

**Evolution
of
Sex Determining Mechanisms**

EVOLUTION

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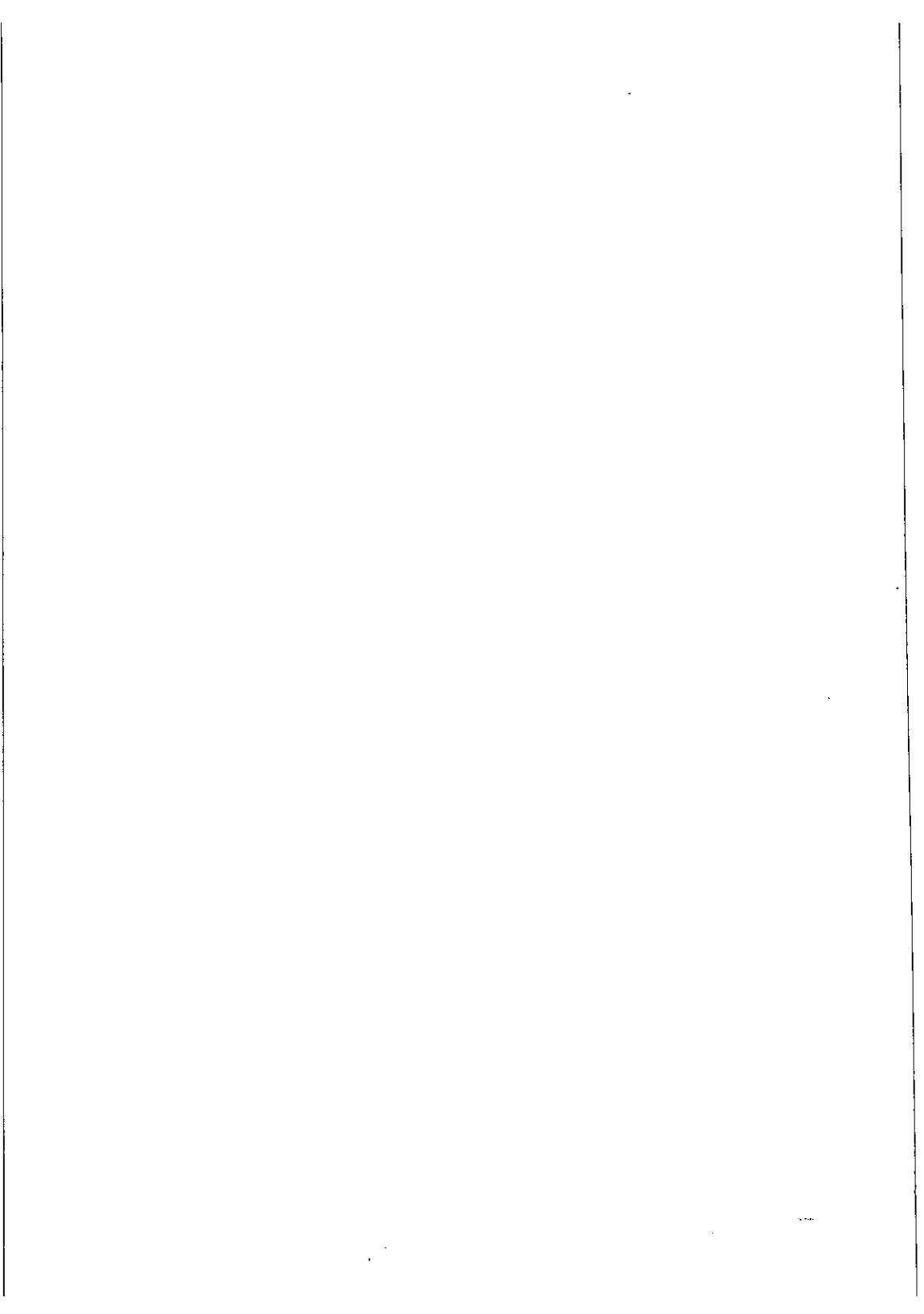
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University of Texas
Austin, Texas



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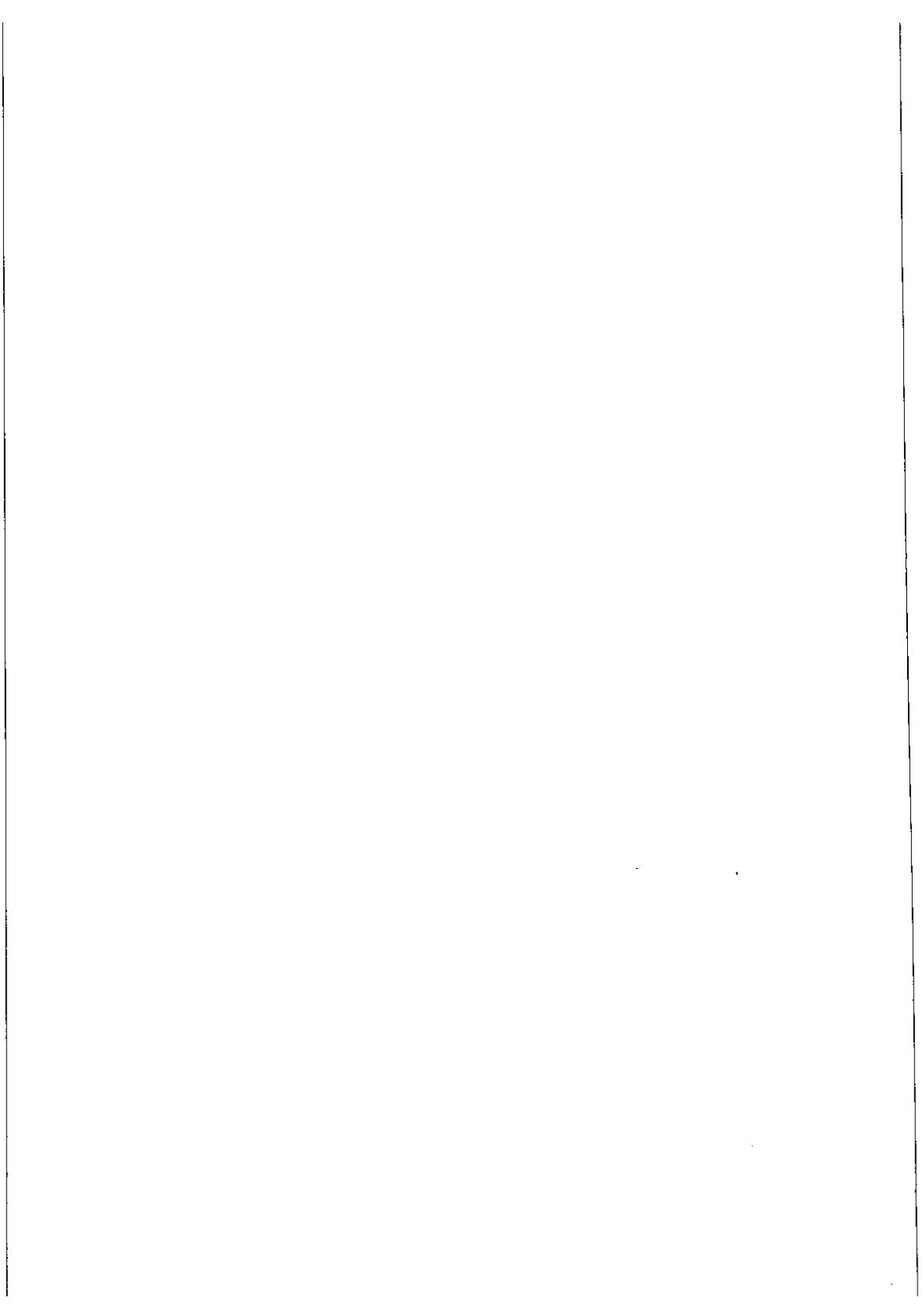
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To
Becky, Greg
and
Jimi



Contents

List of Illustrations xv

List of Tables xvii

Preface xix

PART ONE Classical Sex Determining Mechanisms

1.	Introduction	3
A.	<i>An Evolutionary Perspective of the Problem</i>	3
B.	<i>Terminology</i>	6
2.	Male and Female Heterogamety: 2-Factor Systems	11
A.	<i>Introduction</i>	11
B.	<i>Diagnosing the Heterogametic Sex</i>	13
C.	<i>Taxonomic Patterns</i>	15
D.	<i>Recessive-X and Dominant-Y Systems: The Sex of XO and XXY</i>	20
E.	<i>The Sex of YY</i>	22
F.	<i>The Origins of Heterogametic Sex Determination</i>	24
G.	<i>Summary</i>	25
3.	Multiple-Factor Systems	26
A.	<i>A Commonly Observed System in Diptera</i>	27
B.	<i>Platypfish</i>	28
C.	<i>Lemmings</i>	29
D.	<i>Houseflies</i>	30
E.	<i>Midges</i>	32
F.	<i>Complementary Sex Determination in Hymenoptera (A Preview)</i>	33
G.	<i>Summary</i>	34

4.	Genetics of Sex Development and the Nature of Sex Factors	35
A.	<i>Fruitflies</i> 36	
B.	<i>Nematodes</i> 40	
C.	<i>Transformer Genes in Mammals</i> 42	
D.	<i>Goldschmidt on the Gypsy Moth</i> 46	
E.	<i>The Theory of Genic Balance and the Additive-Value Model of Sex Determination</i> 48	
F.	<i>Summary</i> 53	
5.	A Combinatorial Enumeration of Sex Determining Mechanisms: 2-Factor and Multiple-Factor Systems	54
A.	<i>Introduction</i> 54	
B.	<i>2-Factor Systems</i> 55	
C.	<i>Three Factors Assorting in Opposition</i> 58	
D.	<i>2-Locus Systems</i> 61	
E.	<i>Summary</i> 64	
6.	Evolution in Multiple-Factor Systems	66
A.	<i>Sex Ratio Evolution</i> 66	
B.	<i>Equilibria in Multiple-Factor Systems: Fitnesses Equal</i> 69	
C.	<i>Multiple-Factor Systems When Fitnesses Differ</i> 73	
D.	<i>Biological Examples and Possibilities</i> 77	
E.	<i>Summary</i> 85	
7.	Evolution of the Heterogametic Mechanism of Sex Determination	86
A.	<i>A Theory Based on Multiple-Factor Systems</i> 86	
B.	<i>Difficulties of the Theory and Alternatives</i> 89	
C.	<i>Other Topics Concerning the Evolution of Heterogametic Mechanisms</i> 90	
D.	<i>Summary</i> 92	
8.	Polyfactorial Sex Determination	93
A.	<i>Introduction</i> 93	
B.	<i>Criteria and Examples of Polyfactorial Sex Determination</i> 94	
C.	<i>A 2-Factor Model with Environmental Variance</i> 97	
D.	<i>The Number of Factors</i> 100	
E.	<i>A Formal Model and Its Evolutionary Implications</i> 102	
F.	<i>Coexistence of Polyfactorial and Major-Factor Sex Determination</i> 104	
G.	<i>Summary</i> 107	

9.	Environmental Sex Determination (ESD)	109
	A. <i>The Meaning of Environmental Sex Determination</i> 109	
	B. <i>A Marine Worm</i> 110	
	C. <i>Nematodes</i> 111	
	D. <i>Reptiles</i> 115	
	E. <i>Silverside Fish</i> 123	
	F. <i>Other Examples</i> 123	
	G. <i>Environmental Alterations of Genotypic Sex Determination</i> 124	
	H. <i>Summary</i> 126	
10.	Evolution of Environmental Sex Determination	128
	A. <i>When is ESD Favored?</i> 128	
	B. <i>Sex Ratio Evolution When Fitness Varies</i> 129	
	C. <i>The Transition Between GSD and ESD</i> 132	
	D. <i>Selection Against ESD</i> 134	
	E. <i>The Evidence: When Is Sex Environmentally Determined?</i> 137	
	F. <i>Summary</i> 144	
11.	Uniparental Males: Arrhenotoky (Haplo-Diploidy) and Paternal Genome Loss	145
	A. <i>Introduction</i> 145	
	B. <i>Arrhenotoky</i> 148	
	C. <i>Sex Determination in Arrhenotokous Hymenoptera</i> 150	
	D. <i>Paternal Genome Loss</i> 152	
	E. <i>Fungal Gnats: Germ Line Loss</i> 155	
	F. <i>Scale Insects</i> 158	
	G. <i>Summary</i> 159	
12.	Advantages of Producing Uniparental Males	160
	A. <i>A Segregational Advantage for the Mother</i> 161	
	B. <i>The Mechanics of Producing Uniparental Sons</i> 163	
	C. <i>The Disadvantage of Uniparental Males—To the Father</i> 166	
	D. <i>Inbreeding and Non-Random Mating</i> 168	
	E. <i>Ecological and Sex Ratio Advantages of Arrhenotoky</i> 170	
	F. <i>Conclusions</i> 172	
	<i>APPENDIX 12.I. Why Always Uniparental Males?</i> 173	
13.	Joint Evolution of Uniparental Males and Sex Determination	177
	A. <i>Arrhenotoky</i> 177	

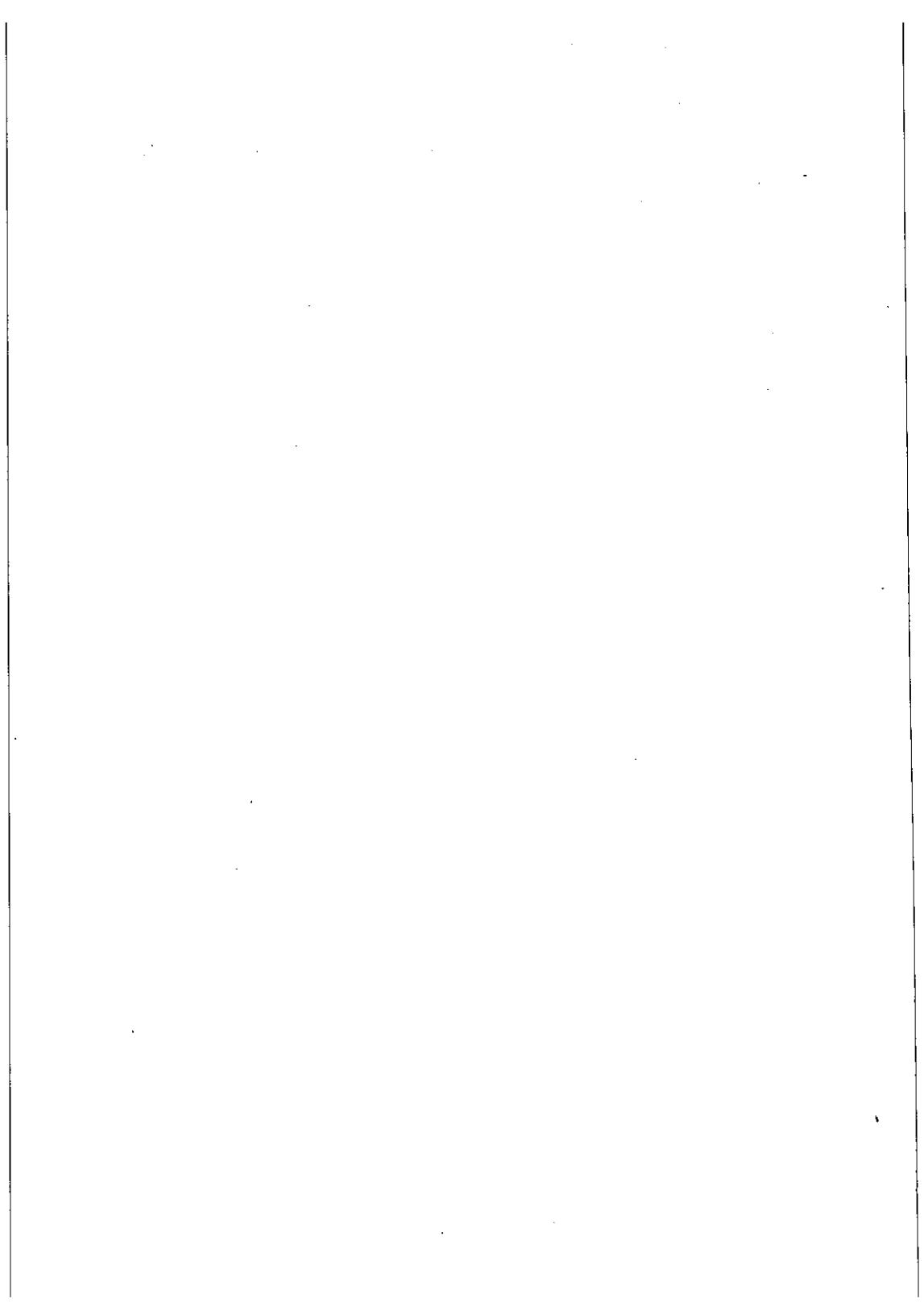
B.	<i>A Model of Hymenopteran Arrhenotoky</i>	181
C.	<i>Paternal Genome Loss</i>	185
D.	<i>Summary of Chapters 11-13</i>	188
<i>APPENDIX 13.I. Sex Ratio Evolution Under PGL:</i>		
	<i>Zygotic Control</i>	189
14.	Cytoplasmic Sex Determination	192
A.	<i>Introduction</i>	192
B.	<i>Amphipods: Gammarus</i>	193
C.	<i>Amphipods: Orchestia</i>	195
D.	<i>Isopods: Armadillidium</i>	199
E.	<i>Evolution of Sex Ratio Modification by Cytoplasmic Factors (Models)</i>	204
F.	<i>Joint Evolution of Cytoplasmic and Nuclear Sex Factors (Models)</i>	206
G.	<i>The Interpretation of Sex Factors: Another Caution</i>	209
H.	<i>Summary</i>	210
15.	A Parental Mechanism of Sex Determination: Maternal Monogeny	211
A.	<i>Examples</i>	211
B.	<i>Monogenic Houseflies</i>	213
C.	<i>Evolution of Monogeny (Models)</i>	214
D.	<i>Summary</i>	215

PART TWO

Sex Chromosome Evolution

Introduction	217	
16.	Characteristics of Sex Chromosomes: Extreme X-Y Heteromorphism	219
A.	<i>Historical Background</i>	219
B.	<i>The Nature of Extreme Heteromorphisms</i>	220
C.	<i>Meiosis and Crossing-Over</i>	227
D.	<i>Multiple Sex Chromosomes</i>	228
E.	<i>Dosage Compensation</i>	229
F.	<i>Degenerate X's</i>	234
G.	<i>Summary</i>	234
17.	Slight X-Y Heteromorphism and Evidence of a Transition	239
A.	<i>Examples of Slightly Heteromorphic Sex Chromosomes</i>	239

B.	<i>From Homomorphism to Heteromorphism</i>	243
C.	<i>Conserved Systems</i>	246
D.	<i>Summary</i>	247
18.	Evolution of Sex Chromosome Differences: Models and Theory	248
A.	<i>Crossover Suppression</i>	249
B.	<i>Degeneration of the Y</i>	254
C.	<i>Haploid Expression and Haploid Sexes: Plants</i>	259
D.	<i>Summary</i>	264
	<i>APPENDIX 18.I. Evolution of Genes with Sex-Specific Fitnesses as a Function of Linkage to Sex Factors</i>	265
	References	271
	Name Index	299
	Subject Index	307



Illustrations

Figure

1.A	A perspective for the evolution of sexuality and related problems	7
2.B	Sex chromosome heteromorphism	14
5.B.1	The two anisomorphic 2-factor phenotype systems for a diploid organism with two sexes	56
5.B.2	The two population systems for a diploid population with 2-factor sex determination	58
5.C	The six anisomorphic 3-factor phenotype systems with two sexes	59
5.D.1	The 48 2-locus/2-factor phenotype systems	62-3
5.D.2	Sixteen possible 2-locus/2-factor population systems	65
6.B.1	Equilibrium conditions in system P(2.2.2)	71
6.B.2	As in Fig. 6.B.1, illustrating here that the two endpoints of the path of equilibria represent different systems of male heterogamety	71
6.B.3	A De Finetti diagram of the equilibrium frequencies of the three female genotypes in the platyfish system	73
6.C.1	Evolution in system P(2.2.2) when the $Aa\ bb$ male is superior	75
6.C.2	Evolution in the platyfish system when fitnesses differ	76
6.D	Equilibria in the platyfish system when sons cost more to rear than daughters	84
8.C	Distributions of the true family sex ratios under 2-factor sex determination with environmental variance	99
8.E	Model of polyfactorial sex determination	103
8.F.1	Model of polyfactorial and major-factor sex determination	104
8.F.2	Equilibrium conditions for the coexistence of major-factor and polyfactorial sex determination	106
9.A	A graphical representation of the distinction between environmental and genotypic sex determination	110
9.C	Sex determination in a mermithid (<i>Romanomermis culicivorax</i>) as a function of the size of host (mosquito larva)	113
9.D.1	Sex ratio as a function of incubation temperature in Ouachita Map Turtles	116
9.D.2	Response of sex ratio to incubation temperature in reptiles	117

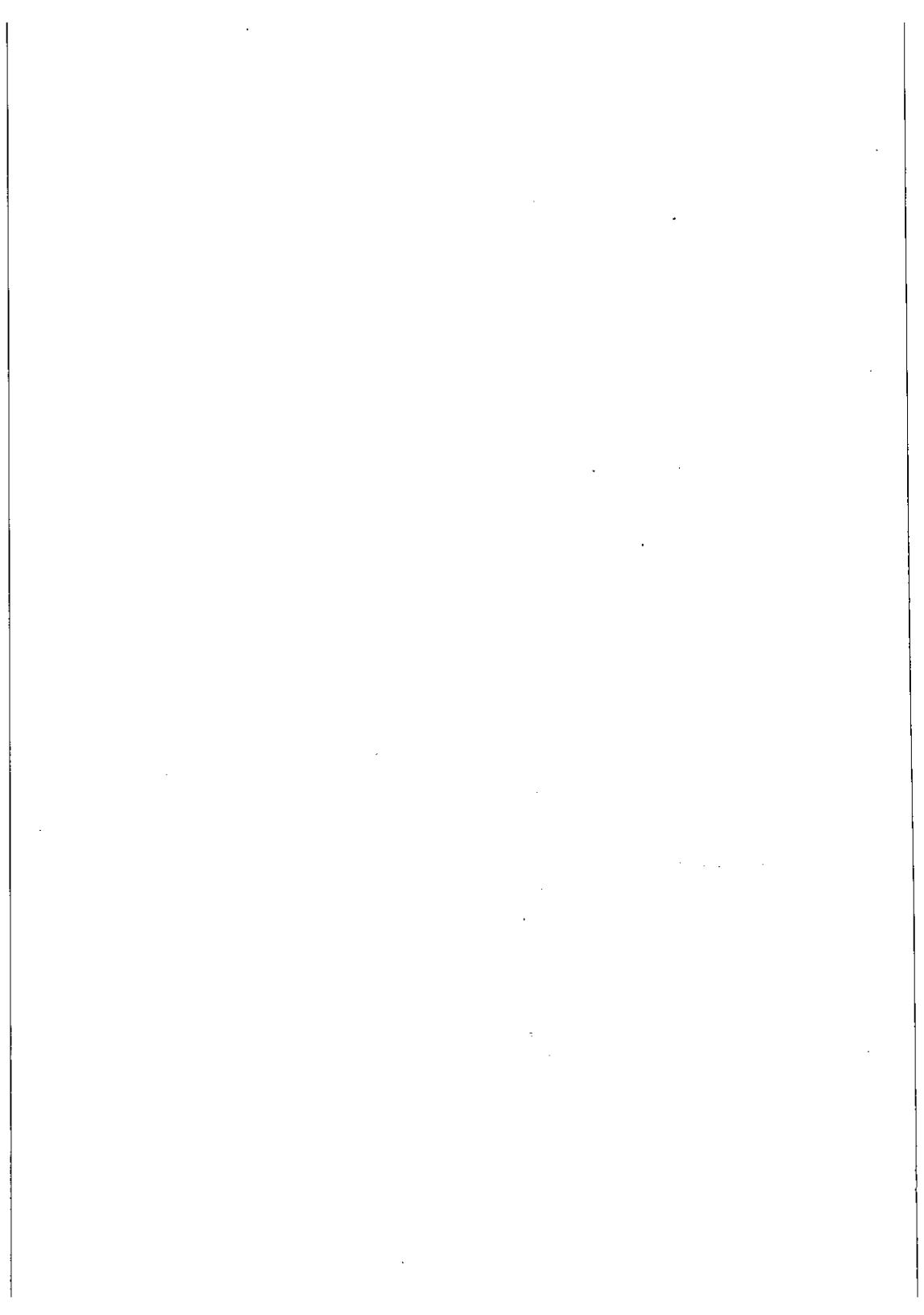
Figure

10.B	The evolutionarily stable sex ratio when fitness varies according to an environmental variable	131
10.C	Equilibrium conditions for the coexistence of major-factor and environmental sex determination	135
10.D	The effect of environmental fluctuations on the selected sex ratio under environmental sex determination	138
11.A	Two distinct types of systems with uniparental males: arrhenotoky and paternal genome loss	146
11.D	Two forms of paternal genome loss	153
11.E	The chromosomes during development and gametogenesis in <i>Sciara</i>	156
12.A	The probability of gene identity-by-descent is doubled between a female and her biparental grandchildren if she produces uniparental sons instead of biparental sons	162
12.C	Diagrammatic summary of the evolution of paternal genome loss for three different modes of inheritance of the trait	167
13.A	The possible equilibria between pure diploidy and arrhenotoky in the Hartl-Brown model	180
13.I	Sex ratio evolution under paternal genome loss	191
16.B.1	(PLATE) Sex chromosomes in rodents and a fly	236-7
16.B.2	(PLATE) Sex chromosomes in two reptiles with slight X-Y heteromorphism	238
18.A	Model for the evolution of X-Y crossover suppression	251
18.B	Muller's ratchet and the degeneration of the Y chromosome	257
18.C	Sex chromosome inheritance in haploid dioecy versus diploid dioecy	263
18.I.1	The conditions for allele α to evolve when unlinked to the sex factors	267
18.I.2	The evolution of allele α when completely linked to the sex factors	268
18.I.3	The set of fitness values for which α can invade when completely linked to the sex factors but not when unlinked	269

Tables

Table

2.C.1	The heterogametic sex in Angiosperm plants	16
2.C.2	The heterogametic sex of invertebrate groups	17
2.C.3	The heterogametic sex in Diptera	18
2.C.4	The heterogametic sex of vertebrates	18-19
2.C.5	The heterogametic sex in lizards	20
2.D	The sex of XXY and XO individuals with a normal complement of autosomes	23
2.E	The sex of YY individuals	24
3.A	Examples of multiple-factor system 3.A.1 (all Diptera)	27
4.A	Sex transformer mutations in <i>Drosophila melanogaster</i>	37
4.B	Sex transformer mutations in <i>Caenorhabditis elegans</i>	41
6.D	Sex ratios in the platyfish system with unequal costs of sons and daughters	83
9.D	Heteromorphic sex chromosomes and temperature-dependent sex determination in families of reptiles studied for both	119-20
9.G	Environmental extremes influencing sex determination in species with genotypic sex determination	125
11.B.1	Groups with arrhenotokous species	148
11.B.2	Arrhenotoky and alternative systems within some groups	149
11.C	Species of Hymenoptera reported to have diploid males	151
14.C	Brood compositions from <i>Orchestia</i> females of thelygenous populations	196
14.D	Sex ratios in broods from <i>Armadillidium</i> females of amphogenous origin induced to thelygeny by tissue transplants from Niort thelygenous females	201
16.E	X-linked <i>Ace-1</i> activity in a nematode	233
17.A	Examples of slight X-Y differentiation	241



Preface

My interest in the evolution of sex determining mechanisms began when studying reptile chromosomes with R. J. Baker and G. A. Mengden during my undergraduate days at Texas Tech University. At this time Ohno's book *Sex Chromosomes and Sex-linked Genes* (1967) appeared. We were first of all inspired by Ohno's evolutionary perspective on sex chromosomes, and at the same time puzzled by the rigidly conserved systems of male heterogamety in mammals and female heterogamety in birds, compared with the existence of both systems in reptiles. Could male and female heterogamety be readily derived from an ancestor of either type? This question puzzled me for several years, and my association with two people, Richard Shine and Eric Charnov, helped me anticipate some possible solutions for this problem and thereby contemplate what has become the scope of this book. It was with R. Shine that I first considered the evolution of the sex ratio, which proved to be an important aspect in the evolution of sex determination. In this endeavor we both owe a major intellectual debt to G. C. Williams' *Adaptation and Natural Selection* (1966). Then with Eric Charnov at Utah, I began to directly address the topic of the evolution of sex determining mechanisms. Charnov taught me the basics of population genetics, while sharing with me his enthusiasm and insights into what he designated "sex allocation theory." Charnov was the inspiration for this book, having originally provided me with the confidence needed to accomplish my goals.

Since leaving Utah, I worked with several people who helped develop my understanding of theoretical population genetics: J. F. Crow, C. W. Cotterman, R. Lande, C. Denniston, K. Aoki, A. Gimelfarb, W. Engels, M. Moody, M. Rose (Wisconsin), J. Maynard Smith, B. and D. Charlesworth, P. Harvey (Sussex), and M. G. Bulmer (Oxford); and in my experimental work on turtles: J. M. Legler (Utah) and R. C. Vogt (Wisconsin). Charles Cotterman deserves special mention because of the inspiration he shared with me on the use and possibilities of the combinatorial method. Russell Lande also greatly influenced me by demonstrating how detailed genetic studies motivate population

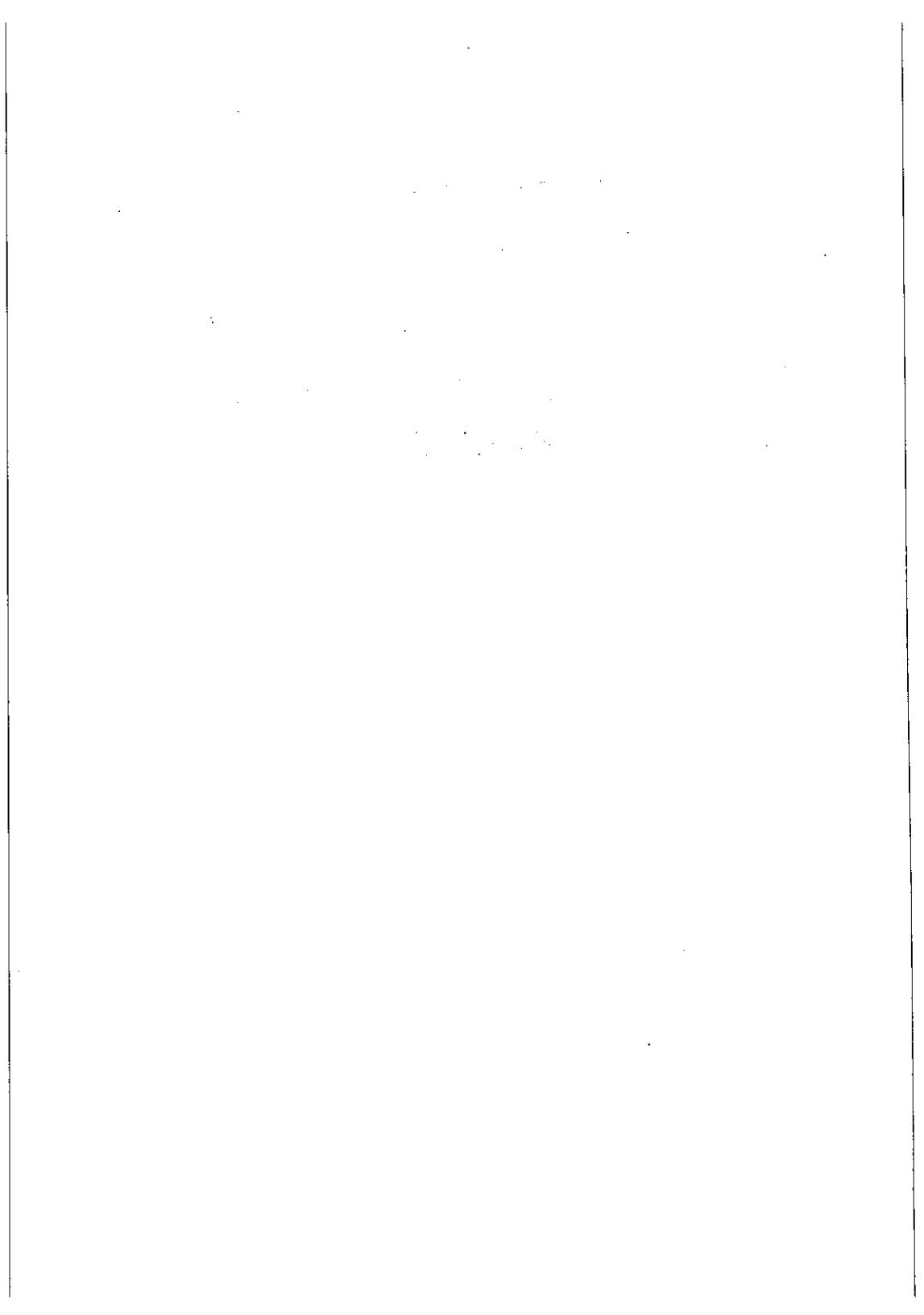
genetics models of the evolutionary process. Raissa Berg offered valuable insights to the theory of genic balance.

This book was written from late 1981 to early 1983 while in residence at the University of Utah and was completed at the University of Texas. Drafts were read and criticized by Brian and Deborah Charlesworth, Paul Harvey, John Maynard Smith, Eric Charnov, and especially Sam Skinner (Utah). The first half of the book was read and criticized by David Crews and Allen Billy (U. Texas). H.-P. Bulnheim reviewed the chapter on cytoplasmic factors, K. Kallman reviewed the chapter on polyfactorial sex determination and other sections relevant to the fish literature, P. Anderson and B. Baker each reviewed the chapter on the genetic regulation of sex development, and J. Oliver provided a table of different genetic systems in mites and ticks. I thank all of them for useful suggestions and for correcting some of my misconceptions about the literature. Kerry Matz was delightfully creative and prompt in preparing the illustrations. Finally, Joni Moody provided her services toward editing the penultimate draft; only the few colleagues who read an early draft can appreciate the many improvements that stem directly from her work.

James J. Bull

PART ONE

Classical Sex Determining Mechanisms



1

Introduction

A. An Evolutionary Perspective of the Problem

This book is mostly about the diversity of sex determining mechanisms, or the manifold ways in which sex is inherited in animals with separate sexes. Beginning around 1900, the rediscovery of Mendelian genetics inspired studies which provided the first clear understanding of the inherited basis of males versus females in animals and plants, so that now, 80 years later, sex determining mechanisms have been evaluated in thousands of species. The demonstrated variety of sex determining mechanisms serves as an essential foundation for the evolutionary perspective proposed here, and I suggest ways in which sex determining mechanisms might further be studied to better understand the existing variety.

Evolutionary biology addresses the topic of variety among species, but there are two levels at which this variation is commonly investigated: the basic description of variety, and the processes which lead to the variety. Both levels of investigation will be adopted here.

The Classification of Variety: A Combinatorialist Perspective

In the simplest analysis one may observe that certain forms of a system are present and others are absent. This approach represents the combinatorialist

perspective, i.e., the categorization of known systems among those which are theoretically possible. The value of the combinatorialist approach is simply that it enables the investigator to consider the possible and perhaps probable existence of as yet undiscovered variety. This investigative process in turn may lead to the recognition of new variety or to the realization that some forms are invariably absent. To quote three inspiring combinatorialists,

We need scarcely add that the contemplation in natural science of a wider domain than the actual leads to a far better understanding of the actual.

(Eddington, 1929, pp. 266-7)

No practical biologist interested in sexual reproduction would be led to work out the detailed consequences experienced by organisms having three or more sexes; yet what else should he do if he wishes to understand why the sexes are, in fact, always two?

(Fisher, 1930, preface)

Often it will be found that the domain dreamed of by the combinatorialist is not really much wider than the actual.

(Cotterman, unpubl.)

One of the striking features of sex determination is the enormous variety of different types: male and female heterogamety, polyfactorial, environmental, and haplo-diploidy. And within these categories, there is further possible variety. For example, species with heterogametic sex determination may differ with respect to which sex is heterogametic, or with respect to the locus of heterogamety. Under environmental sex determination, sex is determined in response to temperature in some species but by other environmental factors in other species.

One of the major goals here will be to present the variety of mechanisms known and to cast this variety in terms of a larger set of possible mechanisms. For each of the major types of sex determination, the *known* mechanisms will be first described, followed by a presentation of the mechanisms *possible*. In some cases the alternatives are obvious and do not warrant enumeration. For example, under environmental sex determination, the possible variety of mechanisms is simply a list of the different environmental variables which could conceivably be used to determine sex. For other systems there is a well-defined set of possibilities, and a complete enumeration is desirable (e.g., male and female heterogamety).

The presentation of the variety of mechanisms known, coupled with the variety possible, could well stand on its own as a self-contained discipline in evolutionary biology. That is, one would be justified in looking no deeper. However, this appreciation for the variety of mechanisms is an almost essential prerequisite for the second objective, which is to understand how the different mechanisms evolve.

The Processes which Generate Variety: Transitions

A second level of investigating variety is to consider how and why certain characteristics exist in populations—the processes that bring about change. The second objective, therefore, will be to describe the evolutionary transitions between different mechanisms. In some cases it is possible to describe *how* one mechanism changes to another; furthermore, it is sometimes possible to propose *why* such a change is favored. Heavy emphasis will be placed on descriptions of how sex determining mechanisms might change, especially for male and female heterogamety. Where empirical support of the transitions is lacking, some models will be offered as possibilities, not exclusive of others. For a few systems, such as environmental sex determination and haplodiploidy, I will further suggest that there are general selective advantages for the transition. Based on this evolutionary framework, therefore, sex determining mechanisms will be presented along the following guidelines: (1) describe the variety known, (2) present the possible variety, (3) describe how the transitions might occur from one mechanism to another, and (4) consider why the transition might be favored.

Part I (Chapters 1–15) represents the major portion of the book and addresses almost exclusively the inherited and environmental bases of sex differences in animals. Under normal circumstances, sexual development is directed toward the production of a male or a female by an initial set of factors, such as the XX/XY genotype, and then proceeds as a highly integrated series of genetic and physiological steps which results in a male or female. These chapters will consider the genetic and environmental factors exerting the initial influence on which developmental pathway is to be followed, without considering the details of how the steps within each developmental pathway are coordinated. The chief reason for excluding a serious consideration of the details of sex development and differentiation is that the evolution of the inherited basis of sex may be described without understanding these various details. Rather, in its simplest form, an evolutionary model merely needs to specify inheritances and fitnesses of the different phenotypes, along with population breeding structure, all of which can be observed in ignorance of the physiological and molecular interactions which bring about these events. Chapter 4 does, however, review recent studies of genetic regulation of sex development in mammals, *Drosophila*, and *Caenorhabditis*.

Part II (Chapters 16–18) investigates the structural differences in the X and Y sex chromosomes. The evolution of sex chromosome differences is not to be equated with the evolution of sex determination, since the changes which occur on the sex chromosomes involve genes linked to those determining sex. However, the evolution of sex chromosome differences does indeed depend on the sex determining mechanism, and so sex chromosome evolution will be considered in this book as well.

Readers may wish to know how the present book relates to the recent literature on the evolution of sex. Four previous books (Williams, 1975; Maynard

Smith, 1978; Bell, 1982; Shields, 1982) were concerned with the evolution and maintenance of sexual reproduction, in which there are several major problems (Fig. 1.A). From a chronological perspective, the first steps in the evolution of sex may have been the evolution of biparental reproduction, or gametic union, followed by evolution of the male/female phenomenon, or small and large gamete producers, respectively. Superimposed upon these is the possibility for the evolution of parthenogenesis, in which biparental reproduction is abandoned. These problems rest completely outside the scope of this book. The topics addressed below concern sex determining mechanisms in populations maintaining sexual reproduction between males and females, while excluding questions on the origin of males and females or the evolution of parthenogenesis (Fig. 1.A).

The present book parallels and complements sex allocation theory (Charnov, 1982). Sex allocation theory considers the evolution of hermaphroditism (or sex change) versus separate sexes, the sex ratio, and the allocation to sperm versus eggs by a hermaphrodite. Sex allocation theory and the present book overlap with respect to the sex ratio: sex ratio selection appears to be the dominant force in molding sex determining mechanisms. However, these two bodies of theory diverge in the problems considered. This book will consider the evolution of mechanisms which produce the sex ratio, whereas sex allocation theory considers sex ratio evolution (or its counterpart in hermaphrodites) without regard to the sex determining mechanism.

B. Terminology

The topic of sex, and its legitimate progeny, sex determination, is of certain interest to many people, with the result that various meanings may be implied by these terms until they are defined. Even among biologists, various meanings exist: sex may refer to gender, male or female, to the act of copulation, or to the process of gametic union (biparental reproduction as opposed to parthenogenesis). With respect to "sex determination" one again finds a term capable of encompassing multiple definitions, including the ascertainment of sex, the artificial manipulation of sex, or others. This problem with semantics has been recognized by several authors (McCarrey and Abbott, 1979; Austin et al., 1981), and in the effort to clarify the terminology used in this book, this section provides definitions for a few key words which might otherwise prove ambiguous.

(1) *Sex and Sex Determination*: Sex is defined as gender, male or female, with sex determination defined by extension as gender determination, the natural means by which a son or daughter is produced.

(2) *Sex Determining Mechanisms*: In the sense that differences in pea color might be studied from various perspectives such as (1) classical genetics

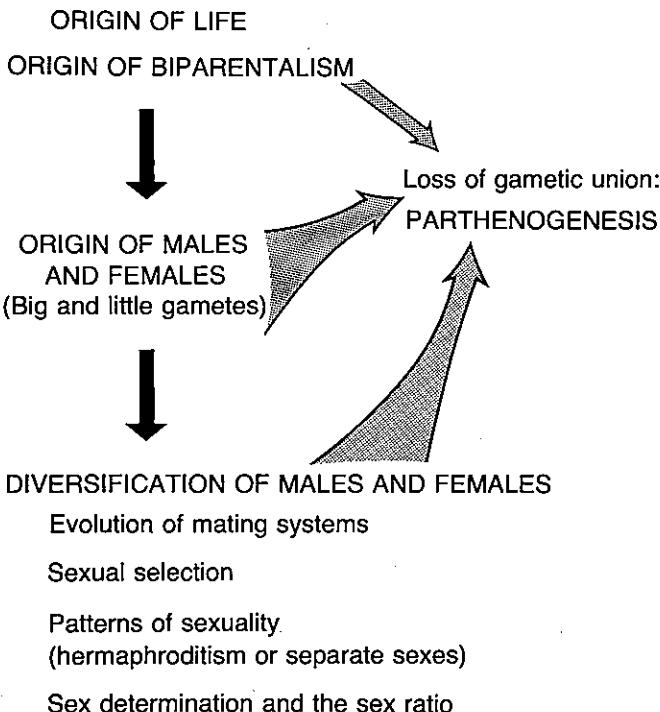


FIGURE 1.A. A perspective for the evolution of sexuality and related problems (based on the text of Maynard Smith, 1978). Historically, one of the first events in the evolution of sex may have been the development of biparental reproduction, in which offspring were produced from the union of two gametes at some stage of the life cycle. It is presumably difficult to know whether life itself originated with this form of reproduction, or if biparentalism was a subsequent development. Initially, biparentalism may have involved the union of equal-sized gametes (isogamy), as now found in some unicellular organisms. The next step in the evolution of sex would then have been a gamete dimorphism, so that small gametes always united with large ones (anisogamy), representing the essence of males and females. The origin of males and females then generated a new set of phenomena, such as sexual selection, the mating system, and sex determination. Superimposed on these processes is the possibility for the loss of biparental reproduction through the evolution of parthenogenesis. The present book is restricted to the topic listed at the bottom of the figure: sex determination and the sex ratio.

(inheritance of color), (2) molecular genetics (structure of color genes), and (3) physiology (biochemistry of pigment synthesis), a sex determining mechanism may also be described according to these different levels. Therefore, describing a mechanism as male heterogamety indicates the inherited basis of males versus females, but the mechanism may be equally described according to its physiology, molecular genetics, and so forth.

This book addresses the inherited and environmental basis of males versus females. The term “sex determining mechanism” therefore refers merely to a description at this level, without regard to other details such as the molecular or physiological properties of the system. It is sufficient that the reader understand this usage, but as reinforcement, I will refer to this level of description as the *classical* mechanism of sex determination, since this level of analysis has historical precedence. Specifically, the classical mechanism refers to the earliest elements in ontogeny common to one sex that distinguishes it from the other sex, including environmental and genetic effects acting in parents or zygotes that differentially influence the probability of producing or becoming male/female. For further clarification, some of the more common sex determining mechanisms are defined and explained in this context.

Male Heterogamety—All adult males are XY, adult females are XX. All zygotes are therefore XX or XY, and XY develops into male, XX into female. The X and Y are the inherited basis of sex determination, sex being determined at conception (in the zygote). (Chapter 2)

Female Heterogamety—As in male heterogamety, except that females are ZW, males ZZ. (The tradition of using the notation X and Y for male heterogamety, Z and W for female heterogamety, is retained here.) Depending on the meiotic mechanism, sex may be determined prior to or after fertilization, but sex is determined no later than the formation of the zygotic nucleus, so I shall refer to this as a zygotic mechanism. (Chapter 2)

Polyfactorial (Polygenic) Sex Determination—Sex is determined in the zygote by many factors with individually small effects, perhaps also with an arbitrary environmental effect. Thus the cumulative effect of many factors controls sex, rather than just two factors with a major effect. (Chapter 8)

Environmental Sex Determination—Sex is determined during embryogenesis in response to the local environment, with some environments producing males and others producing females. Sex cannot be predicted by zygotic genotype, because of the subsequent environmental influence. (Chapter 9)

Arrhenotoky (Haplo-diploidy)—A genetic system in which males arise from unfertilized eggs, females from fertilized eggs. Sex determination could be environmental (based on fertilization) or could be genotypic (based on ploidy or other). (Chapter 11)

(3) *Sex Development*: Although the emphasis in this book is on the classical sex determining mechanism, it is necessary to refer to other levels of sex determination, if only at a superficial level. To distinguish these other levels from the classical mechanism, the term “sex development” will be used. (“Sex differentiation” would be equally appropriate.) Sex development refers collectively to the various molecular, genetic, and physiological processes that produce a male or a female from a zygote of a given genotype and parents in a given environment.

(4) *Sex Factors*: Populations with separate sexes usually exhibit inherited differences in the probability of male or female determination. Consider male heterogamety: the inheritance of the X and Y can be said to determine sex because those zygotes inheriting two X's become female and XY becomes male. The segregating units that provide the inherited basis of differences in sex determination are defined as *sex factors*. In the simple systems of male and female heterogamety, the sex factors are X and Y, but multiple-factor systems have three or more factors, and polyfactorial systems may have several factors. It is also useful to distinguish between *major* and *minor* factors, the former having individually large effects and the latter small effects. Thus the X and Y of heterogametic systems are major factors, but the majority of sex factors in polyfactorial systems may be minor.

Sex factors may be defined as influencing sex determination either in the zygote or in the parents, controlling the offspring sex ratio according to the parental genotype. A *parental effect* on sex ratio would exist if, in the context of a particular mating, the average progeny sex ratio differed from that which would be obtained under Mendelian segregation of all sex factors from the parent, and sex determined among the zygotes according to their genotype and a random environment. This definition of parental influence excludes variation in family sex ratio due solely to differences in zygotic sex factors among the parents. Sex factors are assumed to be zygotic unless stated otherwise, and in this book there are in fact only a few mechanisms for which a parental effect is considered.

A sex factor may be inherited at a single locus or as several loci tightly linked on a chromosome (supergene). However, in the case of sex chromosomes, sex factors are inherited with many genes whose functions are independent of sex determination. I prefer to regard sex factors as the genes and their homologues responsible for controlling the inheritance of sex, and to differentiate them from genes which are incidentally co-inherited, even though in practice the sex factors may never be separated from the other linked genes. This definition, however, has the desirable effect of distinguishing the evolution of sex chromosome rearrangements and X-Y crossover suppression from changes in sex determination (the inheritance of sex). I consider these two processes as separate.

(5) *Sex Tendency*: A description of the inheritance of sex offers little information on how sex factors control sex development. For example, under male heterogamety, the X may dispose the embryo toward becoming female or the Y toward becoming male, or both, and the autosomes may also dispose the embryo toward one sex or the other. Beginning with Bridges (1922), the term "sex tendency" has been used to describe this underlying contribution toward male or female development. Specifically, a sex tendency is a number assigned to a gene (sex factor or otherwise) that reflects its contribution to whether the zygote develops as male or female, usually assumed to be invariant across different genotypes (see the additive-value model in Sec. 4.E). This concept was central to a model of gene action used by many early workers, often displayed

as $M > F$ = male, $M < F$ = female (e.g., Witschi, 1929; Bridges, 1925; Winge, 1932, 1934, 1937; Hartmann, 1956; Bacci, 1965; Yamamoto, 1969). The M and F in these formulae refer to net male- and female-tendency values calculated for the entire genome.

"Sex tendency" is an attempt to describe the underlying mechanism of gene action in sex determination, and this concept is distinct from that of "sex factor" in three ways. First, one member of a sex factor pair may have no sex tendency even though the other member does, but this factor nonetheless influences the inheritance of sex by segregating opposite the one with sex tendency. Second, a gene may be assigned a sex tendency even if it does not segregate for differences and is therefore not a sex factor. Third, some mechanisms of sex determination are not compatible with this notion of sex tendency, and assigning values to sex factors does not lead to a valid description of sex determination. Most importantly, however, sex tendency is a *model* of gene action, which can be refuted by observation, whereas a sex factor is more an observation than a hypothesis.

(6) *Sex Chromosomes*: It is a common observation with male heterogamety (XX females/XY males) and female heterogamety (ZW females/ZZ males) that the X and Y (Z,W) are cytologically distinguishable from each other even though they pair at meiosis. The X and Y in this case are referred to as heteromorphic sex chromosomes, with the X carrying one sex factor and the Y the other. However, as described in Chapter 17, the sex factors are not always accompanied by cytological heteromorphism, as exemplified by some amphibians, fish and flies. To some readers, the use of the letters X and Y (or Z and W) may connote a cytological as well as genetic distinction. In Part I, a notational difference is used to distinguish cases in which X and Y are intended as cytological sex chromosomes from cases in which X and Y may be considered as the sex factors themselves, not tightly linked to other genes on the chromosome. Boldface letters (**X**, **Y**) are used when heteromorphic sex chromosomes are implied, lightface X and Y are used otherwise, when heteromorphism may apply but is not implied. Similarly, boldface **A** represents an autosomal chromosome (or haploid set of autosomes), whereas an italic *A* (as well as other italic characters) are used for an allele at a single locus.

2

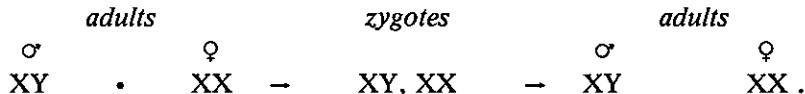
Male and Female Heterogamety: 2-Factor Systems

The inheritance of sex may be influenced by three measurable effects: (i) major sex factors, (ii) minor sex factors, and (iii) environmental differences, and the study of sex determination is one of quantifying the relative magnitudes of these effects as well as their evolutionary consequences. This chapter and the following five chapters (2, 3–7) will consider mechanisms in which sex is inherited chiefly according to a few major factors. This chapter specifically considers XX/XY systems. A list is provided of taxa in which XX/XY systems are known, and tables are also provided for two properties of the X and Y which are not evident merely from their inheritance: the sex of YY, and recessive-X versus dominant-Y systems.

A. Introduction

Male and female heterogamety are probably the two most common sex determining mechanisms known in animals, as they have been discovered in many invertebrates and vertebrates. Male heterogamety is described as an XX female/XY male system in which males produce X and Y sperm, females produce only X ova, and fertilizations yield either XX or XY zygotes. The system

is maintained because XX zygotes become female and XY zygotes become male:



This 2-factor system (the sex factors are X and Y) is denoted as *genotypic* sex determination because the X-Y genotype is the earliest ontogenetic characteristic distinguishing males from females. It is also a *zygotic mechanism*, because sex is determined in the zygote. Parents differing in their tendency to produce sons versus daughters, perhaps by altering the segregation ratios of X and Y, may offer a further variation of these mechanisms, and these will be designated as *parental mechanisms*. The X and Y *sex factors* may be inherited as a single locus, recombining freely with other genes on the chromosome, or they may be inherited in a tightly linked chromosome segment that incorporates other genes as well. Also, no assumptions are made concerning the molecular or physiological regulation of sex by the X and Y. These sex factors may consist of allelic differences at a single regulatory locus, or instead involve many tightly linked genes that collectively regulate sex. My definition of a sex factor does not address the nature of sex development, but rather concerns just the inheritance of sex.

Female heterogamety, denoted here as ZW female/ZZ male, differs from male heterogamety only in a reversal of the heterogametic sex. Both types of heterogamety are regarded here as zygotic mechanisms, even though in some cases of female heterogamety, meiosis may lead to the determination of sex prior to conception. A consequence of the formal similarity between male and female heterogamety is that arguments which apply to one system usually apply to the other. Henceforth, descriptions adopting the perspective of male heterogamety will be assumed to apply to female heterogamety unless indicated otherwise.

In some species, two or more *chromosomes* assort with respect to sex (e.g., $\mathbf{X}_1\mathbf{X}_1\mathbf{X}_2\mathbf{X}_2$ female/ $\mathbf{X}_1\mathbf{X}_2\mathbf{Y}$ male, or \mathbf{XX} female/ $\mathbf{XY}_1\mathbf{Y}_2$ male). These *multiple sex chromosome systems* (not to be confused with multiple-factor systems) are usually thought to have arisen by translocation of an autosome to the X or Y, as shown, or by fission of the X or Y (e.g., White, 1973):

	σ	\varnothing	Comments
<i>Basic XX/XY system</i>	\mathbf{AA}	\mathbf{XX}	\mathbf{AA} \mathbf{XY}
<i>Multiple-Y</i> notation	$\dot{\mathbf{X}}\dot{\mathbf{X}}$	$\dot{\mathbf{X}}$ \mathbf{Y}_1 \mathbf{Y}_2	Unlinked autosome indicated by \mathbf{A}
interpretation	\mathbf{AA} \mathbf{XX}	\mathbf{A} \mathbf{A} \mathbf{Y} \mathbf{X}	The neo-X ($\dot{\mathbf{X}}$) is a fusion of an auto- some and the ancestral X

Multiple-X

notation	$X_1 X_1 X_2 X_2$	$X_1 X_2 \dot{Y}$
interpretation	AA XX	A X A ↓ Y

The neo-Y (\dot{Y}) is the ancestral Y fused to an autosome.

According to the definition of a classical sex determining mechanism, the evolution of a multiple sex chromosome system does not constitute a change in sex determination. The location of the sex factors does not change, but rather the sex linkage increases. There is in fact no fundamental difference in this respect between the evolution of multiple sex chromosomes and the evolution of crossover suppression along the XY chromosome pair. Therefore, the notation XX/XY includes multiple sex chromosome systems, except where indicated.

Other systems are known which lack a Y (XX/XO), or in which only the Y is present (OO/OY). Systems such as these are also regarded as two-factor systems because the regularity of meiosis ensures that the inheritance of sex is the same as with XX/XY . Indeed, even when X and Y chromosomes are both present, one almost never knows if the sex factor locus is present on both chromosomes.

B. Diagnosing the Heterogametic Sex

There are commonly three methods of diagnosing the heterogametic sex in species with separate sexes: cytogenetics, sex linkage of markers, and the breeding of animals whose sex has been experimentally altered by environmental factors (reviewed in White, 1945, 1954, 1973; Westergaard, 1958; Gallien, 1959; Bacci, 1965; Crew, 1965; Mittwoch, 1967, 1973; Ohno, 1967).

Cytogenetics

The chromosomes of diploid animals generally occur in duplicate, with one copy from each parent. In meiosis, the chromosomes align together in pairs, and one member of every pair is transmitted to each gamete. Usually the two chromosomes from each pair, called homologues, are similar in size and shape. However, in many species, the study of chromosomes has revealed a consistent asymmetry involving one of the chromosome pairs in either the males or the females. This asymmetry is commonly manifested as an odd number of chromosomes, or as a heteromorphism—two homologues differing in size and/or shape. These heteromorphisms (or unpaired chromosomes) are usually the sex chromosomes (Fig. 2.B). One chromosome, the Y (W), is restricted to one sex, and its meiotic partner, the X (Z), occurs in both sexes,

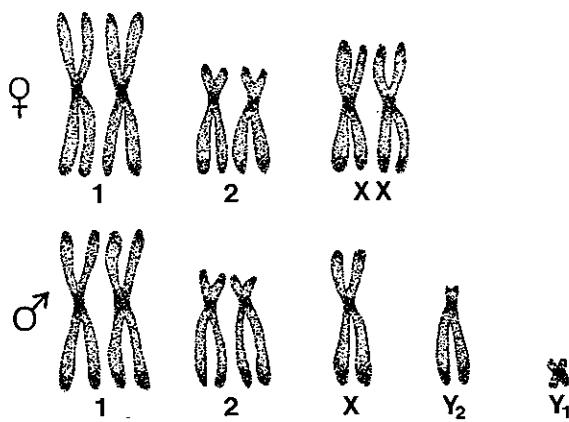


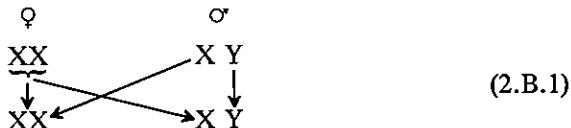
FIGURE 2.B. Sex Chromosome Heteromorphism. The diploid chromosome complement of the male and female muntjac deer is illustrated schematically. The chromosomes have been artificially arranged in homologous pairs, according to approximate size. The female has two X chromosomes, while the male has one X and two Y chromosomes (a condition known as multiple sex chromosomes). (Drawing based on D.H. Wurster and K. Benirschke. 1970. "Indian Muntjac, *Muntiacus muntjak*: a new deer with a low chromosome number." *Science* 168: 1364-6, Figure 1.)

although with multiple sex chromosomes, more than one X or Y are present. The majority of species in which the heterogametic sex has been reported have been studied by examination of chromosome heteromorphisms.

Cytological studies offer only indirect evidence for the presence of heterogametic sex determination, because chromosomal differences between the sexes could conceivably arise from reasons other than sex determination (e.g., sex-specific lethals). This objection is offered more in principle than in practice, as there do not appear to be many examples in which the cytological evidence of heteromorphic "sex" chromosomes has misidentified the sex factors. Further evidence that the X and Y chromosomes carry the sex factors may be obtained by observing the sex of (occasional) XXX or XO individuals (see Sec. 2.D). Of course, the absence of cytologically detectable sex chromosomes does not imply that heterogametic sex determination is lacking.

Sex Linkage

The inheritance of X and Y sex factors is readily distinguished from autosomal inheritance:



Therefore, segregation of a visible marker which is sex-linked, or partly so, can be used to identify the heterogametic sex. Such polymorphisms have led to the identification of the heterogametic sex in a variety of animals: Y-linked color genes are known in a few fish and flies, Z-linked polymorphisms are known in some birds and lepidopterans, and many X-linked genes are known in flies and mammals (general reviews in Gallien, 1959; Bacci, 1965; Crew, 1965; for mammals, Ohno, 1967; fish, Atz, 1964; Yamamoto, 1969; Kallman, 1968; Lepidoptera, Cock, 1964; Johnson and Turner, 1979; flies, Tsukamoto et al., 1980; Franco et al., 1982). This method can reveal the heterogametic sex even if sex chromosomes are not cytologically distinguishable, but it requires the fortuity of detecting a polymorphism linked with the sex factor. It also suffers from some of the same limitations as the cytological approach in properly identifying the sex factors.

Alteration of Sex by Environmental Factors

A more direct demonstration of heterogametic sex determination is possible if means are available to artificially circumvent genetic control of sex determination, such as with the external application of hormones, temperature, or other extrinsic factors. Suppose, for example, that hormones are used to produce males in all individuals. If the male is heterogametic, XX and XY males will be created, and mating of the XX males to normal (XX) females will produce all daughters. If the female is heterogametic, then some males will be ZW, and those mated to normal females will yield 1/4 ZZ, 1/2 ZW, and 1/4 WW. The sex ratio will depend on WW's sex and whether it survives. By producing unusual genotypes and sex ratios, this method diagnoses the heterogametic sex and provides information about how the X and Y influence sex determination. A variation of this method may be applied to species with occasional hermaphrodites. The hermaphrodite is bred to normal males and females, and the sex ratio is studied in both cohorts. Even though the sex genotype of the hermaphrodite is unknown, the alternatives of male and female heterogamety may be distinguished. A limitation of this method is that it assumes that sex is determined according to male or female heterogamety, and other sex determining mechanisms may provide results consistent with these expectations.

C. Taxonomic Patterns

The following tables indicate many of the taxa in which male and female heterogamety are known, though these compilations are by no means complete (Tables 2.C.1-5). Some major groups are not represented here, but in some cases these groups consist primarily of species that are hermaphroditic, haplo-diploid, or have some other genetic system which does not facilitate the

evolution of sex chromosomes or heterogamety; the detail to which groups are listed reflects both the available information and the variety of heterogametic mechanisms within the group. Male heterogamety is extraordinarily prevalent in some of the invertebrates, such as nematodes, arachnids, and insects, but female heterogamety is not uncommon otherwise. It may be noted that the heterogametic sex is conserved in some groups, but that it varies within other groups, and the conserved system may be either male heterogamety (nematodes, arachnids, most insects, mammals) or female heterogamety (Lepidoptera and Trichoptera, birds).

The heterogametic sex is nearly always diagnosed from cytological evidence, i.e., the observation of a chromosomal difference between the sexes; but there are some cases in which the evidence is also genetic, based on observation of sex-linked markers or the sex ratios obtained from breeding "sex reversed" individuals. It is understood here that evidence of the heterogametic sex is purely cytological unless indicated otherwise. If instead the evidence is genetic, those cases are indicated by (G); if the evidence is both genetic and cytological, those cases are indicated by (B). Cytological evidence of the heterogametic sex is sometimes questionable, especially in fishes, so these tables should not be used as final sources on the heterogametic sex in any species of particular interest. Instead, individual entries in the table should be used as guides to the original sources (usually found in the reviews cited for each table).

TABLE 2.C.1. The Heterogametic Sex in Angiosperm Plants

Family	Heterogametic Sex	
	Male	Female
Moraceae	♂ (B)	
Polygonaceae	♂	
Caryophyllaceae	♂ (B)	
Amaranthaceae	♂ (G)	
Liliaceae	♂ (G)	
Cucurbitaceae	♂ (B)	
Caricaceae	♂ (G)	
Euphorbiaceae	♂ (G)	
Chenopodiaceae	♂ (G)	
Ranunculaceae	♂ (G)	
Vitaceae	♂ (G)	
Asteraceae		♀ (G)
Rosaceae		♀ (G)

Sources: Winge, 1931; Westergaard, 1958; Lloyd, 1974; Charlesworth and Charlesworth, 1978.

Note: Dioecy is uncommon in most of these families.

(G)—indicates that the evidence of heterogamety is genetic; (B)—indicates that the evidence of heterogamety is both genetic and cytological; otherwise the evidence is cytological.

TABLE 2.C.2. The Heterogametic Sex of Invertebrate Groups

Taxon	Heterogametic Sex	
	Male	Female
Phylum Platyhelminthes		
Class Trematoda		
F. Schistosomatidae		♀
Phylum Nematoda		
Class Phasmida (4 Orders)	♂ (XO in 4 Orders)	
Phylum Arthropoda		
Class Arachnida		
Sc. Acarina	♂ (XO)	
O. Parasitiformes	♂ (XO)	
Acariformes	♂ (XO)	
Sc. Araneae	♂ (XO)	
Class Crustacea		
Sc. Branchiopoda		
O. Anostraca	♂	♀ (B)
Sc. Ostracoda	♂ (some XO)	
Sc. Copepoda		♀
Sc. Malacostraca		
O. Decapoda	♂	
O. Isopoda	♂ (G)	♀ (B)
O. Amphipoda	♂ (G)	
Class Chilopoda	♂	
Class Insecta		
Sc. Apterygota	♂ (XO)	
Sc. Pterygota		
Div. Exopterygota		
O. Ephemeroptera	♂ (XO)	
Odonata	♂ (XO)	
Orthoptera	♂ (XO)	
Dermaptera	♂	
Isoptera	♂ (XO)	
Embioptera	♂ (XO)	
Plecoptera	♂ (XO)	
Psocoptera	♂ (XO)	
Hemiptera	♂ (XO)	
Div. Endopterygota		
O. Mecoptera	♂ (XO)	
Trichoptera		♀
Lepidoptera		♀ (B)
Diptera*	♂ (B)	♀ (B)
Siphonaptera	♂	
Neuroptera	♂	
Coleoptera	♂ (XO)	

Source: Data from White, 1973, Chs. 16, 17. More recent data substantially improve the information available for some groups: Grossman et al., 1981 (Trematoda); Triantaphyllou, 1973 and 1976; Chitwood and Chitwood, 1974 (Nematoda); Oliver, 1971, 1977 (Acarina).

Note: Sc.—Subclass; O.—Order; (XO)—a true XX/XO system is documented for a large number of species, the absence of Y not being an artifact of a multiple sex chromosome system.

*See Table 2.C.3.

TABLE 2.C.3. The Heterogametic Sex in Diptera

Family	Heterogametic Sex	
	Male	Female
Tipulidae	♂	
Culicidae	♂	
Chironomidae	♂	♀
Simuliidae	♂ (B)	
Tephritidae	♂	♀
Drosophilidae	♂ (B)	
Muscidae	♂ (B)	♀ (G)
Calliphoridae	♂	
Phoridae	♂ (B)	
Anthomyidae	♂	

Source: Data from White, 1973, Chs. 16, 17. Chironomids and muscids are discussed further in Secs. 3.A, D, E.

TABLE 2.C.4. The Heterogametic Sex of Vertebrates

Taxon	Heterogametic Sex	
	Male	Female
Class Osteichthyes		
O. Anguilliformes		
F. Anguillidae		♀
Congridae		♀
O. Salmoniformes		
F. Bathylagidae	♂	
Galaxiidae	♂	
Salmonidae	♂ (B)	
Sternopychidae	♂	
O. Cypriniformes		
F. Cyprinidae	♂ (G)	
Parodontidae		♀
O. Siluriformes		
F. Bagridae		♀
Loricariidae	♂	
Siluridae	♂	
O. Myctophiformes		
F. Myctophidae	♂	
Neoscopelidae	♂	
Synodontidae		♀
O. Atheriniformes		
F. Goodeidae	♂	
Poeciliidae	♂ (G)	♀ (B)
Cyprinodontidae	♂ (B)	
O. Beryciformes		
F. Melamphaeidae	♂	

TABLE 2.C.4. (continued)

Taxon	Heterogametic Sex	
	Male	Female
O. Gasterosteiformes		
F. Gasterosteidae	♂	♀
O. Scorpaeniformes		
F. Cottidae	♂	
O. Perciformes		
F. Belontiidae	♂	
Cichlidae	♂	
Gobiidae	♂	
Osphronemidae		♀
Scatophagidae	♂	
O. Pleuronectiformes		
F. Cynoglossidae	♂	
O. Tetraodontiformes		
F. Balistidae	♂	
Class Amphibia		
O. Anura (Frogs)		
F. Pipidae		♀ (G)
Ranidae	♂ (G)	♀
Leptodactylidae	♂	
Hylidae	♂ (G)	
O. Urodele (Salamanders)		
F. Salamandridae	♂	♀ (G)
Ambystomidae		♀ (B)
Proteidae		♀
Plethodontidae	♂	♀
Class Reptilia		
O. Testudines	♂	
O. Squamata*	♂	♀
Class Aves		♀ (B)
Class Mammalia	♂ (B)	

Sources: Fish: general reviews in Yamamoto, 1969; Ebeling and Chen, 1970; Gold, 1979; Sola et al., 1981; Additional observations on fish include Thorgaard, 1978; Johnstone et al., 1979 (Salmonidae); Yamamoto, 1975 (Cyprinidae); Moreira Filho et al., 1980 (Parodontidae); Murofushi et al., 1980 (Balistidae); Park and Kang, 1979; Park and Grimm, 1981 (Anguilliformes). No comprehensive reviews are available for the Amphibia, since most of the findings are recent; these references are the following: Mikamo and Witschi, 1964 (Pipidae); Richards and Nace, 1978; Schmid, 1980 (Ranidae); Iturra and Veloso, 1981 (Leptodactylidae); Kawamura and Nishioka, 1977 (Hylidae); Schmid et al., 1979; Gallien, 1959 (Salamandridae); Sessions, 1982; Humphrey, 1945 (Ambystomidae); Sessions, 1980 (Proteidae); Kezer and Sessions, 1979 (Plethodontidae). For the Reptilia, see Sec. 9.D. For birds, two major references are Ray-Chaudhuri, 1973; Tagaki and Sasaki, 1974. For mammals, see Sec. 4.C.

Note: Symbols and notation as in preceding tables.

*See Table 2.C.5.

TABLE 2.C.5. The Heterogametic Sex in Lizards

Taxon	Heterogametic Sex	
	Male	Female
Infraorder Gekkota		
F. Gekkonidae		♀
Pygopodidae	♂	
Infraorder Iguania		
F. Iguanidae	♂	
Infraorder Scincomorpha		
F. Lacertidae		♀
Scincidae	♂	
Teiidae	♂	
Infraorder Platynota		
F. Varanidae		♀

Source: King, 1977. "The evolution of sex chromosomes in lizards." In: *Evolution and Reproduction*, edited by J. Calaby and H. Tyndale-Briscoe. Australian Academy of Science, Canberra, pp. 55-60, Table 1.

Note: F-Family.

In several species with heterogametic sex determination, the inheritance of sex may occasionally deviate from XX/XY, due either to environmental extremes or to rare combinations of autosomal sex factors (e.g., Secs. 8.B, 9.G). This variation may, on the one hand, provide the basis for the evolution of radically different sex determining mechanisms, and so it is important to acknowledge this phenomenon in the proper context (Secs. 8.F, 10.C). At the same time, occasional exceptions to an otherwise simple mechanism for the inheritance of sex do not warrant abandoning the overriding theme of simplicity. For the purposes of the combinatorial classification, a mechanism that determines sex according to XX females and XY males in 95% of the individuals may be classified as male heterogamety just as meaningfully as mechanisms in which sex is always inherited according to XX female/ XY male. Furthermore, there is no basis from an evolutionary perspective for distinguishing slight variations in heterogametic sex determination: models for the transition between different types of mechanisms seem robust to small magnitudes of "atypical" sex determination. Thus, without hesitation, I classify mechanisms as male and female heterogamety even if they are known to produce occasional exceptions.

D. Recessive-X and Dominant-Y Systems: The Sex of XO and XXY

The inheritance of sex under male and female heterogamety is described fully by XX/XY, but this formula provides only a rudimentary understanding of the nature of these sex factors. Heterogametic systems have sometimes been studied in special ways to further characterize the X and Y, and these studies

enrich our knowledge about the variety of systems that remains hidden when only the inheritance of sex is known. This section and the following one will consider two further aspects of heterogametic sex determination which have often been studied.

An XX/XY system may be accomplished by various possible mechanisms of gene action, as emphasized quite early by Muller (1932). Considering male heterogamety, for example, the X might have a female tendency or the Y a male tendency, or both, with the autosomes also exhibiting a sex tendency. Thus XX/XY may represent

♀	♂
$\mathbf{A}_m \mathbf{A}_m \mathbf{X}_f \mathbf{X}_f$	$\mathbf{A}_m \mathbf{A}_m \mathbf{X}_f \mathbf{Y}_o$
or,	$\mathbf{A}_f \mathbf{A}_f \mathbf{X}_o \mathbf{X}_o$
or,	$\mathbf{A}_o \mathbf{A}_o \mathbf{X}_f \mathbf{X}_f$
	$\mathbf{A}_o \mathbf{A}_o \mathbf{X}_f \mathbf{Y}_m$
	,

or other combinations, where (**A**) represents a haploid set of autosomes, the subscript (o) the absence of sex tendency, (f) a female tendency, and (m) a male tendency (modified from Beermann, 1955; Bush, 1966). Sex could even depend upon heterozygosity versus homozygosity (XY versus XX), so that the concept of sex tendency was not even applicable (see Sec. 3.F).

Recognition of this possible variety within systems of male or female heterogamety has stimulated studies to identify the roles of X and Y in initiating sex development. One well-known approach to this problem has been to study the sex of individuals with an atypical complement of sex factors, such as XO and XXY. These studies have usually been conducted in species with heteromorphic sex chromosomes, so that the atypical individuals were distinguishable by their odd number of sex chromosomes. It is fortunate for this work that, in systems with heteromorphic sex chromosomes, the Y is often highly degenerate and does not seem to have nearly as many gene functions as the X. Consequently its presence or absence often does not affect viability.

Bridges (1916, 1925) was the first to use this approach, and he applied it to study sex determination in *Drosophila melanogaster*. This species normally has XX females and XY males, but through occasional accidents of meiosis, flies were obtained with a normal complement of autosomes but a sex chromosome constitution of XO or XXY. The former were males and the latter were females, as though the X played an active and recessive role in producing females, while the Y was passive, influencing sex merely by segregating opposite the X. In the study of these and other genotypes, Bridges further showed that sex was determined according to the number of X's relative to the number of autosomes, rather than according to the absolute number of X's: a fly with three sets of autosomes and two X's (3A + 2X) possessed some male characters, whereas a completely triploid 3A + 3X fly was fully female.

There have since been similar studies of a few other species (Table 2.D). If one considers whether XO and XXY individuals with two sets of autosomes are male or female (no intersexes), there are four possible outcomes:

		XXY	
		♂	♀
XO	♂	(a)	(b)
	♀	(c)	(d)

However, species usually fall into one of two categories, which are denoted as follows:

Recessive-X Systems (b above): XO male, XXY female. Sex varies according to the presence of one or two X's, irrespective of the Y. (Previous terms include "genic balance" and "X-autosome ratio"; e.g., White, 1973, Ch. 16.)

Dominant-Y Systems (c above): XO female, XXY male. Sex varies according to the presence of the Y, irrespective of the presence of one or two X's.

From Table 2.D, most species with a Y chromosome have a dominant-Y system, although a recessive-X system is known in a few cases. Of course, the many **XX/XO** species also have recessive-X systems (Table 2.C.2). Many studies infer dominant-Y and recessive-X systems from the analysis of atypical genotypes other than or in addition to these (e.g., polyploids), but these other genotypes are not included in this table.

The terms recessive-X and dominant-Y are convenient descriptions of these characteristics, and do not imply any particular model of gene action. One possible interpretation of both these systems is that one of the sex factors (X or Y) is essentially null regarding gene action in regulating sex development. Under the principle of sex tendency, this interpretation implies that only one member of a sex factor pair need have a prominent sex tendency, although it may be either the X or the Y. The autosomes may therefore also have a sex tendency. Consequently, there may be far more genes with sex tendency than there are sex factors, and apparently not all sex factors have a sex tendency. (Recall that "sex factor" is defined according to the inheritance of sex; "sex tendency" reflects a supposed underlying contribution toward developing as male or female and thus may apply to a locus even if there are no segregating differences.)

E. The Sex of YY

The heterogametic mechanism may be further characterized as to whether or not YY is the same sex as XY. This characterization is again distinct from the

TABLE 2.D. The Sex of **XXY** and **XO** Individuals with a Normal Complement of Autosomes

Taxon	Sex of			Interpre- tation	References
	XY	XO	XXY		
Mammals					
<i>Homo sapiens</i> (man)	♂	♀	♂	Dom-Y	Cattanach, 1961; Ohno, 1967; Lyon et al., 1981
<i>Mus musculus</i> (mouse)	♂	♀	♂	Dom-Y	
<i>Bos taurus</i> (cow)	♂	—	I	?	Scott and Gregory, 1965
<i>Macropus eugenii</i> (wallaby)	♂	I(f)	I(m)	?	Sharman, 1970
Diptera					
<i>Drosophila melanogaster</i>	♂	♂*	♀	Rec-X	Bridges, 1925
<i>Musca domestica</i> (housefly)	♂	♀	♂	Dom-Y	Rubini et al., 1972
<i>Phormia regina</i> (blowfly)	♂	♀	♂	Dom-Y	Ullerich, 1963
<i>Lucilia cuprina</i> (blowfly)	♂	♀	—	Dom-Y	Ullerich, 1963
<i>Pales ferruginea</i> (tipulid)	♂	—	♂	Dom-Y	Ullerich et al., 1964
<i>Glossina palpalis</i> (tse tse)	♂	♂	♀	Rec-X	Southern, 1980
Lepidoptera					
<i>Bombyx mori</i> (silkworm)	♀	♂	♀	Dom-Y	Kihara, 1953
Plants					
<i>Melandrium</i> (<i>Silene</i>) <i>alba</i>	♂	—	♂	Dom-Y	Westergaard, 1958
<i>Rumex acetosa</i> group	♂	—	♀	Rec-X	Smith, 1963; Zuk, 1970a, 1970b

Note: I—Intersex, an individual with characteristics of both male and female; I(f)—intersex tending toward female; I(m)—intersex tending toward male.

This table excludes species which are regularly **XX/XO**, and excludes multiple sex chromosome systems (except for *Rumex*), since there is ambiguity as to which of the multiple X's or Y's carries the sex factor. A few of these references provide a more extensive listing of atypical sex chromosome genotypes, especially for *Rumex* (above references, plus Love, 1944), *Bombyx*, *Melandrium*, and *Drosophila*.

*—XO is male in several other species of *Drosophila* (Voelker and Kojima, 1971; Hess and Meyer, 1968).

inheritance of sex, and the information is useful in revealing the nature of sex factors. Since YY does not normally occur in the population, some method is required to cause XY to develop as the same sex as XX; the mating of XY males to XY females then produces YY genotypes. There are two common methods of influencing the sex of XY: environmental effects (such as external application of hormones or temperature extremes), or additional sex factors (e.g., the W of the platyfish system generates WY females, so that YY can be obtained). The sex of YY is evaluated in the absence of these additional factors. A possible complication may ensue if YY is inviable, as commonly occurs in species with heteromorphic sex chromosomes (Chapter 16).

Table (2.E) lists cases in which the sex of YY is known. All examples conform to the rule that XY and YY are the same sex. The only clear exception to this rule is observed in a mechanism from some hymenopteran insects. These

TABLE 2.E. The Sex of YY Individuals

Taxon	Sex of			References
	XX	XY	YY	
Fishes				
<i>Oryzias latipes</i>	♀	♂	♂	Aida, 1936; Yamamoto, 1963
<i>Xiphophorus</i> (3 spp.)	♀	♂	♂	Kallman, 1983
<i>Poecilia reticulata</i>	♀	♂	♂	Winge and Ditlevson, 1947
<i>Carassius auratus</i>	♀	♂	♂	Yamamoto, 1975
Amphibia				
<i>Xenopus laevis</i>	♂	♀	♀	Mikamo and Witschi, 1963, 1964
<i>Pleurodeles waltlii</i>	♂	♀	♀	Gallien, 1959; Collenot, 1975
<i>Ambystoma mexicanum</i>	♂	♀	♀	Humphrey, 1945, 1948
<i>Hyla arborea</i>	♀	♂	♂	Kawamura and Nishioka, 1977
Diptera				
<i>Musca domestica</i> *	♀	♂	♂	Milani et al., 1967; McDonald, 1971; Franco et al., 1982
Crustacea				
<i>Orchestia gammarella</i>	♀	♂	♂	Ginsburger-Vogel and Magniette-Mergault, 1981a,b
<i>Armadillidium vulgare</i>	♂	♀	♀	Juchault and Legrand, 1972
Plants				
<i>Thalictrum fendleri</i>	♀	♂	♂	Westergaard, 1958
<i>Asparagus officinale</i>	♀	♂	♂	Westergaard, 1958
<i>Mercurialis annua</i>	♀	♂	♂(st)	Westergaard, 1958

Note: X and Y are not necessarily to be interpreted as heteromorphic sex chromosomes. Instead, they may be inherited as single genes on a freely recombining pair of chromosomes. ♂(st)—a nearly sterile male.

*—Applies both for a heteromorphic XY pair and also for cytologically indistinct factors.

hymenopterans have halpo-diploid sex determination, rather than male or female heterogamety, but the genetic basis of sex determination is such that individuals heterozygous for sex factors are female, and homozygotes (and haploids) are male (Secs. 3.F, 11.B). If these hymenopterans had heterogametic sex determination, XX and YY would develop as the same sex.

F. The Origins of Heterogametic Sex Determination

In admiring the immense number of species with male or female heterogamety, it is natural to inquire how these systems arose. One might first entertain the possibility that, for some groups, heterogametic sex determination originated when separate sexes first arose. Of course, for some groups the origin of separate sexes is too remote for inferences about the sex determining mechanism at that time, but in other groups the origin of separate sexes is

quite recent, and one may study sex determination in these. For example, in flowering plants hermaphroditism is the common form of sexual reproduction, and in at least a few cases the origin of separate sexes (dioecy) is so recent that it can be traced to particular species. Substantial empirical and theoretical evidence demonstrates that one common pathway for the evolution of dioecy from hermaphroditism leads to heterogametic sex determination (Westergaard, 1958; Charlesworth and Charlesworth, 1978; described in Sec. 7.C).

Separate sexes may also evolve from a condition known as "isogamy," a condition illustrated by some algae. Isogamy involves reproduction in which two gametes of equal size join to form a zygote. The evolution of males and females (small- and large-gamete producers, respectively) conceivably could be the result of a dominant or recessive gene with a major effect on gamete size, and the establishment of such genes would in turn effect heterogametic sex determination. If the system is to accurately represent separate sexes, gametes of the same size must also be prevented from fusing, which could be accomplished if the gamete-size factor was linked to a mating-type locus. There have been some interesting models proposed for various aspects of this process, but there is not yet a strong empirical foundation for these evolutionary pathways (Parker, Baker, and Smith, 1972; Bell, 1982; Maynard Smith, 1978; Parker, 1982).

It should be emphasized that the above cases consider the origin of heterogametic sex determination as coinciding with the evolution of separate sexes. Many, if not the majority of existing systems of male and female heterogamety probably did not arise from a hermaphroditic or isogamous ancestor. Rather, they probably evolved in ancestors with separate sexes. That is, separate sexes have been continually present but the sex determining mechanisms have changed. These latter processes will be a major focus of this book.

G. Summary

This chapter introduced the most widely recognized systems of sex determination, male and female heterogamety. Two factors control the inheritance of sex in both systems, so that one sex is heterozygous or heterogametic for sex factors and the other is homozygous for one of these factors. (The notation XX female/XY male is reserved for male heterogamety, ZW female/ZZ male for female heterogamety.) Heterogametic sex determination has evolved on many occasions and in different groups, so it provides a major focus for studies in the evolution of sex determination. The ubiquity of these systems further implies that they may provide a common ancestral state for the evolution of alternative sex determining mechanisms. A second purpose of this chapter was to illustrate some of the variety known within these mechanisms, regarding recessive-X and dominant-Y systems, and the sex of YY. This appreciation of variety provides a useful perspective for the introduction of the next chapter.

3

Multiple-Factor Systems

Some examples of genotypic sex determination are slightly more complicated than male or female heterogamety because three or more sex factors segregate in the population. These mechanisms are perhaps derivatives of the simple two-factor systems, and they may also be intermediates for the evolutionary transition from one type of two-factor system to another. This chapter reviews examples of multiple-factor systems known from natural populations, restricting attention to those which are characterized in detail and where relatively few major sex factors seem to occur in the population.

The characterization of multiple-factor systems is based on principles similar to those for two-factor systems, although the details of the characterization are often more tedious. It is generally desirable to have an abundance of markers for studying multiple-factor systems, because the sex factors are not often associated with the cytological heteromorphism typical of sex chromosomes. A marker closely linked to a sex factor is not transmitted equally to sons and daughters, at least in certain crosses, and this property helps identify sex factor loci. The biased sex ratios of particular crosses provides an addi-

tional useful diagnostic property for some multiple-factor systems (e.g., Scudo, 1967). Generally, however, one may anticipate that only the simplest multiple-factor systems will prove amenable to a complete characterization. The evidence used in ascertaining the presence of multiple-factor systems will be indicated below.

A. A Commonly Observed System in Diptera

Most of the observed multiple-factor systems are known from only one or two species, but one system is observed in a variety of dipterans. A symbolic representation of it is as follows:

$$\begin{array}{ccc} \text{♀} & & \text{♂} \\ aa\ bb & & Aa\ bb \\ & & aa\ Bb, \end{array} \quad (3.A.1)$$

where the A - and B -loci are distinct, as in the case of independent segregation (although linkage is irrelevant in this system). Except for mutation, no other combinations of sex factors occur and two mechanisms of male heterogamety coexist:

	<i>Parents</i>		<i>Progeny</i>
	♀ ♂		♀ ♂
1)	$aa\ bb \cdot Aa\ bb$	→	$aa\ bb \quad Aa\ bb$
2)	$aa\ bb \cdot aa\ Bb$	→	$aa\ bb \quad aa\ Bb.$

This system has been documented in several species of Diptera (Table 3.A), and some species of *Chironomus* not included in this table also reveal sex determining mechanisms that are possibly consistent with this system (Beermann, 1955; Rosin and Fischer, 1972; Martin et al., 1980).

With appropriate markers, the detection of system 3.A.1 is straightforward, because males are always and only associated with A or B , and all

TABLE 3.A. Examples of Multiple-Factor System 3.A.1 (All Diptera)

Species	References
<i>Chironomus tentans</i> (midge)	Beermann, 1955
<i>Culex tritaeniorhynchus</i> (mosquito)	Baker et al., 1977
<i>Megaselia scalaris</i> (phorid)	Mainx, 1964
<i>Musca domestica</i> (housefly)	Milani et al., 1967; Franco et al., 1982; Hiroyoshi, 1964

family sex ratios are 1/2. In houseflies, these holandric factors (*A* or *B*) may be of three types: (i) a Y chromosome, which segregates opposite a larger X; (ii) a Y-autosome translocation, which segregates opposite the non-translocated autosome; or (iii) a cytologically indistinct sex factor which may be present on almost any of the chromosomes other than the X or Y, revealed in crosses with marker genes, (Wagoner, 1968, 1969; Milani, 1975; Tsukamoto et al., 1980). In midges (*Chironomus*) the inheritance of sex factors is usually detected in association with chromosomal inversions (described later in this chapter).

The two-locus system 3.A.1 is readily generalized to an arbitrary number of loci:

♀	♂	
<i>aa bb cc ...</i>	<i>Aa bb cc ...</i>	(3.A.2)
<i>aa Bb cc ...</i>		
<i>aa bb Cc ...</i>		
⋮		

In this version, there exists one female genotype, homozygous at all sex factor loci, and *n* distinct male genotypes, each one heterozygous at one of the *n* loci: A three-locus model of this sort may be appropriate for most populations of *Megaselia* (Mainx, 1964). One population of houseflies reported to have a four-locus version shows the Y chromosome to be absent, with sex factor pairs on four of the chromosomes distinct from the X (Tsukamoto et al., 1980).

The sex factors represented with capital letters occur only in males (holandric inheritance), and in the literature on Diptera, the cytologically indistinct holandric sex factors are generally referred to as *M* factors. Green (1980) suggested that the *M* factors of different loci may be homologous in ancestry, at least within a species, and are capable of being transposed to different sites, hence their multiple positions. This hypothesis assumes that *M* factors function according to a dominant-Y scheme (recall Sec. 2.D).

B. Platypfish

A thoroughly studied multiple-factor mechanism occurs in the platypfish (*Xiphophorus maculatus*), a small, tropical poeciliid fish often reared by aquarium fanciers. The earliest captives proved to be heterogametic in the female, whereas subsequent collections yielded male heterogamety (Gordon, 1946, 1954). Further work of Kallman (1965, 1968, 1970, 1973) showed that many natural populations were polymorphic for three factors (W, X, Y) assorting in opposition:

♀	♂	
XX	XY	
WX		
WY	YY.	(3.B.1)

This system has been inferred from sex-linked pigment genes and the sex ratios in the different crosses. The genotype WW does not normally occur, but it has arisen in some special cases and is generally female. There is as yet no known cytological distinction among X, Y and W. Furthermore, YY males have normal fertility. It is not known if the sex factors are alleles at one locus or if they are comprised by many, tightly linked loci, although two other species of *Xiphophorus*, *X. milleri* and *X. variatus*, have male heterogamety, and their sex factors are homologous (assort in opposition) to those of *maculatus* (Kallman and Atz, 1967; Kallman, 1983). It is clear that both male and female heterogamety can be isolated from the platyfish system, thereby accounting for the differences among early strains.

Overall exceptions to this system (such as XX, WX, or WY males) are less than 1%, but frequent exceptions occur in certain strains and crosses (Kallman, 1968, 1983). One particular cross, involving strains *Np* and *Cp*, generated up to 50% males in the genotypes WX and WY, yet less than 5% of the XX individuals were males (Kallman, 1968). The incidence of exceptions within each strain was considerably smaller than 50%, so this represented a (non-additive) genetic interaction between the two strains. This result is interesting, because it is one of the few examples of sex determination which cannot be accounted for under the simple principle of sex tendency. (That is, this result violates the concept of additivity of sex factors, a point that will be clarified in Sec. 4.E, following the introduction of the additive-value model of sex determination.)

C. Lemmings

Lemmings are microtine rodents found in the northern polar region. Most mammals are XX in the female and XY in the male, with a marked heteromorphism between the X and Y. However, a multiple-factor system resembling the system in the platyfish is known in the wood lemming (*Myopus schistocolor*) and in the varying and bog lemmings (*Dicrostonyx torquatus*, *D. groenlandicus*) (Fredga et al., 1976, 1977; Gileva, 1980; Gileva and Chebotar, 1979). Lemmings are heterogametic in the male, just as in other mammals, but some females possess an X variant (X*) causing X*X and X*Y to be female. (The Y is apparently absent in some *Dicrostonyx*, so the proper notation would substitute O for Y, although the inheritance of sex remains unaffected: Gileva, 1980; Gileva et al., 1982.) The lemming system has the same representation as in platyfish, except that YY is inviable:

♀	♂	
XX	XY	
X*X		
X*Y	(YY) dies.	(3.C.1)

Females with a **Y** are distinguishable when analyzed cytologically, but the **X*** is derived from the standard **X** chromosome, such that **X** and **X*** are not as cytologically distinct from each other as they are from the **Y**. In wood lemmings, **X*** and **X** have been distinguished with special stain techniques (Herbst et al., 1978), but no cytological distinction is yet known in varying lemmings. Consequently, the distinction between **X** and **X*** in varying lemmings has been inferred from pedigree analysis (Gileva, 1980). The death or absence of **YY** lemmings precludes the isolation of female heterogamety, in contrast to platyfish. These systems will be discussed further in Sec. 6.D. Lobato et al. (1982) and Lizzaralde et al. (1982) described possibly similar systems in South American rodents of the genus *Akodon*.

D. Houseflies

The common housefly (*Musca domestica*), with its cosmopolitan distribution, has been the subject of sex determination studies on several continents. Although sex determination in houseflies was discussed at the beginning of this section in the context of systems 3.A.1 and 3.A.2, other multiple-factor systems are also known.

Genome and Karyotype

The standard housefly karyotype consists of five euchromatic pairs, I-V, and a heterochromatic pair, which stains more darkly than the euchromatic pairs. In most literature, the euchromatic pairs I-V are referred to as "autosomes," and the **X** and **Y** as "sex chromosomes," regardless of which chromosomes carry the sex factors in the particular strains. This terminology will be adopted here, with appropriate clarification.

The two heterochromatic chromosomes in females are the same size and shape (**XX**), while the males are heteromorphic for an **X** and a smaller **Y**. Three lines of evidence suggest that the **X** and **Y** are both largely, though not completely, inert. First, both chromosomes stain positively for C-band heterochromatin (Jan and Shu, 1972). This type of staining is often associated with chromosome regions suspected of having little somatic function (John and Miklos, 1979; see Sec. 16.B). Second, aside from the male tendency of the **Y**, there are no known functions of the **X** or **Y**, despite many functions having been mapped to all the autosomes (Milani, 1975; Tsukamoto et al., 1980). Third, the number of **X**'s and **Y**'s in the karyotype may be selected up or down without difficulty, whereas aneuploidy for the autosomes is extremely rare (reviewed in Rubini et al., 1972). Flies **XX**, **XY**, **YY**, **XO**, and **OY** were reported in several studies, but flies without at least one **X** or **Y** were never observed (Boyes, 1967; Milani et al., 1967; Rubini et al., 1972). Thus there appears to be some vital function on both the **X** and **Y**. It is interesting to note that most other muscid flies have five pairs of euchromatic chromosomes, similar to the "autosomes" of houseflies, but several species lack the

heterochromatic pair (Boyes, 1967). One might consider, therefore, that the sex chromosomes of houseflies are recent additions to the genome.

Multiple Factors

As indicated above, there are various visible markers for the "autosomes," and these may be used to diagnose the positions of the sex factors. Due to the usual absence of significant recombination in males (e.g., Rubini et al., 1980; although see Lester, Crozier, and Shipp, 1979a, for an exception), markers of *M* factors need only lie on the same chromosome as *M* (Rubini et al., 1980). Sex factors have now been observed on all chromosomes of the housefly karyotype.

Houseflies isolated from the wild have shown any of three types of sex factor pairs: (i) the **X** and **Y** sex chromosomes; (ii) polymorphism for *M* factors, thus far known for all autosomes except IV; and (iii) polymorphism for a feminizing factor *F*, of which one copy is epistatic to apparently any number of **Y**'s and *M* factors. *F* was located on autosome IV in the one strain in which it was localized (McDonald et al., 1978). All three types of sex factor pairs have been discovered in Australia, Japan, and Europe, but *F* has not been found in North America (Wagoner, 1969; Tsukamoto et al., 1980; Franco et al., 1982). A fourth type, a **Y**-autosome translocation, has been found only rarely in the wild (Lester, Crozier, and Shipp, 1979b).

The relationships between these different sex factors may be expressed as a multiple-factor system in the following condensed fashion:

$$\begin{array}{ccc} \text{♀} & & \text{♂} \\ Ff + \text{ any } M, Y & & ff + \text{ at least one } M \text{ or } Y \\ ff XX mm & & \end{array} \quad (3.D.1)$$

(although the sex of specific genotypes has not been carefully studied in many cases). Here, *F* is the feminizing factor, with *f* as its alternative, and *M* is the masculinizing factor with *m* as its alternative. The **X** and **Y** are the respective sex chromosomes.

From these, the following strains* show some of the possibilities which have been or may be isolated (Milani et al., 1967; Milani, 1971):

	♀	♂	<i>Comments</i>
i)	XX mm ff	XY mm ff	As in 3.A.1 and 3.A.2
ii)	XX mm ff	XX Mm ff	
iii)	XX MM Ff	XX MM ff	Female heterogamety with XX males
iv)	YY mm Ff	YY mm ff	Female heterogamety with YY males

*Based on R. Milani. 1971. Genetics of factors affecting fertility and of sex ratio distortions in the housefly. Sterility principle for insect control or eradication. In Proceedings of a Symposium, Athens, 14–18 September 1970. International Atomic Energy Agency Proceedings Series, Vienna. pp. 381–397, Table on p. 392.

The nature of the European *F* factor is not clear. *F* was initially isolated in a strain of **YY** males and females, as in (iv) above. In the early stages, out-crosses between males of this strain (**YY mm ff**) and standard females (**XX mm ff**) produced all males, as expected. However, after more than 20 generations, **YY** males from this strain produced some daughters in this cross, indicating that *F* was no longer the simple epistatic factor as originally supposed (Rubini et al., 1972; Milani, 1971). These authors suggested that *F* may have been comprised of multiple loci, having become separated in this **YY** strain. But a hypothesis more compatible with subsequent results is that *F* may instead have been incompletely penetrant (see Sec. 6.D).

Wild populations studied in Japan, Europe, and North America exhibited both **XX** and **XY** males, the **XX** males resulting from the presence of "autosomal" *M* factors (Hiroyoshi, 1964; McDonald et al., 1975; Franco et al., 1982). The latter two studies reported geographical variation in the frequency of **XX** males, and Franco et al. (1982) described what appeared to be altitudinal and latitudinal clines in these frequencies. Based largely on the many early studies of Milani, the study of Franco et al. (1982) suggested that the frequency of autosomal sex factors may have been increasing through time, since **XX** males and holandrically inherited autosomal mutants apparently did not exist at the time the early housefly studies were published. They also observed in their own studies at one locality a significant increase over five years in the frequency of **XX** males.

E. Midges

Many observations have been reported on the sex determination of these dipterans (genus *Chironomus*). It appears from those studies that highly heteromorphic sex chromosomes are absent in most midges, and that sex is inherited according to single-locus factors. The markers commonly used to identify sex factors are chromosomal inversions. (An inversion is a rearrangement which causes a reversal of gene order within the chromosome.) Midges have readily accessible, banded, polytene chromosomes (as in *Drosophila*), so the detection of even a small inversion is straightforward.

One species of midge, *C. tentans*, has been extensively studied. Most populations are heterogametic in the male, sometimes with the multiple-factor system 3.A.1 (Table 3.A). However, Thompson and Bowen (1972) reported female heterogamety in a population, and crosses between midges from this female heterogametic population and midges from a nearby male heterogametic population were studied to observe the sex of different combinations of sex factors. The two populations segregated for sex factors in different parts of the genome, as follows:

	♀		♂	
<i>Population I</i>	<i>Ff</i>	**	<i>ff</i>	**
<i>Population II</i>	— —	<i>mm</i>	— —	<i>Mm</i>

It is not known whether (*) in population I corresponded to M or m of population II or to something else, and likewise for (—) in population II. Although there was no evidence of a multiple-factor system within either population, the hybridization of these populations initiated a multiple-factor system. The sexes of the genotypes assayed were

$F - M^*$	♂
$f - M^*$	♂
$F - m^*$	♀
$f - m^*$	♀

Possibly, population I consisted of $Ff mm$ females/ $ff mm$ males, and population II consisted of $FF mm$ females/ $FF Mm$ males, but further crosses are needed in order to accept this hypothesis. Additional genotypes would have been created upon further matings, so the observed genotypes did not constitute a complete multiple-factor system.

The Thompson and Bowen experiment highlights a point that will be noted in subsequent chapters. Two populations of a species that have different sex determining mechanisms may be hybridized, and the hybrid population may reveal a multiple-factor system. The multiple-factor system generated in this fashion—which was not observed in either natural population—may nonetheless once have been present and may have fostered the change in sex determining mechanisms that led to the difference between the two populations.

Martin et al. (1980) presented data on the positions of sex factors in several Australian *Chironomus* species, and they surveyed the literature on sex factors in other *Chironomus*. The homologies of chromosome arms were easily established in these different species, so the location of sex factors could be compared straightforwardly. They concluded that present data were compatible with the existence of five to six different sex factor sites. Although no single population was known to segregate at all sites, different species often had sex factors at potentially the same sites. Multiple-factor systems were suspected in some of these populations, although they were not studied in detail (except as listed in Table 3.A).

F. Complementary Sex Determination in Hymenoptera (A Preview)

A system of multiple sex factors is known in some hymenopterans (ants, bees, wasps). Several factors (A_i) assort in opposition, and heterozygotes become females, while diploid homozygotes as well as haploids become males:

$A_i A_j$	A_i	$i \neq j$	(3.F.1)
	$A_i A_i$		

This system is sometimes referred to as “complementary” sex determination (Whiting, 1943, 1945; Crozier, 1977). Hymenopterans with this mechanism have a haplo-diploid genetic system (arrhenotoky), with unfertilized eggs producing males and most fertilized eggs producing females. Diploid males are either inviable, or they produce diploid sperm, and so they do not have normal progeny. (More details will be given in Sec. 11.B.)

Haplo-diploidy renders system 3.F.1 outside the classification of multiple-factor systems in the strict sense of this chapter, but there are two reasons that warrant its inclusion here. First, it simply illustrates another system with more than two major sex factors. Second, and more importantly, system 3.F.1 represents a type of sex factor interaction (complementarity) not otherwise known. For example, if complementary sex determination is described in the notation of 2-factor systems (Z and W), ZW is female, but both ZZ and WW are male, in contrast to the usual result that ZW and WW are the same sex (Table 2.E). The observation of complementary sex determination, although not from a normal diploid population, enriches our understanding of variety among sex determining mechanisms and thereby helps motivate adoption of the combinatorialist perspective (Chap. 5).

Although this complementary mechanism is known only in some haplo-diploid hymenopterans, in principle it may also occur in diploid populations, and recognition of this possibility may help lead to its further discovery. In a diploid population, the complementary mechanism should produce female heterogamety with a dominant-W scheme, since ZZW would likely be female and ZO male, independent of which sex factors were chosen as Z and W. Only a demonstration that ZZ and WW were the same sex would distinguish this system from the more common type of female heterogamety (Table 2.E).

G. Summary

Although a great many species are suspected or known to have male or female heterogamety, there are some species with multiple-factor systems, and these systems may be derived from 2-factor systems by the addition of one or a few sex factors. Multiple-factor systems are known in diverse groups, including dipterans, mammals, and fish. The evidence suggests that some mechanisms of male and female heterogamety are periodically invaded by new sex factors, with the potential to maintain a multiple-factor system for at least short evolutionary periods. The following chapter continues with this theme, by reviewing the studies of sex transformer genes in mammals, *Drosophila*, and *Caenorhabditis*, in the context of their relationship to the origin and nature of sex factors.

4

Genetics of Sex Development and the Nature of Sex Factors

The previous two chapters described the inheritance of sex factors in some simple sex determining mechanisms, but these descriptions did not consider the constitution of sex factors. This chapter addresses the genetics of sex development and further provides a perspective on the nature of sex factors. Regulatory mutations of sex development are known in the fruitfly *Drosophila*, in the nematode *Caenorhabditis*, and in several mammals, with each mutation simultaneously controlling the expression of an entire set of sex-specific characters. In the two invertebrates, these mutations have been thoroughly studied according to how they influence sex development and also how they interact with each other. These mutations may be fundamentally the same as sex factors, and therefore they unveil a dimension of sex determination not to be found in population studies. This chapter also discusses the work of two pioneers in the theory of sex determination as it relates to the nature of sex factors: Goldschmidt's work on sex determination in gypsy moths, and the theory of genic balance as formulated by Bridges.

As a starting point, consider the physical size of sex factors. Observations from several species of Diptera indicate that their sex factors occupy only a small portion of the chromosome (Gilchrist and Haldane, 1947; Beermann, 1955; Mainx, 1964; Green, 1980; Martin et al., 1980). Even in mice and man, in which there are heteromorphic sex chromosomes with a dominant-Y system,

studies on Y chromosome deletions have shown that only a tiny part of the Y is necessary to cause male development (Ohno, 1979; Singh and Jones, 1982); the same may be true in the silkworm, although the evidence is less compelling (Tazima, 1964). These results suggest that sex factors may often be regulatory genes at a single locus, as anticipated by Muller (1932) and in part by Aida (1936). The next three sections address this possibility as well as other details of the genetics of sex factors.

A. Fruitflies

The fruitfly *Drosophila melanogaster* is characterized by male heterogamety with heteromorphic sex chromosomes, XX females/XY males. A brief but thorough review of sex determination in *D. melanogaster* is given by Baker and Lindsley (1983). In addition to the sex chromosomes, there are three pairs of autosomes, one which is dot-like. As described in Sec. 2.D, XXY flies with two sets of autosomes (XXY AA) are female and XO AA are male, as if the Y has no male tendency. Bridges (e.g., 1939) further showed that flies (or tissues) were female if they were haploid X A, triploid XXX AAA, or tetraploid XXXX AAAA, but that XX AAA flies were intersexual. Therefore, he suggested that sex was determined according to the ratio of the number of X chromosomes to the number of sets of autosomes.

Bridges' work led to studies concerning the positions of sex factor genes on the X. This problem was analyzed by constructing XO AA flies in which an additional segment of the X was present in two copies (Patterson, 1931, 1938; Patterson, Stone, and Bedichek, 1937; Crow, 1946), or by constructing XX AAA flies in which an arbitrary segment of the X was present in triplicate (Dobzhansky and Schultz, 1931, 1934). With both methods, the extra portion of the X should have caused a shift toward female development when the sex factor locus was included in the segment, but should not have caused a shift otherwise. A shift toward female development was observed in some experiments, but rather than being attributable to a particular site on the X, the magnitude of the shift was proportional to the size of the euchromatic portion of the X present in excess. Rather than a single site for a sex factor gene on the X, it seemed that individually small female tendencies were scattered over much of the X.

A search was also undertaken to determine the position of male-tendency sites in the autosomes (Pipkin, 1960, and references therein). These studies again investigated the phenotype of flies with additions or deletions of individual chromosome segments, most commonly in flies triploid, XXX AAA, except for the aneuploid autosomal region. Individual analysis of a large set of fragments, which together incorporated all portions of the autosomes, failed to identify any segment with an appreciable male tendency, even though comparable lengths of X fragments had been shown to harbor readily detectable female tendencies (Pipkin, 1960).

Some of the most interesting work on *Drosophila* concerns mutations isolated in the laboratory which transform major parts of the somatic sexual phenotype. Five such loci are known, and they are given the following designations: (a) *transformer* (*tra*), (b) *transformer-2* (*tra-2*), (c) *doublesex* (*dsx*), (d) *intersex* (*ix*), and (e) *sex lethal* (*sxl*) (Table 4.A). Each of these five sex loci regulates the expression of a large set of sex-limited traits, and the mutant alleles appear to disrupt or abolish the regulatory functions. In this respect the normal and mutant alleles at each locus are characteristic of sex factor pairs in other species, but the sterility or lethality, and in some cases the incomplete sex transformation of the mutant alleles (hence their virtual absence in natural populations), distinguishes them from the sex factors described in preceding chapters. Mutations from the first four of these loci were studied in detail by Baker and Ridge (1980) and Belote and Baker (1982), and the *sex-lethal* mutations were studied by Cline (1979a). The coverage here was derived largely from these papers.

The effects of most of the sex transforming mutations in *Drosophila* are readily obtained from Table 4.A, except perhaps for those of the *sex-lethal* locus. The mutations of *tra*, *tra-2*, and *ix* affect sex development in only one direction, by masculinizing **XX**. The mutations of *dsx* and *sxl* differ from those

TABLE 4.A. Sex Transformer Mutations in *Drosophila melanogaster*

Symbol of Mutation	Chromosome Map Position	Phenotype of		Notes
		XX	XY	
wild type		♀	♂	
<i>tra</i>	3-45	♂(st)	♂	recessive; indistinct from deficiency
<i>tra-2</i>	2-70	♂(st)	♂(st)	recessive; indistinct from deficiency
<i>tra-2</i> ^{ts}		♂(st)	♂(st)	recessive; transforms only at high temperature
<i>dsx</i>	3-48.1	I	I	recessive; indistinct from deficiency; apparently causes simultaneous expression of ♂ and ♀ characters
<i>dsx</i> ^D		I	♂	dominant
<i>ix</i>	2-60.5	I	♂	recessive
<i>sxl</i> ^{f1}	1-19.2	♂(l)	♂	recessive; lethal in XX; elevates X activity in XX and causes male development
<i>sxl</i> ^{m1}		♀	♀(l)	dominant; lethal in XY/XO; lowers X activity in XY/XO and causes female development

Sources: Baker and Ridge (1980), Belote and Baker, (1982), and Cline (1979a, b). A more complete listing of mutations at these loci are available in these references. I have chosen those mutations which illustrate the most extreme transformations. The above table is based on B.S. Baker and K.A. Ridge. 1980. "Sex and the single cell. I. On the action of major loci affecting sex determination in *Drosophila melanogaster*." *Genetics* 94:384-423, Table 1.

Note: ♂—normal, fertile male; ♂(st)—sterile male; ♂(l)—lethal male; I—intersex (sterile); ♀—normal female; ♀(l)—lethal female.

in that both **XX** and **XY** are affected, though not necessarily by the same mutant. (Even in the case of *sxl*, it is hypothesized that wild-type function is limited to **XX**, and the mutation influencing **XY** causes constitutive expression of the locus.) Transformations induced by mutations at the first four of these loci are invariably sterile, apparently because the germ line is not transformed (Marsh and Wieschaus, 1978; Schupback, 1982). Transformations due to *sxl* are lethal and can only be studied in patches of tissue in mosaic flies.

Sex-lethal mutations affect at least four characteristics of the fly: (i) dosage compensation of **X**-linked genes (cf. Sec. 16.E), (ii) sex development, (iii) sex-specific viability (some mutations are male-lethals, others are female-lethals). A fourth characteristic of *sxl* mutants is that they are influenced by mutations at the daughterless locus (Cline, 1978, 1979a, b). The various effects of *sxl* mutations are not necessarily independent, however. The *sxl^{m1}* mutation is lethal to **XO** and **XY** genotypes and also causes feminization of these genotypes, but it does not affect the viability or male development of **XX tra/tra** flies (Cline, 1979a). It is suspected that the activity of **X**-linked genes in **XO** and **XY** flies is considerably reduced from normal by the *sxl^{m1}* mutation, which is possibly the basis of its lethality (Lucchesi and Skripsky, 1981). The *sxl^{f1}* mutation is recessively lethal and causes the masculinization of **XX** flies. In contrast to the above mutation, *sxl^{f1}* apparently elevates **X** activity above normal, thus possibly accounting for its lethality in **XX** genotypes (Lucchesi and Skripsky, 1981). The *sxl^{f1}* allele interacts with other mutations influencing dosage compensation, so that partial sex transformations sometimes occur in flies heterozygous for this mutation (Uyenoyama et al., 1982). On the basis of these results, it has been suggested that, in responding to the **X-autosome** ratio, the *sxl* locus has a dual role in establishing the level of dosage compensation and in triggering the male or female pathway of sex development (Cline, 1979a; Lucchesi and Skripsky, 1981).

Two major questions have been investigated with these sex transforming mutations: when and for how long during development their function is required, and also how the loci interact. The first question, which addresses the "window" of required activity during development, has been investigated with the following two techniques. The first technique simply involves the use of temperature-sensitive mutants. The sex phenotype of flies with known **XX/XY** genotype is compared for different intervals of exposure to the permissive temperature. Only a few temperature-sensitive sex transforming mutations are known, however (Table 4.A). The second technique induces homozygous cells in a fly heterozygous for a recessive sex transformer. Cells that remain heterozygous will develop normally, but cells that become homozygous for the mutation (through mitotic recombination induced by irradiation) will be transformed if homozygosity was induced prior to the time of activity. This technique works well with flies, because there are external sex differences on many different parts of the fly, and because the sex in one patch of tissue is not influenced by the sex in other parts of the fly. (This method is in fact used to

demonstrate the clonal autonomy.) Recessive markers closely linked to the transformer mutations are used to identify groups of cells homozygous for the mutation, and the size of the group of homozygous cells indicates how early in development the homozygosity occurred.

The results from both experimental methods indicate that expressions of wild-type *tra*, *tra-2*, and *dsx* are required as late as the pupal stage for some characteristics of female differentiation (abdominal tergites) but not so late for other characteristics (foreleg, Baker and Ridge, 1980). Some especially interesting results are available for the temperature-sensitive *tra-2^{ts}* (Belote and Baker, 1982). The wild-type function of this locus is required from the second larval instar to early-mid pupal period. Within this period, however, different characteristics are determined at different times, and control of one characteristic is perhaps independent of others. For example, the number of bristles on the foreleg is approximately determined at the time of pupariation, while bristle morphology is determined later. Flies were constructed with the number of bristles as in males and the morphology as in females, and vice versa. Another discovery was that wild-type *tra-2* function in the gonadal primordia of XX caused both proliferation of the female primordia as well as suppression of the separate, male primordia (Belote and Baker, 1982).

In addition to the effects of single mutations, combinations of *dsx*, *tra*, *tra-2*, *ix* and *sxl^{m1}* have been studied. Invariably, XX flies homozygous for two of these mutants displayed the phenotype of just one mutant, and the pattern of epistasis (dominance across loci) was transitive (Baker and Ridge, 1980):

$$dsx > tra, tra-2 > ix$$

("A > B" is read "A is epistatic to B.") The complete epistasis combined with the linear hierarchy of epistasis is expected if these loci function sequentially in a single pathway of sex development, and Baker and Ridge offered a model along these lines. The sequence of initial gene effects they proposed is (*tra*, *tra-2*) followed by *dsx* and then *ix*, although expression of these loci also overlaps in time. Certain observations of the *dsx* mutants preclude a simple role for this locus independently of *tra-2* (e.g., *dsx* > *tra-2* > *dsx^D*), but this offers only a small modification of what seems to be an otherwise simple scheme of the genetic control of sex development.

XX flies homozygous for both *sxl^{m1}* and *tra* developed as males with perhaps normal viability (Cline, 1979a). If *sxl^{m1}* is interpreted as a mutation causing female development in both XX and XY flies, then this result indicates that *tra* > *sxl^{m1}*. Based on this conclusion, it was hypothesized that *sxl* had an earlier influence than the other sex transforming loci (Cline, 1979a; Baker and Ridge, 1980). However, the interpretation of epistasis between *sxl* and *tra* remains incomplete until this combination is assayed in XY and XO tissue, since it can also be argued that any effect of *sxl^{m1}* on sex determination is limited to haplo-X.

B. Nematodes

The free-living nematode *Caenorhabditis elegans* is normally a self-fertilizing hermaphrodite. The first cells produced by the gonad become sperm, which are stored, and the gonad otherwise is an ovary for most of the adult life. Males are known as the result of various mutations, but most commonly they arise from non-disjunction of a particular chromosome (designated **X**), so that males are **XO AA**, while hermaphrodites are **XX AA**, letting **A** represent a haploid set of autosomes. (There are five pairs of autosomes in addition to the **X**'s.) It is tempting to suppose that hermaphroditism ultimately arose from an **XX/XO** system with separate sexes, since the **XX/XO** mechanism is so common in other nematodes (cf. Table 2.C.2). Although the phenomenon of hermaphroditism is outside the scope of this book, the genetics of sex development are especially well-studied in *Caenorhabditis*, and for this purpose it does not seem totally unwarranted to compare males and hermaphrodites in the same light as males and females.

Since males are **XO** and hermaphrodites **XX**, the inheritance of sex is of the recessive-X scheme (Sec. 2.D). Further details have been obtained from crosses of tetraploid and diploid strains (Madl and Herman, 1979; and Nigon, 1949a,b, 1951a,b, as described by Madl and Herman):

<i>Hermaphrodite</i>	<i>Male</i>
XX AA	XO AA
XXX AAA	XX AAA
XXX AAAA	XX AAAA
XXXX AAAA	

The ratio of the number of **X**'s to sets of autosomes seems to control the direction of sex development, just as in *Drosophila*. By employing techniques similar to those used for *Drosophila*—adding fragments of the **X** to the genome—it was again indicated that there was no single site responsible for the entire “female” tendency of the **X**. Rather there appeared to be at least three sites with lesser female tendencies, although there could have been many more sites (Madl and Herman, 1979).

As in *Drosophila*, various sex transforming mutants are known at different autosomal loci (Table 4.B): (a) *transformer-1* (*tra-1*), (b) *tra-2*, (c) *tra-3*, (d) *her-1* (hermaphrodite or female), (e) *her-2* (perhaps inseparable from *tra-1*), and (f) *intersex* (*isx*). The major distinction between these mutations and those in *Drosophila* is that some of the transformations in *Caenorhabditis* are fertile. When segregating in a population these mutations qualify as sex factors, and so from a developmental or evolutionary perspective there is no necessary distinction between sex factors and these mutations.

Temperature-sensitive mutants of *isx* and *tra-2* were studied to determine at what interval during development their expression was required (Klass, Wolf, and Hirsh, 1976; Nelson, Lew, and Ward, 1978). The results parallel

TABLE 4.B. Sex Transformer Mutations in *Caenorhabditis elegans*

Mutation	Chromosome	Phenotype of		Notes
		XX	XO	
wild type		♀	♂	
<i>tra-1</i>	III	♂	♂	
<i>tra-2</i>	II	♂(p)	♂	Temperature-sensitives known
<i>tra-3</i>	IV	♂(p)	♂	
<i>her-1</i>	V	♀	♀	Temperature-sensitives known
<i>her-2</i>	III	♀	♀	Tightly linked to <i>tra-1</i>
<i>isx</i>	IV	♀	♂(g)	Temperature-sensitive; influences the gonad but not secondary sex characters

Sources: Hodgkin (1980), Klass et al. (1976), and Nelson et al. (1978). Not all variants of each locus are included. The above table is based on J. Hodgkin. 1980. "More sex determination mutants of *Caenorhabditis elegans*." *Genetics* 96:649-664, Table 1.

Note: All mutations are recessive except *her-2*, which is almost completely dominant. Transformations are not necessarily fertile. ♂—male; ♂(p)—male, but transformation not complete or of low fertility; ♂(g)—male with intersex gonad due to a lack of sperm; ♀—hermaphrodite; ♀—female, a hermaphrodite lacking sperm.

those of *tra-2* in *Drosophila*. Each mutation controls several characteristics of the sex phenotype at different times, and the wild-type function is required for a lengthy period of development (such as from prehatching into the first or second larval instar). In many but not all cases the sensitive periods overlap for different characteristics controlled by the same locus. In some cases these sensitive periods occur prior to any morphological evidence of sexual dimorphism (Klass, Wolf, and Hirsh, 1976; Hodgkin, 1980, for *her-1*).

Double combinations of the *tra* and *her* mutants, assayed in both XX and XO genotypes, again revealed a linear sequence of epistasis (Hodgkin, 1980):

$$\textit{tra-1} > \textit{tra-2}, \textit{tra-3} > \textit{her-1}$$

$$\textit{her-2} > \textit{tra-2}, \textit{tra-3}.$$

The remaining combinations enabling placement of all these mutations into one hierarchical scheme were either not produced, or could be ordered because both mutations produced indistinguishable phenotypes. These results parallel those found for *Drosophila* in the linearity of epistasis, suggesting that all mutations function sequentially in a single pathway of sex development, a pathway producing either a male or a hermaphrodite. Combinations of *isx* with *tra-1* and *tra-2* were also studied in XX worms (Nelson et al., 1978). The patterns of epistasis were reversed for different characteristics controlled by these mutations, but the interpretation of these results is ambiguous, because the double-mutant combinations were not studied in XO individuals.

Hodgkin (1980) offered a model for the genetic control of sex development in *Caenorhabditis* that specified an essentially linear order to the roles of the *her-1* and different *tra* loci. Again, some observations require the assumption

of nonlinear effects, but the overall picture is potentially simple at this level. Hodgkin's model for *Caenorhabditis* is quite similar to Baker and Ridge's model for *Drosophila*.

In summary, one may consider two somewhat opposite impressions from the work on sex transformers in *Drosophila* and *Caenorhabditis*. First, these regulatory loci of sex development are indeed complicated. They control several developmental dichotomies at separate times in different tissues. Some double-mutant combinations suggest complicated interactions. Second, however, there is an equally overriding simplicity to interactions among these loci. It is indeed remarkable that although each of these loci seems to control different subsets of its phenotype at different times, so that multiple effects of a locus can be separated, double-mutant combinations are uniformly characteristic of one mutation. For example, studies of sex transforming mutations in hermaphroditic plants illustrate how these double-mutant combinations might instead have developed. Combining a mutation causing pollen sterility with a mutation causing seed abortion often produces a plant sterile in both sex functions (Westergaard, 1958; Charlesworth and Charlesworth, 1978). The mutations at the loci regulating sex development in *Drosophila* and *Caenorhabditis* are perhaps fundamentally similar to sex factors in natural populations, and the thorough research with these species leads to a further understanding of the role sex factors play in the process of sex development.

C. Transformer Genes in Mammals

More work is available on sex differentiation in mammals than in any comparable animal group, but the emphasis is usually placed more on behavior, morphology, physiology, and biochemistry than on genetics. Consequently, genes affecting sex are often interpreted in the context of these other disciplines. This section will first briefly discuss two dimensions of work on mammals relevant to the interpretation of sex transformer genes (hormones and H-Y antigen), and it will subsequently review the known transformer genes.

Hormones

The secondary sex differences—the extragonadal differences between males and females in morphology and behavior—are expressed in response to circulating gonadal steroid hormones. A complete, or at least contemporary, picture of the role of hormones in affecting the sex phenotype would be quite complicated (e.g., see Austin and Edwards, 1981; the overview here is extracted from Ohno, 1979). However, there is one aspect of sex development in which hormones have a simple interpretation. Since sex hormones circulate throughout the body, there is often a uniform secondary sex phenotype, even in genetically mosaic individuals. Whereas a fly mosaic for **XO** and **XX** will have patches of male and female tissue, a mammal mosaic for sex chromo-

some differences (e.g., **XO** and **XY**) will have a uniform appearance. Furthermore, some hormones have a major effect on sexual phenotype.

Consider the effects of testosterone, in anticipation of the mutation *testicular feminization*. If the gonads of a placental mammal are removed early in embryogenesis, the secondary sex characteristics develop as female, even in **XY** individuals (Jost, 1965). In these castrated embryos, the early and continued administration of testosterone, normally produced by Leydig cells in the testes, induces most secondary sex characters to develop as male. (Regression of the Mullerian ducts—precursors of the uterus—is induced by a hormone from the testicular Sertoli cells, rather than by testosterone.) In adults, circulating testosterone is responsible for the maintenance of these secondary male characteristics. Hormones do not control gonadal differentiation, however, because **XY** gonads develop as testes and **XX** gonads develop as ovaries, irrespective of the hormones administered.

Gonadal Differentiation and H-Y Antigen

The initiation of testicular development in mammals may be influenced by H-Y antigen (reviewed in Ohno, 1979; Wachtel and Koo, 1981). H-Y antigen was first detected as a male specific antigen in inbred strains of mice: males accepted skin grafts from both sexes within the same strain, but females rejected skin grafts from males (Eichwald et al., 1958; reviewed in Wachtel and Koo, 1981). However, the most common assay of H-Y antigen is now performed with antisera: females are immunized against males from the same strain and build antibodies against the male factor. This antiserum is used to identify H-Y antigen on cells of mammals and even in other vertebrates. It is now suggested, however, that the serological assay may detect a male specific antigen distinct from the tissue-rejection antigen, because some individuals show a positive response by the skin-graft assay and a negative response by the serum assay, or vice versa (Wachtel and Koo, 1981; Silvers, Glasser, and Eicher, 1982; Muller, 1982). The serum-defined antigen is secreted by the testicular Sertoli cells, but since it has also been detected on most cells of males, it is likely that a soluble state as well as the membrane-bound state of H-Y exists (Muller, 1982).

Assays using mouse serum antibody to identify H-Y have detected a sex specific antigen in various mammals, birds, reptiles, frogs and fish, suggesting extreme conservation of the antigen as well as a fundamental role in sex development (Wachtel et al., 1975a, b; Wachtel and Koo, 1981). In some fish, however, no detectable differences were observed between the sexes in the level of H-Y antigen (Muller and Wolf, 1979). In mammals, the hypothesis of a prominent role of H-Y in gonadal development was strengthened by *in vitro* experiments showing that (i) testis-secreted H-Y would bind only to gonadal cells, (ii) a testis-secreted substance causing ovarian cells to associate in testicular structures was bound by H-Y antiserum, and (iii) **XX** cultured

gonads were induced to form testis-like structures by serum containing H-Y (reviewed in Ohno, 1979; Wachtel and Koo, 1981; Muller, 1982).

The research on H-Y antigen is so recent that despite the wide interest in this phenomenon, many questions remain, and there is still controversy over the exact role of H-Y in sex development. The serum method of assaying H-Y has not always produced repeatable results. For example, X^*Y female wood lemmings were originally reported to be H-Y⁻ (Wachtel et al., 1976) and more recently to be H-Y⁺ (Wiberg et al., 1982). Silvers et al. (1982) challenged the theory that either form of H-Y antigen controls gonadal development in vertebrates, and they proposed instead that H-Y may be a consequence of gonad development. This challenge was based in part on the observation that, in frogs (*Xenopus*) and birds, the early administration of hormones to ZZ genotypes induced H-Y expression along with partial or complete sex reversal (Muller et al., 1979; Wachtel et al., 1980; Zaborski et al., 1981). In birds and *Xenopus*, the ZZ genotype is normally male and lacks H-Y expression. Even in mammals, where the most extensive evidence on the role of H-Y antigen in gonadal differentiation exists (Muller, 1982), there are unexplained exceptions to the rule that H-Y antigen is associated with testes (Haseltine et al., 1982). Therefore, while H-Y antigen appears to have a major role in directing gonadal differentiation in mammals, no consensus exists on the exact nature of this role.

Conserved Sex Chromosomes

Placental and marsupial mammals possess male heterogamety with a heteromorphic X and Y (the cytological work was reviewed by Vorontsov, 1973). As first recognized by Ohno (1967), these mammals possess the same set of X-linked genes, as if these sex chromosomes were inherited from an ancestor common to both groups, and this pattern has been corroborated by subsequent evidence (Cooper et al., 1977; McKusick, 1978; VandeBerg, 1983). Cytological studies of the X chromosome in different species are also consistent with this hypothesis (Pathak and Stock, 1974). Circumstantial evidence suggests that the sex chromosomes of monotreme mammals (platypus, echidnas) are not homologous with those of placentals and marsupials (VandeBerg and Cooper, 1978). The only known fertile exceptions to XX female/XY male in mammals are lemmings and akodont rodents (Sec. 3.C) and some other rodents (Ohno, 1979), but sex transforming mutations are known to induce sterile transformations in some species. These mutations are not as thoroughly characterized as in *Drosophila* and *Caenorhabditis*, but they again exemplify regulatory genes controlling development of large portions of the sex phenotype.

Testicular Feminization

The mutation *testicular feminization* (*tfm*) illustrates the separation of gonadal from secondary sex differentiation (Lyon et al., 1981; Ohno, 1979).

This mutation affects XY individuals: they develop testes and are H-Y⁺ (serum assay), but the testes do not descend and the individuals are feminine in non-gonadal characteristics. Derivatives from the Mullerian duct are also absent (recall that Mullerian duct regression is due to a hormone of testicular Sertoli cells). *Tfm* is a defect of the androgen receptor, and it thereby prevents the binding of testosterone to its cellular substrate. Consequently, *tfm* XY individuals are not responsive to testosterone, and they manifest most secondary sex characteristics as female, while the initial differentiation of the testes is unaffected (Ohno, 1979). The *tfm* syndrome is known in mice, rats, dogs, cattle, and man, and it is X-linked, at least in mice (Lyon and Hawkes, 1970). In contrast to *tfm*, the following transformer genes apparently influence gonadal development and thus also influence secondary sex characteristics.

XY Females and XY Gonadal Dysgenesis

There are several examples of sterile XY humans who manifest a typically feminine appearance, but are not *tfm* mutants (reviewed in Ohno, 1979; Moreira-Filho et al., 1979; Wachtel and Koo, 1981; Wiberg et al., 1982). Some of these individuals are H-Y⁺ and others are H-Y⁻. There is a greater teratogenicity among the H-Y⁺ individuals, so it has been suggested that there are at least two distinct causes of this syndrome. X-linkage was suggested in one case of the H-Y⁻ syndrome (Bernstein et al., 1980). The gonads of H-Y⁻ individuals are similar to those of XO human females, so the sterility of these XY individuals may be due in part to the single X in the ovary (German et al., 1978; Burgoyne, 1978). The deleterious effect of a single-X ovary may be anticipated because the principle of dosage compensation, whereby one X of female mammals is inactivated, does not apply to female germ cells, and both X's are active in many stages of oocyte development (reviewed in VandeBerg, 1983).

Sterile XY females with ovaries have also been observed at high frequency in hybrid mice (Eicher et al., 1982). The XY females occurred if the Y chromosome was derived from *Mus poschovianus* (= *domesticus*), with the X and perhaps half the autosomes derived from a particular laboratory strain of *Mus musculus*. Since XY females were absent in parental strains, the XY female condition in hybrids involved an "interaction" between the two genomes. The XY females were typed H-Y⁺ for both the skin graft and a cell-mediated assay (possibly similar to the serum assay).*

XX Males

Various mammals produce sterile XX males at low frequency, although strains have been selected in which XX males are frequent (reviewed by Ohno, 1979,

*Note: A dominant autosomal mutation causing XY mice to be female was reported recently. (Washburn and Eicher, 1983.)

p. 42; Lyon et al., 1981). The most thoroughly studied XX males are mice with the mutation *sex reversal* (*sxr*). A single copy of *sxr* causes XX and XO individuals to be males. The inheritance of *sxr* was for a long time puzzling, but the problem was recently solved (Singh et al., 1982; Hansmann, 1982; Evans et al., 1982). *Sxr* is derived from an aberrant Y chromosome, say Y'. XY' males are fertile and normal, and hence allow the propagation of *sxr*. At high frequency, though, Y' crosses over with one end of the X to produce an X' with part of the male factor. Progeny inheriting this X' become males (without a Y), but they are sterile. XX males are also known in goats, pigs, dogs, and humans, although the masculinization may not always be complete.

Three lines of evidence suggest that the sterility of XX males in mammals may be due in part to the XX spermatogonia. First, XXY trisomics in humans are male but sterile (Klinefelter's syndrome). In this case the sterility is due to the trisomy, since no point mutations are involved. Second, XO *sxr* male mice produce sperm (although not fully functional), whereas XX *sxr* males do not (Lyon et al., 1981). Third, male mice which are mosaic for XX and XY cells invariably transmit only the XY line (McLaren, 1981).

One final observation of XX males involves a brief account of the rodent *Ellobius talpinus* (Vorontsov et al., 1980). The glucose-6-phosphate dehydrogenase locus was heterozygous in some males of this rodent. Since G-6-PD is X-linked in the other mammals studied to date, and since male mammals are XY, males should have only one copy of this locus. *E. talpinus* may therefore be homozygous for part of the ancestral X. These authors indicated that one bivalent showed end-to-end pairing in spermatogenesis, but no heteromorphism was apparent from the size and shape of mitotic chromosomes. The absence of cytological heteromorphism is expected if both sexes are homozygous for the ancestral X. *Ellobius lutescens* is well known for its XO condition in both sexes (Ohno, 1979), so the discovery of unusual sex chromosome systems was not without precedent in this genus. However, there are no further indications that the situation in *E. talpinus* is similar to that in *E. lutescens*.

D. Goldschmidt on the Gypsy Moth

The inheritance of sex was first elucidated for diploid species around 1900. The next few decades witnessed many cytological studies on sex chromosomes in different species, but the work of two scientists, R. B. Goldschmidt and C. Bridges, emerged as among the most penetrating investigations into the genetics of sex. Goldschmidt performed extensive analyses of sex determination in the gypsy moth (*Lymantria* = *Porthetria dispar*) and also wrote books on sex determination (1920a, 1931). This section briefly discusses Goldschmidt's work on *Lymantria*. (Bridges' work will be considered in the following section.) Goldschmidt's observations are interesting in the context of this chapter, because they suggest geographic variation in the strength of sex factors, a result unprecedented in the examples cited thus far. Goldschmidt's

work on *Lymantria* is summarized in a lengthy monograph (Goldschmidt, 1934), although the data for his conclusions are found in earlier papers (e.g., 1920b).

Goldschmidt's studies on the gypsy moth compared the sex of hybrids among different geographic races. The gypsy moth occurred from Europe to Japan (and was also introduced to North America), and Goldschmidt performed a series of crosses among moths from different localities, especially from Japan and Europe. Frequently, the males *or* females from a cross would be intersexual, and it was the characteristics of these intersexes that Goldschmidt attended closely.

Intersexes showed both male and female characteristics in various structures, such as genitalia, antennae, genital ducts, gonads, wing color, and behavior. Extreme transformations were sterile or inviable. A few sexually dimorphic characteristics were observed in the pupa, but most were observed in the adult. As a rule, the degree of intersexuality within a moth was roughly the same in these different characteristics, rather than some moths being intersexual only in wings, others intersexual only in antennae, and so forth. Furthermore, Goldschmidt indicated that the degree of intersexuality was constant in a particular cross and was repeatable in other crosses among the same races.

Goldschmidt inferred female heterogamety in gypsy moths, partly from his experiments, and no doubt partly from observations of female heterogamety in other moths, such as the silk moth (Table 2.D). Yet he had no sex-linked markers and could not recognize a cytological heteromorphism among the 62 metaphase chromosomes in this species.

Goldschmidt interpreted his intersex data as if, within a cross, only the genotypic males (ZZ) or only the genotypic females (ZW) became intersexual. If intersexuality was slight, the genotypic males and females could be distinguished despite the intersexuality. But in some crosses, one sex was essentially absent. In these crosses, Goldschmidt inferred that the "missing" sex had been transformed into the other sex. However, no ZZ female was ever known to be bred (he thought that this condition was lethal). He claims to have only once bred with certainty a known ZW male, but this assertion is unfounded (1934, p. 37), although he thought that fertile ZW males occurred frequently in his cultures even though they were not deliberately bred to observe their progenies. On the basis of his results, Goldschmidt assigned values to geographic races that reflected their tendency to cause intersexuality. Observations of the variances in F_2 and subsequent progenies from the hybrids convinced Goldschmidt that these values were properties of the Z and W chromosomes. (He reversed his opinion on whether the egg cytoplasm, rather than the W, was the bearer of the matroclinous feminizing factor. Both have identical inheritance in normal moths. He seems to have eventually adopted the hypothesis that the W was the bearer of the female factor, 1955, p. 431.)

According to his interpretation, Goldschmidt's results possibly indicated geographic variation in the sex tendencies of sex factors, or in some other

genes involved in sex development. Such a finding would be interesting because it would contrast with the invariant XX females/XY males of mammals and *Drosophila*, except for deviations due to transformer genes. The *Lymantria* results did not necessarily indicate variation of sex factors, but since intersexuality was simultaneously characteristic of many traits within a moth, we may suppose that some major regulatory process of sexual development was involved.

However, some points of Goldschmidt's work need further clarification before his conclusions can be accepted. Several problems in the interpretation of his data stem from the absence of an independent diagnosis of ZZ and ZW genotypes. By analogy, we may consider the work of Sturtevant (1920) in hybridizing *Drosophila melanogaster* with *D. simulans*. The reciprocal crosses produced wildly different sex ratios (all females versus an excess of males), yet sex corresponded to XX females and XY males in all cases. In the absence of this assay of sex chromosomes, it might have been concluded (incorrectly) that the sex ratio biases were due to variation in sex factors. In fact, in order to account for his various results, Goldschmidt invoked one or more of the following hypotheses on different occasions: (i) autosomal modifiers of intersexuality, (ii) an autosomal, incompletely penetrant, sex-specific lethal, and (iii) an autosomal lethal of both sexes. He does not seem to have provided statistical treatments of his data (e.g., 1920b, 1934), and indeed, his conclusion that a brood of 33 females and 28 males was inconsistent with a sex ratio of 1/2 (1934, p. 38) renders suspect his other conclusions requiring statistical treatment.

It is not my wish to suggest that Goldschmidt's overall interpretation of the gypsy moth data was inaccurate, but rather to emphasize that some of it be repeated and verified. Clarke and Ford (1980) have repeated some of Goldschmidt's crosses to study intersexes, but they introduced the important technique of distinguishing ZZ from ZW on cytological grounds—the W chromosome is heterochromatic and is evident in the resting nuclei of many tissues (see Sec. 16.B). The initial findings of Clarke and Ford were in the direction proposed by Goldschmidt, but the proportions of intersexes were far below those stated by Goldschmidt. Therefore, further repetition of this work is still in order.

E. The Theory of Genic Balance and the Additive-Value Model of Sex Determination

Goldschmidt's and Bridges' early work led to a theory that Bridges called "genic balance," as an attempt to account for the action of genes in sex determination and development. The advent of molecular genetics has rendered much of this theory obsolete, since there are now direct methods of analyzing gene action, but it is of some historical interest to review this concept and its early role in theories of sex determination. It is difficult to ascertain exactly

what Bridges meant by genic balance, so the ideas that Bridges considered central to sex determination have been assembled here.

Bridges emphasized two theories of sex determination. One theory was that the underlying basis of sex determination in *Drosophila* was according to the X:A ratio (a recessive-X system, Secs. 2.D, 4.A). The other theory was genic balance, which included his X:A ratio model as a special case. In its broadest sense, the theory of genic balance merely proposed that sex determination was influenced by many genes, not just those comprising the X and Y. From Bridges (1925, p. 129):

From such studies [of aneuploids] the view had been reached that each character of an individual is the index of the point of balance in effectiveness of a large but unknown number of genes, some of which have a tendency to change development in one direction and others in the opposite (Bridges, 1922). This conception of "genic balance" was applied to the sex characters of the intersexes as follows: In chromosome constitution the intersexes differ from females only in that they have an extra set of autosomes. This proves that the autosomes are concerned with the determination of sex.

If this statement is interpreted simply to mean that many genes are concerned with sex development, I think few people today would challenge this view. However, this idea was put forth less than a decade after the first published proof of the chromosome theory of heredity (Bridges, 1916), and it could not have been considered obvious then that the sex phenotype was controlled in this general fashion. However, Bridges apparently regarded the various genes concerned with sex development as equivalent to sex factors, and this aspect of his theory is far from accepted (see below).

The Additive-Value Model

Early theories of sex determination were addressed at a more specific level beyond this general view. Goldschmidt's work with gypsy moths and Bridges' work with *Drosophila* lent themselves to simple quantitative interpretation, from which a quantitative model of sex determination was born—a model that persists today. I refer to this as the *additive-value model* of sex determination, with previous examples found in Goldschmidt (1920b, 1934, and probably earlier), Heslop-Harrison (1919), Winge (1932, 1934), Yamamoto (1969), Bulmer and Bull (1982), and many others. Under the additive-value model, a number (i.e., a sex tendency) is assigned to each sex factor, and perhaps to other parts of the genome, and sex is determined in the zygote according to its total value. In the simplest formulation, a single "threshold" is specified, so that all values larger than the threshold are one sex, and values less than the threshold are the other sex. Alternatively, an intermediate range may be specified, and individuals whose values lie within the interval are intersexes.

Consider the following illustration. Under male heterogamety, assign the X a value of 4, assign a haploid set of autosomes a value of -3, and assign the Y a value of zero. These values are chosen somewhat arbitrarily. Under this model, an individual's total value is the sum of its component parts, and the following values apply:

<i>Genotype</i>	<i>Value</i>	
XX AA	+ 2	
XY AA	- 2	
XO AA	- 2	(4.E.1)
XXY AA	+ 2.	

Letting positive values be female and negative values be male (i.e., a threshold of zero), this is a recessive-X system, because XO and XY are male, and XX and XXY are female. According to this threshold, therefore, the X has a female tendency (+ 4), the autosomes a male tendency (- 3), and the Y has no sex tendency (0). Other sex factors may be incorporated, and if haploids or polyploids are considered, their values may be scaled according to the number of autosome sets. Thus, haploids and triploids (XA and XXX AAA) should have the same value of + 2 instead of + 1 and + 3.

The additive-value model found appeal because it had explanatory power, and as the above example illustrates, male and female heterogamety were compatible with this framework. Although this illustration was of a recessive-X system, the additive-value model is consistent with any possible set of observations for the sexes or intersexes of XO and XXY (p. 22). However, despite widespread acceptance of the additive-value principle, opinions diverged on which parts of the genome harbored the sex tendencies—the autosomes, X or Y—and on how many such factors existed (discussed in Winge, 1937).

Bridges preferred a ratio formulation rather than an additive one. This preference was based on his observations of polyplloid *Drosophila*, in which XXX AAA flies were indistinguishable from XX AA flies. On the additive scale these two genotypes would generally have had different values, but the X:A ratio was the same in both cases. While it now seems reasonable to remove the effect of ploidy in these artificially constructed flies, Bridges also advocated his ratio formulation in applications to diploid populations. However, he never suggested how this ratio model should be formulated.

I do not think that the ratio formulation offers a significant difference from the additive model, at least in the usual context of its use. In the simple case that sex is determined according to the ratio of two quantities (for example, M/F , as used by Goldschmidt, 1934), the ratio model can be transformed readily into an additive model by taking the log of this ratio, which becomes $\log M - \log F$. In practice, M and F are never measured, so the choice of scale is arbitrary—we may as well assign the value $\log M$ as M , and so forth. The two models are not generally equivalent, but regarding the manner in which any of these models have been applied to diploid populations, a ratio formulation offers no advantage over the additive-value model.

It is not clear how Bridges perceived his ratio model in the context of his theory of genic balance. The data for *Drosophila* clearly fit his ratio formulation, but the complementary sex determining mechanism in many hymenopterans (Sec 3.F) does not; Bridges nonetheless argued that the complementary mechanism fit the genic balance theory (1939, p. 58). He also accepted evidence that the Y had a sex tendency in some species (e.g., in *Lymantria*, 1925). It seems without doubt that Bridges did not restrict his genic balance theory to merely the X:A ratio model or even to the additive-value model of sex determination.

Bridges reached the curious conclusion that flies with an X:A ratio outside the usual range were supersexes (e.g., X AAA, and XXX AA). There was no observational basis for this conclusion; rather, it was an assumed outcome of his model of sex determination. Therefore, Bridges did not consider "thresholds" in his ratio model of sex determination, but assumed that individuals with progressively larger ratios tended increasingly toward the female extreme, and those with smaller values tended toward the male extreme.

In concluding this discussion, it may be noted that the additive-value model is a model of gene action in sex determination. It serves a useful purpose in providing a simple explanation of certain observations, but there is no more reason to believe that an additive-value model is correct than, say, a multiplicative model, or some other formulation. The additive-value model (as well as Bridges' ratio model) is incompatible with the complementary sex determination of Hymenoptera described in Sec. 3.F. It is also incompatible with the atypical males observed in certain crosses of platyfish, as mentioned in Sec. 3.B. Pipkin's (1960) failure to detect any autosomal male tendency sites in *Drosophila* may also reflect a form of sex determination inconsistent with this model. As more multiple factor systems are described, more exceptions to the additive-value model are likely to be discovered.

Regulation of Sex Development

A further component of Bridges' theory of sex determination specified how sex chromosomes regulated sex development, and he perhaps intended the application of these ideas only to *Drosophila*. While the concept of genetic regulation has taken on concrete meaning in the context of modern genetics, it was nonetheless clear to these early investigators that the difference between males and females involved the simultaneous expression or suppression of many genes.

The initial sections of this chapter have reviewed evidence that regulation of sex development involves a small set of mappable genes whose sole function is apparently the regulation of large parts of the sex phenotype, a result anticipated as early as 1932 by Muller, and in 1936 by Aida. Bridges proposed a very specific form of genetic regulation, a point brought to my attention by Raissa Berg. Bridges apparently thought that sex development was regulated by

the combined actions of the many sex-limited genes (those with different effects in males and females). Thus, the *Drosophila* X caused female development because it was concentrated with genes producing various female characteristics. This subtle point is suggested in the following quotation (Bridges, 1939, p. 42):

From the numerous examples of mutant sex-characters in *Drosophila*, *Zea* and other forms it is clear that a fairly large proportion of the genes must be concerned with the production of the normal sex organs in their normal grade of development. All those genes whose action is part of the normal sex-development, which would have another outcome if mutant alleles were present instead of these normal genes, one may call "sex-producers." . . .

Any of the above producers of sex may become a "differentiator" of sex in mutant form as contrasted to the standard form in the same cross. Some may require the special circumstances such as the sensitive condition in 2X3A intersexes or the cooperation of other genes to bring about their differential action. . . .

The difference between a producer and differentiator of sex may be illustrated by an analogy. As equal weights are added to the pan of a balance the beam finally tips. Let us say ten weights left it untipped and after the eleventh was added it tipped. But this eleventh weight has no more intrinsic significance in the tipping than each of the weights added before. . . . The last one is the differentiator of the position of the beam.

From these statements it seems that Bridges did not regard the regulatory genes of sex development as fundamentally different from those merely contributing to the many sex differences, an idea that integrated well with the other components of his genic balance theory, such as the concept of supersexes, which would have an unusual preponderance of genes for one sex.

This theory of regulation could be falsified by a straightforward test. Berg (1937a,b, 1938) studied the incidence of autosomal and X-linked sterility mutations in *Drosophila*. If Bridges was correct, then one might expect that the number of female-sterile mutations relative to male-sterile mutations should be highest in the X and lowest in the autosomes. Berg's observations did not support this expectation. (B. Baker, however, informed me that it now appears there may be such varied causes of sex-limited sterility, that this comparison may not bear directly upon Bridges' model; Baker and Lindsley, 1983.) Bridges' theory of gene regulation in sex development was also challenged by Aida (1936).

Overview

A striking feature of the early studies of sex determination is that a major emphasis was placed on explaining sex determination at an underlying level, a level outside the scope of their direct observations (e.g., the physiology and nature of genetic regulation). The theory of genic balance and its ramifications (additive-value model) were used by Bridges, Goldschmidt, and others as a

means of organizing the observed diversity of sex determining mechanisms. Each new variety was molded into this framework, in order to uphold this single view as the underlying basis of sex determination. While this early work on sex determination greatly enriched our understanding and appreciation of sex determination, it did not lead to a comprehensive understanding of gene action in sex development. The underlying nature of gene action in sex development is of great interest, but it is a problem more directly analyzed with the tools of molecular genetics. The basic facts and observations of the variety of sex determining mechanisms remain from this early work and provide material for current interests.

F. Summary

This chapter considered the regulatory nature of sex factors, both in the context of modern studies and also from the classical works of Goldschmidt and Bridges. In mammals, *Drosophila*, and the nematode *Caenorhabditis*, single genes have been identified with major regulatory functions in sexual development. Detailed analyses of these mutations in the two invertebrates suggested the existence of single regulatory hierarchies of sex development, but comparable studies have not been conducted with mammals. Sex factors may therefore be genes which act at a high level in these regulatory hierarchies.

The studies of Goldschmidt and Bridges in the early part of this century fostered various attempts to explain the "physiology" of sex determination, attempts which included the additive-value model and the theory of genic balance. Some aspects of these studies were reviewed and discussed for their relevance to modern theories.

5

A Combinatorial Enumeration of Sex Determining Mechanisms: 2-Factor and Multiple-Factor Systems

A. Introduction

The naturally occurring 2-factor and multiple-factor systems described in Chapters 2 and 3 indicated much about the variety of mechanisms known in animals. These chapters did not, however, indicate what additional variety might be considered possible. This chapter enumerates the sex determining mechanisms theoretically possible for some simple classes (2, 3, and 4 factors).

The systems enumerated here comprise a set of possibilities and therefore are not necessarily known in natural populations. This chapter might therefore seem to be an abstract exercise of little practical value, except that the combinatorial study serves at least four useful functions. First, it provides a framework in which the known variety can be displayed. Second, by identifying the systems as yet undiscovered, it encourages the investigation of additional variety and will perhaps lead to the discovery of systems previously unknown. Third, in identifying unknown systems, this approach may facilitate the understanding of why they are absent or have not been detected. And finally, any attempt to unify these mechanisms into a broad context would be incomplete without considering all possible mechanisms, a point which will be made evident in the following chapter.

At the outset, I would like to identify three inspiring papers relevant to this chapter. Cotterman (1953) provided a comprehensive enumeration of one class of systems (phenotype systems, explained below); it was his work, both published and unpublished, that led me to appreciate the combinatorialist perspective. Scudo (1964, 1967) specifically enumerated different sex determining mechanisms, though not always with the intention of completeness. Many original ideas concerning the population genetics of sex determining mechanisms are found in his two papers.

The following presentation involves a two-step process of enumeration, and a distinction is made between two types of mechanisms. One the one hand, we are interested in the possible sex determining mechanisms that can actually be observed in populations, such as XX/XY systems and the multiple-factor systems presented in Chapters 2 and 3. There are, however, characteristics of the sex determining mechanism not evident from a study of genotypes within the population, because certain genotypes are absent. These characteristics may nonetheless be ascertained experimentally. For example, YY is absent in XX/XY populations, but it has been possible to describe its sex in some species (Sec. 2.E).

We may thus enumerate two types of sex determining mechanisms: *phenotype systems* and *population systems*. In a phenotype system, sex is assigned to all possible genotypes (under the constraint of a fixed number of sex factors and loci, c.f. Cotterman, 1953). In a population system, however, sex is assigned only to those genotypes maintained in the population. The simplest example of the distinction between a phenotype system and a population system is found with heterogametic sex determination. In the phenotype system, sex is assigned to all three possible genotypes, XX, XY, and YY. Yet YY does not occur in the population, so the population system consists of only XX and XY. Phenotype and population systems will be enumerated below for 2-factor systems, 3-factor systems, and 2-locus/2-factor systems. Phenotype systems will be identified with the label $\phi(a.b.c)$, indicating a loci, b factors per locus, and identification number c . Population systems will be identified with label $P(d.e.f)$. All phenotype and population systems will assume that each genotype develops only as one sex.

B. 2-Factor Systems

Phenotype Systems

If an individual's sex is determined strictly by its own genotype, there must be at least two genotypes and hence two sex factors in the population. The simplest case, therefore, is the one in which two factors (A and B) assort in opposition, as with two alleles at a locus. There are three possible genotypes and two distinctly different ways to assign sexes—two phenotype systems—(cf. Cotterman, 1953, p. 201; Scudo, 1964, p. 98) as illustrated in Fig. 5.B.1.

Genotype Key

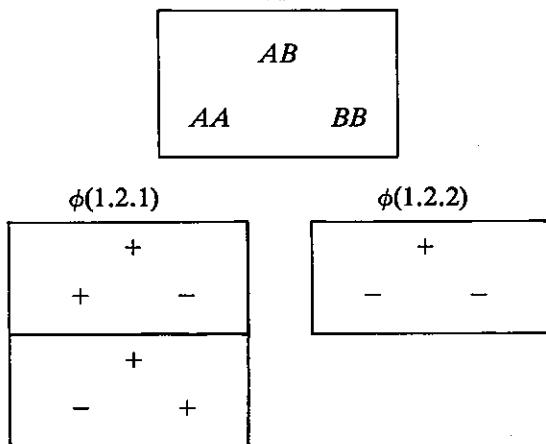


FIGURE 5.B.1. The two anisomorphic 2-factor sex determining systems (phenotype systems) for a diploid organism with two sexes. There are two permutational images of $\phi(1.2.1)$. Genotypes of like sign are the same sex. (Based on C.W. Cotterman. 1953. "Regular two-allele and three-allele phenotype systems." *American Journal of Human Genetics* 5:193–235, Figure 1.)

Before proceeding with the biological implications, some remarks are offered to facilitate understanding the symbolism in this figure. Genotypes have not been labeled "male" or "female"; they are shown only with (+) for one sex and (-) for the other. From a biological perspective it may be useful to distinguish two sex determining mechanisms with the same phenotype system if the sexes are reversed, such as male versus female heterogamety, but it is unnecessary here to list each system twice for this simple operation. Thus, $\phi(1.2.1)$ represents

<i>Sex 1</i>	<i>Sex 2</i>
<i>AA</i>	<i>BB</i>
<i>AB</i>	,

which is equivalent to both

σ	φ	σ	φ
<i>YY</i>	<i>XX</i>	<i>ZZ</i>	<i>WW</i>
<i>XY</i>	,	and	<i>ZW</i> .

The two forms of $\phi(1.2.1)$ are "permutational images" of each other. Merely interchanging *A* and *B* generates one image from the other, so they are regarded as essentially the same system and identified with the same number. Systems

$\phi(1.2.1)$ and $\phi(1.2.2)$ are distinctly different, or *anisomorphic*, because interchanging *A* and *B* does not generate one system from the other.

These phenotype systems are listed merely as the complete set of theoretical possibilities within specified restrictions. From these systems, the goal is to determine which ones exist in nature, and this necessarily depends on the biological (e.g., molecular) basis of sex determination, hence on the nature of mutations. Distinguishing between $\phi(1.2.1)$ and $\phi(1.2.2)$ is possible only if the sexes of all three genotypes, XX, XY, and YY are known. These data were presented in Table 2.E and indicated that only $\phi(1.2.1)$ is known in diploid animals (including insects, crustaceans, fish, and amphibians). Although $\phi(1.2.2)$ is unknown, the type of gene action upon which it depends exists in the complementary sex determining mechanism of haplo-diploid Hymenoptera (heterozygotes become female, but homozygotes and haploids become male, Sec. 3.F). It is therefore plausible that $\phi(1.2.2)$ may yet be found in some populations of diploid animals.

The phenotype system does not specify a sex tendency or other underlying means by which sex determination could be further characterized. To specify additional properties would further increase the variety, but not all phenotype systems would necessarily be consistent with a particular model of sex determination. Consider the notion of sex tendencies in the context of the additive-value model in Section 4.E. Section 2.D has already shown three possible interpretations of $\phi(1.2.1)$, in terms of assigning sex tendency to *A* and *B* (X and Y), and a numerical example was provided in 4.E. However, the additive-value model cannot be used to describe $\phi(1.2.2)$, because the two homozygotes are the same sex. This type of comparison offers an interesting possibility for elucidating the underlying property of sex determination in a group of organisms which varies in phenotype or population systems. If all *observed* systems are consistent with the additive-value model (or some other scheme), it might suggest that the model reflected a general underlying property of sex determination.

Population Systems

For a majority of species with heterogametic sex determination, it is not possible to determine if the mechanism corresponds to $\phi(1.2.1)$ or to $\phi(1.2.2)$, because the sex of YY is unknown. Since the phenotype system specifies more about the sex determining mechanism than is necessarily observed in a population, one may wish to carry the analysis forward and consider systems of genotypes actually maintained in a population under each of the phenotype systems. As indicated above, these are designated as "population systems."

Two population systems may result from the above phenotype systems (Scudo, 1964; and Fig. 5.B.2). Both of these are forms of the ubiquitous heterogametic sex determination: one sex is heterozygous and the other homozygous for sex factors. Three points are to be noted about these population

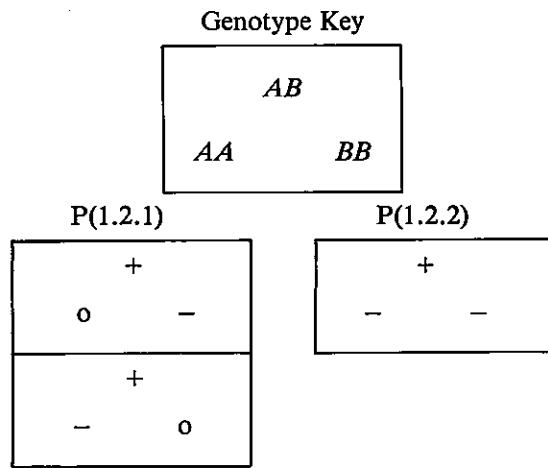


FIGURE 5.B.2. The “population systems” (possible genotype compositions maintained in the population) for a diploid population with 2-factor sex determination. Genotypes of like sign are the same sex; (\ominus) indicates that the genotype is not maintained in the population. As with the phenotype systems, P(1.2.1) has two images.

systems. First, some population systems retain all genotypes from the phenotype system: P(1.2.2) is identical to $\phi(1.2.2)$. Second, one system may collapse into another by the loss of one or more genotypes. For example, the loss of *AA* or *BB* in P(1.2.2) leads to P(1.2.1). In this case, the change is neutral, because there is no selection against the loss of one or the other male genotype. Thus, two population systems may be the same even though they represent different phenotype systems. The third point is that in practice it may be difficult to distinguish between different population systems. For example, distinguishing P(1.2.2) from P(1.2.1) would require either linked markers, artificial control of sex determination, or observation of a structural difference between *A* and *B* (assuming that both *AA* and *BB* were obtained in the sample of the former).

C. Three Factors Assorting in Opposition

Phenotype Systems

The enumeration of phenotype systems is readily extended to the three-factor case, in which there are six genotypes. Cotterman (1953) enumerated the six anisomorphic 3-factor systems with two sexes (Figure 5.C), and Scudo (1964)

Genotype Key

<i>AB</i>	
<i>AA</i>	<i>BB</i>
<i>AC</i>	<i>BC</i>
<i>CC</i>	

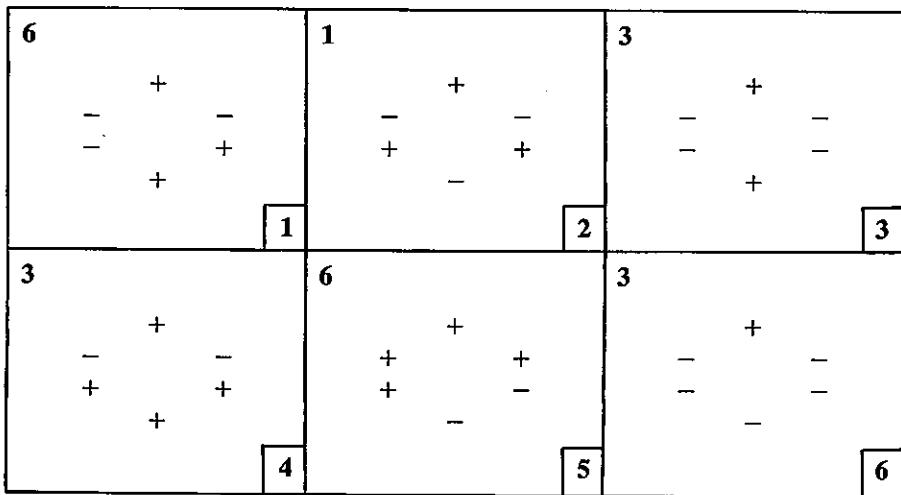


FIGURE 5.C. The six anisomorphic 3-factor phenotype systems with two sexes, $\phi(1.3.-)$, from Cotterman (1953). Genotypes of like sign are the same sex. The identification number for each phenogram is given to its lower right, the number of images to its upper left. (Based on C.W. Cotterman, 1953. "Regular two-allele and three-allele phenotype systems." *American Journal of Human Genetics* 5:193-235, Figure on p. 207.)

analyzed four of them.* The only 3-factor systems known are in platyfish and lemmings. The platyfish system corresponds to $\phi(1.3.5)$, since WW is female. The sexes of two genotypes from the lemming system, X^*X^* and YY , are unknown, so this phenotype system cannot be specified. System $\phi(1.3.2)$ corresponds to the "complementary" sex determination observed in diploid males and females of the hymenopteran mechanism described in Sec. 3.F.

*There are three additional anisomorphic systems which might be described as 3-allele systems; Cotterman used "degenerate." In each of these, two of the alleles are identical in their effects on sex determination, so they are not recognized as distinct sex factors. Therefore, these are essentially 2-factor systems.

Population Systems

The number of 3-factor population systems is further reduced from these six phenotype systems. Just as in the 2-factor systems, it is often the case that some genotypes are not produced in the population. For example, if a sex factor is absent from males (or females) in the phenotype system, homozygotes for that factor cannot occur in the population. In addition, some genotypes and even sex factors may be present for several generations (given arbitrary starting frequencies), but continually decrease and become vanishingly rare. Their gradual loss is due to sex ratio selection, which results even when no fitness differences exist within a sex (Sec. 6.A).

In these cases it is necessary to specify how the population system is defined. In this book, a *population system* represents a set of genotypes that can coexist at a stable or neutral equilibrium in a random-mating population in which fitnesses are the same for all genotypes within a sex.* Population genetics methods, either analytical or numerical (computer), are used for determining which genotypes from a phenotype system are maintained. These methods will be considered briefly in the next chapter and were illustrated extensively in two papers on this subject by Scudo (1964, 1967).

The six 3-factor phenotype systems yield two population systems that retain all three factors. In some cases, two or more phenotype systems may lead to the same population system, so again we observe that a single population system may correspond to more than one phenotype system. Conversely, two population systems may correspond to the same phenotype system.

However, only one of these two population systems is now "recognizable" as a 3-factor system, even though all three factors have been retained. Consider $\phi(1.3.2)$, with heterozygotes as one sex and homozygotes the other sex.

$$\begin{array}{ccc} AB & & \\ + & & \\ AA - & & - BB \\ AC + & & + BC \\ - & & \\ CC & & \end{array}$$

All three factors are distinguishable on the basis of sex determination in this phenotype system, but the only 3-factor population system that results is

$$\begin{array}{ccc} + & & \\ - & & \circ \\ + & & \circ \\ & & \circ \end{array}$$

*In view of this definition, it should be noted that some multiple-factor systems observed in nature may not correspond to multiple-factor population systems, due to unequal fitnesses or other effects. This is unfortunate, but phenotype and population systems are best accepted in the spirit of a simplification around which further variation can be organized.

or any equivalent permutational image, with "o" indicating the absence of the genotype (cf, Scudo, 1964). This population system might be interpreted as

♀	♂
XX	XY
XY'.	

Although Y and Y' are sex factors in the context of the phenotype system, they do not differ either in inheritance or in their effects on sex determination among the genotypes retained in the population. Only special experiments creating additional genotypes would enable distinguishing them. Therefore, this cryptic multiple-factor system would be diagnosed as the 2-factor system P(1.2.1).

Only one population system segregates three factors such that they can be detected by the existing genotypes (changing the notation to facilitate its recognition):

P(1.3.1)

$$\begin{array}{ccc} \text{WX} & & \\ + & & \\ \text{WW o} & + & \text{XX} \\ \text{WY} & + & - \text{XY} \\ - & & \\ \text{YY} & & \end{array}$$

This system is exactly the one observed in platyfish (Sec. 3.B), and it may also represent lemmings, except that YY's sex is unknown in mammals. (The lemming systems are maintained by selection, so the set of genotypes maintained in lemmings does not necessarily correspond to a population system, in which fitnesses are assumed equal.) Since the sex of WW is not specified, this population system could represent either of two phenotype systems, $\phi(1.3.5)$ or $\phi(1.3.1)$. In platyfish, the former phenotype system applies. Again it is the case that these 3-factor population systems may, from random drift, lose all but two genotypes and collapse into 2-factor systems (Chap. 6). For example, we have already noted that the platyfish system may produce male and female heterogamety.

D. 2-Locus Systems

The last sex determining mechanisms to be enumerated here are those with two "loci" and two factors per locus. There are 48 anisomorphic 2-locus/2-factor phenotype systems (Figure 5.D.1), and from these, there are at least 16

Genotype Key

AA BB	Aa BB	aa BB
AA Bb	Aa Bb	aa Bb
AA bb	Aa bb	aa bb

4	4	4	8	2	2	8
+	-	-	+	-	-	+
-	+	-	-	-	-	-
-	-	-	-	-	-	-
4	5	6	7	8	9	10
4	4	8	2	8	4	4
+	+	-	+	-	+	+
-	+	-	-	-	+	-
-	-	-	-	-	-	-
12	13	14	15	16	17	18
4	4	8	8	8	8	8
+	-	-	+	+	+	+
-	-	-	+	-	-	-
-	+	-	-	-	-	-
20	21	22	23	24	25	26

4	4	4	4	4	4	4	4
+ + +	+ + -	+ - +	- + -	+ + +	- + -	+ - +	- + +
- + -	- + -	- + -	- + -	- + +	- + -	+ + -	+ + -
- - -	- - -	- - -	- - -	- - -	- + -	- - -	- - -
26	27	28	29	30	31	32	33
8	8	8	8	4	8	4	8
+ + -	+ + -	+ + +	+ + +	+ + +	+ + -	+ + -	+ + -
- + -	- + -	- - -	- - -	- - -	- - -	- - -	- - -
- - +	- + -	- - -	- - -	- + -	- + -	- + -	- + -
34	35	36	37	38	39	40	41
8	8	4	4	4	1	1	1
+ + -	+ + -	+ + -	+ + -	+ + -	- + -	- + -	- + -
- - -	- - +	- - +	- - +	- - +	+ - +	+ - +	+ - +
+ - +	+ - -	- - +	- - +	- + +	- + +	- + +	- + +
42	43	44	45	46	47	48	48

FIGURE 5.D.1. 2-Locus/2-Factor Phenotype Systems. The 48 anisomorphic 2-locus/2-factor phenotype systems for sex determination in diploids, $\phi(2,2,-)$. The identification number is located under each system, and the number of images is given at the upper left. Genotypes indicated by (+) are the same sex, different from the sex of genotypes indicated by (-). The number of anisomorphic 2-allele/2-locus systems was correctly given as 50 by J. Haigh, in Scudo (1967); two of these 50 are degenerate so they have been omitted from this figure. (Produced in collaboration with C. W. Cotterman.)

2-locus/2-factor population systems in which both factors at each locus are distinguishable among the existing genotypes (Fig. 5.D.2). (Population systems were derived numerically, assuming free recombination between the two loci, and I am not confident that I have discovered all of them.) A catalogue of these phenotype and population systems is provided, partly as a basis for comparison to observed systems, but also because the investigation of various problems in the evolution of male and female heterogamety is facilitated by having such a catalogue. The number of 2-locus/2-factor population systems is much larger than for the 2-factor and 3-factor systems, and it would be tedious to enumerate categories with even more sex factors.

The most commonly observed 2-locus/2-factor population system is the common system in Diptera, P(2.2.2): one sex is homozygous at both loci and the other sex is heterozygous at either locus (Table 3.A). This system is known only for male heterogamety. There is the further suggestion that P(2.2.6) has been constructed in housefly strains (recall Sec. 3.D). However, the number of 2-locus/2-factor systems known among animals is far less than the number possible. In no case are the sexes known for all genotypes of a 2-locus/2-factor phenotype system.

E. Summary

A number of concepts and properties of sex determining mechanisms have been presented here.

1. There are many possible mechanisms in which sex is determined strictly by zygotic genotype (phenotype systems), their number increasing with the number of sex factors allowed. A catalogue is provided for some of the simpler cases. The variety of phenotype systems which occurs naturally depends on the mutations generating new sex factors.
2. All possible genotypes of sex factors specified in the phenotype system are not necessarily maintained in the population (e.g., YY is absent in the usual XX/XY system, even if it is viable). A catalogue of these population systems is provided for the set of phenotype systems listed. A principle illustrated here is that the sex determining mechanism of a population in nature (population system) is a consequence of the mutational basis of sex factors (i.e., the phenotype system that nature produces) but also depends on the maintenance of the various genotypes and sex factors within the population.
3. Since the population system does not necessarily contain all genotypes of the phenotype system, two species with the same population system do not necessarily have the same phenotype system. For example, two populations with male heterogamety may differ in the sex of YY.

Genotype Key

AA BB	Aa BB	aa BB
AA Bb	Aa Bb	aa Bb
AA bb	Aa bb	aa bb

+ + +	+ - o	o + -	+ + -
+ - +	- o o	+ + -	- + -
+ + +	o o o	- - -	- - -
			4
+ + -	+ + -	- + +	+ + +
+ - -	- - -	+ - -	- + -
- - o	o o o	- - o	- - -
			8
+ - +	o + -	+ - +	o + +
- + -	+ + -	+ + -	+ + -
- + -	- - +	- - -	- - -
			12
+ + -	+ + -	- + +	- + -
- + -	+ - -	+ - -	+ - +
- - +	- + -	- + -	- + -
			16
13	14	15	

FIGURE 5.D.2. Sixteen possible 2-locus/2-factor population systems of sex determination P(2.2.-). Seven of these were identified by Scudo (1967). The identification number is at the lower right of each system. Figure 5.D.1 provides the phenotype systems from which these were derived. Otherwise as in Figure 5.B.2.

- From this combinatorialist approach, it is seen that male/female heterogamety provides the simplest basis for genotypic sex determination in zygotes, but that the further addition of sex factors to a heterogametic system offers the potential for an increasing variety of mechanisms. The degree to which nature is confined to a subset of these possibilities is yet to be shown.

6

Evolution in Multiple-Factor Systems

This chapter describes how natural selection influences the evolution of multiple-factor systems. The first section (A) offers a brief presentation of sex ratio evolution, which is a major selective force in multiple-factor systems. Sections B and C then describe models of multiple-factor systems in random-mating populations, first in the absence of, and subsequently incorporating genotypic fitness effects (fertility and viability effects). These models illustrate that many multiple-factor systems provide a ready transition from one 2-factor system to another, and may therefore be intermediaries for natural changes in the heterogametic mechanism. The final section (D) will consider specific biological effects relevant to evolution in multiple-factor systems and will also describe the few quantitative studies of laboratory and natural populations with multiple sex factors.

A. Sex Ratio Evolution

By controlling the inheritance of sex, the sex determining mechanism also controls the sex ratio among zygotes. Consequently, *the evolution of the sex determining mechanism depends fundamentally on the population sex ratio*. In

ideal, random-mating populations, it is usually difficult to evolve from a primary sex ratio of 1/2 (proportion of males in zygotes equal to 1/2), so it is difficult to evolve any sex determining mechanism that causes the population sex ratio to deviate from 1/2. This principle is fundamental to many of the arguments presented in the following chapters, and it also accounts for the previously noted loss of particular genotypes and sex factors in population systems.

Fisher (1930) first explained the nature of sex ratio selection within a population. While the "success" of the population may be enhanced by a biased sex ratio (e.g., a female bias), selection within the population is indifferent to population success and favors 50% males at conception (assuming that the number of offspring is independent of sex ratio). This result may be illustrated by the following example. Suppose that in the population as a whole, there are 10 females for every male at conception:

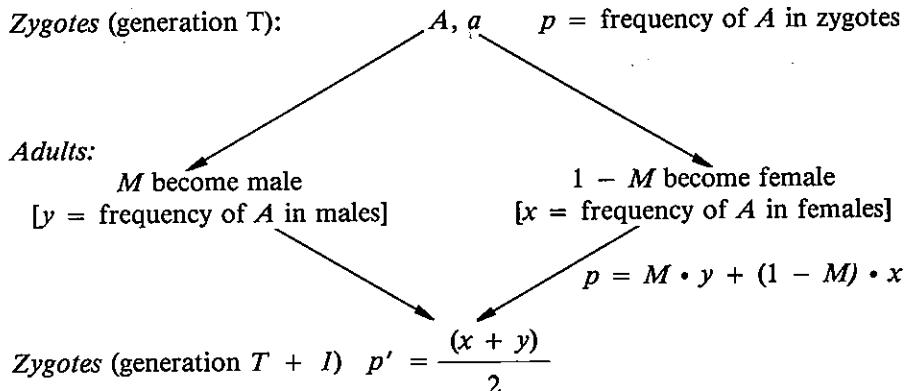
	♂	♀
Zygote numbers	N	10N
Expected contribution to the next generation per zygote	10X	X.

It necessarily follows that each of these male zygotes will have *on average* 10 times as many children as each female zygote. This result will hold regardless of whether there is monogamy, polygamy, or any amount of differential mortality. It follows that parents which overproduce sons will have more grandchildren, since a male will contribute more genes than a female, and a heritable tendency to overproduce sons will increase in the population and thereby reduce the sex ratio bias. The argument is symmetrical—males and females could have been interchanged—and at equilibrium there is an equal number of males and females at conception. While some special population structures can be interpreted as if selection between subpopulations is important enough to favor a biased sex ratio, it is otherwise usually regarded that selection within a population represents the dominating force in sex ratio evolution (Hamilton, 1967, 1979; Charnov, 1982).

Several variations of this basic sex ratio argument have been studied, and there is presently a large literature on models of sex ratio evolution as well as empirical observations of sex ratios in various species. The basic sex ratio formalizations have also been extended to various aspects of hermaphroditism, in a discipline of evolutionary biology known as sex allocation theory (Charnov, 1982). For the most part, however, the models in this book require an understanding of only the basic argument outlined above and as developed in the following paragraphs.

A simple and useful algebraic statement of selection for a sex ratio of 1/2 was offered by Nur (1974). Suppose that in a diploid, random-mating population there are two alleles at a locus (A , a), and these alleles have different

effects on the sex ratio or sex determination, but are otherwise identical in their effects on viability and fertility. Let the frequency of A in zygotes from generation T be p . The life cycle is such that the zygotes mature, reproduce, and then die. Consider the frequency of A in zygotes of generation $T + 1$ (p'). The entire argument is based on two observations: (i) if x is the frequency of A in females and y is for males (enumerated after the zygotes mature), then $p' = (x + y)/2$. This result merely reflects the observation that each zygote has a mother and a father, and that the zygotic frequency of an allele is the average of its frequencies among the mothers and fathers (with random mating).



(ii) if M is the sex ratio (proportion of males) among zygotes in generation T , then $p = x(1 - M) + yM$. That is, the number of A alleles in zygotes equals the number in females plus the number in males, dividing by population size to obtain frequencies.

From these two expressions, the result follows that

$$\Delta p = p' - p = (y - x)(1/2 - M) \quad (6.A.1)$$

If half the zygotes become male ($M = 1/2$), the zygotic frequency of A does not change. If males are in excess ($M > 1/2$), then A increases only if its frequency in females (x) is greater than in males (y), and so forth. This result is particularly instructive, because for many sex factors, the frequency is always higher in one sex than the other. One application of this result is that it provides the conditions under which a sex factor can invade a population with a biased sex ratio.

It should be noted that various circumstances do not lead to the evolution of a sex ratio of 1/2, but the details of these arguments are beyond the scope of this book (see Charnov, 1982): (i) sex-linked genes which distort the segreg-

tion ratios of sex factors, (ii) number of offspring varying with sex ratio, (iii) certain types of structured matings, and (iv) a covariance between fitness and sex ratio (see Sec. 10.B). In addition, the above result is not easily extended to multiple loci or even to predict sex ratio evolution once a sex factor invades. However, a sex ratio of 1/2 is nonetheless fundamental to many problems presented in this book, and Nur's formula will be useful in explaining many results.

B. Equilibria in Multiple-Factor Systems: Fitnesses Equal

In the last chapter several multiple-factor systems were described in which several genotypes could remain in the population at equilibrium (multiple-factor population systems). These population systems were generated by assuming random mating and equal fitness within a sex. The following three points apply to the equilibria in these population systems.

(i) The population sex ratio is apparently 1/2 at equilibrium in all but one case (neglecting unstable equilibria). This result was derived analytically for some cases and numerically for others, although not all systems have been thoroughly studied (Scudo, 1964, 1967; Bull and Charnov, 1977; unpubl. results). In some systems all families produce a sex ratio of 1/2 [e.g., systems P(2.2.2), P(2.2.16) Fig 5.D.2, p. 65], but in most systems the sex ratio is female biased in some families and male biased in others. From Nur's result (6.A.1), a population sex ratio of 1/2 would be anticipated as a common outcome in these systems. The only known exception to a sex ratio of 1/2 in a population system is P(2.2.1), in which the double heterozygote is one sex and all other genotypes are the other sex. All matings produce a sex ratio of 1/4 (if the double heterozygote is male), and there is no means by which a sex ratio of 1/2 can evolve, unless other sex factors invade. This system is in fact susceptible to invasion by sex factors which increase the frequency of the rare sex.

(ii) In the multiple-factor population systems with a sex ratio of 1/2 there is often an infinity of genotype frequency equilibria (Scudo, 1964, 1967; Bull and Charnov, 1977). The sex ratio is 1/2 at these equilibria, and there is a continuous path (or surface) of equilibria, over which the frequency of sex factors changes but the sex ratio does not. This path of equilibria is most simply illustrated by the system P(2.2.2), in which the double homozygote has been labeled female:

♀ <i>aa bb</i>	♂: <i>Aa bb</i> <i>aa Bb</i>	<i>frequency in population</i>
		<i>x</i>
		$1 - x$.

Suppose now that matings occur in proportion to the frequency of each male genotype:

Frequency	Matings		Progeny	
	♀	♂	♀	♂
x	aa bb	Aa bb	1/2 aa bb	1/2 Aa bb
1 - x	aa bb	aa Bb	1/2 aa bb	1/2 aa Bb.

The frequency of *Aabb* males in the next generation is simply

$$x' = \frac{x/2}{(x + 1 - x)/2} = x.$$

Therefore, regardless of the frequencies of the two male genotypes, they are not expected to change in the absence of fitness effects, mutation, or chance fluctuations. There is only one female genotype, and there is a continuous, infinite set of possible equilibria for the two male genotypes, as shown in Figure 6.B.1. The sex ratio is 1/2 at all these equilibria, but a sex ratio other than 1/2 cannot evolve, because *all* matings produce a sex ratio of 1/2. However, most multiple-factor systems have the potential to evolve a sex ratio other than 1/2 because the sex ratios in some families are not 1/2, yet the equilibria observed for these systems are nonetheless characterized by a sex ratio of 1/2. Again, this has been established analytically for some systems and numerically for others (Scudo, 1964, 1967; Bull and Charnov, 1977).

(iii) In many, if not all systems with these infinite sets of sex ratio equilibria, the paths (surfaces) of equilibria connect different systems of 2-factor sex determination (Bull and Charnov, 1977). The term *recurrent genotype pair* indicates any two genotypes of opposite sex, that when mated, produce only the two parental genotypes, and produce them in a 1:1 ratio (e.g., *Aa* × *aa* → 1/2 *Aa* + 1/2 *aa*). A recurrent genotype pair, when taken in isolation, necessarily constitutes heterogametic sex determination.

The manner in which two recurrent pairs are connected by a path of equilibria is again most simply illustrated by the system P(2.2.2), as shown above. The endpoints of this path represent two different mechanisms of male heterogamety (Fig. 6.B.2). To illustrate how male and female heterogamety may be connected, recall the platyfish system,

♀	♂
XX	XY
WX	
WY	YY.

The two recurrent pairs in this system are XX/XY (male heterogamety) and WY/YY (female heterogamety). There is again a continuous set of equilibria

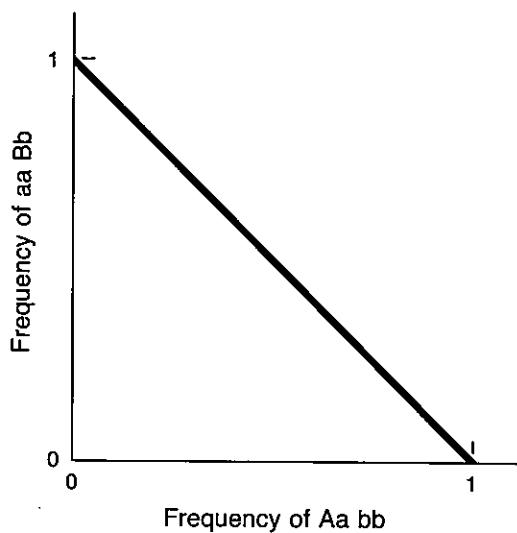


FIGURE 6.B.1. The diagonal line represents the path of equilibria for system P(2.2.2), in which there are two male genotypes ($aa\ Bb$ and $Aa\ bb$) and just one female genotype ($aa\ bb$). The frequencies of the two male genotypes must add to unity (by assumption), but these genotypes may coexist in a population at any frequencies satisfying this condition.

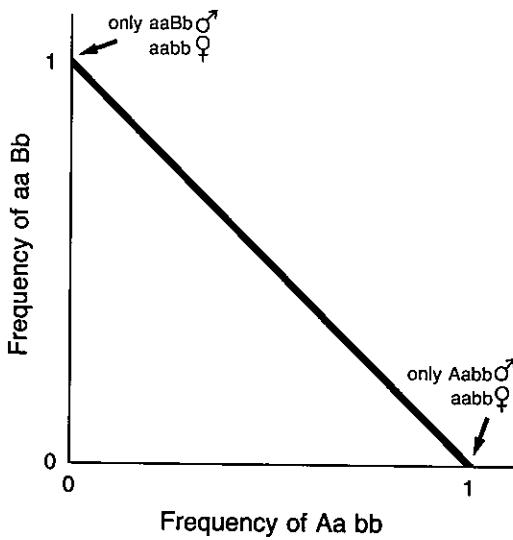


FIGURE 6.B.2. As in Fig. 6.B.1, illustrating here that the two endpoints of the path of equilibria represent different systems of male heterogamety.

connecting these two endpoints, albeit somewhat more complicated than in the preceding example (Fig. 6.B.3; Bull and Charnov, 1977).

The relationship between recurrent pairs and paths of equilibria is not this simple in all population systems. Of the 16 2-locus/2-factor systems, 15 have two or more recurrent pairs (always an even number), and P(2.2.1) has none (p. 65). The recurrent pairs are easily found through inspection of the population system, whose genotypes are represented by:

<i>AA BB</i>	<i>Aa BB</i>	<i>aa BB</i>
<i>AA Bb</i>	<i>Aa Bb</i>	<i>aa Bb</i>
<i>AA bb</i>	<i>Aa bb</i>	<i>aa bb</i>

Any two adjacent genotypes of opposite sex on the same edge comprise a recurrent pair. The sex of each genotype is of course obtained from the population system (Fig. 5.D.2). For example, P(2.2.3) is the following system

$$\begin{array}{ccc} \circ & + & - \\ + & + & - \\ - & - & -, \end{array}$$

and there are two recurrent pairs (shown connected by dots),

$$\begin{array}{ccc} \circ & + \dots - \\ + & + & - \\ \vdots & & \\ - & - & -, \end{array}$$

and similarly for the other population systems. All the population systems analyzed by Bull and Charnov (1977) possessed two recurrent pairs, apparently connected by a continuous path of equilibria (some systems were only analyzed numerically). All but one population system analyzed by Scudo (1964, 1967) had two recurrent pairs (one system had none), although he did not consider his models in the context of recurrent pairs connected by paths of equilibria.

There are also population systems with four, six, and eight recurrent pairs. In system P(2.2.16), there is an interior surface of equilibria interconnecting all eight recurrent pairs. In systems P(2.2.10) and P(2.2.13) there are four recurrent pairs and two paths of equilibria, each one connecting two different recurrent pairs. Is there, then, a general rule that the recurrent pairs in these systems are always connected by paths of equilibria (at least in pairs)? Most of these systems have been studied numerically only, so no conclusive answer can be offered at present. My numerical work suggests that paths of equilibria exist in all these population systems, but the paths in some systems either fail to connect two recurrent pairs (a possibility I regard as unlikely), or the paths have such a narrow zone of attraction in some regions that equilibria are difficult to locate.

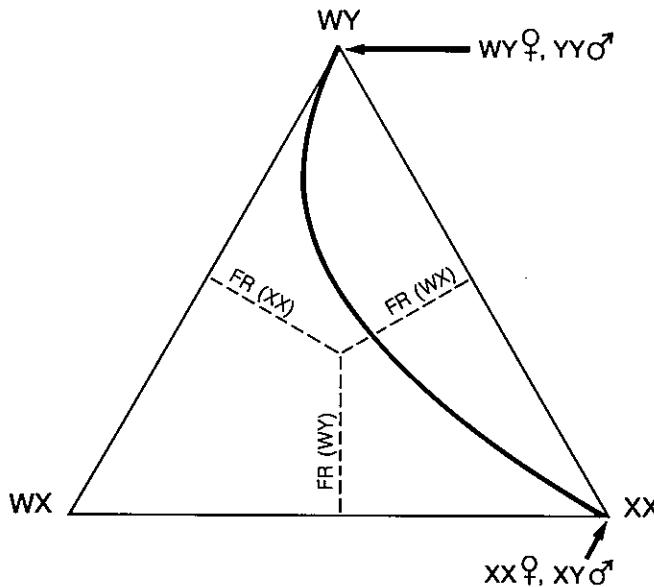


FIGURE 6.B.3. A De Finetti diagram of the equilibrium frequencies of the three female genotypes in the platyfish system (XX, WX, WY). Each point inside the triangle represents a different set of frequencies for these genotypes; the frequency of a genotype is given by the perpendicular distance from the point to the axis opposite the vertex labeled with that genotype (as shown). Distances are measured as a fraction of the triangle's altitude, and the three frequencies necessarily add to unity. The solid curve indicates the complete set of equilibrium frequencies for XX, WX, and WY in the platyfish system, and the curve connects the two endpoints of male and female heterogamety, as indicated by the arrows. The frequencies of the two male genotypes are not evident from this figure, but the equilibrium frequencies of all genotypes are related by the following formulae (Bull and Charnov, 1977): $YY = p$, $XY = 1 - p$, $XX = (1 - p)^2 / [(1 + p)^2]$, $WX = 2p(1 - p) / [(1 + p)^2]$, $WY = 2p / (1 + p)$.

These results are relevant to the overall understanding of the evolution of genotypic sex determination because they reveal how different mechanisms of male and female heterogamety are connected through paths of equilibria in multiple-factor systems. In one sense, the models are highly artificial, as they assume strict random mating in an infinite population with equal fitnesses. Yet, they offer a framework in which more realistic models and actual populations may be studied.

C. Multiple-Factor Systems When Fitnesses Differ

A multiple-factor system is expected to remain at any of the various neutral equilibria only in an idealized random-mating, infinite population, assuming

that fitnesses within a sex remain equal. These assumptions, of course, never exactly apply to natural populations, so it will be informative to consider the consequences of more realistic assumptions. For example, with finite population size, the genotype frequencies in a multiple-factor system would not remain indefinitely at any of the internal neutral equilibria, and random changes in gene frequency would eventually cause the system to collapse to just two factors (Scudo, 1964, 1967). Therefore, only recurrent mutations or stabilizing selection would lead to the long-term maintenance of a multiple-factor system. The effect of fitness differences among genotypes provides the most interesting set of possibilities for study and is therefore the topic of this section.

There has been little analytical work on models that incorporate fitness differences into multiple-factor systems. Some special cases were described by Scudo (1964, 1967), and the platyfish system was investigated by Orzak et al. (1980). Bull and Charnov (1977) investigated simple cases of fitness differences in some "population" systems with just two recurrent pairs. (The strict definition of population system does not admit fitness differences, hence the cautious use of this term.) In the equal fitness case, all the systems studied by Bull and Charnov (1977) contained a single curve of equilibria connecting the two recurrent pairs. Numerically, the fitness (viability or fertility) of one genotype was then altered and the evolution of the system was studied. The conclusions were as follows.

(i) If the fitness of one recurrent-pair genotype was increased, selection led to the loss of all genotypes except that recurrent pair; if its fitness was decreased, only the other recurrent pair was retained. This result may again be illustrated with the simple system P(2.2.2):

♀ $aa\ bb$	♂ $Aa\ bb$ $aa\ Bb.$
------------------------	-------------------------------------

If the fitness of one male (e.g., $Aa\ bb$) is consistently higher than the fitness of the other male, evolution proceeds along this path of former equilibria toward fixation of the $Aa\ bb$ male (Fig. 6.C.1).

(ii) If the fitness of a non-recurrent-pair genotype was increased, the system evolved to a stable, multiple-factor equilibrium; if the fitness was lowered, an unstable internal equilibrium resulted, and either recurrent pair was fixed, depending on the starting conditions. This result cannot be illustrated in the above system, because all genotypes contribute to a recurrent pair. A non-recurrent-pair genotype is found in the platyfish system, however:

♀ XX WX WY	♂ XY $YY.$
------------------------------------	-----------------------------

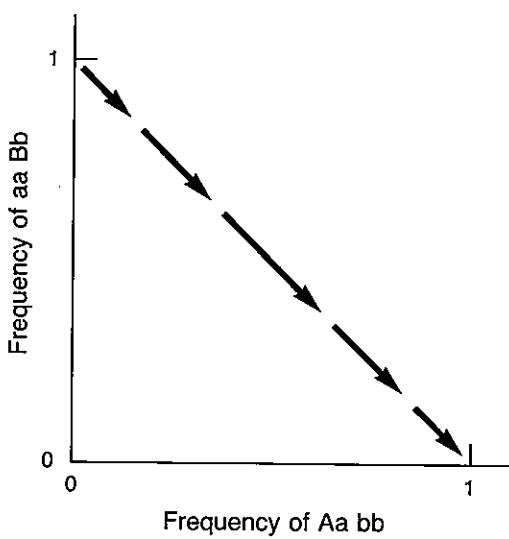


FIGURE 6.C.1. Assigning an advantage to the *Aa bb* male eventually leads to its fixation in P(2.2.2), the arrows indicating the direction of evolution along the former path of equilibria. (Otherwise as in Fig. 6.B.1.)

The WX female genotype does not form a recurrent pair with any of the male genotypes; increasing its fitness above that of the other females leads to a stable equilibrium with W, X, and Y present; decreasing its fitness leads to an unstable equilibrium, and the XX/XY or the WY/YY endpoint eventually evolves.

(iii) With weak selection, and prior to equilibration, evolution of the sex factor frequencies progressed close to or on the path of former equilibria (from the equal fitness case), and the sex ratio remained near, if not exactly, 1/2 (e.g., the platyfish system, Fig. 6.C.2). The set of genotypes defined under the concept of population system was therefore the relevant set of genotypes to consider when fitnesses differed.

The extent to which these conclusions generalize to the more complicated multiple-factor systems is unknown. These results are limited by their failure to consider fitness alterations of more than one genotype simultaneously, although in some cases the consequences of altering the fitnesses of several genotypes can be predicted from these results.

One interesting implication from these results is that the invasion of a new sex factor in an XX/XY system is hindered if it leads to the production of any subvital YY genotypes. If YY is produced and is inferior to XY, the invading sex factor is selected against, *even if the invading sex factor never occurs in YY individuals*. This result can also be seen in the platyfish system, shown just above. If YY males are even slightly inferior to XY males, W is eliminated and

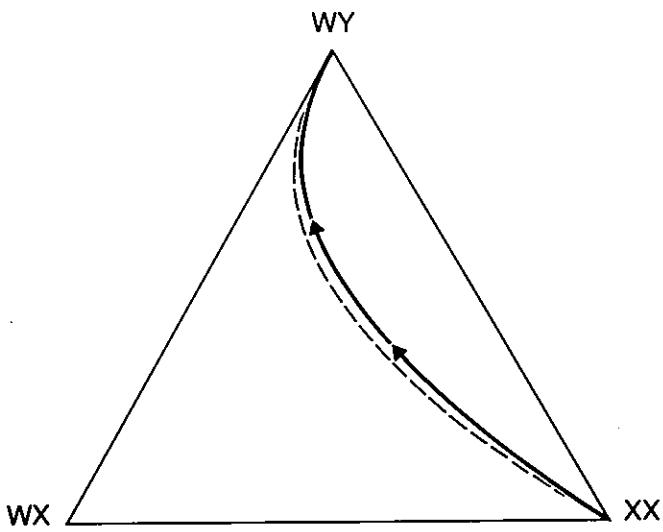


FIGURE 6.C.2. The solid, arrowed curve is a trajectory of genotype frequency change in the platyfish system when fitnesses differ. (Frequencies are illustrated only for the three female genotypes.) The trajectory passes near the set of equilibria from the equal fitness case (dashed curve). The solid curve is drawn for the case when WY females have a fitness of 1.2 relative to other females, with no differences among males.

XX/XY evolves, even though W occurs only in females and has no direct fitness effect in males.

Other Considerations

In addition to direct fitness differences between genotypes, there are other alterations concerning the assumptions of multiple-factor population systems that may affect the equilibria: non-random mating, occasional environmental alterations of sex, and segregation distortion. The first two effects have not been studied in multiple-factor systems (although see Sec. 10.C for a model of 2 sex factors with an environmental effect), and it would be helpful to know how such models compare to those presented above. Segregation distortion was considered in this context by Scudo (1964), Maynard Smith (1978), and Bull and Charnov (1977). The latter study showed that models with segregation distortion behaved in somewhat similar ways as did models incorporating fitness differences among the genotypes. Under segregation distortion, for example, the multiple-factor system either evolved to a stable, internal equilibrium or degenerated to a 2-factor endpoint. One interesting result concerned the sex ratio. If segregation distortion was present in an XX/XY system, producing a biased sex ratio, a rare sex factor at another locus was not

necessarily favored, even if its evolution would ultimately have led to a sex ratio of 1/2. The invading sex factor must have a higher frequency in the rare sex than in the common sex in order to increase (from Nur's formula, 6.A.1).

D. Biological Examples and Possibilities

This section offers specific examples of the biological nature of fitness effects that may influence the evolution of multiple-factor systems. In a few cases, data are available on the sex ratios and/or frequencies of sex-factor genotypes in multiple-factor systems, along with the corresponding fitness effects. In other cases, the fitness effects experienced by sex factors may be anticipated, and the evolutionary consequences for multiple-factor systems may therefore be predicted.

Hitch-hiking: Houseflies

A spectacular demonstration of selection for **XX** males occurred in a housefly strain selected for DDT resistance (Kerr, 1970). The ancestral strain consisted mostly of **XX** females and **XY** males, and segregated for DDT resistance on the second autosome. Whether by mutation, or initially present at low frequency, **XX** males heterozygous for sex factors on autosome II appeared:

♀ XX mm	♂ XY mm XX Mm.
----------------------------	---

The **M** factor was on the same chromosome as the DDT resistance gene, and since recombination in housefly males is generally quite low (recall Sec. 3.D), **M** was always inherited with DDT resistance. Within a few generations of exposure to DDT, **XX Mm** males replaced **XY mm** males. Since DDT resistance was otherwise not fixed, the **XX** males were always at a higher fitness than **XY** males and so increased.

XX males also gained prominence in a strain selected for early adult emergence, a characteristic shown to covary with DDT resistance (Kerr, 1970). Following selection for early emergence, the males in this strain became heterozygous for a holandrically inherited resistance gene (the same resistance gene as above), while females were entirely DDT sensitive. This result was puzzling because, in the ancestral stock, *late* emergence was associated with DDT resistance and early emergence with DDT sensitivity. Therefore, under selection of early emergence, **XX** males should have evolved with a holandric sensitive allele rather than resistance allele. It is possible, of course, that early

emergence was associated with DDT resistance in these particular XX males, but the needed observations were not reported.

There exists the intriguing possibility that the prevalence of autosomal *M* factors in housefly populations was selected from the widespread use of insecticides (Franco et al., 1982). Several autosomal housefly loci confer resistance to DDT, with major effects on autosomes II and III, and V (Milani, 1975; Rupes and Pinterova, 1975). Resistance to other insecticides was also shown for autosomes II-V, and the same process that occurred in Kerr's laboratory experiment may have occurred in nature, as anticipated by Milani (1969). In Europe, Japan, and Australia, *M* factors were most commonly observed on autosomes II and III, less so on V, and almost never on I or IV, consistent with the DDT selection hypothesis.

A Progressive Female Bias Causing Extinction of a Housefly Strain

Milani (1971) and Rubini et al. (1972) reported the establishment of a housefly strain with male heterogamety, supposed to be as follows:

$$\begin{array}{ccc} \text{♀} & & \text{♂} \\ F'F' \text{ YY} & & F'f \text{ YY.} \end{array} \quad (6.D.1)$$

F' was derived from the *F* factor of Sec. 3.D, but *F'* was never mapped, and consequently no direct evidence was available to indicate that sex was inherited according to this system. This strain was maintained for six generations with a sex ratio near 1/2, but by generation 14 the sex ratio was less than .1 (with several males intersexual), and in generation 20 no males were produced (reviewed in Milani, 1971). Therefore, not only did a biased sex ratio evolve, but one sex was lost completely.

If this example had demonstrated the reverse—an initial female bias converging to a sex ratio of 1/2—I would have applauded it as one of the few experimental demonstrations of the evolutionary stability of a sex ratio of 1/2, hence strongly supporting the models in this chapter. Instead the result is contrary to these models and has no plausible explanation in the data provided, so it presents an important challenge to an understanding of the evolution of sex determination.

A progressively female biased sex ratio may evolve for several reasons, and it is important to determine whether any of these accounts for this unusual result in houseflies. Discriminating among these possibilities will likely require further work, so housefly strains similar to the original one would need to be established. One point should be emphasized: as suggested by the analyses in this chapter, the evolution of a female bias cannot be explained merely by proposing that the sex determining mechanism in this strain incorporated more sex factors or loci than in system (6.D.1); rather, a qualitatively different effect

is required. One explanation consistent with many observations is that the sex ratio bias resulted from a maternally inherited cytoplasmic sex factor that arose after the isolation of the strain. Cytoplasmic sex factors will be discussed in Chapter 14, but here it is important to add that they (i) are associated with extreme female biases, (ii) sometimes cause intersex males, and (iii) can cause population extinction by eliminating males. They are unknown in houseflies, however. Alternatively, it may be considered that the sex ratio bias evolved through segregation distortion of a sex factor—in system (6.D.1), by $F'f$ males producing only F' sperm. Segregation distortion of a sex factor is not necessarily associated with a female bias, nor with intersex males, but it can cause population extinction from a progressive sex ratio bias (Howard, 1942; Shaw, 1958; Hamilton, 1967; Lyttle, 1977).

A final possibility to consider is that F' was a sex factor of partial penetrance and was fixed in the strain, so that both sexes were $F'F'$. An environmental change reverting F' to full penetrance could have caused the extinction. Although partial penetrance does not accord with the sex determining mechanism reported for this strain (6.D.1), F' was not mapped, and no observations were reported that rule out the model of partial penetrance. It should be possible to re-isolate F' from the original F -strain to study its penetrance. Until resolved, this example of a progressive female bias offers one of the most serious contradictions to the views of the sex ratio evolution presented in these chapters.

Segregation Distortion and Compensation: Lemmings

The two lemming systems described in Section 3.C were represented as

♀	♂
XX	XY
X^*X	
X^*Y	(YY).

The systems in varying lemmings (*Dicrostonyx torquatus*) and wood lemmings (*Myopus schisticolor*) differ in one major respect. As the result of an embryonic duplication process, the X^*Y female wood lemmings develop an X^*X^* ovary lacking the Y , so these females transmit only X^* to offspring (Gropp et al., 1976). Their fertility is consequently normal (Fredga et al., 1976, 1977). The inviability of YY is irrelevant here, since YY zygotes are not usually formed. The expected equilibrium is 25% males with an equal frequency of all three female genotypes (Bengtsson, 1977; Bull and Bulmer, 1981).

The X^*O female varying lemming apparently segregates X^* and O in equal frequency (Gileva, 1980; Gileva et al., 1982). Therefore, in mating with a male (XO), 1/4 of X^*O 's progeny should be OO and inviable. (If these progeny occur, they seem to die so early that they are unknown, except as tiny

embryos.) With this hypothesis, it might be expected that **X*O** females would demonstrate only 3/4 the fecundity of an **XX** female, but the fecundities of these two genotypes are indistinguishable. These lost zygotes are compensated in part by a greater ovulation rate in **X*O** than in **XX** mothers (Gileva et al., 1982). In contrast, the net fecundity of **X*X** females has been estimated at approximately 1.4 times that of **X*O** and **XX** females, and as chiefly the result of larger brood sizes in **X*X** (Gileva et al., 1982). (The confidence interval of this ratio is no doubt large, since both the numerator and denominator are products of independent estimates of two fitness components.)

The predicted sex ratio and frequency of **X*O** females in varying lemmings is contingent upon the fecundities of all three female genotypes. If brood sizes from all three types of females were the same (complete compensation for the loss of **OO** offspring in broods from **X*O**), the expected sex ratio would be .42, with 20% of the females **X*O** (Bull and Bulmer, 1981). If instead, the fecundity of **XX** and **X*O** were equal but **X*X** was 1.4 times as high, the expected sex ratio would be .36, with .30% of the females **X*O**.

The sex ratio and the frequency of **X*Y** females in both lemming genera has been reported only from laboratory colonies. Bull and Bulmer analyzed these data assuming equal fitness among all females. In wood lemmings as well as varying lemmings, sex ratios were sometimes in agreement with predictions, but in many cases were significantly too female-biased, and the observed frequency of **X*Y** females significantly exceeded the predicted value in all studies (Bull and Bulmer, 1981). The study of Gileva et al. (1982) was not available for Bull and Bulmer's analysis, and if the high relative fecundity of **X*X** varying lemmings is taken into consideration, the model predicts an equilibrium more in line with the *Dicrostonyx* results. However, even if **X*X** females have 1.4 times the fecundity of **XX** and **X*O**, most of the discrepancies would still be significant. The quantitative disagreement between predicted and observed sex ratios and genotype frequencies in both genera of lemmings is thus unexplained.

Platyfish

The fitnesses of the different genotypes in the 3-factor W, X, Y platyfish system may be affected by color genes closely linked to the sex factors (Kallman, 1965, 1968, 1970; Kallman and Atz, 1967). In poeciliids, for example, brightly colored males are common. Bright fish suffer greater predation than cryptic fish, but bright males gain a mating advantage because females prefer them to dull males (reviewed in Kallman, 1970; Endler, 1978, 1980). Several color genes in platyfish are tightly linked to the W, X, Y "locus," occurring commonly on the Y, and perhaps equally or less so on the X, but essentially never on the W (Kallman, 1970, pers. comm.).

Kallman (1970, 1983) proposed the hypothesis that the ancestral sex deter-

mining mechanism in platyfish was male heterogamety (XX females and XY males) with color genes present on both the X and Y. In support of this hypothesis, he noted that male heterogamety is the common form of sex determination among other *Xiphophorus*, and that the sex factor locus of two species with male heterogamety, *X. variatus* and *X. milleri*, is homologous with that in platyfish (Kallman and Atz, 1967). Kallman proposed that the W may have been able to invade because it lacked genes for bright color. Since brightly colored females are at a disadvantage over cryptic females, a gene reducing the occurrence of bright coloration in females might indeed be advantageous.

Evaluation of Kallman's hypothesis requires a detailed understanding of the inheritances and fitnesses associated with color genes, and the available evidence is insufficient for a rigorous evaluation. Two hypothetical examples offered here will demonstrate that evolution of W varies according to these parameters. It is assumed throughout these examples that males as well as females which carry the genes for bright color also express them according to the specified dominant/recessive mode of action. This is an appropriate assumption for platyfish (Kallman, 1970), but not for some other poeciliids, such as guppies (Haskins et al., 1970). First consider a model in which W is selected against: a dominant gene for bright color occurs only on the Y. All XX and WX females are therefore cryptic, but some or all WY females are brightly colored and so W is at disadvantage (recalling the results of Sec. 6.C). A second hypothetical example demonstrates selection for W. Suppose a recessive gene for bright color is fixed on both the X and Y (its disadvantage in females more than compensated by its advantage in males). A W that lacks the allele for bright color will occur only in cryptic females and thus evolve.

Kallman (pers. comm.) suggested that dominant color genes were polymorphic and may have been at similar frequencies on both the X and Y, but absent from the W. In this case, a lower fraction of W females would inherit the color gene than would XX females, thereby favoring W. Yet, the above example illustrated that W would be selected *against* if the color gene was located only on the Y, so there exists a critical frequency of X- versus Y-linked color genes at which the selection of W reverses. In reality, if color genes are advantageous in males but not in females, the opposing selection will lead to a higher frequency of them on the Y than the X, even with free X-Y recombination. The above assumption of equal frequencies of pigment genes on the X and Y is therefore unreasonable. A quantitative evaluation of these effects is required in order to further interpret evolution of the W within this framework.

Orzak et al. (1980) considered the possibility that W is maintained in platyfish from a superiority of YY males to XY males, and they derived the conditions for existence of a stable polymorphism of W, X, and Y under this assumption. In their experiments, YY males were more successful than XY males, but the effect was not statistically significant.

Sex Chromosome Systems

The evolution of heteromorphic sex chromosomes often entails changes affecting the fitness of individuals with **XX**, **XY**, and **YY** karyotypes. Most of these effects mitigate against the evolution of new sex factors. The most obvious complication is that **YY** individuals are subvital, sterile, or lethal in many heteromorphic sex chromosome systems (Chaps. 16 and 18). Invading sex factors that lead to **YY** genotypes are therefore at a disadvantage and are likely to be eliminated. If **YY** individuals cannot reproduce at all, the only new system of heterogamety than can evolve must have **XX** males and females, and nearly half the evolutionary pathways to new heterogametic systems are thereby precluded.

Sex chromosomes may also interfere with the fertility of **XX** males or **XY** females, and these effects are well-documented in mammals (Sec. 4.C). Complications stem from the fact that, prior to the origin of the multiple-factor system, **XX** occurred only in females and **XY** only in males, so selection against deleterious effects on these chromosomes limited to **XX** males or **XY** females did not exist. If these deleterious effects build up, sex factors that produce **XX** males or **XY** females are at a disadvantage.

Not all effects of heteromorphic sex chromosomes necessarily interfere with the invasion of a new sex factor. **XY** males with a degenerate **Y** chromosome have only one dose of sex-linked loci, and they may consequently be exposed to the harmful effects of deleterious, recessive, **X**-linked genes. **XX** males do not have this problem. (Conversely, **XY** females should suffer more than **XX** females from this effect.) In support of this hypothesized deleterious effect of a single **X**, experiments with *Drosophila* have shown that **XX** adult males are more apt to survive short exposures to insecticides than are **XY** males (J. F. Crow, pers. comm.).

On the basis of these effects, it seems that species with extremely heteromorphic sex chromosomes should be less likely to evolve new systems of heterogamety than species without heteromorphic sex chromosomes, if only because of **YY** inviability. The evidence in support of this hypothesis is limited, however (Sec. 17.C).

Unequal Cost of Sons and Daughters

Fisher (1930) proposed that sex ratios would evolve toward the point at which the "expenditure" on daughters would equal the expenditure on sons. The model often used to illustrate this result is the case in which a daughter "costs" more to rear than a son (or the reverse), so that the number of progeny in a family increases linearly with the sex ratio. If the cost of a son relative to a daughter is u , the Fisherian sex ratio equilibrium would be $1/(1 + u)$. (This formula gives the value to which the sex ratio is expected to evolve under arbitrary genetic variation in sex ratio and will be referred to in these paragraphs

as the "optimal" sex ratio.) Yet it has been questioned whether the sex ratio in XX/XY systems can evolve away from 1/2, despite a differential cost of sons and daughters, because Mendelian segregation may preclude a large departure from 1:1 segregation (e.g., Maynard Smith, 1978, 1980; Williams, 1979; Charnov, 1982).

As an alternative to segregation distortion, the sex ratio may change through the incorporation of additional sex factors. I will illustrate here that a differential cost of sons and daughters influences the evolution of multiple-factor systems, so that a polymorphism of multiple factors is sometimes stable, and an XX/XY system with a sex ratio of 1/2 is consequently unstable. Thus, in this context, an XX/XY system is not expected to persist under selection for a biased sex ratio, if various multiple-factor systems arise.

Several multiple-factor population systems have families in which the sex ratio deviates from 1/2. If the number of progeny in a family depends on its sex ratio, then the fitness of genotypes contributing to these biased sex ratios may be affected and so influence the evolution of the multiple-factor system. To illustrate, consider again the platyfish system:

♀	♂
XX	XY
WX	
WY	YY

Four of these matings produce a sex ratio of 1/2, but the mating XX • YY produces all sons, and WX • XY produces 1/4 sons. Assigning a higher cost to sons than daughters (so that a family with all daughters is larger than one with all sons) generated a stable equilibrium in this system, with W, X, and Y all maintained. But if daughters cost more than sons, the polymorphism decayed to a two-factor system (Table 6.D, Fig. 6.D).

TABLE 6.D. Sex Ratios in the Platypus System with Unequal Costs of Sons and Daughters

Cost (σ/φ)	Fisherian Sex Ratio Optimum	Platypus Sex Ratio
1	.50	.50 (infinity of equilibria)
1.1	.476	.498
2	.33	.481
4	.20	.464
10	.099	.448
<1	>.50	.50 (evolution toward XX/XY or WY/YY, depending upon initial conditions)

From these results, the sex ratio in the platypus system indeed evolved from 1/2 toward the Fisherian optimum, but the deviation from 1/2 was never

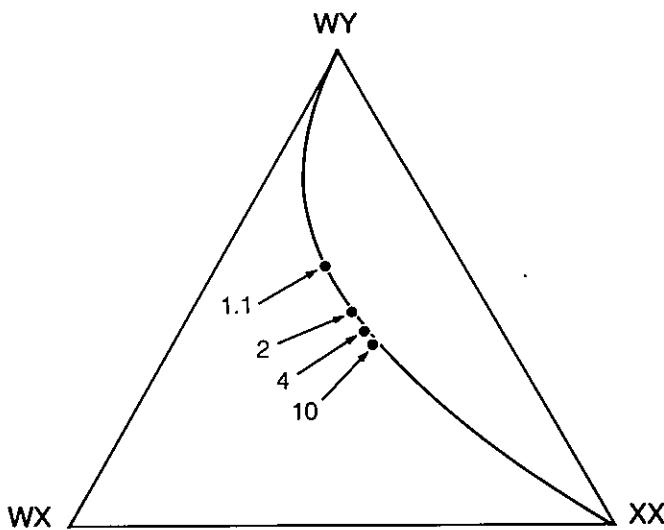


FIGURE 6.D. Equilibria in the platyfish system when sons cost more to rear than daughters. Equilibria differ according to the relative cost of sons (arrowed dots). The equilibria correspond to the values listed in Table 6.D. The curve indicates the former set of equilibria when fitnesses are equal and both sexes are equally costly to rear (from Fig. 6.B.3).

great, even for an unrealistically high relative cost for sons. As a conjecture, I suggest that while the platyfish system is maintained polymorphic under these conditions, it can be invaded by other sex factors that move the sex ratio even farther from 1/2 toward the Fisherian optimum. This may further increase the number of sex factors.

The above results are interesting in a broader context. First, a sex ratio of 1/2 is not the automatic consequence of a multiple-factor system. Rather the sex ratio of 1/2 results from selection under a set of environmental conditions favoring a sex ratio of 1/2. Second, when viewed over long periods of time, the evolution of male and female heterogamety should be regarded as a process reflecting selection of a sex ratio of 1/2. The chance loss of multiple factors could generate male or female heterogamety amid selection for a biased sex ratio. But mutation could continue to introduce multiple factors, and if the above conjecture is correct, enough sex factors would eventually invade so that male or female heterogamety did not persist.

Differential investment in sons versus daughters is apparently not a widespread phenomenon in animals, although I know of few actual studies measuring this effect. In many species, the total investment in offspring is provided in the egg, and the eggs are provisioned prior to sex determination. Two groups which have some capacity to invest differentially in sons and daughters are mammals and birds, because investment is provided after conception. In these groups, sex chromosomes are well established (and perhaps were

established prior to the evolution of post-conception parental care), so there is now probably only a limited potential for the evolution of multiple-factor systems.

E. Summary

This chapter analyzed models of evolution in multiple-factor systems for random-mating populations. A universal feature of these analyses is that selection for a sex ratio of 1/2 plays a key role in affecting the evolution of sex factors. When fitnesses were assumed equal within a sex, most of the multiple-factor systems presented here contained continuous paths of equilibria connecting different recurrent genotype pairs (2-factor systems), and the sex ratio of these equilibria was 1/2. Under a wide range of fitness differences among genotypes, a new recurrent pair evolved from the ancestral one via a multiple-factor intermediate, a transition that occurred approximately along the path of former equilibria. In addition, certain combinations of fitness effects led to stability of a multiple-factor system, so that a recurrent pair did not evolve. The equilibrium sex ratio when fitnesses were not all equal was not necessarily 1/2, but the deviation from 1/2 was not great for slight fitness effects. Some plausible types of fitness effects were discussed, but as yet there are only a few detailed quantitative studies of multiple-factor systems.

7

Evolution of the Heterogametic Mechanism of Sex Determination

Male and female heterogamety are the most prevalent forms of sex determination known, occurring in diverse plants and animals (recall Tables 2.C.1-5). These systems therefore warrant a central place in any comprehensive evolutionary theory of sex determination. This chapter combines the results of preceding chapters to formalize and evaluate a theory for the evolution of differences in the heterogametic sex determining mechanism.

A. A Theory Based on Multiple-Factor Systems

It was proposed as early as 1932 by Winge and by Muller that a mechanism of heterogametic sex determination could change by relatively simple means within a population. Winge had selected a strain of XX male and female guppies from a former system of male heterogamety, thus demonstrating the feasibility of change to a new system, although the mechanism in the XX strain was never identified. These early studies, therefore, provided the insight for a major focus of this book.

Chapter 6 demonstrated that multiple-factor systems may act as intermediates in the transition from one heterogametic mechanism (recurrent pair) to another. These changes can have several consequences on the properties of the sex determining mechanism. To illustrate, suppose that the ancestral mechanism is symbolized as XX females/XY males, and consider the evolution of the multiple-factor system P(2.2.2) by introducing the factor *M*:

♀ $\text{XX } mm$	♂ $\text{XX } mm$ $\text{XX } Mm.$
-------------------------------	---

From the results in Sec. 6.C, if $\text{XX } Mm$ males have a consistent advantage, they will replace $\text{XY } mm$ males. Two consequences of this transition are (i) the locus of heterogamety changes, and (ii) the population becomes entirely XX. This latter change would be observed as the loss of sex chromosome heteromorphism if the X and Y were heteromorphic but *M* and *m* were not (cf. Winge, 1932, 1934). An additional consequence of the evolution of $\text{XX } Mm$ males is (iii) the recessive-X and dominant-Y relationships of the heterogametic mechanism may change. For example, the $\text{XX } mm/\text{XY } mm$ system might have operated on a recessive-X principle, while $\text{XX } mm/\text{XX } Mm$ operated on a dominant-*M* principle.

Changes in the heterogametic sex offer no additional complication. The platyfish system has been illustrated above frequently. Another example is P(2.2.6):

♀ $\text{XX } mm$	♂ $\text{XY } mm$ $\text{XY } Mm$ $\text{XY } MM$ $\text{XX } Mm$
-------------------------------	--

In the absence of fitness differences, the two recurrent pairs $\text{XX } mm/\text{XY } mm$ and $\text{XX } Mm/\text{XX } MM$ are connected by a path of neutral equilibria, and a slight advantage to either recurrent pair in the absence of other effects leads to its establishment (Bull and Charnov, 1977). This system illustrates that the heterogametic sex can change without creating YY genotypes in the population.

A Theory for Changes in the Heterogametic Mechanism

Evolution in multiple-factor systems can lead to the diverse types of 2-factor systems observed within different groups, and they therefore provide the basis of a theory for the evolution of differences in heterogametic sex determining mechanisms. Comprehensive evaluation of this theory must await substantially

more evidence than presented in this book, but it is possible here to identify some major issues in such an evaluation.

(i) If multiple-factor systems have been responsible for changes in the heterogametic mechanism, one would expect them to be most common in groups with varied heterogametic mechanisms and rarest in groups with conserved mechanisms. Multiple-factor systems seem relatively common in dipterans, a group with at least moderate variety of sex determining mechanisms. But multiple-factor systems are rare in mammals, a group which has characteristically conserved mechanisms. Only one multiple-factor system was presented for fish, but at least in poeciliids, several other systems are known with multiple factors, except that these systems have not been thoroughly characterized, or they have a major environmental component to sex determination and thus were not included in the above chapters (see instead Chapter 8).

The multiple-factor systems observed in nature are likely to be stable ones. Yet some unstable multiple-factor systems will lead to changes in the heterogametic mechanism, and these will not be observed as often as stable multiple-factor systems. Therefore, the above comparison presumes that the abundance of observed multiple-factor systems reflects the abundance of those which lead to new 2-factor systems. Furthermore, an overall paucity of multiple-factor systems is therefore not itself a major obstacle to the hypothesis that they provide many of the transitions from one heterogametic mechanism to another, since most of the changes in sex determination may occur so rapidly that the multiple-factor systems occur only briefly.

(ii) In some cases it should be possible to observe a transition from one heterogametic system to another through a multiple-factor system. The most convincing evidence at this level exists for housefly populations, where it seems that *M* factors have led to the evolution of XX males from XY males. While the actual transition through a multiple-factor system will no doubt be uncommonly observed, there is a powerful, indirect method of demonstrating that multiple-factor systems have led to changes in the heterogametic mechanism. Two populations of the same or closely related species that have different mechanisms of heterogamety may be hybridized to regenerate the intermediate mechanism. If a multiple-factor system was involved, this system should appear after a few generations in the hybrid population, provided that both parental populations have not undergone subsequent changes in sex determination. This approach was suggested by Avtalion and Hammerman (1978) in a study of fish, and it was described above for midges in Sec. 3.E.

(iii) To understand the role of multiple-factor systems in the evolution of sex determining mechanisms, quantitative evaluations of the models are desirable, if only to verify that natural systems evolve approximately according to the results of models. Quantitative analyses of multiple-factor systems may be performed at several levels. A particularly simple characteristic to study is the sex ratio, which is expected to equilibrate near 1/2 except under ex-

treme fitness effects. In addition, genotype frequencies may be studied. They may be studied first to see if they lie near any part of the set of equilibria from the equal fitness case, since the models indicate that genotype frequencies remain near this set even when fitnesses differ. At the most sophisticated level, genotype frequencies may be compared to the actual predicted values, based on fitness estimations for each genotype. The only rigorous analysis at any of these levels is of the genotype frequencies and sex ratios in the lemming systems, which agree qualitatively, but not quantitatively, with predicted values.

B. Difficulties of the Theory and Alternatives

Despite few attempts to rigorously evaluate the above theory, there are already some observations which present difficulties and which might therefore lead to its falsification in specific cases. As noted in Sec. 6.D, the genotype frequencies and sex ratios observed in lemmings deviate significantly from predicted values. Another and more serious unexplained observation is the extinction of the housefly strain resulting from its eventual failure to produce males (Sec. 6.D). This result is contrary to all of the results presented above. Further work is needed to determine whether the extinction resulted from some effect of general importance which should be incorporated into other models for the evolution of sex determination.

The sex chromosomes in *Drosophila* and *Caenorhabditis* pose a subtle difficulty for the theory. In both species multiple loci, rather than a single major locus, contribute to the X's role as a sex factor (Secs. 4.A, B). It is difficult to imagine that these systems arose in their present form directly from an alternative mechanism—the sex factors involve too many genes to have originated in one step and to have segregated as a unit at the outset. The remote ancestry of sex chromosomes in *Drosophila* and in nematodes invites the speculation that these sex factors have a different genetic structure now than originally, but their obscure origins likewise preclude a solution to this problem. It is ironic that, while these sex factors are comprised by several loci on each X, both species also reveal a hierarchy of single, major regulatory genes involved in the control of sex development.

The theory presented here does not predict which multiple-factor phenotype systems should arise. The origin of a phenotype system depends upon the genetic variation created by mutation, and the models here merely propose the evolutionary consequences once the phenotype system is present. It would be immensely interesting to understand enough molecular genetics of sex factors to suggest why some phenotype systems occur and others do not, but there does not seem to be any basis for generating such predictions from the methods used in this book.

The models of preceding chapters have been limited to multiple-factor systems, but these should not be regarded as the only means by which differences in heterogametic mechanisms may evolve. In reptiles, for example,

it is plausible that various heterogametic mechanisms evolved independently from environmental sex determination (Sec. 9.D). Section 2.F considered that heterogametic sex determination may have evolved from ancestors lacking separate sexes altogether (hermaphroditism, isogamy). However, alternatives to multiple-factor systems are not equally plausible for all groups. For example, nearly all sexually reproducing insects have separate sexes with some form of genotypic sex determination, so isogamy, hermaphroditism, and environmental mechanisms are too rare to account for many of the changes in their sex determination.

Winge (1932, 1934) proposed an extreme variation of the multiple-factor theory. He argued that in XX/XY systems, many loci segregate for minor sex factors, and occasional combinations of minor sex factors override the major ones, thereby producing, for example, XX males. Selection of XX males could lead to the loss of XY males and, he supposed, lead to heterogamety at a new locus. This theory emphasized the importance of many rather than few sex factors, but it is otherwise similar to the multiple-factor theory. Winge's model encounters one serious problem, however. If the inheritance of sex is controlled by many factors with individually small effects, no single pair is likely to have a major influence on sex determination. Therefore, if an XX strain is created by selecting this underlying "polyfactorial" variation, a new system with just two major factors is not likely to evolve unless a major sex factor reinvades. The polyfactorial theory is therefore not a plausible way of generating new systems of male or female heterogamety.

C. Other Topics Concerning the Evolution of Heterogametic Mechanisms

Except for the enormous success of a few predominantly haplo-diploid invertebrate groups (e.g., Hymenoptera, Acari), male and female heterogamety are overwhelmingly the most common sex determining mechanisms observed in animals with separate sexes. This evidence is based on the many cytological studies that demonstrate heteromorphic sex chromosomes. It is natural to ask why these simple mechanisms should be so common. I am unable to answer this profoundly interesting question, but I can suggest two directions in which its solution may be pursued. Heterogametic mechanisms have two notable properties: (i) they experience few environmental influences on sex determination, and (ii) they have just two sex factors. To understand why heterogametic mechanisms are so common requires understanding both properties, but insights to either of these would be rewarding. The lack of environmental effects on sex determination may simply be an unalterable property of these mechanisms—major regulatory genes of sex development are perhaps not susceptible to external influences. However, in contradiction to this hypothesis of genetic constraints, there is considerable evidence that environmentally sensitive sex factors exist and may be selected (Sects. 4.A, 4.B and 9.G). The second prob-

Item identified here is why systems with only two factors are so common. In some species, such as *Drosophila melanogaster*, the solution is straightforward, because functional sex factors other than X and Y apparently do not arise. Functional multiple-factor systems do occur in some groups, however, and for these one wonders why sex factors do not simply accumulate in large numbers. Perhaps the maintenance of multiple-factors requires such a delicate balance of fitness effects that the vast majority of multiple-factor systems which arise are simply not stable (cf. Lewontin et al., 1978; Aoki, 1980).

Male Versus Female Heterogamety

While female heterogamety is nearly as common as male heterogamety among vertebrates, it seems to be grossly under-represented among some invertebrates (Tables 2.C.1–3). However, the mere analysis and interpretation of the relative frequencies of male and female heterogamety is difficult, because the heterogametic sex in a group may have been retained by most species since their common ancestry. No argument has been offered here that male heterogamety *should* prevail, and no explanation for this asymmetry emerges from the study of multiple-factor systems. There may be in part the observational bias that chromosome studies are often limited to males, and as a consequence, instances of female heterogamety may be missed, but male heterogamety still seems to be overwhelmingly popular in insect groups, nematodes, and in the Acari (mites and ticks). Although male heterogamety is the dominant form in Diptera, female heterogamety is also known in some flies, indicating that it can indeed arise. A careful study of the origins and ancestries of male and female heterogamety in well-known groups would be helpful in distinguishing between a bias against the origin of female heterogamety versus a bias against its maintenance. A solution to this problem would be welcome, as would a proper analysis of the extent of the asymmetry.

Male heterogamety is also more common in dioecious flowering plants: 23 cases of male heterogamety are known versus only three cases of female heterogamety (Westergaard, 1958; Lloyd, 1974; Charlesworth and Charlesworth, 1978). The prevalence of male heterogamety in plants, however, can be explained by the nature of the evolution of dioecy. A common transition for the evolution of dioecy in these plants is from hermaphroditism through a “gynodioecious” intermediate (a population of females and hermaphrodites). This process begins with the invasion of the hermaphrodite population by a mutation converting the hermaphrodite into a female by suppressing its pollen production. Under appropriate conditions, gynodioecy evolves—a mixture of females and hermaphrodites. The second and final step to dioecy occurs with the evolution of a gene converting the hermaphrodite into a male by suppressing its seed production. This pathway from hermaphroditism to dioecy is supported both empirically and by mathematical models (Westergaard, 1958; Lloyd, 1974; Charlesworth and Charlesworth, 1978).

To understand why this process leads to dioecy, the nature of these sex factors and the constraints placed on their evolution must be considered. Under a wide range of conditions, the mutation suppressing seeds cannot evolve unless closely linked to the locus of the mutation suppressing pollen (Charlesworth and Charlesworth, 1978). This restriction arises because certain combinations of mutations produce a neuter plant, with both pollen and seeds being suppressed. Free recombination would lead to frequent neutrals. Because close linkage is required when dioecy evolves via this route, both loci segregate together, as though there is one sex factor locus. The dioecious population therefore segregates two factors—one factor suppresses seeds but not pollen (a male factor), and the other suppresses pollen but not seeds (a female factor). The population therefore evolves to male or female heterogamety (Charlesworth and Charlesworth, 1978).

The above pathway will lead to male heterogamety if the first mutation arising is a *recessive* pollen-suppressor, whereas the pathway will lead to female heterogamety if this first mutation is a *dominant* pollen suppressor. Since recessive mutations are generally more common than dominant ones, especially for those that destroy gene function, this theory has been proposed as the basis for the prevalence of male heterogamety in plants.

D. Summary

This chapter formalized and evaluated the theory that multiple-factor systems are one of the common types of intermediates for changes in the heterogametic sex determining mechanism. Although it will no doubt be difficult to actually observe the evolution of one heterogametic mechanism to another, indirect assessments of this theory are possible. Most importantly, the hybridization of two populations differing in heterogametic sex determination should reconstitute the ancestral system. If the change in heterogametic sex determination involved a multiple-factor system, this system should result in the hybrid population, provided that no further changes in sex determination occurred subsequent to the original change. Also, groups exhibiting many variations of heterogametic mechanisms are expected to exhibit more multiple-factor systems than are groups of conserved heterogametic mechanisms. Some difficulties and alternatives to this theory were discussed. Two additional questions concerning the evolution of heterogametic sex determination were posed: why are heterogametic mechanisms so common, and why is male heterogamety more common than female heterogamety in many invertebrates?

8

Polyfactorial Sex Determination*

A. Introduction

Polyfactorial sex determination is usually regarded as a mechanism with sex determined by many factors, so that no few of them have a major influence (Kosswig, 1964; Bacci, 1965; Yamamoto, 1969; Kallman, 1983; usually referred to as polygenic sex determination). Polyfactorial mechanisms have not been so extensively researched nor are they as widely renowned as heterogametic mechanisms and multiple-factor systems, except in the literature on poeciliid fish. The earliest formulation of a polyfactorial model was provided by Winge (1932, 1934) as simply the additive-value model of sex determination (Sec. 4.E) in which many sites on each chromosome segregated sex factors. The main component of this model—a large number of loci with sex tendencies—stemmed directly from Bridges' theory of genic balance (Sec. 4.E), a fact that may have led to frequent acceptance of the polyfactorial concept even without direct evidence of many sex factors.

*The term "polyfactorial" combines the Greek prefix "poly" with the Latin term "factor," which violates an etymological tradition of combining terms only if they have similar origins. A superior alternative is not apparent, however. "Polyfactorial" is preferable to "polygenic" (the term commonly used for this mechanism) because the sex determining mechanism describes the inheritance of *sex factors*. The other feasible alternative, "multi-factorial" (multiple-factor) was used above for a different class of systems. "Polyfactorial" has previously been applied to sex determining mechanisms in the sense of this chapter (Kallman, 1983).

It is not clear whether models of polyfactorial sex determination subsequent to Winge have retained the emphasis of many sex factors, or whether some authors would include the above multiple-factor systems (Chap. 3) as examples of polyfactorial sex determination. While there is necessarily an arbitrary distinction between the categories of multiple-factor and polyfactorial systems, the distinction which seems most practical is that multiple-factor systems are those which have a relatively simple characterization: once a multiple-factor system is known, its evolution may be treated in an exact manner. Systems lacking a simple characterization require a superficial means of analysis, and these may be lumped under the polyfactorial classification: as will be shown below, no practical method is available for ascertaining the number of sex factors in these "polyfactorial" systems, so this classification does not generally exclude systems with only a few sex factors.*

This chapter will first review two well-established examples of polyfactorial sex determination from poeciliid fish (Sec. B). These examples will be followed by a demonstration that the evidence used in support of polyfactorial sex determination does not necessarily indicate the presence of many sex factors (Secs. C and D). Finally, models will be offered to illustrate some evolutionary properties of polyfactorial sex determination (Secs. E and F).

B. Criteria and Examples of Polyfactorial Sex Determination

Criteria

Polyfactorial mechanisms are generally difficult to characterize according to the effect of individual sex factors, so diagnosing them has been based on certain superficial properties. In particular, three criteria have been used as evidence for the presence of polyfactorial sex determination: (i) a large between-family sex ratio variance, (ii) paternal and maternal effects on family sex ratio, and (iii) a sex ratio response to selection. Not all these lines of evidence are always available, and polyfactorial mechanisms have sometimes been inferred merely from the observation of a wide between-family sex ratio variance.

One must first be convinced that the three criteria presented above are indeed properties of polyfactorial sex determination. A simple illustration is provided by the platyfish system:

♀	♂	
XX	XY	
WX		(from 3.B.1)
XY	YY	

*I adopt the view that no assumptions should be made about the number of sex factors in the absence of evidence. Some workers may prefer to adopt the view that all systems are XX/XY unless shown otherwise, and alternatively, some may adopt the view that all mechanisms have polyfactorial inheritance unless shown otherwise.

There are six types of matings, four which produce sex ratios of 1/2. One mating, $XX \bullet YY$ produces all sons, and another, $WX \bullet XY$, produces only 1/4 sons. Consequently, the sex ratio varies between families, satisfying the first criterion. (This fact implies little about the population sex ratio, which is expected to evolve to 1/2 in large, random-mating populations.) Also, the family sex ratio varies according to the genotype of both the father and the mother, satisfying the second criterion. Third, if XY or YY males could be identified, their frequency could be selected (cf. Chap. 6). Systems with more than three factors will generally have these properties as well, whereas the basic system of male or female heterogamety lacks all these properties (although male or female heterogamety with parental influences on the segregation of X and Y would exhibit some of these properties).

Examples

The remainder of this section will briefly consider studies on two poeciliid fish, swordtails and medakas, that satisfied these criteria and were therefore interpreted as having polyfactorial sex determination.

Swordtails

The most famous case of polyfactorial sex determination is in the swordtail, *Xiphophorus helleri* (Breider, 1935; Kosswig, 1964; Peters, 1964). Although two-factor and three-factor systems have been reported in several other species of *Xiphophorus*, as diagnosed from closely linked color genes (Kallman and Atz, 1967; Kallman, 1983), there is no evidence in swordtails of male or female heterogamety or other sex factors of major effect. Furthermore, inspection of family sex ratios reveals a wide between-family variance, too large to be accounted for by sampling error under the assumption of male or female heterogamety. Of many possible examples, consider the following set of family sex ratios from Breider* (1935) (with brood sizes in parentheses):

.16	.24	.29	.52	.54	.56	.72	.73	.81	.85	.94
(50)	(141)	(137)	(79)	(95)	(78)	(50)	(84)	(59)	(88)	(49).

These are the broods larger than 40 recorded from the month of August (Breider, 1935, p. 392), the month in which the largest such set of sex ratios is available in Breider's table. (Comparisons have been restricted to families born in the same month to avoid possible seasonal effects on sex ratio, such as those suspected in guppies and medakas; see Sec. 9.G.) Based on a simple heterogeneity test, there is a significant between-family sex ratio variance.

*Data from H. Breider. 1935. "Über Aussenfaktoren die das Geschlechtsverhältnis bei *Xiphophorus helleri* Heckel kontrollieren sollen." *Zeitschrift fuer Wissenschaftliche Zoologie* 146:383-416, Tables 13 and 14.

Additional work on swordtails has shown that both parents influence the family sex ratio (reviewed in Kosswig, 1964). A striking case of paternal influence was observed by Peters (1964). Two types of males were distinguished, early-maturing and late-maturing, and the sex ratios differed between these two types. In particular, all 12 broods recorded from the late males were female biased, but only 2 of 8 broods recorded from the early males were female biased (Peters, 1964, p. 235). Again, this difference is not likely to arise by chance ($P < 0.002$, 2-tailed Fisher's exact test), and it suggests that the early males used in this study were more prone to produce sons than late males. (This test excluded broods of less than 40 and also excluded three additional broods that improved the correlation but perhaps confounded the effect of sire with a common ancestry of dams.)

I am not aware of experiments designed to select sex ratio in swordtails, but Kallman (1983) listed cumulative and sequential sex ratios for different strains of swordtails. Some stocks had cumulative sex ratios different from $1/2$, and a male biased sex ratio seemed to have stabilized for the last 15 generations recorded from the *Cd* stock (Kallman, 1983, App. A). Each generation of fish was usually produced from a single pair of parents, so a biased sex ratio could easily have resulted from random loss of sex factors despite selection for a sex ratio of $1/2$.

XX Males in Medakas

In three well-known studies of poeciliid and cyprinodontid fish, XX males were selected from a stock originally having XY males. The XX males were originally rare, but their frequency was increased greatly under selection. In all cases, the XX males could not be accounted for by a single autosomal factor invariably producing males (i.e., an *M* factor; recall from Chapter 3 several examples of XX male flies that resulted from an epistatic, autosomal *M* factor). These studies were performed with guppies (*Poecilia reticulata*, Winge, 1932, 1934), platyfish (*Xiphophorus maculatus*, Oktay, 1959a, b), and medakas (*Oryzias = Aplocheilus latipes*, Aida, 1936), and the results have been interpreted as evidence of polyfactorial sex determination (Winge, 1932, 1934; Kosswig, 1964; Yamamoto, 1969). Only Aida's work will be described here.

There are three results in Aida's (1936) work relevant to this chapter. First, while XX males were rare in wild populations, XX males were selected to a high frequency in a laboratory stock. Second, there was a significant between-family sex ratio variance within the laboratory strain. Third, this variation at least in part resulted from the mother. (Aida also claimed to have demonstrated paternal influence on sex ratio, but this conclusion is equivocal because each sire in this experiment was bred only to his sisters, thus confounding the effects of sire and dam.) These three results* can be illustrated in one of Aida's several experiments:

*Data from T. Aida. 1936. "Sex reversal in *Aplocheilus latipes* and a new explanation of sex differentiation." *Genetics* 21:136-153, Table 3.

	Sire 1		Sire 2		Sire 3	
	Mother		Mother		Mother	
	lab	wild	lab	wild	lab	wild
♀	49	120	155	153	103	310
♂	58	0	41	0	12	0 .

In this experiment, each of three XX sires was mated to two females, one from the laboratory stock and the other from "wild" animals, as indicated. The Y was therefore absent in these matings. The sex ratios differed significantly between dams mated to the same sire, with the laboratory mothers producing a significantly higher frequency of XX sons than the wild females, perhaps because their ancestors had been selected for XX males. Furthermore, sex ratios from the three mothers of laboratory origin were significantly heterogenous. It is interesting that Aida interpreted his results as variation in the female tendency of the X rather than as polyfactorial sex determination; Yamamoto (1969) reinterpreted these results as indicative of an underlying polyfactorial mechanism.

Reviews of additional examples of polyfactorial sex determination were given by Kosswig (1964), Bacci (1965), and Yamamoto (1969); Sections 9.E and 9.F will describe a fish and amphipod with environmental effects on sex determination that may have polyfactorial influences as well. The evidence from these other species is rarely as complete as in poeciliid fish, however.

C. A 2-Factor Model with Environmental Variance

The three properties used above to diagnose polyfactorial sex determination do indeed apply to most mechanisms with many sex factors, but these properties also apply to some mechanisms with just a few factors. This conclusion is evident merely from the fact that the 3-factor platyfish system was used to illustrate all three properties. This section will show that systems with only two sex factors can account for a wide range of effects previously attributed to systems with supposedly many sex factors. The view presented in this section—that the criteria commonly used to diagnose polyfactorial sex determination do not imply the existence of many sex factors—was pioneered by Kallman (1965, 1983).

A model will be developed below which exhibits the above properties of polyfactorial sex determination, except that only two sex factors will be assumed. This model, as well as models of polyfactorial sex determination in general, require introducing the concept of *environmental effects* on sex determination. While some species show sex ratio variation in response to certain environmental characteristics such as temperature (Chap. 9), that is not necessarily what is required here. In the context of polyfactorial sex determination, the environmental effect of interest is best described as "environmental

noise": if identical genotypes could be reared under the same environmental conditions, some would develop into males while others of the same genotype would develop into females. Such data are available for clones of zebra fish (G. Streisinger, pers. comm.):

<i>Clone</i>	♀	♂
B	71	2
18	35	26
21	25	0
26	19	7.

Fish from the same clone were known to be genetically identical (Streisinger et al., 1981), so sex differences within a strain could not have resulted from genetic differences; rather the differences were the result of unmeasurable environmental effects, or environmental *variance*. Environmental effects are commonly encountered in the development of other characteristics in animals; for example, if the right and left halves of the same individual differ unpredictably in the number of bristles, toes, eye facets, or other such trait (Falconer, 1981; Wright, 1968).

The model that will now be introduced incorporates genetic as well as environmental effects. Suppose that G and g are two sex factors assorting in opposition, and that because of environmental effects, none of the three genotypes, GG , Gg , and gg are consistently one sex. (This supposition now violates the earlier notion of a 2-factor phenotype system, because environmental effects were not allowed.) Specifically, let the following sex ratios obtain:

<i>Genotype</i>	<i>Probability of Being Male</i>	
GG	$1/2 - p$	
Gg	$1/2$	
gg	$1/2 + p$	$(0 < p < 1/2)$

(8.C.1)

The value of p may be interpreted as reflecting the magnitude of environmental effects on sex determination; the environmental effects are smallest with p near $1/2$ and largest at $p = 0$. Conversely, the sex factors have larger effects with p near $1/2$ than near 0. Due to the symmetric effects of G and g about a sex ratio of $1/2$, and because the selected sex ratio is $1/2$, the equilibrium for this system is with G and g equally common in zygotes (under the usual assumption of random mating). Since G is more common than g in females but less common in males, the frequency of genotypes depends on p in a complicated way.

With three genotypes in each sex, there are nine possible ordered matings, and five distinct family sex ratios: $1/2 - p$, $1/2 - p/2$, $1/2$, $1/2 + p/2$, and $1/2 + p$. The frequency of these different family types varies with p , but in general, the sex ratio variance between families increases with p , as the magnitude of environmental effect decreases (Fig. 8.C). This figure shows the

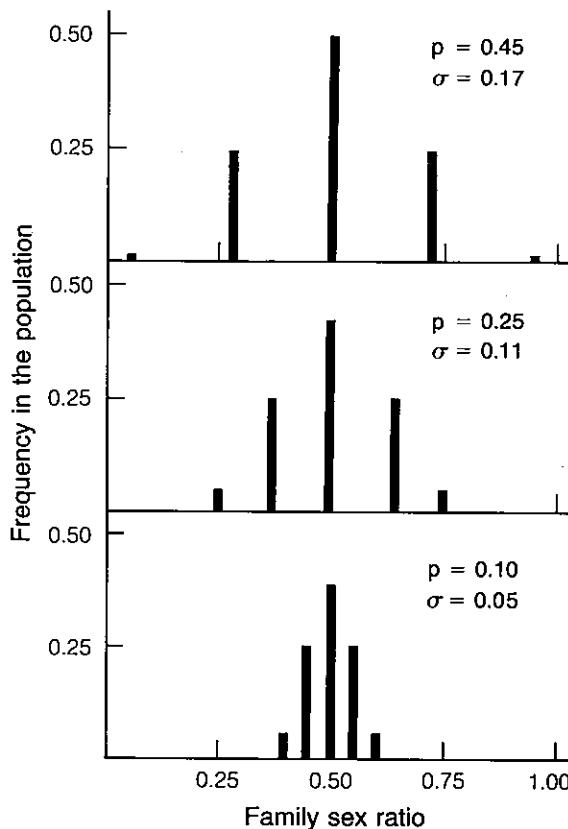


FIGURE 8.C. Distributions of the true family sex ratios under 2-factor sex determination with environmental variance. The population sex ratio is 1/2. GG becomes male with probability $1/2 - p$, Gg with probability 1/2, and gg with probability $1/2 + p$. The standard deviation of the between-family sex ratio variation (σ) is shown for each value of p .

distribution of the five theoretical family sex ratios for three values of p . The distribution consists of five spikes, but a plot of the *observed* family sex ratio would be considerably smoother, if family size was small and there were mild environmental influences on family sex ratio.

This model demonstrates that there can be a large between-family variance in sex ratio, even though only two sex factors are present. Furthermore, in this model, mothers and fathers differ in their tendency to produce sons, and the sex ratio could be selected in either direction. These are the criteria usually regarded as evidence of polyfactorial sex determination, yet the system has only two factors. While it certainly would be difficult to experimentally diagnose this system as a 2-factor system for most values of p , and it therefore might have to be treated the same as systems with many sex factors, any

conclusion about the number of sex factors from these observations should be avoided.

D. The Number of Factors

As illustrated above, the three properties cited in support of polyfactorial sex determination do not discriminate between systems with few sex factors and those with many. How, then, can the number of sex factors be calculated? This question turns out to be a problem of interest in the field of quantitative genetics, quite aside from sex determination, and one aspect of it—estimating the number of loci—has been studied in detail (reviewed in Wright, 1968, Chapter 15; Lande, 1981). Unfortunately, an analysis of sex determination using these methods may prove difficult.

(i) Perhaps the most generally useful method of estimating the number of loci influencing a typical quantitative trait is based on the “segregation variance.” If two strains differing in the mean value of a trait are hybridized, there is an increase in the variance of the trait between the F_1 and F_2 generations, resulting from the segregation of loci affecting the trait. The magnitude of this increase enables calculating an “effective” number of loci (i.e., assuming that all loci are unlinked and have equal effects). Unfortunately, there are serious complications in applying this method to polyfactorial sex determination, because there are no simple methods of measuring variances in the unseen distribution of genetic and environmental effects controlling sex determination. These methods could be applied to some forms of environmental sex determination, since the variance of the underlying distribution may be measured according to the relation between sex ratio and the environmental factor (Chap. 9).

(ii) A second and similar method lends itself to this problem, although it has restricted applications in practice. (I will discuss it only as it applies to sex determination.) Visible markers heterozygous in parents and linked to sex factors appear disproportionately in sons and daughters. This method is of course commonly used to identify male and female heterogamety and multiple-factor systems (Chaps. 2 and 3), but the same principle applies to weaker sex factors. For example, a male heterozygous at a sex factor locus and at a closely linked marker locus will transmit the marker differentially to sons and daughters, according to the sex factors’ effects and their linkage to the markers. The best species for this type of analysis may be poeciliid fish, because they often have many color polymorphisms that could serve as markers. In fact, some swordtail data presented by Breider (1935, pp. 413–4), although intended to reveal the effect of different sires on progeny ratio, seem also to reveal a sex factor linked to the *Mo* locus. Heterozygous females were mated to homozygous males, and the sex ratios were the following (family sizes are in parentheses):

Parents		Progeny Genotype	
(mm x Mm)		Mm	mm
Sire	Dam		
1	1	.37 (142)	.62 (104)
1	2	.28 (38)	.70 (28)
2	1	.06 (35)	.44 (47)
2	2	.08 (43)	.63 (30)

Of the eight sex ratios, all four from the *Mm* progenies were lower than each of the sex ratios from *mm* progenies, a difference not likely the result of chance (2-tailed Fisher's exact test, $p = 1/35$). (A more sophisticated analysis is made possible by incorporating family sizes, but the sex ratios given by Breider—to three significant figures—do not correspond in many cases with sex ratios which can be attained in these family sizes, so I have omitted them from the comparisons.)

These results indicate that the linkage group of *Mo* had a substantial effect on sex determination. This conclusion is not surprising in view of the fact that *Mo* is actually a sex-linked gene of *X. maculatus*, so Breider's fish probably had *X. maculatus* sex chromosomes carrying the *Mo* gene (Kallman and Atz, 1967; Kallman, pers. comm.). Yet despite the fact that these fish were not pure *X. helleri*, the data provide a valid illustration of how markers may be used to identify linkages containing sex factors. The next step would be to consider how much of the sex ratio variation between families is accounted for by the *Mo* linkage (assuming the presence of just two factors) and thus whether there are sex ratio effects attributable to more than just two sex factors.

This method is reliable only for species with an abundance of markers, because in order to obtain a significant result, the markers must be closely linked to the sex factors. If only a few loci segregate sex factors, and only a few markers are available, the markers and the sex factors may occur on different chromosomes, and the lack of a correlation between sex ratio and the markers could be interpreted (incorrectly) as indicative of many minor factors. However, if this method was used merely to identify individual factors, the number of factors detected would necessarily be a minimum of the actual number.

(iii) A straightforward method of estimating the number of factors influencing sex determination may be feasible with clones of the zebra fish (Streisinger et al., 1981). Clones of genetically homozygous fish may be produced artificially; data presented in Section 8.C illustrated that the sex ratio varies between clones. The number of clones with distinct sex ratios indicates a minimum number of sex factors, and their magnitudes of effect can be estimated from the sex ratio differences (assuming that differential mortality may be excluded). Strains with different sex ratios may be crossed to study the genetics and interactions of the factors.

E. A Formal Model and Its Evolutionary Implications

This section develops the additive-value model of Section 4.E for polyfactorial sex determination, following the models proposed by Winge (1934), Kosswig (1964), and Yamamoto (1969). The model assumes that many minor sex factors segregate in the population, and that each sex factor is assigned a numerical value (sex tendency). An individual's sex is determined by its total value relative to some threshold, where the individual's total value is the sum of values over all loci plus an environmental effect (Sec. 8.C). If the threshold is taken arbitrarily as V , then individuals whose value exceeds V are males, and if their value is less than V , they are females.

Before progressing with this model, three points of clarification will be offered. First, although the observations on polyfactorial mechanisms do not indicate whether the assumption of many sex factors is appropriate, the results of this model may not depend greatly upon the number of factors as long as they have individually weak effects. Second, it makes no difference if sex tendencies are assigned to all loci or only to sex factors; the absolute values of sex tendencies are also irrelevant except among sex factors at the same locus. Variations of these types are equivalent under appropriate translation of the threshold. Third, the magnitude of the environmental effect is assumed to be arbitrary, merely influencing the probability that particular male genotypes become female and vice versa. The magnitude of the environmental effects within a particular population may be ascertained from the analysis of family sex ratios (cf. Bull, Vogt, and Bulmer, 1982).

To continue with the presentation of this model, the letter S is used to represent the sex determining variable, which is now the sum of sex tendencies over all loci plus an environmental effect (Fig. 8.E). Each individual is born with a particular value of $S = s$ and becomes male if $s > V$ or female if $s < V$ (the threshold value, V , is arbitrary). It is therefore assumed that no intersexes occur; observations on poeciliid fish presumed to have polyfactorial sex determination suggest that intersexuality is in fact almost non-existent (Yamamoto, 1969; Kosswig, 1964; Kallman, 1983). The distribution of S generated under this model has not been studied, although Yamamoto (1969) and Bulmer and Bull (1982) supposed that it would be normal. Normality may not be strictly appropriate because mating is always between individuals from opposite sides of the threshold. The sex ratio in the population is determined by the mean and variance of S relative to the threshold V (Fig. 8.E).

A polyfactorial system of this sort exhibits a property known as *heritability*, which describes collectively the transmission of the sex factors. Some males and some females will be more inclined than others to produce sons because they have large relative values of S , and the heritability determines the extent to which parents with different values of S produce different sex ratios. In turn, the heritability determines the rate at which the mean population value of S evolves in response to selection of the sex ratio. While heritability is a highly superficial description of heredity, a more detailed specification of inheritance

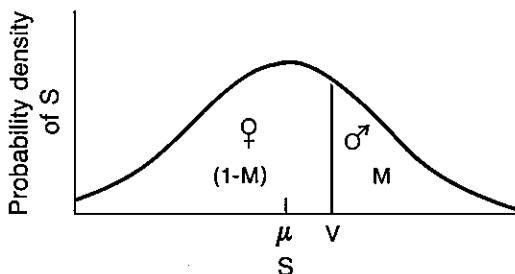


FIGURE 8.E. Model of polyfactorial sex determination. Each zygote is born with a value of the character $S = s$, determined as the sum of sex tendencies over all loci plus an environmental effect. Sex is male if $s > V$, female if $s < V$, where V is the threshold value. The sex ratio in the population is M ; μ is the mean value of S in the population. (From M.G. Bulmer and J.J. Bull. 1982. "Models of polygenic sex determination and sex ratio evolution." *Evolution* 36:13–26, Figure 1. Reprinted by permission of the Society for the Study of Evolution.)

proves cumbersome. The heritability specifies some useful properties of the system, and it is readily measurable, so further description of the system is rarely warranted. Formally, the heritability is defined as the ratio of the additive genetic variance in S to the total variance in S , so that it must lie between 0 and 1, and the heritability decreases as the environmental effect increases (explained further in Falconer, 1981; Crow and Kimura, 1970).

There are three important evolutionary consequences if the character S is heritable: (i) some parents from each sex are more inclined to produce sons than others, so that (ii) the between-family variation in sex ratio is greater than that experienced in families with XX/XY mechanisms, and (iii) the sex ratio may be selected. These properties are of course the ones regarded as evidence of polyfactorial sex determination (Sec. 8.B).

This model of polyfactorial sex determination was analyzed by Bulmer and Bull (1982). Assuming that S was normally distributed in a randomly mating population, the following conclusions were drawn: (i) the sex ratio evolved toward 1/2 at a rate proportional to the heritability times the deviation of the population sex ratio from 1/2 (this held true even in the absence of the normality assumption). Thus the magnitude of the environmental effect on sex determination influenced the rate of evolution. (ii) The genetic variation in S increased as the sex ratio evolved toward 1/2, partly through an increase in heterozygosity of sex factors. The variance in S was not selected once the sex ratio equilibrated. (iii) There was a negative correlation ($-.64$) between the S -values of eggs and sperm, because males tended to have high values and females have low values. The negative correlation creates an excess of heterozygotes and negative linkage disequilibrium: if the factors did not affect sex determination, there would be fewer heterozygotes and a higher frequency of gametes with similar values at the different loci.

One obvious consequence from both the environmental component and the multiple-factor effect on sex determination is that the distinction between a heterogametic and homogametic sex is no longer observed: some males and some females will be heterozygous and others homozygous for each sex factor. Winge (1934) apparently neglected this point when arguing that he had selected a new system of male or female heterogamety in his XX strain of guppies (derived from an XX/XY strain). There was in fact a large seasonal effect on the sex ratio in the XX strain, suggesting a major environmental effect on sex determination (temperature), and he further supposed a polyfactorial basis for the rare XX males in the ancestral XX/XY strain. In either case, a heterogametic mechanism would not have resulted in his XX strain. Similarly, claims of discovering the heterogametic sex in species with environmental sex determination are unfounded (e.g., Engel et al., 1981).

F. Coexistence of Polyfactorial and Major-Factor Sex Determination

Up to this point, polyfactorial sex determination has been treated separately from major-factor sex determination. What happens when sex is determined according to many minor factors and two major ones? This question is motivated by the studies of fish in which strains of XX males and females were selected from male heterogamety (as above), since it seemed that minor factors led to the occurrence of XX males.

An appropriate model was provided by Yamamoto (1969), presented here and modified slightly: a polyfactorial system with minor factors also segregates two major factors, X and Y (Fig. 8.F.1). The major factors are each assigned large *S*-values, and the distribution of minor factors is superimposed. A threshold *V* is chosen so that XY is essentially always male and XX is usually

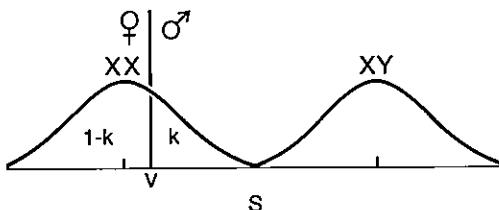
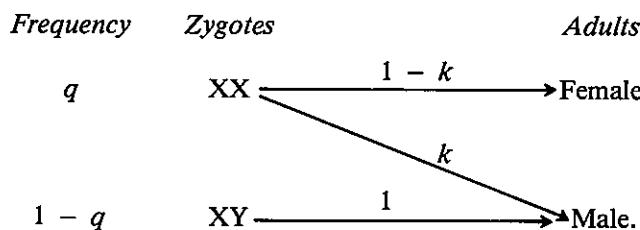


FIGURE 8.F.1. Model of polyfactorial and major-factor sex determination. XX usually becomes female, XY is always male, but there is an underlying polyfactorial distribution of sex factors with small effects, and XX zygotes whose combined XX and polyfactorial value exceeds the threshold *V* are male. (Based on T. Yamamoto. 1969. "Sex differentiation." In: *Fish Physiology*, Vol. 3, edited by W.S. Hoar and D.J. Randall. Academic Press, New York, pp. 117-177, Figure 6.)

female, but for unusually large values of the underlying polyfactorial character, XX becomes male. (A similar scheme could be proposed for XY females, but the math is straightforward if XY is always male, and no qualitatively unique conclusions are lost by this restriction.)

Assume that a proportion q of the zygotes are XX, and let a fraction k of XX become male. The value of k is determined by the distribution of minor sex factors relative to the threshold V and by the S -value of XX, so the value of k may therefore evolve. The value of q is also selected. It is complicated to describe the joint evolution of both q and k , and only q is considered in this superficial treatment. Therefore this analysis will be confined to a single generation, so that the value of k does not change:



This system is analyzed as follows (see Scudo, 1964, for an analysis with fixed k). The sex ratio is simply

$$M = qk + 1 - q = 1/2 - (1 - k)(q - 1/[2(1 - k)]). \quad (8.F.1)$$

The frequency of XX zygotes in the next generation is given by

$$q' = \frac{qk + (1 - q)/2}{M}, \quad (8.F.2)$$

which becomes

$$\{q' - 1/[2(1 - k)]\} = \frac{k}{M} \{q - 1/[2(1 - k)]\}. \quad (8.F.3)$$

To complete this set of equations, the evolution of k must be specified, but the important conclusions are evident without considering the evolution of k . (A model which specifies the evolution of both q and k is presented and studied numerically in Bull (1981a), although it ignores covariances between the major and minor factors.)

From equation 8.F.3, the value of q does not change if $q = 1/[2(1 - k)]$; there is also no selection of k under these conditions (not shown here). These results indicate that *a continuous path of equilibria exists from polyfactorial sex determination to major-factor sex determination* (Fig. 8.F.2). At the endpoint representing male heterogamety, XX is always female and all males are

XY ($k = 0$ and $q = 1/2$). At the other endpoint, half the XX zygotes become male, and XY is absent ($k = 1/2$ and $q = 1$), so sex is determined entirely by the polyfactorial character S . As expected, the sex ratio is $1/2$ at all these equilibria (from equation 8.F.1). Numerical studies indicated that this set of equilibria is approached without complication (Bull, 1981a).

If either male genotype, XX or XY , is superior to the other, the system should evolve to the establishment of the most fit male. Again, with weak selection, this transition occurs approximately along the former path of equilibria. The only known examples relevant to this process are the XX males selected from male heterogametic strains of poeciliid fish (Sec. 8.B; Winge, 1934; Aida, 1936; Oktay, 1959a, b). In these experiments, however, selection of XX males was extreme and rapid, rather than gradual, and the sex ratio did not necessarily evolve to $1/2$ once the XX males replaced the XY males. The failure to evolve a sex ratio of $1/2$ in the XX strains may have been due to exhaustion of genetic variability, either from the extreme selection and/or from maintaining stocks with few individuals. In nature, a slight advantage of XX males

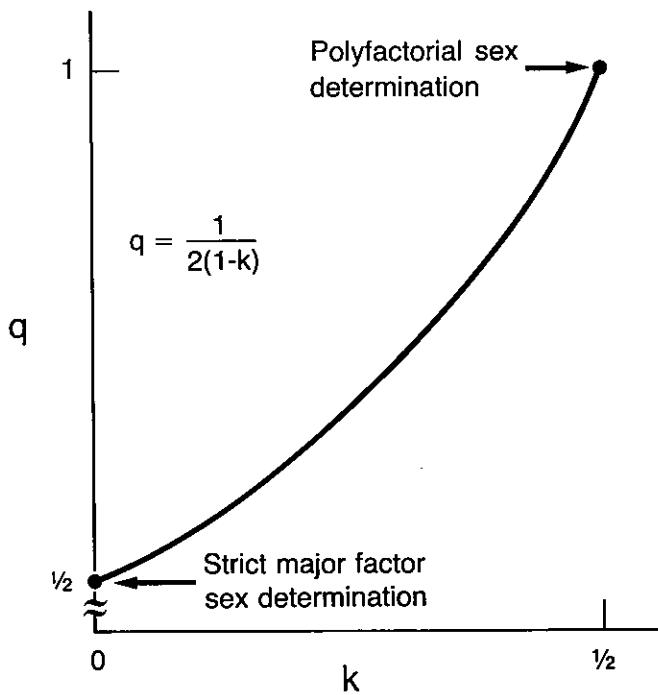


FIGURE 8.F.2. Equilibrium conditions for the coexistence of major-factor and polyfactorial sex determination. q is the frequency of XX zygotes, k is the fraction of XX which become male. All points on the curve are equilibria, so there is a continuum of equilibria between strict major-factor sex determination ($k = 0$) and strict polyfactorial sex determination ($k = 1/2$).

would cause a more gradual evolution, and mutations would perhaps maintain variation throughout the process, with the sex ratio remaining near 1/2.

The polyfactorial concept formulated by Winge (1934), and the extent that it derived from Bridges' genic balance theory, was not merely a theory advocated for sex determination in some fish. Winge regarded the polyfactorial theory as most soundly supported by the guppy data, but he also extended it to explain atypical sex determination occasionally observed in other species. Thus Winge (and Bridges) regarded minor polyfactorial variation as a common feature of sex determining mechanisms. As Winge was well aware, the underlying polyfactorial variation should sometimes lead to XX males or XY females (assuming male heterogamety). However, such exceptional sex determinations are unreported in a great many species with heterogametic sex determination, or, as is now known, they occur as the result of well-defined transformer mutations of major effect. There is no evidence of a significant polyfactorial influence from many species, in contradiction to the supposed ubiquity of minor sex factors. Of course, since exceptional sex determinations have been carefully studied in only a few species, they may have been overlooked in many others, so it will be important to have this problem investigated specifically before firming conclusions from this evidence on the general existence of underlying polyfactorial variation in sex factors.

An absence of minor sex factors could either stem from an absence of appropriate mutations, or from selection against weak sex factors. Nothing in this analysis suggests whether major factors are superior to minor ones, since both types coexist at equilibrium in the above model. However, disadvantages of polyfactorial systems can be anticipated: (i) individuals whose *S*-value lies near the threshold may be prone toward intersexuality (although intersexes are essentially unknown in poeciliid fish), or (ii) minor factors may be susceptible to systematic environmental effects, leading to fluctuations in the population sex ratio (explained further in Sec. 10.D). At present, the apparent absence of minor sex factors in systems of male and female heterogamety is unexplained.

G. Summary

This chapter considered several aspects of polyfactorial sex determination. Here, polyfactorial sex determination was used as a heterogeneous classification, to include sex determining mechanisms with many sex factors as well as mechanisms with few factors that also have a substantial environmental component (although excluding environmental sex determination, Chapter 9). I distinguished polyfactorial systems from the multiple-factor systems of previous chapters because multiple-factor systems are subject to an exact description, whereas polyfactorial systems are not usually amenable to exact characterization, either because of the many factors or because of the environmental component. The earliest model of polyfactorial sex determination

was one in which weak sex factors were assumed to segregate at many loci (Winge, 1934), a concept that seemed to gain prominence in part because of its parallel with the theory of genic balance. However, the evidence used to document the existence of polyfactorial sex determination has not indicated whether many sex factors are present in these systems. The two final sections considered the evolutionary consequences of a polyfactorial system: the sex ratio evolves toward 1/2 under random mating, and major factors may coexist in a population with an underlying polyfactorial mechanism of weak sex factors. Some of the most important work remaining for these mechanisms concerns evaluating the number of sex factors and loci, as well as investigating heterogametic sex determining mechanisms for exceptional sex determinations (e.g., XX males or XY females under male heterogamety), which may bear upon the existence of underlying polyfactorial variation.

9

Environmental Sex Determination (ESD)

The first part of this chapter will describe detailed examples of environmental sex determination in a marine worm (Sec. B), mermithid nematodes (Sec. C), some reptiles (Sec. D), and a fish (Sec. E). The end of this chapter will review several less thoroughly studied examples of environmental sex determination (Sec. F); it will also review systems of genotypic sex determination subject to occasional or artificial environmental influences (Sec. G).

A. The Meaning of Environmental Sex Determination

In some species sex is determined after conception according to the immediate environment. Some environments are therefore associated with male production and others with female production. This mechanism is called environmental sex determination (henceforth ESD), because the earliest ontogenetic distinction between the sexes is an environmental one (from the definition of the classical sex determining mechanism). The individual's genotype therefore has little influence on whether it becomes male or female, although it is not supposed that sexual development occurs without the participation of genes. The examples of ESD described in this chapter are confined to mechanisms in

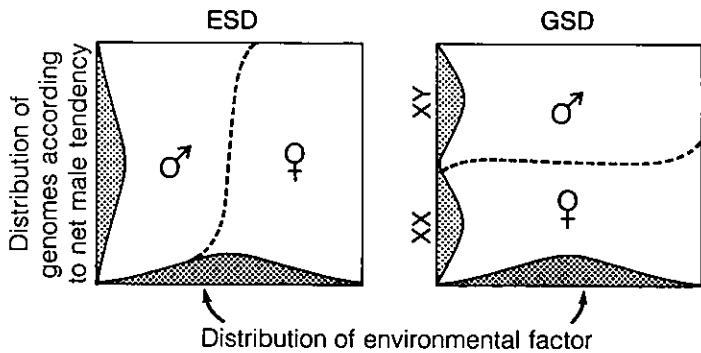


FIGURE 9.A. A graphical representation of the distinction between environmental and genotypic sex determination. Under ESD, genetic differences among individuals have little influence on sex determination relative to differences of some appropriate environmental factor. Under GSD, such as male heterogamety, XY is usually male and XX is female, regardless of environmental variation.

which sex is determined prior to maturity for the remainder of the individual's life. Various types of environmental influences on sex determination are also known from individuals that change sex, but sex change will not be considered here (see Charnov, 1982, for a treatment of sex change).

Graphically, ESD may be contrasted with genotypic sex determination (GSD) as in Figure 9.A. A mechanism is classified as ESD if *any* environmental factor commonly influences sex determination in nature, even if all other environmental factors are without sex determining influence. The distinction between ESD and GSD is necessarily one of degree, since all ESD systems probably experience at least slight inherited effects on sex determination, and many GSD systems may experience rare environmental influences (see Sec. 9.G). Thus the capacity for ESD is apparently common, but it is uncommonly manifested to such an extreme that environmental effects on sex determination dominate over genetic effects.

B. A Marine Worm

ESD was first observed in *Bonellia viridis*, a marine, echiurid worm (Baltzer, 1912, 1914; Leutert, 1975; the summary here of Baltzer's work was derived from reviews in Bacci, 1965, and Crew, 1965). As adults, these largely sessile worms inhabit the marine substrate. The females possess a long proboscis for feeding; the males live a dwarf, parasitic existence on females. Larvae are planktonic and differentiate sex after settling from the water column: those which settle on adult females become males and those which settle in isolation

become females (Baltzer, 1912, 1914; Bacci, 1965; Crew, 1965; Leutert, 1975).

The basic observation from these studies is that nearly all developing larvae become females if raised in isolation or become males if raised in association with adult females (or with substances derived from females). By itself, this observation can be explained either by ESD or by GSD with differential mortality of larvae, but two experiments refute the differential mortality hypothesis. First, Leutert (1975) observed that, under laboratory conditions, significantly more than half the initial number of larvae differentiated as male under the influence of adult females, while more than half differentiated as females when unexposed to this stimulus. The proportions differentiating as one sex significantly exceeded one half even if all dead and undifferentiated larvae were assumed to belong to the rarer sex. Second, Baltzer observed that intersexual development was induced if larvae were exposed to adult females before being raised in isolation; at least for short periods of exposure, the degree of intersexuality increased with the length of exposure to the adult females (reviewed in Bacci, 1965; Crew, 1965). Neither observation can be plausibly explained under a hypothesis of strict GSD and differential mortality of the male and female larvae.

Not all larvae under a particular environmental regime differentiated in the same direction. In Leutert's experiments, about 3% of the larvae differentiated as male when unexposed to a female (proboscis) while as many as 10% differentiated as female when unexposed to a proboscis. The possibility of a hereditary basis for these exceptions was not investigated.

C. Nematodes

Environmental sex determination has also been observed in nematodes (round-worms) of the family Mermithidae (see Charnov, 1982, for a treatment similar to the one given). Mermithids are free living as adults, but as larvae they parasitize insects. In this parasitic stage, the larvae are nourished entirely by the host insect, and the worm's growth therefore depends on the resources extracted from the host. The host is killed when the worm finally exits the host. (See Christie, 1929, Welch, 1965, and Poinar, 1979 for life history details.)

Mermithids utilize host resources so efficiently that a crowding effect occurs. Smaller hosts produce smaller worms, and in the case of multiple infections, the average worm size decreases with the number of worms inhabiting the host. Small worms may also require a shorter developmental time than large worms. The worm's growth apparently ceases when it leaves the host, although in some species, the worm does not mature for several months after leaving the host. Mating invariably occurs outside the host. Several factors influence sex determination in mermithids, all of which seem to reflect the nourishment available to the worm.

Host Crowding. The first observation of environmental sex determination in mermithids was discovered in relation to the number of worms present in the host. Caullery and Comas (1928) and Christie (1929) showed that the proportion of male worms found within a host increased with the number of worms per host: hosts with one or two mermithids produced nearly all females, while hosts with many worms produced nearly all males. Christie's data for *Mermis subnigrescens* were as follows (here in condensed form)*:

No. of Worms per Host	Total No. of Worms		Sex Ratio
	♂	♀	
1-5	8	107	.07
6-10	18	47	.27
11-15	48	81	.37
16-72	770	17	.98.

Christie (1929) also investigated the possibility that the sex ratio variation was due to differential mortality. He fed grasshoppers a fixed number of nematode eggs and counted and sexed the resulting worms**:

No. of Eggs/Host	Total No. Eggs	Adults		Sex Ratio
		♂	♀	
20-30	100	86	0	1.00
4-5	102	6	67	.08.

Some of the eggs failed to develop, but even assuming that all these unknowns were of the rare sex, these data still depart significantly from the hypothesis that sex is determined genotypically, independent of host crowding (Fisher's exact test).

The host-crowding effect has been demonstrated in other mermithids, especially those parasitizing midges, blackflies, and mosquitoes (a few studies are Johnson, 1955; Petersen, 1972, 1977; Ezenwa and Carter, 1975; Harlos et al., 1980). From these and other studies it is possible to elaborate on the nature of the crowding effect. Petersen (1972, 1977) showed that host size at the time of entrance by the nematode had little effect on sex ratio, and Christie (1929) and Petersen (1972, 1977) showed that, with a given number of worms per host, smaller host species were more inclined to produce male worms than

*Based on J.R. Christie. 1929. "Some observations on sex in the Mermithidae." *Journal of Experimental Zoology* 53: 59-76, Table 1.

**Based on J.R. Christie. 1929. "Some observations on sex in the Mermithidae." *Journal of Experimental Zoology* 53: 59-76, Tables 2 and 3.

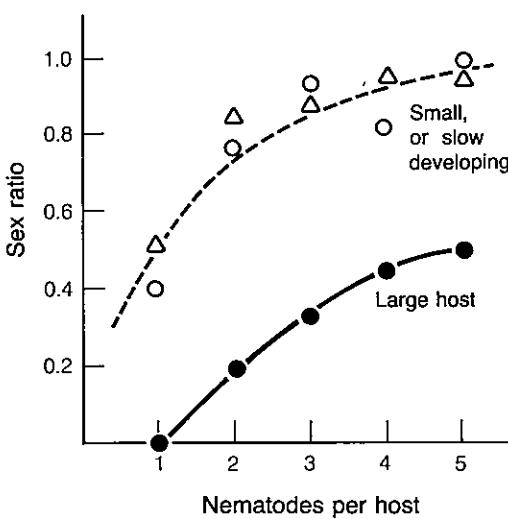


FIGURE 9.C. Sex determination in a mermithid (*Romanomermis culicivorax*) as a function of the size of host (mosquito larva). At a given infection rate, worms were more likely to be male in small hosts than in large hosts. Solid circles—*Psorophora confinis*, a large species; open circles—*Uranotaenia sapphirina*, a small species; triangles—*Culiseta inornata*, a large species that develops slowly; this last species was effectively a small host because worms emerged before the host reached its largest larval stage. (Based on J.J. Petersen. 1972. "Factors affecting sex ratios of a mermithid parasite of mosquitoes." *Journal of Nematology* 4:83-87, Figure 4.4.)

larger species (Fig. 9.C). These studies demonstrated that sex is determined according to the amount of host available to the developing worm, rather than according to the infection rate *per se*.

Parenti (1965) investigated sequential infestation of mosquito larvae by *Paramermis*. Curiously, worms were more inclined to become female if they entered a host already harboring a male than if they entered a host not previously parasitized. This observation is not expected if sex is determined strictly according to host crowding, unless there was a bias such that hosts harboring two parasites were in fact larger than those harboring one parasite. Moreover, the sex of the later worm may be irrelevant, if the first worm emerges and kills the host before the later worm fully develops.

Host Nutrition. The nematode sex ratio becomes increasingly female-biased with increased nutrition of the host. Petersen (1972) infected mosquito larvae with *Romanomermis culicivorax* and separated the hosts into two groups,

those that were starved and those fed normally. The starved mosquitoes produced a much higher proportion of males than those fed normally*:

Worms/ Host	Sex Ratio			No. of Hosts (starved/fed)
	Starved Host	Fed Host		
1	.92	.13		97/26
2	.97	.46		39/81
3	1.00	.64		3/60
4	—	.67		0/22
5	—	.76		0/5
6	—	.83		0/2

Also, nematode parasites of mosquitoes were more apt to become female if their host was fed a blood meal rather than only sucrose (Harlos et al., 1980): in sucrose-fed female mosquitoes, only 2% (3 of 125) of the infecting worms became female, but in female mosquitoes fed both blood and sucrose, 27% (27 of 104) of the worms became female. In field collections, female worms were obtained only from female mosquitoes, and there were usually multiple infections in these as well.

Ancestry. The ancestry of ESD in mermithids is unknown, although XX/XO sex chromosome systems and multiple sex chromosome derivatives are widespread in other groups of nematodes (discussed in this context by Bull, 1981a). The XX/XO systems are so well established, that the hermaphroditic nematode *Caenorhabditis elegans* produces occasional (XO) males by non-disjunction of what may be this ancestral X (recall Sec. 4.B). If similar observations were obtained for mermithids, it would suggest that ESD ultimately originated from male heterogamety.

Parthenogenesis. Some female mermithids are capable of producing offspring in the absence of males. Christie (1929) stated that female *Mermis subnigrescens* were capable of parthenogenesis, while virgin female *Agameris decaudata* did not produce offspring and so were perhaps incapable of parthenogenesis. Parthenogenetic reproduction by an individual *Culicimermis sp.* was reported by Harlos et al. (1980), although the total number of worms studied for this phenomenon was not stated. In these species capable of parthenogenesis, the frequency of parthenogenetic births in the population is unknown, but the high frequency of males in nature suggests that parthenogenesis is not commonly practiced.

*Based on J.J. Petersen. 1972. "Factors affecting sex ratios of a mermithid parasite of mosquitoes." *Journal of Nematology* 4:83-87, Table 5.

Plant Parasites. Nematodes from the taxonomic family Heteroderidae may have ESD, although the evidence is equivocal (reviewed by Triantaphyllou, 1973, 1976). These worms infect plant roots, and the adult sex ratio becomes increasingly male biased under stressful or crowded conditions. Ellenby (1954) reported ESD in *Heterodera*, based on the sex ratio difference between crowded and uncrowded conditions, but now it seems more likely that sex differential mortality is the proper explanation (Triantaphyllou, 1973). ESD has been demonstrated in *Meloidogyne incognita* as a response to nutrition (Triantaphyllou, 1973). Under favorable conditions, worms become female; under unfavorable conditions, worms become male. By altering the state of the environment from favorable to unfavorable at a critical stage during development, the worms developed as male with testes, but the gross morphology of these testes was otherwise characteristic of female gonads, thereby excluding the possibility that the sex ratio biases were due to differential mortality. Surprisingly, this species' reproduction is exclusively parthenogenetic, without males (Triantaphyllou, 1976). Not all *Meloidogyne* species are totally parthenogenetic, so it may be that ESD operates in some of the partly sexual (amphimictic) species, but this hypothesis has not been investigated.

D. Reptiles

In a variety of lizards, turtles, and crocodilians, sex is determined during embryogenesis by the incubation temperature (reviewed in Bull, 1980; with original data in Charnier, 1966; Pieau, 1971, 1972, 1973, 1974, 1975a, 1976, 1978, 1982; Yntema, 1976, 1981; Yntema and Mrosovsky, 1980, 1982; Bull and Vogt, 1979; Bull, Vogt, and McCoy, 1982; Ferguson and Joanen, 1982; Vogt et al., 1982; Wagner, 1980; Moreale et al., 1982; Miller and Limpus, 1981). This phenomenon was originally discovered in reptiles by Charnier, but Pieau's extensive work was instrumental in characterizing it and in bringing it recognition. The reptiles in which this mechanism is known are all egg-layers that place their eggs in the ground or, as in some crocodilians, eggs are placed in constructed mounds. The ambient temperature of the external environment is therefore likely to have a major effect on sex determination. The hatchlings do not mature for months, or usually years, so there is never mating within the nest. Few live-bearing species have been studied for temperature-dependent sex determination.

The sex ratio biases under these ESD mechanisms are often extreme. In the majority of species studied, most incubation temperatures produce only males or only females, with a narrow range of temperatures producing both sexes. In map turtles, for example, only males are obtained at 23–28 °C, both sexes are obtained in the range 28–30 °C, and essentially only females are obtained above 30 °C (Fig. 9.D.1). This abrupt change in sex ratio over a narrow temperature range is visually suggestive of a threshold, so the temperature

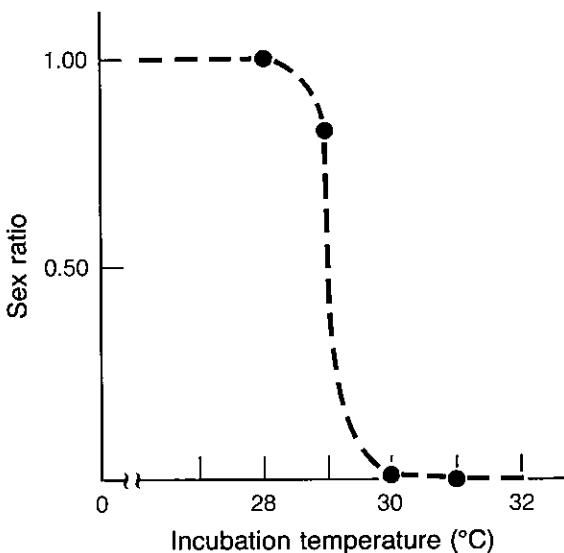


FIGURE 9.D.1 Sex ratio as a function of incubation temperature in Ouachita Map Turtles from eggs incubated at constant temperature. There is an abrupt change, over 2 C°, from all males to all females. The dashed line is the hypothetical relation based on the data points. (Data from Bull and Vogt, 1979, and Bull, Vogt, and McCoy, 1982; redrawn from M.G. Bulmer and J.J. Bull, 1982. "Models of polygenic sex determination and sex ratio evolution." *Evolution* 36:13–26, Figure 2.)
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producing a sex ratio of 1/2 is called here the "threshold temperature" (Yntema and Mrosovsky, 1980; and Mrosovsky, 1980, use the term "pivotal" temperature).

Temperature-dependent sex determination has been documented in the laboratory under constant and fluctuating temperature regimes, and in natural nests for a few species, but most studies are confined to constant-temperature incubation (reviewed in Bull, 1980). It has also been shown for several species that sex ratio biases associated with temperature are not due to differential mortality of the sexes (Bull and Vogt, 1979). In most studies, sex has been diagnosed by gonadal inspection of hatchlings, so it is a point of concern that these reptiles might change sex prior to maturity. However, the hatchlings from some turtle species were raised for three months, and the sexes still corresponded to incubation temperature (Yntema, 1976; Bull and Vogt, 1979); Wagner's (1980) demonstration of temperature-dependent sex determination in a lizard was based on the sex of animals that were nearly mature, so there is at least circumstantial evidence that the temperature effect is permanent.

Considerable variation exists among the reptilian mechanisms of temperature-dependent sex determination (Fig. 9.D.2). In lizards and alligators, warm temperatures produce males and cool temperatures produce

females (Charnier, 1966; Wagner, 1980; Ferguson and Joanen, 1982). This pattern is reversed in most turtles (above references, reviewed in Bull, 1980). A third pattern of ESD is shown with females developing at extremely low as well as high temperatures, and males developing at intermediate temperatures. This third pattern is known in snapping turtles (Yntema, 1976, 1979), and probably also occurs in mud and painted turtles and at least one species of crocodile (Vogt et al., 1982; Gutzke and Paukstis, 1983a; Webb et al., 1983).

Temperature-Sensitive Stages. Temperature-sensitivity in the embryonic stages has been studied in snapping turtles (Yntema, 1979), emydid turtles

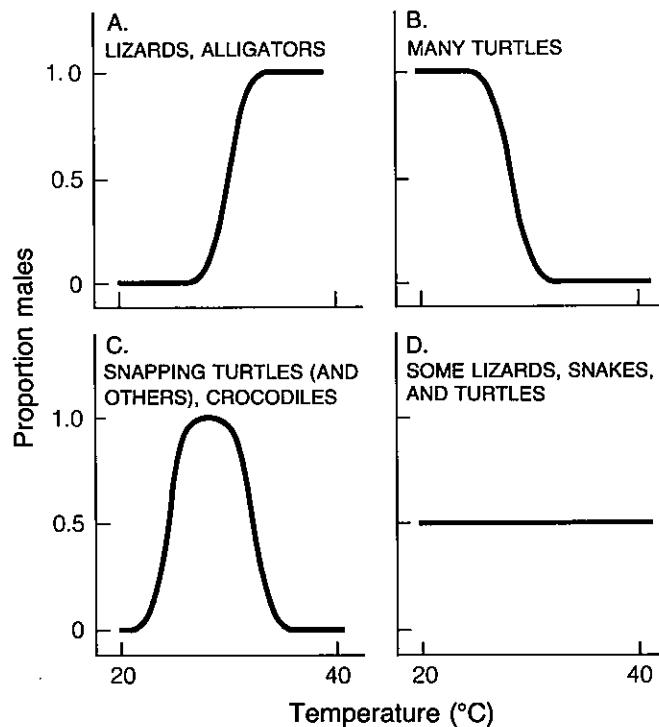


FIGURE 9.D.2. Response of sex ratio to incubation temperature in reptiles. These graphs represent only the approximate form of the response and are not drawn according to any single species. There are four patterns recognized at present. (A) Females develop at low temperature, males at high temperature, as in two lizards and in alligators. (B) The reverse of A, males develop at low temperatures and females at high ones, as in most turtles studied. (C) Females at low and high temperatures, males at intermediate ones. This pattern may be widespread, as it occurs in snapping turtles and perhaps other turtles (see text) and in an Australian crocodile. (D) The hatchling sex ratio of some species is not significantly influenced by incubation temperature. (See text and Table 9.D for references.)

(Bull and Vogt, 1981; Pieau and Dorizzi, 1981), loggerhead sea turtles (Yntema and Mrosovsky, 1982), and alligators (Ferguson and Joanen, 1982). These studies employ two developmental temperatures: male-producing and female-producing. Eggs are incubated at one of the temperatures for a specified part of development, and shifted to the other temperature for the remainder of development. An experiment producing males indicates that sex was determined during the stages exposed to the male-determining temperature, and so forth. The general finding has been that sex is determined during roughly the middle "third" of development, coinciding somewhat with gonadogenesis, although the temperature-sensitive period may be earlier in alligators. In some species there is also an asymmetry in the effect of sequential cool and warm temperatures on sex determination, with one temperature seeming to have a stronger effect. In map turtles, cool temperature seems to dominate over warm, but in snapping turtles the opposite holds (Yntema, 1979; Bull and Vogt, 1981).

Other Factors. Recent work has suggested that sex determination is influenced not only by temperature, but also by the "water potential" available to the egg. At a particular temperature, eggs incubated under dry conditions produced a different sex ratio than eggs incubated under wet conditions, and again this did not seem to be the result differential mortality (Gutzke and Paukstis, 1983b; Paukstis et al., 1983). These results are well-documented, but there are still insufficient data to anticipate generalizations about the influence of dryness on the sex ratio. Since most previous studies investigated just temperature effects, without necessarily controlling water potential, it should be considered that the variation in sex ratios may not have been exclusively the result of variation in temperature.

Patterns of Sex Determination in Reptiles

At least in comparison to a group such as fish, reptiles have conserved sexual patterns. Parthenogenesis is known in several species (Cole, 1975; Peccinini-Seale, 1981), while hermaphroditic species are lacking entirely. However, among reptiles with separate sexes, a diversity of sex determining mechanisms has been observed (Table 9.D). Heteromorphic sex chromosomes are known in many snakes, several lizards, and a few turtles; only male heterogamety is known in turtles, only female heterogamety in snakes, but both are known in lizards (recall Table 2.C.5). Temperature-dependent sex determination is known in two lizards, many turtles, and three crocodilians—in all three orders in which it has been investigated—but many species remain to be studied (Table 9.D). Several species studied for TSD apparently lack it (Raynaud and Pieau, 1972; Vogt and Bull, 1982; Osgood, 1980; Muth and Bull, 1981).

It is likely that species with heteromorphic sex chromosomes do not also exhibit temperature-dependent sex determination. If a species did show both,

TABLE 9.D. Heteromorphic Sex Chromosomes and Temperature-Dependent Sex Determination in Families of Reptiles Studied for Both

Turtles		
Family	HSC	TSD
Chelidae	– (11)	– (1)
Cheloniidae	– (3)	+(3)
Chelydridae	– (2)	+(2)
Emydidae	– (24) + (1)	+(4) – (1)
Kinosternidae	– (3) + (1)	+(2)
Trionychidae	– (3)	– (1)

Sources: for HSC: reviews in Bickham and Carr, 1983; Bickham, 1982; Bull and Legler, 1980; for TSD: from text, plus unpublished data of Bull and Vogt of TSD in *Macroclermys* (a chelydrid), and its possible absence in *Clemmys* (an emydid); unpublished data of Bull and Legler for the absence of TSD in *Emydura* (a chelid).

Crocodilians		
Family	HSC	TSD
Alligatoridae	– (4)	+(1)
Crocodylidae	– (3)	+(1)

Sources: for HSC: Cohen and Gans, 1970; for TSD: Ferguson and Joanen, 1982; Webb et al., 1983.

Squamates: Snakes		
HSC	TSD	
Heteromorphic sex chromosomes characterize all snakes except those with the most primitive morphological characteristics (e.g., boas, pythons, blind snakes); all cases of heteromorphism seem to be homologous, involving female heterogamety of the same ancestral pair (Ohno, 1967; Gorman, 1973; Mendgen and Stock, 1980).	TSD is unknown, but only one species has been studied in detail (Osgood, 1980). Sex ratios of newborns are near 1/2 in many species (Shine and Bull, 1977).	

Squamates: Lizards		
Family	HSC	TSD
Agamidae	– (9)	+(1)
Gekkonidae	– (18) + (2)	+(1)
Iguanidae	– (25) + (6)	– (1)
Lacertidae	– (4) + (3)	– (1)

Sources: for HSC: reviews in Gorman, 1973; King, 1977; Peccinini-Seale, 1981; for TSD: Charnier, 1966; Wagner, 1980; Muth and Bull, 1981; Raynaud and Pieau, 1972.

TABLE 9.D. (cont.)

Rhynococphalia: Sphenodon

Heteromorphic sex chromosomes are not evident in the karyotype of the tuatara (Wylie, Veale, and Sands, 1968), but there has been no study of TSD.

Note: The abbreviation "HSC" represents heteromorphic sex chromosomes, and "TSD" represents temperature-dependent sex determination. For each taxonomic family listed, a number in parentheses preceded by + indicates the number of genera studied in which one or more species shows HSC/TSD. A number in parentheses preceded by - indicates those genera in which all species studied failed to show HSC/TSD. No genus is known to contain species with and species without TSD, but some genera have species with and others without detected heteromorphic sex chromosomes, and these are included in those preceded +. The failure to observe the phenomenon (indicated by -) of course does not imply its absence, since not all species of a genus have necessarily been studied, and both sexes have not necessarily been studied. This table includes all families studied for TSD, but not all families studied for (or observed to have) heteromorphic sex chromosomes.

the sex chromosomes would not correspond strictly to sex, a fact that would be evident in karyotypes (e.g., under male heterogamety some XX would be male or some XY would be female if the environment also influenced sex determination). However, no rigorous experiments have been performed to determine if species with heteromorphic sex chromosomes might reveal temperature-sensitivity under abnormal extremes.

The ancestry of sex determination in reptiles remains obscure. Heteromorphic sex chromosomes and temperature-dependent sex determination are found in the lizards and snakes (squamates) and turtles (Table 9.D). Only temperature-dependent sex determination is known in the crocodilians, although sex chromosomes are found in birds (Ray-Chaudhuri, 1973), and crocodilians are more closely related to birds than to other reptiles. On the one hand, temperature-dependent sex determination may be ancestral to reptiles. Consistent with this hypothesis is the fact that all examples of sex chromosome heteromorphism seem to have been recently derived (Bull, 1980). Perhaps the most remote ancestry of heteromorphic sex chromosomes in reptiles is observed in snakes, but the heteromorphism is not observed all major families, suggesting that it evolved subsequent to their common ancestry (Ohno, 1967). However, this evidence from heteromorphic sex chromosomes does not rule out a remote ancestry of *genotypic sex determination*, because GSD may have been present long before the appearance of heteromorphic sex chromosomes.

Ecology

Relatively little is known about the ecology of temperature-dependent sex determination, although this gap may be short-lived because reptiles are easy to study in the field. The following problems are especially relevant to an understanding of the evolution of the sex ratio and sex determining mechanisms in these species: (i) How do different environmental variables affect nest

sex ratio? (ii) What is the population's primary sex ratio, and what factors control it (such as the role of maternal choice of nest site, and variation between embryos in their sex determination under similar conditions)? (iii) Is the year-to-year hatchling sex ratio influenced by climatic variation? Unfortunately, the study of reptilian population sex ratios is complicated by some major problems such as differential mortality and differential capture of males and females, and reliable estimates of primary sex ratios (in the egg) are not likely to be obtained without great difficulty (the case for turtles is reviewed briefly by Gibbons, 1970).

Pieau (1974, 1982) presented temperatures and sex ratios for some natural nests of the European pond turtle *Emys orbicularis*. Nest temperatures varied several Centigrade degrees over the course of most days, and so many of the nests regularly fluctuated from male-producing to female-producing temperatures. The sex ratio varied according to the amount of time spent at warm versus cool temperatures, but the production of a unisexual nest did not require temperatures to be always in the male-producing or female-producing range (as also illustrated in laboratory experiments with map turtles; Bull and Vogt, 1979).

A study of map turtles by Vogt and Bull (1984) addressed the sex ratios in natural nests. Map turtles (genus *Graptemys*) are North American freshwater turtles from the family Emydidae, the same family to which *Emys* belongs. In a collection of hatchlings from over 200 map turtle nests at one locality in 1980, nearly 80% of the nests were all-male or all-female (about 10 hatchlings per nest on average). Nests that produced males were located amid shading vegetation, which cooled the ground, while nests producing females were predominantly in the open sand, and thus exposed to the sun. Therefore, the sex ratio of individual nests varied largely as a consequence of position on the beach. The results from a 1982 study of this population were qualitatively identical in this respect (Bull, unpubl.). However, Wilhoft et al. (1983) found that in snapping turtles the egg position within the nest as well as nest depth played an important role in sex determination. Snapping turtles lay many more eggs per nest than do map turtles and thus have deeper nests, in which thermal gradients apparently exercise a substantial influence on sex determination.

From the nearly 2000 hatchlings obtained in the 1980 map turtle study, the sex ratio was heavily biased toward females (a proportion of only .24 male), as in collections of adults in the parental population (.2 male, Vogt, 1980). The hatchling sex ratio varied significantly between individual nesting beaches, so the observed hatchling sex ratio in this study may not have represented other nest areas for this population. Also, there was a further presumed bias against locating all-male nests, since they were amid vegetation and difficult to detect. Therefore, the hatchling sex ratio of .24 is to be regarded with skepticism. The observed adult sex ratio was also not necessarily representative of the actual adult sex ratio, nor even of the sex ratio at birth. Nonetheless, the agreement between observed adult and hatchling sex ratios is striking and begs further study.

The observed sex ratio of hatchling map turtles in 1982 was significantly more male biased than in 1980 on three of the four nesting beaches studied, while there was no difference on the fourth beach. The June and July average air temperatures in 1982 were also cooler by 3 °C and 1 °C, respectively, than in 1980. The correspondence between sex ratio and relative summer temperature is therefore consistent with the hypothesis that the climate influenced sex ratio, although many alternative hypotheses cannot be excluded on the basis of these two studies.

Ferguson and Joanen (1982) estimated the population primary sex ratio in alligators. Their study extended four years and involved the collection and incubation of 8000 eggs from nests located in a 2000 acre study site. Care was taken to collect eggs only after the embryos had developed past the temperature-sensitive stages, so that artificial incubation did not affect sex determination. The sex ratio among these alligators was heavily biased toward females: 5 ($\pm .7$) females for each male. Further verification that the primary sex ratio was heavily biased toward females was obtained in the following way. Ferguson and Joanen distinguished two types of alligator nests according to their locations in the swamps: levee nests and marsh nests. The marsh nests were consistently cooler than levee nests, so that marsh nests produced nearly all females while levee nests produced nearly all males. Ferguson and Joanen (1982, Ferguson, pers. comm.) indicated that marsh nests were far more common than levee nests, consistent with the observed excess of females in the sample of hatchlings.

The sex ratio in reptiles with temperature-dependent sex determination is influenced by two properties of the population: (i) maternal choice of nest site, and (ii) embryonic response to temperature in becoming male or female (the threshold temperature). Essentially all aspects of the maternal choice of nest site remain unknown, although the map turtle field study did reveal that not all mothers nest at the same temperature within a season. Threshold temperatures have been studied in different populations of emydid turtles from the northern and southern United States (Bull, Vogt, and McCoy, 1982). Despite the fact that summer air temperatures were 2–3 °C warmer at the southern localities than the northern ones, there did not appear to be much variation in threshold temperatures between these closely related turtle species: seven of the eight populations studied had threshold temperatures between 28 and 30 °C, apparently close to 29 °C. Three of these seven populations were southern and four were northern. A North-South intraspecific comparison of threshold temperatures was possible for each of two species, painted turtles (*Chrysemys picta*) and false map turtles (*Graptemys pseudogeographica*), and both comparisons revealed a lower threshold temperature in the southern population. In the southern painted turtles (from Tennessee), the threshold temperature was at least 1 °C lower than in the northern population (Wisconsin), but the magnitude of difference in false map turtles was less. In fact, the threshold temperature of southern painted turtles was lower than that of all other species studied. The implications of this study will be considered in Chapter 10.

E. Silverside Fish

The Atlantic Silverside, *Menidia menidia*, is a marine fish with temperature-dependent sex determination (Conover and Kynard, 1981; Conover, 1983). Cold temperatures produce predominantly females (as in lizards and alligators), and again it has been shown that the sex ratio biases result from ESD rather than differential mortality. The temperature-sensitive period during development occurs late in the larval phase, about 50 days after hatching, and just prior to metamorphosis. Conover and Kynard (1981) studied sex ratios in fish reared under simulated natural temperature regimes corresponding to the warmest and coldest water likely to be experienced in natural populations. The sex ratios in the cold treatment were only about .2 to .4 lower than the sex ratios in the warm treatment, so the sex ratio of silversides is not likely to be as greatly influenced by variation in the natural environmental temperature as in reptiles.

There may also be a large genetic component to sex determination in these fish. In a comparison of broods from six mothers, all fertilized by the same male, the brood sex ratios within a temperature were highly heterogeneous, and the degree of sex ratio response to temperature also varied between broods.

Conover (1983) investigated the details of the silverside's life history with respect to the implications of ESD (the importance of this life history is considered more fully in Sec. 10.E). Individuals from this species live about one year, spawning only in their second spring-summer of life. No parental care is provided after laying. Spawning occurs near shore in May through July. The water temperature increases during this period, so the sex ratio is female biased among fish born in spring, with the proportion of males increasing progressively throughout the spawning period. Essentially all living adults reproduce periodically over the entire course of the spawning season, rather than some individuals reproducing just in the early phase and others just in the late phase.

The young silversides grow throughout their first summer of life, and those that hatch earlier grow to a larger size than those that hatch later (independently of sex). Thus females are larger on average than males, because the fish produced first in spring become females and the last ones become males. These fish overwinter offshore and do not grow appreciably during this period. Conover (1983) thoroughly investigated the reproductive success of males and females as a function of their size. Large fish from both sexes survived winter better than small fish, and large females spawned more eggs than small females, but it was not apparent if large size was important to a male's reproductive success when spawning.

F. Other Examples

The above examples of ESD are among the most thoroughly researched, but there are other cases in which ESD apparently operates.

(i) *Ione thoracica* is a crustacean parasite of fish gills. The larvae are planktonic and begin parasitism in a sexually indifferent state. Sex is determined in response to other individuals already attached to the gills. The first larva to settle on a fish becomes female and the second becomes male (reviewed in Bacci, 1965).

(ii) Bulnheim (1967, 1969; discussed in 1978a,b) demonstrated that, in the brackish-water amphipod *Gammarus duebeni*, sex determination was sensitive to the photoperiod experienced during the post-hatching, sexually indifferent stages. Within the progeny from a single pair of parents, there was a tendency for the sex ratio to be significantly higher at a long photoperiod than at a short photoperiod. (The transition occurred at about 14 hrs light: 10 hrs dark.) He further showed that day length rather than light intensity was responsible for the sex ratio response, and that the effect could potentially operate in natural populations, where light intensity was presumably low. Not all broods were equally sensitive to sex ratio modification by photoperiod, some broods perhaps being totally insensitive. Furthermore, the sex ratio varied significantly between broods, which Bulnheim interpreted as the result of polyfactorial sex determination. No temperature effects on sex ratio were observed. *G. zaddachi* also showed a photoperiod effect on sex determination, similar to but less extreme than in *G. duebeni*. Sex ratios in *G. locusta* were near .5 in both photoperiods studied, so this species presumably lacked ESD according to photoperiod (Bulnheim, 1978b).

(iii) Rubin (1984) studied the effect of pH on sex ratios in some cichlid and poeciliid fish. Acid water (pH 5.0 to 6.2) produced a strong male bias (.8 to 1.0 males), whereas neutral to slightly basic pH (7.0 to 7.8) resulted in a heavy female bias (0 to .2 males). These results have important implications for the interpretation of *genotypic* sex determination in fishes. Further work is needed to verify if the sex ratio biases resulted from male genotypes being converted into females and vice versa.

G. Environmental Alterations of GSD

Some vertebrates are recognized as normally having heterogametic sex determination, but certain environmental extremes override these genetic effects. Studies on these vertebrates have shown that, even though sex is normally determined according to sex factors, the genotypes XX, XY, and YY have the capacity to develop as male *and* as female (e.g., Humphrey, 1948; Mikamo and Witschi, 1964; Yamamoto, 1963, 1969). Therefore, even male and female heterogamety may have the potential to evolve ESD, and this evolution simply requires selecting a greater environmental sensitivity than presently exists. This section presents a superficial review of the effects of four environmental variables on sex determination in some birds, amphibians, and fish which otherwise may have male or female heterogamety, or some other well-defined

system (Table 9.G). Many of these examples lack thorough documentation, but others are well established.

Temperature. Temperature extremes influence sex determination in several amphibians thought to have heterogametic sex determination (Witschi, 1929; reviewed in Foote, 1964; Bacci, 1965; Crew, 1965; Pieau, 1975b; Richards and Nace, 1978). The most thorough demonstration of this effect was in the salamander *Pleurodeles waltl*, a species with ZZ males and ZW females. High temperature produced a ZW male, and in breeding it to a ZW female at a normal temperature, the sex ratio was significantly female biased, indicating that it was not a ZZ male (Houillion and Dournon, 1978). In the normally male heterogametic guppy and medaka (fishes), circumstantial evidence suggested that temperature influenced sex determination in strains of XX males and females (Winge, 1932, 1934; Aida, 1936). In addition, cold temperature produced males in the hermaphroditic fish, *Rivulus marmoratus*, and possibly produced males in the all-female fish, *Mollinesia formosa* (Harrington, 1967, 1968; Hubbs, 1964). Temperature is not known to influence gonad determination in birds, but temperature influenced the regression of genital ducts in quail (Lutz-Ostertag, 1966).

A well-founded precedent for this phenomenon has already been considered—the temperature-sensitive sex mutations of *Drosophila* (Sec. 4.A) and *Caenorhabditis* (Sec. 4.B), with a further example in the mosquito *Aedes* (Craig, 1965). In strains with these mutations, heterogametic sex determination operates at permissive temperatures, but sex ratio biases occur at restrictive temperatures, just as in the above examples of vertebrates (although fertility complications may ensue from these mutations). These mutations further indicate that there may be an inherited basis for the environmental susceptibility, an important result pertaining to theories about the evolution of ESD from GSD.

Hormones. Perhaps the most thoroughly studied form of environmental influence on sex determination is that of hormones. An extensive literature

TABLE 9.G. Environmental Extremes Influencing Sex Determination in Species with GSD

	Influencing Factor			
	Temperature	Egg Overripeness	Hormones	Gonadectomy
Birds	influences retention of Mullerian duct in quail	?	temporary effect on gonad in chicken	+
Amphibians	+	+	+	+
Fish	+	+?	+	+

Note: (+)—indicates there is at least suggestive evidence of a positive influence in some species; (+?)—indicates equivocal evidence of a positive influence (?)—factor not addressed in these sources; see text for references.

exists on artificial sex determination by external hormone application in fishes, amphibians, and amniotes (reptiles, birds, and mammals), and the variety of results is bewildering. Hormones that override sex factors in some species do not necessarily have the same effect in other species, and different doses may have opposite effects (reviewed by Burns, 1961; Atz, 1964; Foote, 1964; Yamamoto, 1969; Schreck, 1974; Witschi, 1951; Kawamura and Nishioka, 1977; Adkins-Regan, 1981). In birds, hormones may have a temporary and partial effect on gonad determination (Taber, 1964; Muller et al., 1979; Zaborski, Guichard, and Scheib, 1981). Although external hormonal influences on sex determination may be absent in nature, the laboratory phenomenon may reflect an inherent susceptibility of sex determination to other environmental factors.

Egg Overripeness. In a few amphibians, delaying fertilization of mature ova has resulted in biased sex ratios (reviewed in Bacci, 1965; Crew, 1965; Richards and Nace, 1978); the evidence for fish is equivocal (Atz, 1964). At least in the frog *Rana*, the sex ratio biases did not seem to be the result of differential mortality (discussed in Bacci, 1965).

Gonadectomy. In some amphibians and fish, the removal or degeneration of a gonad may lead to its regeneration from residual or adjacent tissue. The regenerated gonad may represent the opposite sex as the original gonad (Becker et al., 1975; reviewed in Atz, 1964; Foote, 1964; Crew, 1965; Bacci, 1965; Yamamoto, 1969). The best known example is Bidder's organ in castrated male toads (*Bufo*), which regenerates as an ovary. In female chickens, excision of the ovary (the left gonad) causes the right gonad, which is otherwise indifferent, to develop into a testis with sperm (Miller, 1938; Masui, 1967; Zaborski, Guichard, and Reyss-Brion, 1980).

H. Summary

This chapter reviewed examples of environmental sex determination—mechanisms in which sex is determined after conception in response to the individual's immediate environment. Examples are widespread but apparently uncommon, occurring in a marine worm, in one family of nematodes, in three orders of reptiles, and in at least one fish. There are further suggestions of ESD in other invertebrates and possibly in many fish.

Sex is determined in response to different environmental variables in these different species. Temperature has the major influence in reptiles and one fish, whereas conspecific interactions influence sex in the marine worm *Bonellia*. Sex is determined according to nutrition in mermithid nematodes.

Although ESD mechanisms are not especially common in animals, a capacity for ESD is observed in many systems of GSD. For example, in many

species that normally have an XX/XY system, environmental extremes (such as the external application of hormones) have been used to influence sex determination. Each genotype, XX as well as XY, has been induced to become male as well as female. Furthermore, environmental-sensitive sex transformer mutations are known in some species with XX/XY systems. This combined evidence suggests that no fundamental barriers exist to the evolution of ESD from GSD; rather the transition depends largely upon how these systems are selected. The following chapter addresses the topic of selection for ESD.

10

Evolution of Environmental Sex Determination

This chapter will present some models and theories concerning the evolution of environmental sex determination (ESD). Two general questions will be considered from this perspective: (i) Under what conditions does selection favor sex determination in response to the environment? (i.e., evolution of the mechanism). (ii) Given that sex is determined in response to the environment, how does selection influence the sex ratio?

It may be recalled from the preceding chapter that even though ESD mechanisms are not extremely common in animals, a *capacity* for sex determination in response to environmental extremes exists in many systems of genotypic sex determination (GSD), even though this capacity is realized only in minor ways. This capacity is a necessary ingredient for the evolution of ESD from GSD because it provides an initially low level of ESD which may be increased under selection. The focus of this chapter is therefore to understand selection of ESD, since its evolution does not otherwise seem to be generally precluded.

A. When Is ESD Favored?

Under ESD, sex determination is largely influenced by the environment. Charnov and Bull (1977) proposed that labile sex determination is advan-

tageous when environmental effects have different consequences for males and females. For example, suppose a juvenile encounters an environment in which it is well-fed and will therefore develop into a larger-than-average adult. Assume also that large size increases fitness for females more than males: the large individual can become either a male of nearly average fitness or a female of above-average fitness. Clearly, if an individual develops as female under these circumstances, it will leave more offspring than as a male, and any heritable tendency to become female under these conditions will be selected. More generally, Charnov and Bull (1977) proposed a model in which ESD is favored when the following two conditions occur: (i) an individual early in its life enters a part of the environment that has a lasting effect on its fitness. This environment is spatially variable (patchy) in such a way that some patches enhance (or depress) male fitness more than female fitness, and other patches do the opposite. Mating, however, occurs at random among individuals from different patches. (ii) The parents and offspring have little control over which patch type the offspring enters. Under these conditions, individuals whose sex is determined at conception are at a disadvantage because they often become the sex of lower fitness.

This model for the evolution of ESD will be investigated in subsequent sections of this chapter. Here two observations should be noted: (i) the model predicts that the environmental determinant of sex covaries with fitness differentially for males and females. Recall that sex in *Bonellia* is determined in response to whether larvae settle on adult females, that sex in mermithids is determined in response to available nutrition, and that sex in some reptiles and in silversides is determined in response to temperature. (ii) The model involves two parts: selection favors sex ratio adjustment in response to particular environmental conditions, and selection further favors a *mechanism* to allow this sex ratio control. The following two sections will analyze this model in detail.

B. Sex Ratio Evolution When Fitness Varies

One of the major underlying principles in the evolution of ESD is that of the selected sex ratio. Suppose that offspring are reared in a patchy environment prior to dispersing and mating at random, and the environment encountered in this early phase has an effect on fitness. If some patches increase or decrease fitness more for males than for females (or the reverse) *relative to other patches*, selection favors individuals that become male in patches relatively beneficial to males, and those that become female in patches beneficial to females. This sex ratio argument originated with Trivers and Willard (1973) in their theory for parental control of sex ratio in mammals. It has since been greatly extended and studied analytically, both for the case of parental control of sex ratio (Charnov, 1979, 1982) and for offspring control (ESD, Bull, 1981b; Bulmer and Bull, 1982). The selected sex ratio in both types of models is the same, and it is so unusual that it warrants special treatment here.

Imagine a mermithid nematode in an environment with a nearly continuous range of patch types bounded by certain limits (Fig. 10.B). Patch type can be viewed as the amount of nutrition the worm receives from the host, which may vary both with host size and with the number of worms sharing the same host. (For verbal simplicity, I will consider host "size" as the measure of patch type.) Worm size therefore increases with host size. Random mating is also assumed, meaning that there is open competition for mates among members of the same sex from different patches, along with random dispersal of offspring to different patches. Finally, a worm's fitness is assumed to increase with its size, more steeply for females than for males (Fig. 10.B). While these are the assumptions of this model, they also directly apply to mermithids, as justified in Section 10.E.

The sex ratio is allowed to evolve in this model under arbitrary genetic variation, with sex determined in response to patch type. A complete dynamic treatment is not available, but it can be shown that there is a unique equilibrium around which all minor sex ratio variation is eliminated (an "evolutionary stable strategy" of Maynard Smith, 1978, 1982), and it is this evolutionarily stable equilibrium that is expected to evolve (Bull, 1981b). In the mermithid example, the evolutionarily stable set of sex ratios requires small worms—those from small hosts—to develop as males, and large worms—from large hosts—to develop as females. The exact form of this sex ratio equilibrium is extreme. All worms in hosts below a certain size, say S^* , become male; all in hosts larger than S^* become female (Fig. 10.B). The actual size S^* and the selected sex ratio at this size both depend on various parameters, but the evolutionarily stable set of sex ratios always specifies a threshold response (step function) to patch type. This result may illustrate why ESD is selectively advantageous over GSD in organisms such as mermithids. With arbitrary genetic variation, selection favors all females in some hosts and all males in others. Genes causing individuals to be male or female independently of their environment (i.e., sex factors) are eliminated.

The unusual nature of this sex ratio equilibrium depends strictly on the fact that the ratio of male fitness to female fitness varies between patches. (The male/female fitness ratio is calculated for males and females raised in the same patch, and this ratio is compared for different patches.) Even if patch type influences fitness, if the male/female ratio does not vary across patches, a sex ratio of 1/2 in all patches constitutes an equilibrium in this model, and there is no selection for ESD. (In this case, there is an infinity of neutral sex ratio equilibria, and a sex ratio of 1/2 in all patches constitutes just one of them.) Therefore, the measure of "relative benefit" to which selection responds is the ratio of male/female fitness within a patch; those patches with high male/female fitness ratios are selected for male determination, and those with low ratios are selected for female determination. The absolute values of male and female fitnesses within patches are essentially irrelevant to this aspect of sex ratio evolution.

The population's primary sex ratio (defined as sex ratio per patch times

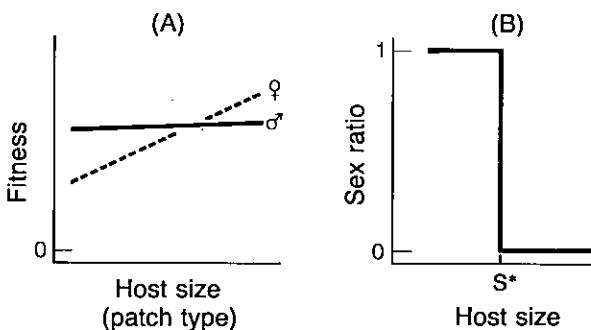


FIGURE 10.B. (A) Fitness specified as a linear function of host size (patch type), differently for males and females, as may approximately obtain for mermithids. (B) The general form of the selected (evolutionarily stable) sex ratio under A is with all males in small hosts (below size S^*), all females in large hosts, and perhaps both sexes in hosts of size S^* .

patch frequency) is not generally 1/2 at the equilibria in this model (Bull, 1981b). Instead, the primary sex ratio is biased toward the sex developing at its low fitness values. In this nematode model, an excess of males is expected because males develop in small hosts, where they are least fit. To offer an intuitive justification for the stability of a biased population sex ratio, consider the extreme case of an environment with just two patches, and all individuals from patch 1 are sterile. Their sex ratio may be all-male, all-female, or anything between without influencing selection of the sex ratio. Since the selected sex ratio in the other patch is necessarily 1/2, the total population sex ratio may differ from 1/2, and the ratio necessarily favors the sex overproduced in the sterile patch. Now suppose that individuals from patch 1 are fertile but of low fitness. At most, the selected sex ratio in patch 2 deviates from 1/2 only slightly, so the population sex ratio can still be extremely biased. Except in special cases, the principle of a population sex ratio equilibrium of 1/2 does not apply whenever there is a correlation between fitness and sex ratio.

Having addressed the evolutionarily stable sex ratio equilibrium in this model, other problems may now be considered: the rate of sex ratio evolution and the influence of patch choice by the parent. The rate of sex ratio evolution under ESD depends on variation in the embryo's sex determining response, and on the distribution of different patch types (Bulmer and Bull, 1982). In turtles, for example, the rate of sex ratio evolution decreases as the between-nest temperature variation increases. This decrease in the rate of evolution occurs because embryos in extremely cool (extremely warm) nests are almost certain to become male (female), irrespective of genotype, but in nests near the threshold temperature, sex determination depends primarily on embryonic differences. Consequently, many more generations of selection are required to incur major changes in sex ratio if there are large temperature differences between nests than if they are all approximately the same temperature.

Patch Choice

The distribution and availability of patch type may be determined in part by the location parents choose for their offspring or by the offspring themselves. In reptiles, the mother may choose between warm and cool nest sites, and in *Bonellia*, a larva could perhaps avoid settling on an adult female. These particular examples do not necessarily violate the assumptions of the Charnov-Bull model, because under GSD (male or female heterogamety) a mother reptile could not preferentially place sons and daughters at different temperatures, and a male *Bonellia* larva would not be guaranteed of meeting an adult female. In fact, there is a special case of parental choice of patch type that even facilitates the evolution of ESD. If an offspring's fitness varies only as a consequence of environmental effects on the mother, and differently for sons and daughters (Trivers and Willard, 1973), ESD is advantageous over GSD in allowing the mother to control the sex of her offspring in response to her condition (Huey, 1982). Analysis of the determinants of maternal choice of nest temperature would indicate whether this mechanism was operating in reptiles, for example.

Sex ratio evolution is influenced in two interesting ways when choice of patch type is allowed (assume maternal choice). First, if the mother can freely choose any patch type without decreasing her fertility other than as reflected in male/female fitnesses within the patch, the population's primary sex ratio evolves to 1/2. Mothers are selected to place offspring in the best patches for each sex, and at equilibrium, fitness is equal for all members of the same sex (otherwise mothers placing their offspring in better patches are selected). When fitness is equal within a sex, the Fisher result once again applies (Bull, 1981b; Charnov and Bull, unpubl.). Second, the sex ratio may evolve through changes in maternal choice of patch type, and perhaps evolve at a faster rate than through changes in the embryonic response. In reptiles for example, the threshold temperature may be slow to respond to sex ratio selection while maternal choice of nest site responds rapidly (Bulmer and Bull, 1982). If there is a single evolutionarily stable sex ratio for the system, the joint evolution of parental and embryonic mechanisms will affect only the rate and direction of approach to equilibrium, but if multiple equilibria exist, the equilibrium which evolves will depend on variation in both parental and embryonic sex determination.

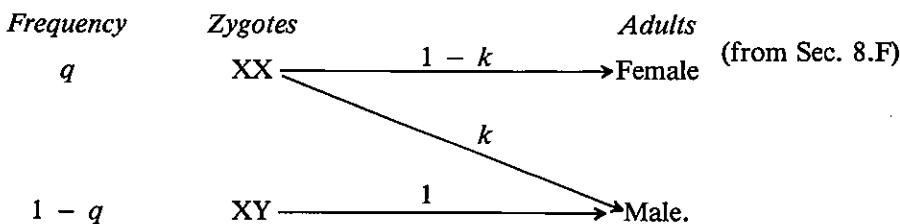
C. The Transition Between GSD and ESD

As suggested above, the argument for the evolution of ESD is in two parts, (i) selection favoring a sex ratio response to the environment, a response which cannot be achieved under GSD, and (ii) selection favoring a mechanism which allows the sex ratio to respond. This section illustrates the second point—that

transitions between GSD and ESD are easily achieved and that they are governed by conditions favoring a sex ratio response to the environment.

Consider the transition between male heterogamety and ESD. Heterogametic sex determination seems a plausible ancestor to ESD because it is so common, although no direct information about ancestral mechanisms is available. The qualitative conclusions do not seem to be sensitive to the mechanism of GSD, so generality is not lost by considering this one case. Under male heterogamety, males are XY and females are XX. Environmental sex determination is introduced by supposing that a fraction (k) of the XX zygotes become male rather than female; that is, a fraction k of the environment is invariably male-determining. (This assumption is motivated by Section 9.G, which described several species with heterogametic sex determination subject to occasional or extreme environmental effects on sex determination.)

The present model is identical to the one studied for a mixture of polyfac-torial and major-factor sex determination (Sec. 8.F), except that here k is fixed. It was also analyzed in Scudo's important paper (1964), although not in the specific context of ESD. From the above assumptions, assign genotype frequencies as follows:



It was shown above that

$$\{q' - 1/[2(1 - k)]\} = \frac{k}{M} \{q - 1/[2(1 - k)]\}, \quad (\text{from 8.F.3})$$

where M is the sex ratio, $kq + 1 - q$. Since k is fixed, we can also derive

$$[M - 1/2]' = \frac{k}{M} [M - 1/2]. \quad (10.C.1)$$

Provided that XY is present, the population sex ratio is always greater than k ($M > k$), and the sex ratio converges toward 1/2 while the frequency of XX zygotes converges toward $1/[2(1 - k)]$. If $k < 1/2$, the sex ratio and frequency of XX equilibrate at these values, respectively, but if $k > 1/2$ (more than half the environment is male determining), XY is lost, and the sex ratio necessarily becomes $M = k > 1/2$.

Consider these results when less than half the environment produces males ($0 < k < 1/2$). The equilibrium sex ratio is 1/2, and the equilibrium frequency

of XX increases as k increases according to $q = 1/[2(1 - k)]$ (Fig. 10.C, reproduced from Fig. 8.F.2). In this case, a continuous path of equilibria extends from strict ESD ($k = 1/2$) to strict GSD ($k = 0$). The evolution of ESD is therefore a matter of changing k .

To model the selection of ESD requires two additional components: (i) inherited variation in k , so that the level of ESD can evolve, and (ii) male/female fitnesses specified as some function of an environmental variable reflected in k . The details of such a model are tedious, but one analysis is available for the specific case of fitness as a linear function of an environmental variable (Bull, 1981a). Two of the major conclusions are (a) in the absence of differential environmental effects on the male/female fitness ratio there is no directional selection on the level of ESD; (b) with differential environmental effects on male/female fitness, ESD evolves so that males develop in environments relatively beneficial to males, and females develop in environments relatively beneficial to females. ESD evolves with a loss of segregation for X and Y so that no trace of heterogamety is retained (all males and females are XX in this example). Both results are as predicted by the Charnov-Bull model. Similar conclusions were reached in a model illustrating the transition between polyfactorial sex determination and ESD (Bulmer and Bull, 1982).

D. Selection Against ESD

The above model offers a satisfying explanation for an advantage of ESD, but it does not suggest why ESD might be inferior to GSD and hence why ESD is so uncommon. For example, in the above model there is never selection of major sex determining genes—those that would establish male or female heterogamety—over genes that determine sex according to the environment. Are there disadvantages to ESD? One possibility is that physiological complications may result if sex is determined in response to the environment, such as intersexes induced by intermediate environments. This hypothesis may not be generally applicable, however. In poeciliid fish, sexual development seems “canalized” such that individuals are essentially never intersexes, even when they have experienced environmental effects on sex determination (Atz, 1964; Kallman, 1983). A more fundamental problem of ESD is that sexually dimorphic characteristics (brain, skeleton, genitalia) cannot begin to develop sex-specific properties prior to the embryonic stages of sex determination. This would possibly limit the magnitude of male/female differences that could arise in early development. Unfortunately, constraints of this nature are unknown, and invoking them superficially in the absence of direct evidence does not lead to an increase in understanding.

Aside from possible physiological complications, however, there is indeed a disadvantage to ESD. If variation in the environment from year to year influences the distribution of patch types, the sex ratio will vary as a conse-

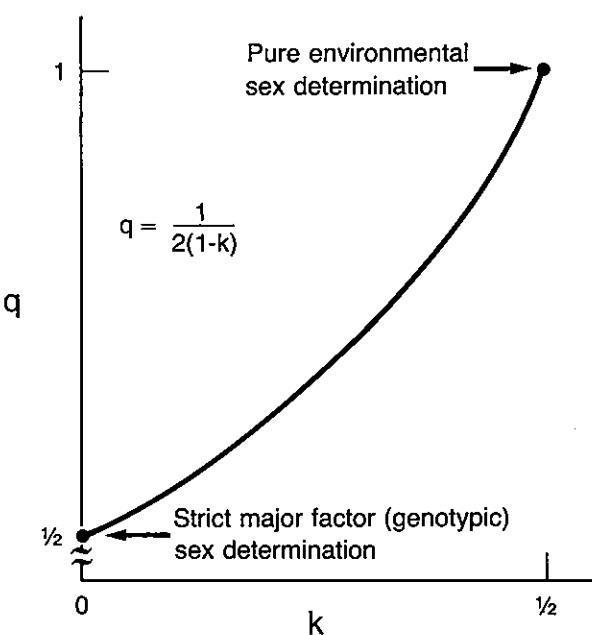


FIGURE 10.C. Equilibrium conditions for the coexistence of major-factor and environmental sex determination. q is the frequency of XX zygotes, k is the fraction of XX which become male. All points on the curve are equilibria, so there is a continuum of equilibria between strict major factor sex determination ($k = 0$) and strict environmental sex determination ($k = 1/2$).

quence. In reptiles and silversides, for example, a cold year will over-produce one sex and a hot year over-produce the other sex. In extreme cases, the sex ratio fluctuations could jeopardize the persistence of the population, but even in the absence of selection between populations, these sex ratio fluctuations constitute a disadvantage of ESD such that GSD will be selected.

To develop this argument further, consider a random mating population of infinite size with discrete, non-overlapping generations ("years"). (An assumption of overlapping generations is more appropriate for many species, but the qualitative conclusions are not likely to be affected and the mathematics are easier if non-overlapping generations are assumed.) For the vast majority of individuals, sex is determined in response to the environment, and the sex ratio is r , in generation t , a random variable due to environmental differences between years. Further assume that the average fitness for all individuals within a sex is the same, so that there is no association between fitness and the environmental determinant of sex.

Introduce the sex factor B into this population: all carriers of B are male (the model is equivalent if all carriers are female). Thus, individuals with genotype bb will manifest environmental sex determination, and Bb will

always be male. To consider whether factor B can invade the population, let the frequency of Bb in generation t be p_t , which is assumed to be small. The frequency of Bb in the next generation is then approximately,

$$p_{t+1} \approx \frac{p_t}{(2r_t)} \quad (10.D.1)$$

This equation was derived as follows. In generation t there are N zygotes, and $p_t N$ are Bb . Of the $(1 - p_t)N$ zygotes that are bb , $r_t N$ become males, and the others are females. Among males, therefore, a fraction

$$\frac{p_t N}{p_t N + (1 - p_t)Nr_t}$$

are Bb , and on average, they transmit B to half their offspring. Assuming p_t is small relative to r_t , the "first-order" approximation (10.D.1) is obtained. (By supposing that exactly 1/2 the offspring of Bb inherit B , N is also assumed to be infinite.)

By extrapolating to previous generations,

$$p_{t+1} \approx p_t \cdot \frac{1}{2r_t} \approx \frac{1}{2r_t} \cdot \frac{p_{t-1}}{2r_{t-1}} \approx \dots \approx p_0 \prod_{i=0}^t \frac{1}{2r_i}.$$

which is approximately correct as long as the frequency of Bb is small.

The sex factor B increases if the product $(1/2r_0)(1/2r_1)\cdots(1/2r_t)$ is greater than unity. If the sex ratio in all years (r_t) is exactly 1/2, then B does not change in frequency, because $1/(2r_t)$ is exactly unity. (The selected sex ratio for this case is in fact 1/2.) But since the sex ratio under ESD is subject to environmental variation, it is reasonable to assume that r_t is only 1/2 on average, varying between generations. Under these conditions, B will usually spread. As further documentation, let r alternate between 1/4 and 3/4, with $1/(2r)$ therefore alternating between 2 and 2/3. The long-term product of $1/(2r_t)$ is therefore $(4/3)^{1/2}$ and is greater than unity. More formally, it can be shown that if the sex ratios in different generations (r_t) are independent, identically-distributed random variables with mean 1/2 and variance V , the factor B has an expected, per-generation rate of increase of approximately $1 + 2V$ (Bull, 1981b, using the methods for studying gene frequency evolution in stochastic environments from Gillespie, 1973; and Karlin and Lieberman, 1974). The factor B will therefore nearly always increase.

In pursuing this matter further, it is seen how heterogametic sex determination may evolve from ESD. The increase of B is accompanied by a male bias in the population. This male bias selects variation—polyfactorial or major-factor—so that bb genotypes become even more inclined to develop as female. Selection of this variation reduces the male bias and allows B to spread

to the point that male heterogamety evolves (all males are Bb). In the final population, the only detectable sex factors are B and b , even though the strict female development of bb may have been selected through minor sex factors which then became fixed in many parts of the genome. The transition to male heterogamety from ESD could also occur in a constant environment, if Bb males were for some reason always superior to bb males. This model has merely shown one plausible reason why Bb (genotypic) males may be superior.

There are three points of further interest here. First, the above model considered temporal variation in the environment, but spatial variation has a similar effect in selecting GSD, if there is limited migration between subpopulations (Bulmer and Bull, 1982). Second, the above model considered a major sex factor pair, B and b , but a fluctuating environment selects GSD under polyfactorial variation by encouraging heterozygosity at all sex factor loci (Bulmer and Bull, 1982). Finally, the model assumed that the environmental determinant of sex did not covary with fitness. However, it has been shown for some special cases that, even if fitness covaries with the environmental determinant of sex, a fluctuating environment selects GSD if the influence of patch type on fitness is the same for males and females (Bull, 1981b; Bulmer and Bull, 1982). In nature, where the existence of annual and spatial variation may be assumed, ESD is selected against in the absence of differential environmental effects on male versus female fitness.

What then, is the final outcome in a fluctuating environment when male/female fitness is affected differently in different patches? A thorough analysis of this problem does not exist, but some limited results suggest the following (Bull, 1981b; Bulmer and Bull, 1982). (i) If environmental variations are small enough relative to differential effects on male/female fitness, the evolutionarily stable sex ratio is unchanged. (ii) If environmental variations are large, partial genotypic control of sex determination is favored, and the amount of genotypic influence at equilibrium increases with the magnitude of environmental fluctuations (Fig. 10.D).

E. The Evidence: When Is Sex Environmentally Determined?

This section compares the life histories of species with ESD to life history traits assumed and predicted under the Charnov-Bull model for the evolution of ESD. The model requires (i) open competition for mates among members of the same sex from different patch types, (ii) no choice of patch type according to the sex of offspring, (iii) sex determined in response to an environmental factor that covaries differently with male and female fitness, and (iv) each sex developing in patches providing the greatest relative benefit. In evaluating this model, it seems reasonable to regard the null hypothesis as the hypothesis that these characteristics do not apply. The null hypothesis will therefore be rejected only when evidence indicates that these requirements are satisfied. It

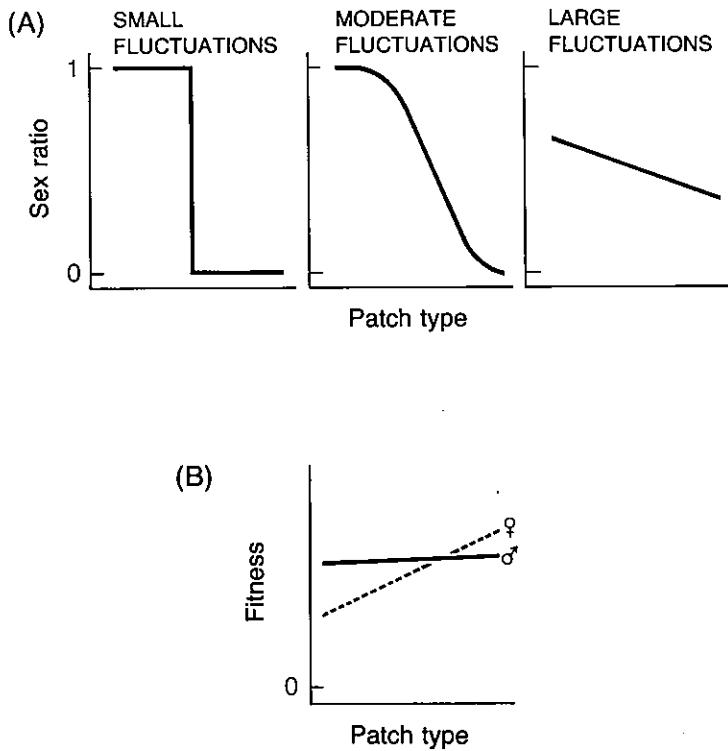


FIGURE 10.D. The effect of environmental fluctuations on the selected sex ratio. In a model of ESD (given the fitness conditions of B), the evolutionarily stable sex ratio in different patch types is influenced by environmental fluctuations that cause the sex ratio to vary between generations. (A) Small fluctuations do not alter the evolutionarily stable sex ratio from the case of no fluctuations (as in Fig. 10.B), and the selected sex ratio is a step function, changing from all males to all females across one patch type. As the magnitude of environmental fluctuations increases above some critical point, a more gradual effect of patch type on sex ratio is selected. (Based on results of Bulmer and Bull, 1982.)

should be noted, however, that merely satisfying these four requirements does not guarantee a species with ESD is fully consistent with the above models. Rigorous evaluation of these models requires quantitative comparisons between predicted and observed sex ratios as well as other characteristics. Some sex ratio considerations are discussed at the end.

Bonellia. As a species, *Bonellia viridis* appears to fit nicely with the model even though detailed measurements have not been made. A two-patch model applies here, with one patch represented by the uninhabited substrate and the other patch represented by adult females. While the above model does not strictly apply here, because patch type depends on sex ratio, the equilibrium

conditions are in the same general form as above. Random mating between patch types is ensured since only males come from one patch and only females come from the other. Patch choice by larvae is at best incomplete: larvae that encounter an adult female can perhaps avoid settling on her, but on the other hand, not all larvae necessarily encounter adult females. Larvae might also be "captured" by adult females, in which case they could not choose to leave. Fitness effects also seem clear: larvae developing as females parasitic on other females would have negligible brood size, while isolated males attempting to fertilize eggs would experience few happy results. The environmental effects on sex determination are therefore consistent with the expected results.

Nematodes. The life histories of mermithid nematodes are also apparently consistent with the proposed advantage of ESD. By maturing long after emergence, these nematodes can be expected to mate with worms from different hosts (different patches), thereby fulfilling the first requirement of the model. The worms are presumably unable to choose patch types, since the level of infection is not evident prior to entry into the host, and alternative hosts may be limited even if worms can assess host size. The fitness effects may also be consistent with the model, although direct evidence is lacking. It is clear that (i) worm size is correlated with the amount of nutrition available from the host (Sec. 9.C), and (ii) potential female fecundity increases with female size (Christie, 1929). There is also circumstantial evidence that male fitness does not increase with size to the extent that female fitness increases with size—males are almost universally the smaller sex in nematodes with GSD, and male mermithids show no overt antagonism toward each other (Chitwood and Chitwood, 1974; Christie, 1929). Sex determination in these nematodes is, of course, consistent with the model only if large size enhances fitness as a female more than as a male.

The possibility of occasional parthenogenetic reproduction is not considered in these models, but parthenogenesis may be occurring in some mermithids (Sec. 9.C). Although facultative parthenogenesis undoubtedly affects the expected sex ratio, I offer as a conjecture that occasional facultative parthenogenesis will not lead to qualitatively different results in the selected sex ratios of these models (all males in small hosts, females in large ones).

Silversides The life history of *Menidia* has been studied by Conover (1983) specifically to test this ESD hypothesis, and there is a tentative agreement between observations and predictions. The environmental patch type in this fish is best interpreted as the date in spring when an individual is conceived. Patch type therefore varies with temperature, the variable of sex determination. Fish are born in spring and early summer, and they overwinter offshore and return to mate together the following spring. Therefore, there is likely to be random mating among individuals born on different dates, satisfying the first requirement. The second requirement provides that, under GSD, parents or offspring cannot match offspring sex with patch type. This requirement is certainly

satisfied if the type of GSD considered is heterogamety or polyfactorial sex determination, because these GSD mechanisms would not allow parents to vary their family sex ratios according to time of year.

Conover demonstrated that fish born early grow to a larger size than fish born late (independent of sex), and that winter survival was enhanced by large size. This established a relationship between fitness and the determinant of sex (temperature), since water temperature changed throughout the spawning season. Conover further considered whether variation in body size differentially affected male versus female fitness. Female fitness seemed to depend largely upon egg number, hence increased with size, but unfortunately, male fitness was not so easily quantified. These fish had external fertilization and spawned *en masse*, suggesting that sperm quantity was a major determinant of male success when breeding, so there was no obvious reason suggesting that body size should differentially benefit male versus female reproductive success.

Conover (1983) investigated the relation between body size and two components of male breeding success, testis size (indicating sperm number) and body build (a measure of emaciation). Testis size increased less steeply with body size than did ovary size, and large size even seemed to handicap a male's endurance over the entire spawning season, so it was tentatively concluded that large size benefitted reproductive success more for females than for males. As Conover acknowledged, however, calculating male reproductive success from these two components would omit other effects of body size on fitness; further, the calculation of total fitness from estimates of two components is itself hampered by statistical problems. A direct measure of male reproductive success, one that employs markers transmitted to offspring, is required before this problem can be resolved. However, if Conover's tentative conclusions prove valid, the third and fourth requirements of the ESD model are satisfied: females are produced in excess early in the season, and they grow to a larger size than males, as predicted if females indeed benefit more than males from large size.

Reptiles. The greatest problem for this theory is posed by the widespread occurrence of ESD in reptiles. There is no difficulty in supposing that reptiles meet the requirement of random mating between patches, and the requirement that parents be unable to match offspring sex with patch type (under most systems of GSD, a mother could not preferentially put sons at one temperature and daughters at another). The difficulty lies in knowing if incubation temperature differentially affects male/female fitness. This problem is especially complicated because various sex ratio responses to temperature are observed in different groups of reptiles. Within lizards and within turtles, some species lack temperature-dependent sex determination altogether and other species show extreme temperature effects. Furthermore, warm incubation temperatures produce males in lizards and alligators but produce females in turtles. In the context of this theory, therefore, warm incubation temperatures are expected to benefit females in turtles but benefit males in lizards and alligators. ("Benefit"

is used here in the relative sense of the male/female fitness ratio.) The model also requires that incubation temperature has no differential effects on male/female fitness ratios in species that lack temperature-dependent sex determination. I am not aware of any comparisons of life histories between different reptiles that suggest the advantages or disadvantages of these different sex determining mechanisms. However, a few recent studies of reptilian life histories do provide results potentially consistent with the Charnov-Bull hypothesis.

In a study of alligators, Ferguson and Joansen (1982) reported that temperature affected hatchling size, and as a consequence, it affected the time required to mature and/or adult size. Alligators hatched from eggs incubated at low temperatures had more yolk reserves than those hatched at high temperatures, even though body weight (minus yolk) was the same. The hatchlings with more yolk grew faster, and they either matured sooner or at a larger size. (Residual effects of incubation temperature on *adult* fitness were not necessarily anticipated.) Ferguson and Joansen further proposed that the advantage of large size early in life was more important to lifetime fitness as a female than as a male, although the justification for this claim was not adequately documented. If this latter claim is true, then ESD in alligators is consistent with the Charnov-Bull theory, since females develop at cool temperatures.

The studies of Gutzke and Paukstis (1983b) and Paukstis et al. (1983) demonstrated that sex determination is sensitive to water potential in some turtles. Water potential also influences embryonic metabolism in these species, so that eggs on dry substrate hatch smaller turtles with more residual yolk than wet eggs (Packard et al., 1981a, b; Gutzke and Paukstis, 1983b; Paukstis et al., 1983). Therefore the water potential during embryogenesis probably affects growth rate in post-hatching life. Since adult size differs between males and females in many turtles (Berry and Shine, 1980), water potential might have differential effects on male and female fitness. It is especially interesting, therefore, that softshelled turtles (genus *Trionyx*) apparently lack ESD, and their embryos are also unaffected by water potential in the incubation substrate (Vogt and Bull, 1982; Packard et al., 1979). These studies of water potential therefore suggest some interesting lines of investigation to pursue in testing the Charnov-Bull model.

It remains to be shown whether ESD in reptiles will generally prove consistent with the above theory. The null hypothesis that temperature has no differential influence on male/female fitness ratios stands unchallenged in most species. Even if reptiles with ESD are found to be consistent with the Charnov-Bull hypothesis, it is hard to imagine *a priori* that species with GSD have life histories so fundamentally different that they completely selected against ESD. It might therefore be considered that genetic variation is lacking for the evolution of GSD (or of ESD) in some species. The situation warrants careful study, but it is clear that the theory did not lead to the anticipation of ESD in reptiles. If the reptiles eventually prove to be consistent with the theory, it may suggest

that superficial assessments of the evolutionary significance of ESD, as was done with mermithids, are not justified.

Sex Ratio Evolution

Few empirical studies of ESD directly address the topic of sex ratio evolution. While the quantitative predictions of the models require detailed knowledge of fitnesses and other parameters that are generally difficult to measure, there are two useful and simple sex ratio characteristics which can be studied at a qualitative level: (i) population sex ratios, and (ii) geographic comparisons of sex determination.

Population Sex Ratios. The population sex ratio under ESD is not generally expected to evolve to 1/2 exactly, but instead should favor the sex overproduced in the poorest patches. In nematodes and silversides the sex ratio is expected to favor males. Collections taken randomly across patch types, also representing the temporal distribution of patch types, could be used to assay the sex ratio, (if biases due to differential mortality/capture are avoided). Few studies provide unbiased samples of primary sex ratios in populations with ESD. Couturier (1963, p. 208) reported a female excess in a sample of mermithids, but he did not indicate if the worms likely represented a random sample by sex. Recall also the female excess observed in hatchling map turtles (p.121), stemming at least partly from a collecting bias.

As described in Sec. 9.D, Ferguson and Joanen (1982) observed a strong female excess in the primary sex ratio of alligators (less than .20 males), and this estimate did not appear to be influenced seriously by collecting biases. Although a skewed population sex ratio usually results at the equilibria in models of ESD, the maintenance of such an extreme value as .20 requires a totally implausible set of ecological conditions for alligators. In fact, recalling results from Sec. 10.B, if the nest sites producing sons are not limiting in this population, a sex ratio of 1/2 is expected to evolve through changes in maternal choice of nest site. The extreme female excess in the primary sex ratio of alligators is therefore enigmatic. It should be considered whether the environments currently inhabited by alligators represent past environments with respect to the distribution of nest sites and temperatures of nests within these sites.

Knowledge of the relation between fitness and patch type, even if only approximate, enables approximate quantitative predictions of the sex ratio and threshold patch type. Such analyses may be readily applied to mermithids and silversides, provided that the patch-type distributions can be assayed without bias. For example, fitness in female mermithids could be estimated based on the number of eggs inside newly emerged females (the number of eggs increasing with female size). A male's fitness could be assumed the same as, or less than, the fitness of a female the same size, even to the extreme of being independent of size. If the size distribution of emerging worms was known, an

expected sex ratio and threshold size could be calculated and compared to observations. Analogous calculations could be performed on silversides. These calculations would be useful because the evolutionarily stable sex ratio is sensitive to the total effect of patch type on fitness, and slight male/female differences are unimportant to the predicted sex ratio when patch type has a major effect that applies equally to both sexes. The calculations proposed here would be especially useful if the models in this chapter are grossly inadequate, because the discrepancies between models and observations then should not be sensitive to the approximations advocated above. There are in fact already some observations that challenge the application of these models—the heavy female excesses in populations of reptiles with ESD.

Geographic Comparisons. The sex ratio is expected to evolve in response to the distribution of patch types. In nematodes, if one population infects smaller hosts on average than another population, female determination at a smaller size will be selected in the former. This relative comparison has been greatly emphasized by Charnov (1979, 1982). Geographic variation of sex determining temperatures was studied from this perspective in turtles (Bull, Vogt, and McCoy, 1982). As described in Section 9.D, threshold temperatures were compared between northern and southern populations of turtles, with summer air temperatures at the southern localities at least 2 C° warmer than the northern ones. The nesting periods for the southern populations began earlier than for the northern ones, but the different nesting times did not compensate for most of the differences in air temperatures. The sex ratio model predicts that if sex ratio evolves according to changes in threshold temperature, higher threshold temperatures should be found in the South. However, it was observed that in many cases no differences were evident, and in the remaining cases the differences were in the *opposite* direction from the one predicted. These results may indicate that nest temperatures do not vary as summer air temperatures do, but nest temperatures have not been studied. In fact, R. Tracy (pers. comm.) informed me why nest temperatures may be as warm in the northern localities as in the southern localities, even if the nests are in equally exposed sites. In summer, the northern localities have a longer day length than the southern localities, and the longer exposure to the sun may cause soil temperatures to be as warm as they are at the southern localities. This warming effect would not explain all the results, but it might account for the overall similarity in threshold temperatures of the northern and southern populations.

Parenti (1962) compared sex ratios and levels of infection for two populations of *Paramermis contorta*. One of these data sets was extracted from Caullery and Comas (1928). The sex ratio in both samples favored females (.44 and .18), the observed levels of infection differed between both populations, and the sex ratio as a function of infection rate also varied between the populations. If the observed distributions of hosts and infection rates represented the natural distributions, the models presented here do not account for the observed sex ratios. In view of the strong female excess observed in

one sample, it should be considered either that small or heavily-infected hosts were missed, or that some reproduction was parthenogenetic. However, the female excess in mermithids parallels the one in alligators.

F. Summary

Environmental sex determination is a mechanism in which zygotes develop as male or female largely according to differences in the environment. Although ESD is apparently uncommon, the previous chapter indicated that many mechanisms of GSD have a capacity for minor levels of ESD, and so this capacity might be increased if ESD was selectively favored. A model in this chapter showed that the transition from GSD to ESD is not intrinsically more difficult than transitions between other types of mechanisms. Furthermore, ESD is at a definite advantage over GSD in life histories where environmental effects encountered early in life have different consequences for males and females. Selection favors individuals developing as male under circumstances benefitting males and as female in circumstances benefitting females; the appropriate measure of benefit here is the comparison of absolute fitness that would be experienced as a male relative to that as a female. The life histories of species with ESD were compared to the characteristics expected under this model. Some species have life histories at least superficially consistent with this model, but the distribution of ESD and GSD in reptiles is yet unexplained.

11

Uniparental Males: Arrhenotoky (Haplo-Diploidy) and Paternal Genome Loss

A. Introduction

There are various genetic systems in which males are uniparental, transmitting only maternal genes, while females are biparental and transmit genes from both parents. These systems present special problems to understanding the evolution of sex determination. The best known system producing uniparental males is haplo-diploidy, or arrhenotoky, in which males arise from unfertilized eggs and females from fertilized eggs (Fig. 11.A). Arrhenotoky holds a special position in many treatments of sex determination, because males inherit a random half of the maternal genome, while daughters inherit both maternal and paternal genes. Arrhenotoky is not compatible with the principle of sex tendency, because factors with a strong sex tendency will produce both haploid and diploid males or females. Arrhenotoky thus provides a clear counter-example to the additive-value model of sex determination, and it has therefore been a source of controversy and interest in the field of sex determination.

A second type of system utilizing uniparental males may be called "paternal genome loss" (PGL). In this system both sexes arise from fertilized eggs but males do not transmit paternal genes (Fig. 11.A). (PGL replaces Hartl and

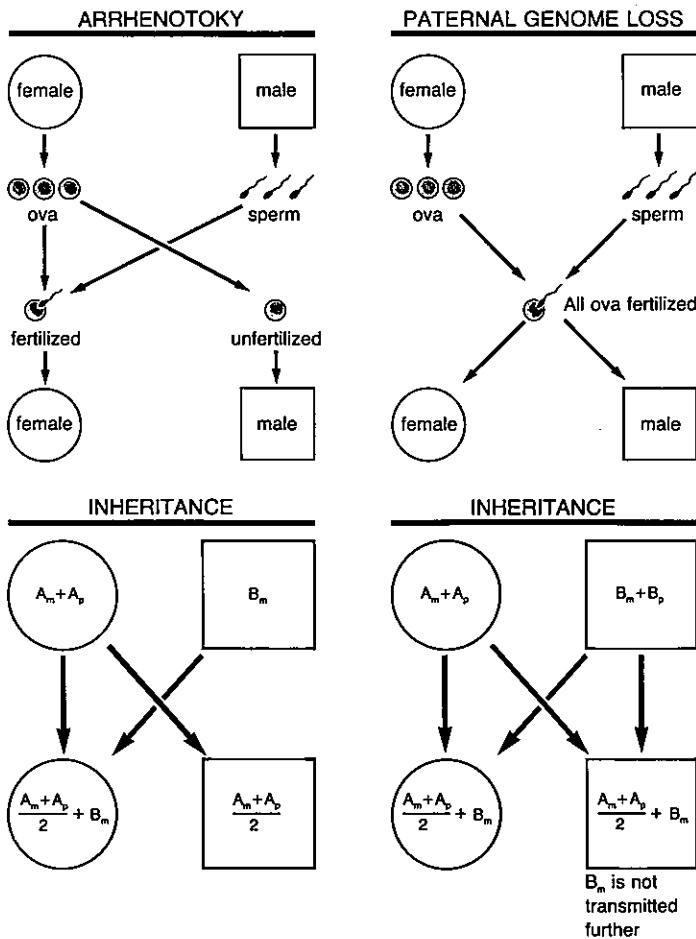


FIGURE 11.A. Two distinct types of systems with uniparental males (males transmit only the maternal genome): arrhenotoky and paternal genome loss. (*Top*) Under arrhenotoky, males arise from unfertilized eggs, females from fertilized eggs; under paternal genome loss, both sexes arise from fertilized eggs. (*Bottom*) The inheritance is the same under arrhenotoky and paternal genome loss. In the parental generation, the letter **A** represents the haploid genome of a female, **B** the genome of a male; the subscripts *m* and *p* indicate the prior source of the haploid genome, whether by maternal or paternal parent, respectively. Females always transmit genes of both parents, $A_m + A_p$, while males transmit only the maternal genome, B_m , even if (under PGL) they inherit a paternal genome as well.

Brown's term "parahaploidy," 1970.) Paternal genome loss also raises problems for sex determination, though not the same ones created by arrhenotoky. The discussion of PGL is included here partly for this reason and partly because the evolutionary advantage of PGL and arrhenotoky may be the same (Chap. 12).

In many arrhenotokous and PGL systems, the males are actually haploid, although there are also systems of arrhenotoky and PGL in which the males are diploid but transmit only maternal genes (see Nur, 1971, 1980 for examples of diploid arrhenotoky; see examples below of diploid PGL males; see White, 1973, p. 685, for a discussion of ploidy levels in male tissues of arrhenotokous species). To avoid confusion over the issue of ploidy, the term *uniparental* will be used to denote males that transmit only maternal genes, and the term *arrhenotoky* is used in place of *haplo-diploidy*. The term *diploidy* refers generally to the common, Mendelian populations, in which both sexes arise from fertilized eggs and transmit genes from both parents.

The treatment here of uniparental male systems includes three chapters. The present chapter describes the known varieties of arrhenotoky and paternal genome loss. The next two chapters (12 and 13) will describe models for the evolution of uniparental males. Chapter 12 will show specifically that a particular advantage applies to the evolution of uniparental males, and that the same advantage applies to both arrhenotoky and PGL. The advantage of uniparental males does not directly concern the sex determining mechanism, but instead stems from the fact that males transmit only their mother's genes. Chapter 12 will merely describe this advantage without considering the sex determining mechanism, whereas Chapter 13 will offer models to show how the evolution of uniparental males is influenced by the sex determining mechanism. The emphasis in these three chapters therefore will not be restricted solely to sex determination, but instead will focus on a two-dimensional evolutionary process, of which only one dimension is sex determination.

Theletoky. The topic of all-female parthenogenesis does not present the same sort of questions with respect to sex determination that arrhenotoky presents. Females produced parthenogenetically inherit only the maternal genome, so no special properties are required of the sex determining mechanism. (Contrast thelytoky to arrhenotoky, in which individuals inheriting only their mother's genes become *male*.) For example, sex determination under thelytoky offers no complications when thelytoky evolves in a population of male heterogamety (all females are XX). There is of course the question concerning why asexual reproduction evolves (Bell, 1982; Shields, 1982; Maynard Smith, 1978; Williams, 1975), but sex determination does not seem to be a limiting factor. For this reason, the evolution of thelytoky will not be considered in this book.

The remainder of this chapter will describe some of the basic facts known about arrhenotoky (Sects. B and C) and paternal genome loss (Sects. D, E, and F).

B. Arrhenotoky

Occurrence

The earliest known correct description of sex determination was Dzierzon's hypothesis in 1845 that female honey bees (*Apis mellifera*) arose from fertilized eggs and males arose from unfertilized eggs. This system is now known as arrhenotoky (haplo-diploidy) and occurs in various arthropods and rotifers (Table 11.B.1), and may characterize all sexual species from the insect orders Hymenoptera (bees, ants, wasps, and sawflies) and Thysanoptera (thrips).

The simplest version of arrhenotoky is the one just described, with all females arising from fertilized eggs and all males from unfertilized eggs, such as is observed in some or most sexual hymenopterans, thrips, scale insects, mites and ticks, and bark beetles. Arrhenotoky also occurs in somewhat more complicated systems, however (Table 11.B.1): (i) In monogonant rotifers and cynipid wasps, arrhenotoky alternates with parthenogenetic production of females during part of the year (reviewed in Bell, 1982; White, 1973). (ii) In the beetle *Micromalthus* and some cecidomyiid gnats, females produce sons by asexual means, but these processes are embedded in bizarre life histories that involve pedogenetic reproduction (reproduction by larval forms). (iii) In the scale insect *Icerya purchasi* most individuals are sequential hermaphrodites (male first) with haploid spermatogonia and diploid oogonia (Royer, 1975); this example is not necessarily one of arrhenotoky, but arrhenotoky does occur in other species of this genus (Nur, 1980).

The detection of arrhenotoky is straightforward because virgin females produce all male offspring. In addition, cytological analysis may reveal the ex-

TABLE 11.B.1. Groups with Arrhenotokous Species

Group	Remarks
ARTHROPODA: Insecta	
Hymenoptera (ants, bees, wasps)	Probably ubiquitous among sexual species
Thysanoptera (thrips)	Possibly ubiquitous among sexual species
Homoptera	
Coccoidae and Margarodidae (scales)	Known from few species
Aleurodidae (whiteflies)	
Diptera (Cecidomyiidae)	Embedded in complex life history with pedogenesis; limited to a few species
Coleoptera	
Scolytidae (bark beetles)	Known from few species
Micromalthidae	Embedded in complex life history with pedogenesis
ARTHROPODA: Acari (Mites, Ticks)	Known from many species, perhaps several origins
ROTIFERA: Monogonanta	
	Alternates with thelytoky

Sources: Reviews by Bell (1982), White (1973), Nur (1980) for coccids, and Oliver (1971, 1977, 1983) for mites and ticks.

istence of arrhenotoky through an aberrant spermatogenesis. Since males from many arrhenotokous species are haploid in the germ line, they require an atypical meiosis readily recognized as unusual.

Origins

Arrhenotoky is a highly successful mode of reproduction as measured by the number of species with this system, but it has arisen only occasionally, and the large number of species currently known appears to be the result of tremendous radiations from a few ancestors. White (1973) proposed a lower limit of eight independent origins of arrhenotoky, and essentially ascribed one to each listing in Table 11.B.1. A lower limit of 12 seems more reasonable, since there are likely several independent origins of arrhenotoky in mites and ticks (Table 11.B.2), but White is certainly correct that they are few. The relatively few

TABLE 11.B.2. Arrhenotoky and Alternative Systems within some Groups

Group	Systems Known
ARTHROPODA: Insecta	
O. Homoptera (scales)	
F. Margarodidae (scales)	A, M
F. Coccidae (scales)	A, P
O. Coleoptera (beetles)	
F. Scolytidae	A, M
ARTHROPODA: Acari (mites, ticks)*	
O. Parasitiformes	
SBO. Gamasida (Mesostigmata)	
SPF. Dermanyssoidae	A, P
SPF. Phytoseioidea	P
SBO. Ixodida	
SPF. Ixodoidea	M
O. Acariformes	
SBO. Actinedida (Prostigmata)	
C. Eleutherengonina	
SBC. Raphignathae	A
SBC. Parasitengonae	2N
SBO. Acaridida (Astigmata)	
SPF. Anoetoidea	A, P
SPF. Acaroidea	M
SBO. Oribatida (Cryptostigmata)	
F. Oppidae	A

Sources: Smith, 1960; Bell, 1982 (beetles); Nur, 1980 (scales); the tabulation for mites and ticks was prepared by J.H. Oliver Jr., and is extracted in part from Oliver (1983).

Note: A—arrhenotoky; M—diploidy with male heterogamety; P—paternal genome loss; 2N—males and females with indistinguishable chromosome complements, sex determination unknown; O—Order; SBO—suborder; C—cohort; SBC—subcohort; SPF—superfamily; F—family.

*—In some of these groups of mites and ticks I have inferred the existence of PGL by the fact that males are cytological haploids but females require insemination before oviposition (Oliver, 1971, 1977). Nelson-Rees et al., (1980) have demonstrated PGL in a phytoseid mite, and suggest that it may be nearly ubiquitous among sexual phytoseids.

origins of arrhenotoky may be contrasted with a plethora of origins for thelytoky in animals (White, 1973; Maynard Smith, 1978, p. 53).

It is not only difficult to assess the number of origins of arrhenotoky, but it is also difficult to identify the ancestral genetic systems. There are no known populations that represent the transitions to arrhenotoky from a plausible precursor, and inferences on arrhenotoky's origins can therefore only be obtained from the analysis of alternative genetic systems in close relatives of arrhenotokous species (Table 11.B.2). A review of these data suggests that diploid and PGL systems are the two likely ancestors of arrhenotoky, although diploidy may be regarded as the only plausible ancestor of arrhenotoky in a few of these groups. (Thelytoky was omitted from consideration here, as it seems an implausible precursor to arrhenotoky.) It is interesting that Schrader and Hughes-Schrader (1931) first suggested that PGL was a predecessor to arrhenotoky based on their analysis of scale insect genetic systems; yet the same association between PGL and arrhenotoky may exist within several groups of mites and ticks. The association between arrhenotoky and PGL does not imply that either is an ancestor of the other, however. An alternative explanation for this association is that both systems have arisen from diploidy, but that species prone to evolve one system are equally prone to evolve the other, hence their frequent association. The next two chapters will show that there are indeed similar advantages for the evolution of PGL and arrhenotoky from diploidy, but there are also lesser advantages for the evolution of arrhenotoky from PGL, so an origin of arrhenotoky from PGL is not implausible.

Sex Determination

Sex determination of arrhenotokous species is understood only for some hymenopterans and is described in the following section. As noted in Sec. A, arrhenotoky is not compatible with the additive-value model of sex determination because individuals inheriting only their mother's genes become male. Male heterogamety is possibly the ancestral mechanism in several cases, since it is the only diploid sex determining mechanism known in the closest relatives (Table 11.B.2), but it is not known whether these particular systems of male heterogamety are compatible with arrhenotoky. In Chapter 13 it will be shown that male or female heterogamety can lead directly to arrhenotoky, but only if uniparental offspring are male; this latter characteristic has not been studied in the diploid relatives of arrhenotokous species.

C. Sex Determination in Arrhenotokous Hymenoptera

From Section 3.F, several arrhenotokous hymenopterans have a 1-locus "complementary" sex determining mechanism with multiple factors—haploids and

diploid homozygotes are male while heterozygotes are female:

$$\begin{array}{ll} \sigma & \varphi \\ A_i A_i & A_i A_j \\ A_i & i \neq j \end{array} \quad i, j = 1, \dots, n \quad (\text{from 3.F.1})$$

It has not been shown that these sex factors represent just a single gene locus, but I will refer to it as a 1-locus system because the factors segregate in opposition. Nine different sex factors have been observed in the parasitoid wasp *Bracon hebetor* (= *Habrobracon juglandis*) (P. Whiting, 1943), and estimates of the minimum number of sex factors in honeybees centers around 12, although some of these estimates are within large confidence intervals (reviewed in Yokoyama and Nei, 1979; Page and Metcalf, 1982).

The evidence revealing biparental homozygotes as male has been obtained from the laboratory studies on a few species (honeybees and *Bracon*) in which inbred females were mated to brothers or sons. Since normal males are uniparental, they carry just one factor, and if the above model (3.F.1) is correct, this incestuous cross is expected to produce diploid homozygotes for sex factors—biparental males—in half the fertilized eggs. Results of inbreeding experiments were consistent with this expectation in a few genera (P. Whiting, 1945; A. Whiting, 1961; Kerr, 1974; Crozier, 1977). In addition, diploid males have been observed at low frequencies in several other species, including ants, bees, and wasps (Table 11.C). However, diploid males have never been observed

TABLE 11.C. Species of Hymenoptera Reported to Have Diploid Males

Species
WASPS
<i>Bracon hebetor</i>
<i>Nasonia vitripennis</i> *
<i>Neodiprion nigroscutum</i>
BEES
<i>Apis cerana</i>
<i>A. mellifera</i>
<i>Bombus atratus</i>
<i>Melipona quadrifasciata</i>
<i>Trigona quadrangula</i>
ANTS
<i>Pseudolasius nr emeryi</i>
<i>Rhytidoponera chalybaea</i>
<i>R. confusa</i>
<i>Solenopsis invicta</i>

Based on R.E. Page, Jr. and R.A. Metcalf. 1982. "Multiple mating, sperm utilization, and social evolution." *The American Naturalist* 119:263–281, Table 3. For *Apis cerana* see Hoshiba et al., 1981.

*—diploid males not biparental.

to be functional. In some cases they are inviable, in honeybees they are killed, and in *Bracon* and other species they are viable but produce diploid sperm because of a failure to undergo a reduction division in spermatogenesis (discussed in White, 1973).

One aspect concerning the molecular basis of the complementary mechanism was revealed in *Apis* and *Bracon*. Following destruction of the egg nucleus by irradiation, two or more sperm sometimes fertilized the egg, and both were independently incorporated in embryonic cells, forming a mosaic, haploid male. When the two paternal genomes carried different sex factors, the border between the two types of male tissue was sometimes characterized by a thin band of female tissue in certain parts of the body (Whiting, 1945; Rothenbuhler, 1957). The production of females therefore seemed to result from the interaction of products from dissimilar sex factors.

Some species inbreed considerably yet fail to produce diploid males. Crozier (1971) suggested that sex determination in these species might also depend on complementary sex determination, but with a mechanism involving multiple loci. Under Crozier's hypothesized mechanism, diploids that were heterozygous at any of the sex loci would be female, while diploids homozygous for all sex loci as well as haploids would be male. Under occasional outbreeding, Crozier suggested that enough heterozygosity would be maintained to ensure that most diploids were female. Kerr (1974) reviewed several possible cases of 2-locus mechanisms of this sort, but Crozier (1977) took a more conservative stance and suggested that there was substantial evidence for a 2-locus mechanism in only one species.

Nasonia (= *Mormoniella vitripennis*) is a wasp parasite of fly pupae in which there is considerable sib-mating without production of diploid males. Diploid males are known, but only from diploid, unfertilized eggs of triploid females (P. Whiting, 1960). Sex determination in this species does not seem to depend on the heterozygosity/homozygosity principle, because carefully controlled long-term inbreeding experiments failed to produce any diploid males or any significant decline in viable offspring (Skinner and Werren, 1984). Equally so, sex determination also does not seem to depend on whether the egg is fertilized, because males have resulted from fertilized eggs in two instances: (i) when the maternal nucleus was destroyed by radiation such that the wasp developed as a haploid from the sperm (Friedler and Ray, 1951); (ii) in some incompatible, interstrain crosses in which sperm penetrated the egg but then degenerated (Ryan and Saul, 1968). The true basis of sex determination in *Nasonia* therefore remains unknown.

D. Paternal Genome Loss

Occurrence

Under paternal genome loss (PGL), both sons and daughters arise from fertilized eggs, but the paternal genome is not transmitted by sons. PGL is known

in three groups of invertebrates: mites (Nelson-Rees et al., 1980), scale insects (Brown, 1964; Nur, 1980), and sciarid flies (Metz, 1938). It may also be widespread in cecidomyiid gnats, but there are no studies indicating whether males transmit just the maternal genome (White, 1973; Brown and Chandra, 1977). The PGL systems of *Sciara* and scales are discussed in detail in Sections E and F, but it can be noted here that these systems are extremely varied in the ways that paternal chromosome loss is achieved in males (Fig. 11.D). In some systems the male genome is retained as active in the somatic tissues and eliminated only in spermatogenesis; in others the paternal genome is heterochromatized in the soma, so it is largely inactive, and it is also eliminated during spermatogenesis. In yet another system, the paternal genome is eliminated from germ and somatic cells during cleavage of embryogenesis, giving rise to a haploid male (except for some special cells).

Origins

The occurrence of PGL parallels the occurrence of arrhenotoky in several ways. First, there seem to be relatively few origins of PGL, although there is

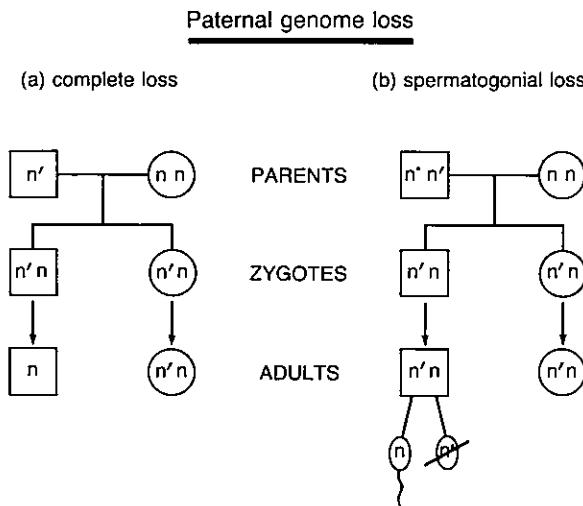


FIGURE 11.D. Two forms of paternal genome loss. (Squares are males, circles are females.) Under paternal genome loss, both sexes arise from fertilized eggs, but males transmit only the maternal genome. In some systems, the paternal genome is eliminated (a) during cleavage, so that paternal genes are absent from the males, or (b) only in the germ line, so that the male is somatically biparental but transmits as a uniparental.

The letters n and n' distinguish genomes of the mother and father in the pedigree (but not when extrapolated to previous generations); n' in (b) indicates the paternal genome in the father, which is not transmitted to his offspring. (From J.J. Bull. 1979. "An advantage for the evolution of male haploidy and systems with similar genetic transmission." *Heredity* 43:361-381, Figure 1. Reprinted by permission of *Heredity*, published by Longman Group Limited, Harlow, U.K.)

not a large radiation of PGL species comparable to the radiation of some arrhenotokous groups. Second, there are no populations known that may represent the transition between PGL and an alternative genetic system. Third, PGL systems are associated with diploidy and arrhenotoky in scales and acarines (Table 11.B.2), and so either system might be entertained as an ancestor to PGL; only diploidy would seem to be a plausible ancestor to PGL in sciarids. It is difficult to offer plausible models for the evolution of PGL from arrhenotoky, and for this reason diploidy seems to be the most plausible ancestor to PGL. Only the transition from diploidy to PGL is addressed in these chapters.

Sex Determination

Sex determination is potentially interesting under PGL. In many PGL systems, the male is haploid, or the paternal genome is heterochromatized and inactive in most somatic tissues (Brown, 1963, 1964; Brown and Chandra, 1977; Nur, 1980). For these systems two quite different perspectives may be entertained (Brown and Chandra, 1977). On the one hand, sex could be determined first, and as a consequence of being male, the paternal genome is eliminated. Alternatively, it may be that paternal genome is eliminated (heterochromatized) in some eggs, and males develop as a consequence of their physiological haploidy. Sciarids are the only PGL species in which sex determination is understood, and in these cases it seems that paternal chromosome loss follows the determination of males (discussed below).

Although the sex determining mechanisms of PGL species are mostly unknown, **XX/XO** systems occur in close relatives of some PGL species of mites and scales with PGL (referenced in Table 11.B.2). An **XX/XO** system is also retained in a peculiar form in sciarids. This prevalence of **XX/XO** systems in close relatives of species with PGL would lead one to speculate that PGL is likely to evolve with male heterogamety. White (1954, 1973) in fact proposed, and Haldane (1957) concurred, that PGL was merely an extreme manifestation of male heterogamety, in which the entire genome became sex-linked and the Y-linkage group degenerated and was lost. But the interesting point here is that PGL *cannot operate* with male heterogamety because there is no transmission from father to son under PGL. Uniparental males produce only one kind of gamete, and there can be no genetic polymorphism among a male's gametes which serve as the basis of sex determination. Thus if **XX/XO** was the ancestral sex determining mechanism, a new mechanism must have evolved prior to the establishment of PGL.

PGL in Mites. Aside from work on *Sciara* and scales, which will be described below, the only thorough cytological and genetic studies of PGL have been on phytoseid mites. PGL is suggested in various mites because males are haploid yet virgin females do not lay eggs (Table 11.B.2), but only one phytoseid, *Metaseiulus occidentalis*, has been studied to observe chromosome loss (Nelson-Rees et al., 1980). Genetic markers and irradiation work on this species suggested that the parental genome had little effect on the viability of sons but had a

major effect on daughters; cytological work observed the heterochromatization and germ-line loss of one chromosome set in some early embryos (presumed males). It was not clear from this study whether the heterochromatic set was also eliminated from all somatic cells, but earlier reports that irradiating the paternal set caused sterility in sons indicated the existence of some paternal genome function in males (Nelson-Rees et al., 1980).

E. Fungal Gnats: Germ Line Loss

A peculiar combination of cytological phenomena occurs with PGL in the genus *Sciara*. A thorough summary of this work was provided by Metz (1938), correcting some of his earlier misinterpretations. The bulk of observations are from a single species, *S. coprophila*, although several other species have been studied superficially and do not contradict the observations on *coprophila*, except as indicated. Here, only the data relating to sex determination and PGL will be described. A diagrammatic summary is given in Figure 11.E.

The *Sciara* genome contains three types of chromosomes: (i) autosomes, (ii) "X" chromosomes, and (iii) in some species, germ line "limited" chromosomes. (Limited chromosomes will be discussed in the following paragraph.) All zygotes are formed with three X's and a full diploid set of autosomes: two of the X's are from the father. *The Germ Line.* Males transmit only the maternal autosomes and maternal X. However, each sperm contains two copies of the maternal X plus a set of her autosomes, so there has been a germ line loss of paternal autosomes and paternal X's, with a doubling of the maternal X. Spermatogenesis lacks crossing over, so there is no exchange of paternal and maternal genes. Females transmit autosomes and X's from both parents. One paternal X is eliminated early from all cells from the female, so females are XX (recall that all zygotes are initially XXX). *Somatic Tissues.* Males and females are biparental in their somatic tissues, retaining both set of autosomes, although one paternal X is eliminated in cells of females and both paternal X's are eliminated in cells of males (see below for sex determination). Chromosomes of the somatic tissues in females are the same as in the germ line of females (except for limited chromosomes). Male somatic tissues, however, retain all autosomes but eliminate both paternal X's, so their soma becomes essentially XO.

"Limited" chromosomes may not be essential to the flies, since they are present only in the germ line and are lacking in some species. (A selfish DNA interpretation comes to mind; cf. Doolittle and Sapientza, 1980; Orgel and Crick, 1980.) When present, there may be up to three limited chromosomes in the zygote, and these are eliminated from all somatic cells early in cleavage. One or more may be eliminated from the germ line of males, but the details were not clear to Metz in 1938, and more recent evidence suggested that paternal limited chromosomes are transmitted through males (reviewed in Brown and Chandra, 1977).

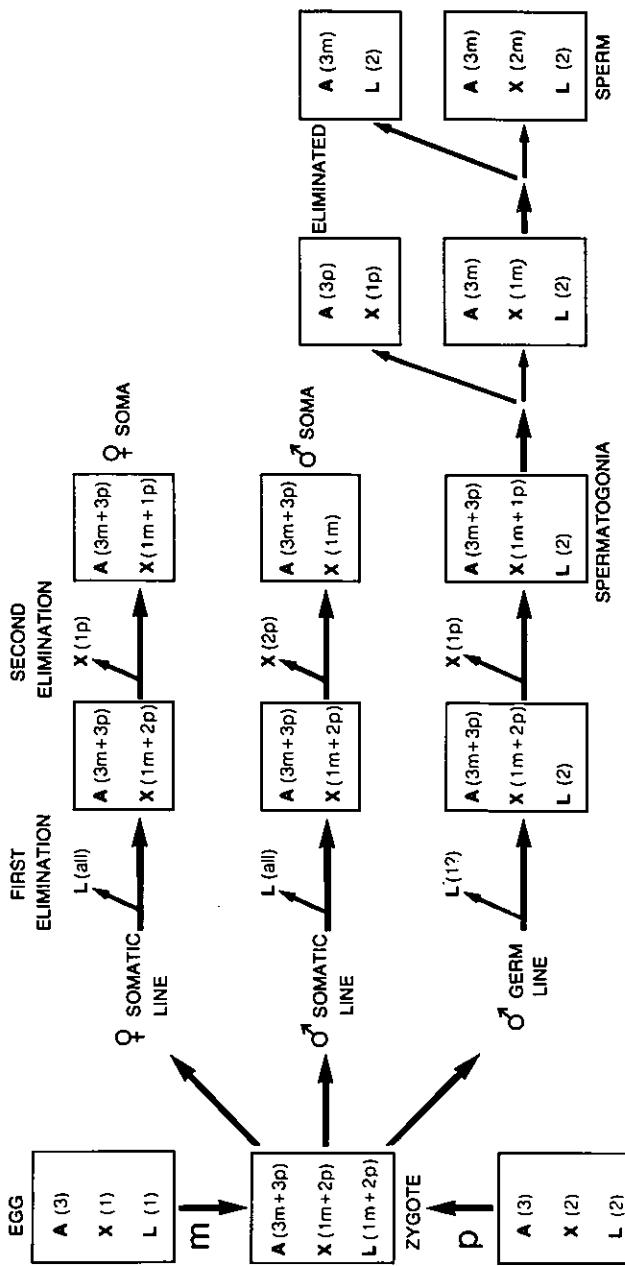


FIGURE 11.E. The chromosomes during development and gametogenesis in *Sciara*, based on *S. coprophila*. There are three types of chromosomes: autosomes (A), X chromosomes (X), and limited chromosomes (L). The chromosomes of the zygote are labeled according to the number of each type of chromosome and their origin, maternal (m) or paternal (p), applying only within a generation, as illustrated. All limited chromosomes are eliminated from the soma early; their number apparently varies from one to two in the germ line of both sexes. At another early stage, X chromosomes are eliminated: the soma of some individuals becomes **XO**, and in others becomes **XX**. **XO** individuals develop as male and **XX** as female. The male germ line eventually eliminates all paternal X's and paternal autosomes, but some paternal limited chromosomes are perhaps transmitted. The female germ line is not illustrated; it is identical to that in males up to gametogenesis, whereupon a normal oogenesis ensues that segregates maternal and paternal chromosomes. (Modified from C.W. Metz. 1938. "Chromosome behavior, inheritance and sex determination in *Sciara*." *The American Naturalist* 72:485-520, Figure 1.)

Sex determination in *Sciara* is equally interesting. All zygotes are formed with three X's, two from the father. The gonadal development of the individual—whether testicular or ovarian—is controlled in an immediate sense by the number of X's eliminated from the soma and is superficially similar to a XX/XO system. The somatic cells in some embryos eliminate two of the three X's (becoming XO) and develop as males, while somatic cells in the other embryos eliminate one X (XX) and become females. The X chromosome constitution of the germ line is XX in both sexes, with one X being lost early in both sexes (the second paternal X in male germ cells is retained until spermatogenesis). Although this *Sciara* system resembles an XX/XO system, it should be realized that the XX/XO condition is not the inherited basis of sex in these flies. All zygotes are initially formed with three X's, and their sex is determined by some (unknown) property of the egg that influences whether one or two X's will be eliminated from somatic cells. Furthermore, males produce only one kind of gamete, so there can be no *heterogamety* in males as the inherited basis of sex.

Sex in *S. coprophila* and perhaps six other species is determined according to the mother. Two types of mothers occur: son-producers and daughter-producers. In *S. coprophila* at least, the maternal sex ratio is inherited as the following 2-factor parental system,

	♀	♂	
daughter-producer	<i>Aa</i>	<i>aa</i>	(11.E.1)
son-producer	<i>aa</i>		

A genetic polymorphism in females for producing all sons or all daughters is therefore established, and the sex of the offspring has nothing to do with the father or the zygote. The locus controlling sex determination is in fact X-linked, so there is polymorphism in females for different X's. What superficially appeared to be some form of male heterogamety in *Sciara* is instead a strange form of parental female heterogamety. (This mechanism is discussed further in Chapter 15 as maternal monogamy.)

As suggested above, the two phenomena of PGL males, their sex and their elimination of paternal chromosomes, may be causally related such that one is a consequence of the other. That is, chromosome loss may be a male-limited function, or instead, a male may develop only after the embryo is committed to chromosome loss. This latter possibility is most applicable to species that eliminate or heterochromatize paternal chromosomes from somatic cells, in which it may be argued that a male results from its physiological haploidy. *Sciara* is atypical of PGL species in that the paternal genome is retained active in somatic tissues of the male. The development of a male is not the result of haploidy, because the male is not haploid. However, it still might be supposed that, for whatever reason, a male is produced in response to whether the egg is programmed to eliminate the paternal genome. Even this secondary hypothesis is inconsistent with a multitude of data, which instead reveals that the sex of the fly depends entirely upon its somatic X-cytotype, regardless of whether it is

derived from an otherwise all-female or all-male brood. Specifically, translocations combining the X and an autosome were used to produce 4X embryos (rather than the usual XXX embryos) from mothers which produce sons. These embryos eliminated two paternal X's, as did their siblings, but since they initially had four X's, two remained in the soma and they were female, transmitting paternal chromosomes (Crouse, 1943, 1960). These translocations have also generated sons from XX embryos in broods otherwise female. It is thus difficult to suppose that males are produced in response to some hypothetical property of the egg that dictates germ line loss (or retention) of the paternal genome, because it must be supposed that the egg anticipates the number of X's retained in the soma.

In some *Sciara* species observed, most females produced both sexes, but the sex ratio variance between families was greater than binomial, suggesting more than just a simple 2-factor system. In addition, there were two species, *S. similans* and *S. ocellaris*, in which some females were strict son-producers, some were strict daughter-producers, and others produced both sexes.

F. Scale Insects

Scales are coccid insects of the Order Homoptera and possess a great diversity of chromosome systems (two comprehensive and enlightening reviews are Nur, 1980; and Brown and Chandra, 1977). Diploid sexual scales with male heterogamety are known (XX/XO) as are species with arrhenotoky and with PGL (Table 11.B.2). The taxonomic occurrence of PGL in scales suggests that PGL has evolved from diploid systems, but there are two cases in which PGL may have reverted to diploidy (Nur, 1980). Even in scales with a diploid genetic system, meiosis is unusual because the first meiotic division is equational (separating sister chromatids), and the second division is reductional. This condition apparently preceded and may have facilitated the evolution of PGL (Brown and Chandra, 1977; Nur, 1980).

Generic names are attached to three of the PGL systems in scales to facilitate distinguishing them (Brown, 1963, 1964): (i) lecanoid, (ii) Comstockiella, and (iii) diaspidid. These three systems are found in the taxonomic Sections Lecanoidae and Diaspidoidae of coccids and they differ only in the details of paternal chromosome elimination. The lecanoid and Comstockiella PGL systems are alike in that both involve spermatogonial loss and somatic retention of paternal chromosomes in males (refer to b in Fig. 11.D, p. 153); the two systems even occur in different cells of the same testis! The paternal chromosomes in males are largely heterochromatic in both systems. They are eliminated from the germ line during spermatogenesis in the lecanoid system, and somewhat earlier in the Comstockiella system. Much of the chromosome behavior in males was studied by irradiating paternal chromosomes; only daughters were seriously affected, and in males, the induced rearrangements were always of the heterochromatic set (Brown and Nelson-Rees, 1961). Brown (1963, 1964) originally suggested that some paternal chromosomes were transmitted by males in the Comstockiella system, but Kitchin (1970) showed

this to be false, a study I failed to note in my previous discussion of these systems (Bull, 1979).

The diaspidid system eliminates all paternal chromosomes from most cells in males during cleavage, resulting in a male that is haploid in both germ and somatic cells (Fig. 11.D, part *a*). However, the paternal set is retained and is euchromatic in the pentaploid mycetocytes, cells that harbor maternal symbionts (Brown and Chandra, 1977). Brown and Chandra suggested that the diaspidid system evolved from the lecanoid/Comstockiella system on several occasions.

A few observations have been noted about the mechanism of heterochromatization in lecanoid and Comstockiella systems. The heterochromatic paternal set of males is late replicating and does not synthesize RNA (Brown and Chandra, 1977; Sabour, 1972). Nur (1967) observed that heterochromatization was reversed in some somatic tissues of species with the lecanoid system. It is also of interest that, in an arrhenotokous scale with diploid but uniparental males, one of the *maternal* chromosome sets became heterochromatic in these males, so heterochromatization is not generally restricted to chromosomes of paternal origin (Nur, 1971).

The inheritance of sex is unknown in scales with PGL, although it seems that sex is often determined by the mother. Nelson-Rees (1960) described and reviewed some environmental and maternal-age effects on secondary sex ratio in a few species. Nur (1963) obtained what may have been both sexes of offspring by a form of parthenogenesis that ensured genetic identity among progeny, so in this instance, sex was not determined by genetic differences among the individuals. Males were merely inferred because one set of their chromosomes was heterochromatic, so their identity as males was equivocal. In the literature on scale PGL systems, there has sometimes been a tendency to regard the physiological haploidy as the cause of becoming male, rather than the reverse—chromosome loss limited to embryos destined to be male. Brown and Chandra (1977) acknowledged both possibilities, but there do not seem to be data which refute either interpretation of sex determination.

G. Summary

This chapter reviewed the various genetic systems of uniparental males—males that transmit only the maternal genome. There are two basic types of systems: arrhenotoky and paternal genome loss. Arrhenotoky is the production of sons from unfertilized eggs, occurring in hymenopterans and several other invertebrate groups. PGL is the production of sons from fertilized eggs, but these males do not transmit the paternal genome. PGL is known in fungal gnats, scale insects and phytoseid mites. Most of the work on these systems has been of a cytological nature to observe chromosome behavior. With the exception of a few species of Hymenoptera and fungal gnats (*Sciara*), little is known about the genetics of sex determination in these systems, nor is anything known about the genetic control of chromosome loss in PGL systems.

12

Advantages of Producing Uniparental Males

Despite many variations among uniparental male systems, each shares the property that males transmit only the maternal genome, and it would be satisfying to offer a general explanation for the evolution of this characteristic. Since the males in these systems are often haploid and consequently have unusual meiotic processes, the initial uniparental males would seem to be at a disadvantage in competing with biparental males. Why, then, should uniparental males replace biparentals?

This chapter describes some possible advantages for the evolution of uniparental male systems, both for arrhenotoky and for paternal genome loss. There is one important message in this chapter: in outbred populations, there appears to be an advantage for the evolution of uniparental males irrespective of whether the system is arrhenotoky or paternal genome loss. Mothers of uniparental sons transmit more genes to grandchildren than mothers of biparental sons as long as uniparental sons are sufficiently fit, but not necessarily as fit as biparental sons. This advantage stems from the "cost of meiosis," a phenomenon recognized previously as an advantage for the evolution of parthenogenesis (Williams, 1975, 1980; Maynard Smith, 1978). While other advantages of uniparental male systems are conceivable in special cases, this particular case is quite general and may provide the insight necessary for understanding the evolution of these systems. Although it is doubtful whether

the past evolution of uniparental male systems can be understood, the models developed here should be useful in studying transition populations yet to be discovered.'

A. A Segregational Advantage for the Mother

In random-mating populations, there is a general set of conditions for which selection increases the frequency of mothers producing uniparental rather than biparental sons. For the moment, the details of sex determination and the type of uniparental-male system may be ignored, in order to simply consider whether mothers of uniparental sons transmit more genes to future generations than mothers of biparental sons. Two components of selection on these mothers are: (i) uniparental males may have fewer offspring than biparental males, and (ii) uniparental males transmit only their mother's genes. These components work in opposite directions. Consider the first component of selection. In many diploid species it is easily imaginable that uniparental males, for one reason or another, would be so inferior to biparental males that they might have no offspring at all. This inferiority would result if uniparental males were haploid, expressing deleterious recessive genes normally masked in the diploid, or if they underwent a haploid meiosis and produced chromosomally unbalanced sperm. Certainly, uniparental males would not evolve if they were inviable or sterile. Nonetheless, it can generally be expected that the initial uniparental males will be inferior to biparental males, a fact which mitigates against their evolution.

Now consider the second fitness component. *Mothers of uniparental sons share a greater genetic identity with grandchildren than mothers of biparental sons.* This increased identity occurs because all the genes transmitted by a uniparental male are of maternal origin, whereas only half the genes transmitted by a biparental male are of maternal origin. The probability of gene identity-by-descent between grandmother and grandchild through uniparental sons is therefore double the probability through biparental sons (Fig. 12.A). (This computation is valid only if uniparental males are as likely to appear in broods sired by either uniparental or biparental fathers, such as under random mating.) The increased genetic identity between grandmother and grandchild resulting from uniparental sons may overcome the potential lower fitness of these sons, such that mothers of uniparental sons have more genes in grandchildren even though fewer grandchildren are produced. The increased genetic identity is a special case of Williams' "cost of meiosis" (1975, 1980) and may provide the key to understanding the advantage of producing uniparental males.

Placed into quantitative terms, assign the fitness of uniparental males as w compared to biparentals, representing the expected number of offspring from a uniparental male zygote relative to a biparental male zygote. The expected

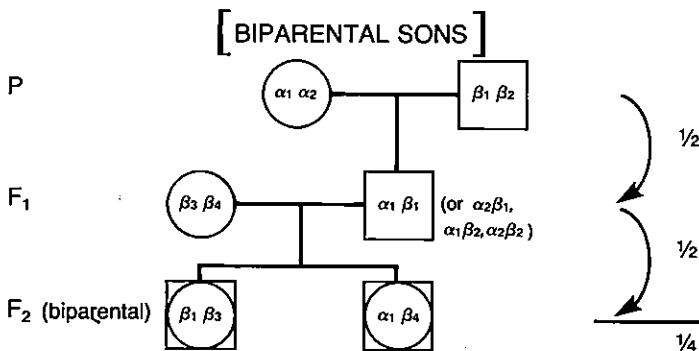
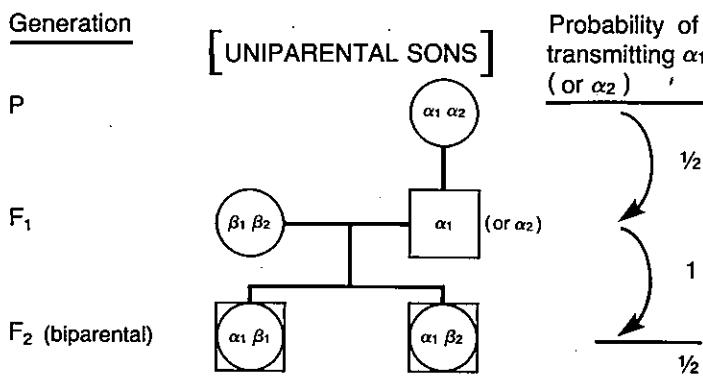


FIGURE 12.A. The probability of gene identity-by-descent is doubled between a P_1 female and her biparental grandchildren (F_2) if she produces uniparental sons instead of biparental sons. Circles are females, squares are males. (Top) Uniparental sons transmit their inherited maternal allele, α_1 or α_2 , to all their progeny. (Bottom) Biparental sons transmit their inherited maternal allele to only half the progeny, because they segregate paternal alleles as well. The right column indicates the probability that a particular maternal allele will be transmitted through the pedigree to the next generation. Alleles are labelled α_i , β_j to denote a distinction by origin rather than by type; the symbol α is limited to P_1 female alleles for ease in identification. F_2 uniparental males do not inherit (transmit) alleles from F_1 males, so they are not represented; arguments in the text assume that the fraction of F_2 uniparental males is the same for both pedigrees.

number of maternal genes transmitted to grandchildren through a uniparental son is $2w$ for every gene transmitted through a biparental son. If $2w > 1$, hence $w > 1/2$, it is expected that a female transmits a greater number of genes to her grandchildren through a uniparental son (Bull, 1979).

How might this model apply to the evolution of uniparental males? Consider a gene that causes a mother to produce uniparental sons instead of

biparental sons. If $w > 1/2$, all the genes in this mother would be transmitted to more grandchildren than would the genes in mothers producing biparental sons. Consequently, the gene causing mothers to produce uniparental sons increases over the alternative allele—the allele associated with mothers producing biparental sons. This argument applies equally to arrhenotoky, where uniparental sons arise from unfertilized eggs, and to PGL, in which sons arise from fertilized eggs but eliminate the paternal genome. Furthermore, once PGL or arrhenotoky has evolved, no further advantage of this kind is gained by evolving to an alternative system of uniparental males (i.e., no similar advantage for the transition from PGL to arrhenotoky or the reverse).

If uniparental male fitness exceeds $1/2$ and biparental males are consequently eliminated from the population, it is expected that biparental males will not later reinvade and displace uniparental males (within the context of this model). Once w exceeds $1/2$ and uniparental males become common, selection will likely improve any cytological and genetic problems they experience from being uniparental, so that w will further increase, perhaps in excess of unity. As long as w does not drop below $1/2$, there is continual selection of mothers producing uniparental sons, and diploid males will not reinvade. However, the subsequent evolution of biparental males may occur for other reasons, as described in Section 12.C.

In recognizing this advantage of uniparental males, the existence of so many species with biparental males requires explanation. There apparently have been only a few origins of uniparental male systems, so we can only surmise that various constraints may prevent many species from making the transition, even though the transition would be favored if the initial complications could be overcome. Several possible constraints mitigating against the evolution of arrhenotoky have been discussed by Whiting (1945), Hartl and Brown (1970), and White (1973), as will also be considered below.

In extending the combinatorialist perspective, it becomes evident that other systems can be enumerated in which the offspring of one sex transmit genes from just one parent. Moreover, it is not difficult to determine that the “cost of meiosis” advantage applies equally to these other systems. It is therefore pertinent to ask why the only systems with uniparental offspring are those in which males transmit the maternal genome. A discussion of this problem is offered in Appendix 12.I.

B. The Mechanics of Producing Uniparental Sons

If the argument is accepted that mothers transmit more of their genes to grandchildren through uniparental sons than through biparental sons when $w > 1/2$, the next question might be: how can a mother produce uniparental sons instead of biparental sons? Contemporary species with arrhenotoky or PGL do not necessarily provide clues, because biparental males are no longer present. We must instead resort to hypothetical models in which both types of

males are assumed present, and ask what distinguishes mothers of uniparental sons from those of biparental sons. Arrhenotoky and PGL differ in this respect, and must be considered separately.

Arrhenotoky. Once arrhenotoky has been established, males arise from unfertilized eggs and females from fertilized eggs, but during the transition to arrhenotoky, males as well as females must have arisen from fertilized eggs. The models proposed for this process assumed a diploid ancestor (biparental males), followed by the evolution of facultative parthenogenesis—eggs awaited fertilization but then developed if unfertilized (Hartl and Brown, 1970; Bull, 1979, 1981c). This process led to a population in which the unfertilized eggs became uniparental males but fertilized eggs became females or males according to the sex determining mechanism. Therefore, a mother could invariably produce a uniparental son by not fertilizing the egg, but she was not assured of producing a daughter from a fertilized egg as long as biparental males remained in the population.

In these models the frequency of uniparental males within a mother's brood depended on the proportion of eggs she left unfertilized. The frequency of biparental males was not directly controlled by the mother but instead responded to the level of unfertilized eggs in the population as a whole. The frequency of biparental males decreased as the frequency of uniparental males increased, and they were eventually lost if uniparental males were sufficiently common (depending somewhat on the sex determining mechanism; see Chap. 13). There was consequently direct selection on the mother for the fraction of uniparental sons she produced, with a feedback on the level of biparental males at the population level. If $w > 1/2$, there was selection of mothers producing enough unfertilized eggs such that biparental males were eventually lost, and the population became arrhenotokous. If $w < 1/2$, there was selection of females producing all fertilized eggs, and diploidy evolved (Bull, 1979, 1981c). So even though a mother could not produce uniparental sons in strict exchange for biparental sons, the evolution of uniparental males nonetheless required $w > 1/2$.

Two major constraints in this process are facultative parthenogenesis and an appropriate sex determining mechanism. The applicable sex determining mechanisms will be addressed in Chapter 13. Facultative parthenogenesis may seem to be extremely rare in diploid species, but any preconception of this sort may be in error, simply from insufficient study. Whiting (1945) reviewed several cases of facultative parthenogenesis in species normally outcrossed and biparental, and the work on ESD in mermithid nematodes has casually observed facultative parthenogenesis in several species (Sec. 9.C). Even more interesting is the work on *Drosophila* (reviewed by Templeton, 1982). Although this genus was the focus of extensive genetic studies during the early to mid 1900's and beyond, facultatively parthenogenetic species were not discovered until the 1950's (Stalker, 1954). Then, once it was specifically sought, facultative parthenogenesis was discovered in approximately 3/4 of the species

(23 of 28), although all impaternal offspring died before reaching maturity in most species. Most of these species produced only a tiny fraction of offspring parthenogenetically if females were uninseminated, so it was not evident unless investigated specifically. The potential for facultative parthenogenesis may be common in many groups of animals and may therefore comprise only a minor hurdle in the evolution of arrhenotoky.

Paternal Genome Loss. Whereas under arrhenotoky a mother produces a uniparental son by failing to fertilize an egg, here all eggs are fertilized, and males do not transmit the paternal genome. There are two possible types of PGL mechanisms with respect to evolution within this framework. In one type (*Sciara*-type), sex is determined first, and chromosome loss is conditional upon becoming male. In the second type, which has yet to be conclusively demonstrated but which could exist in scale insects or mites, paternal chromosomes are eliminated in some embryos, and the haploidy produces males. Under maternal control of chromosome loss, evolution of this latter mechanism is algebraically similar to the evolution of arrhenotoky, because eggs casting out the paternal genome are analogous to unfertilized eggs. There is of course a fundamentally different genetic basis for PGL as there is for arrhenotoky, since one involves chromosome elimination and the other involves parthenogenesis. However, because of the formal similarity between the evolution of arrhenotoky and of this second type of PGL, the discussion here shall be limited to the *Sciara*-type mechanism.

The evolution of PGL has been considered in a simple fashion, given that little is known about the genetic control of chromosome elimination (Brown, 1964; Bull, 1979). The models of Brown and Bull differed in some minor respects, but in general they assumed that a gene with no effect on sex determination caused paternal chromosome loss in males whenever it was inherited from the mother (in the egg). Further, the gene had no effect when transmitted through sperm. Under PGL, the evolution of uniparental males was therefore viewed as selection of a maternal effect causing paternal chromosome loss in sons. With random mating, the gene causing this maternal effect increased if uniparental males were more than half as fit as biparental males ($w > 1/2$), and decreased under the reverse inequality (Bull, 1979; Brown, 1964, assumed that $w = 1$, so there was necessarily always selection of uniparental males). Again, however, the evolution of PGL is constrained by the sex determining mechanism, as discussed in the following chapter.

In the evolution of PGL, it is not necessarily clear how mutations cause the proper type of chromosome loss. First, they must cause the loss of the father's chromosomes, but only in sons, and only in sons of mothers with the mutation. This effect could be achieved through the maternal genotype affecting the constitution of the egg, or through control by the haploid egg genotype itself. However, these are remarkably complicated requirements, and it is not at all clear that they could be accomplished by one gene. Several mutations known from *Drosophila* and a dosage compensation mechanism from

marsupial mammals offer insight to the possibilities of such mutations. In *Drosophila*, the well-known system of *segregation distortion* is a naturally occurring mechanism of chromosome loss in males. Males heterozygous for the relevant chromosome region show a striking transmission bias in favor of one of the chromosomes—nearly 100% in some cases (Hartl and Hiraizumi, 1976). The segregation distortion operates through preferential destruction of spermatids inheriting the disfavored chromosome, irrespective of parental origin.

Other *Drosophila* mutations demonstrate maternal effect and discrimination of paternal versus maternal chromosomes. *Claret* and *mitotic loss inducer* are two recessive mutations causing sporadic chromosome loss in embryos of homozygous mothers, regardless of paternal or offspring genotype (Baker and Hall, 1976; Hall et al., 1976). *Claret* leads to preferential loss of one or more maternal chromosomes during cleavage, while *mitotic loss inducer* causes loss of chromosomes later than cleavage and regardless of parental origin. An additional mutation, described by Levitan (1963), caused breakage of paternal chromosomes in the offspring of mutant mothers, satisfying the requirement of a paternal-maternal chromosome distinction. Therefore, while no mutations in *Drosophila* are known to fulfill all the requirements for a one-gene model of PGL, there are mutations that show some of the requisite characteristics.

The marsupial mechanism of dosage compensation illustrates the preferential inactivation of the paternal X chromosome. In mammals, females are XX, males XY, and the Y lacks most or all X-linked loci. A mechanism known as dosage compensation is present, in which one X in female somatic cells is inactivated, so that both sexes have the same level of expression for X-linked loci. In marsupials, and in some extra-embryonic tissues of placental mammals, the paternal X is preferentially inactivated (Cattanach, 1975; Cooper et al., 1977; Brown and Chandra, 1977; VandeBerg, 1983; VandeBerg et al., 1983). While the paternal X inactivation system exhibits some PGL characteristics, there is as yet no thorough understanding of the genetic steps involved in this process.

C. The Disadvantage of Uniparental Males—To the Father

Uniparental males increase the transmission of maternal genes at the expense of the would-be father. Consequently, there is selection in the most extreme form of genes that, when transmitted through sperm, avoid this elimination (provided they have no deleterious effect when transmitted through females). Under PGL, the paternal genome is present in males, at least temporarily; any tendency for these genes to be transmitted in the male's sperm is selected, because the genes are otherwise eliminated. Fitness of the resulting biparental males could be only infinitesimal, yet the tendency would still increase and the

population would revert to diploidy. Figure 12.C offers a diagrammatic representation of the fitness constraints on the evolution of PGL under maternal, paternal, and zygotic control of chromosome loss. The evolution of PGL is least restricted under maternal control of chromosome loss, and it is impossible under paternal control.

Selection of sex ratio variation among fathers is slightly more complicated under arrhenotoky than it was under PGL, but this process again leads to the evolution of diploidy. Sperm are selected to fertilize eggs, *all* eggs if possible. Under arrhenotoky, these biparental offspring are daughters rather than sons, but as the sex ratio becomes increasingly female biased, the reinvasion of biparental males is facilitated.

Since the evolution of uniparental males is selected in opposite directions under maternal versus paternal inheritance of this characteristic (assuming $w > 1/2$), the population may oscillate through time between systems of uniparental and biparental males. This potential was clearly recognized by Brown (1964) in a very stimulating discussion of the evolution of PGL (although some aspects of his interpretation of scale PGL systems from this perspective have since been shown to be incorrect, Kitchin, 1970). Nur (1980) described two independent examples of apparent reversions from PGL to diploidy, one within the genus *Lachnодиус*. It is of course unknown if these reversions were selected through genes of paternal effect.

The reversion from uniparental males to biparental males may be more apt to occur in some systems than in others, and consequently the most stable systems of uniparental males would be favored. The characteristics of uniparental male systems may be investigated in this light. Arrhenotoky seems

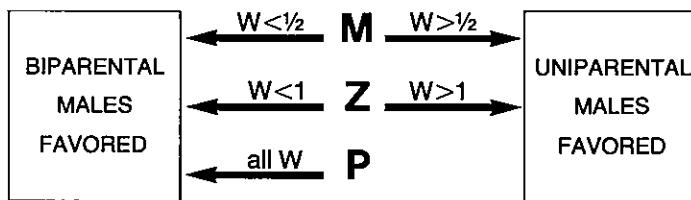


FIGURE 12.C. Diagrammatic summary of the evolution of paternal genome loss for three different modes of inheritance of the trait. If a gene causing paternal chromosome elimination in males does so only when inherited from the mother (M, top), then the fitness (w) of uniparental sons must exceed half that of biparental sons in order to evolve. If elimination occurs in all male zygotes inheriting the gene, (Z, middle, not discussed in the text), the uniparental males must be of greater fitness than biparentals. If the gene acts only when inherited paternally (P, bottom), uniparental males can never evolve. (From J.J. Bull. 1979. "An advantage for the evolution of male haploidy and systems with similar genetic transmission." *Heredity* 43:361-381, Figure 3. Reprinted by permission of *Heredity*, published by Longman Group Limited, Harlow, U.K.)

unlikely to revert to diploidy, since the sex ratio under arrhenotoky can be controlled by whether or not the mother fertilizes her eggs. Once this maternal capacity is perfected it seems that the male can have relatively little effect on increasing the proportion of daughters (although Hamilton, 1967, reviewed a few cases in which the mother may not control fertilization once she is inseminated). PGL systems may be more likely than arrhenotoky to revert to diploidy, since the paternal genome is present in sons at least briefly. However, the early loss or heterochromatization of paternal chromosomes may prevent paternal expression that could lead to biparental sons, and these properties are indeed observed in many PGL systems.

D. Inbreeding and Non-Random Mating

Whiting (1945), Brown (1964), and Hartl and Brown (1970) noted that the fitness of haploid males, when they first arise in a diploid population, is likely to be low because of an unavoidable expression of deleterious genes. (The emphasis here is on *haploid* males.) The supposedly detrimental effect of haploidy is anticipated from the well-known phenomenon of inbreeding depression, whereby sudden inbreeding leads to a marked reduction in viability (Falconer, 1981, p. 225). Inbreeding depression is explained by the fact that in a diploid population, recessive deleterious genes are maintained at low frequency by selection-mutation balance or a weak heterozygote advantage, and few homozygotes for the deleterious genes occur (Crow and Kimura, 1970, p. 260). A rapid increase in inbreeding increases the frequency of individuals homozygous for the deleterious alleles, with a consequent decline in mean fitness (provided that the deleterious genes tend to be recessive). Haploidy is presumably the same as complete homozygosity, since haploids inheriting deleterious genes do not have alternative alleles to mask them. Although the chance that a haploid male would inherit a highly deleterious allele is small for each locus, when considered for the entire genome, the probability of inheriting one or more deleterious genes is large.

Haploid males from inbred populations have a smaller chance of inheriting deleterious genes than do those from outbred populations. Inbreeding in a diploid population increases the frequency of homozygotes above that which would occur under random mating, and the equilibrium level of recessive deleterious genes is consequently reduced. Thus the discrepancy in fitness between a haploid and diploid male is likely to be less for inbred than for outbred populations. This argument led Brown (1964) and Hartl and Brown (1970) to propose that inbreeding enhances the evolution of haploid male systems, since their evolution is facilitated by a relatively high fitness of uniparental males. It should be emphasized that this argument applies only to uniparental males that do not express a paternal genome in their soma (*haploid* males). Uniparental males in *Sciara* do not apply here, since they

presumably express paternal and maternal genes in their somatic tissues, and therefore they would not be inclined to express deleterious genes more than biparental males.

Borgia (1980) emphasized a different point regarding the inbreeding argument. If mating is confined to small groups of individuals by virtue of their location of birth, such that males do not compete at large, a weak male might be able to mate, simply because it is the only male with access to a particular group of females. This phenomenon is known as "local mate competition," and has been studied with respect to sex ratio selection by Hamilton (1967). Local mate competition usually involves the mating of sibs, and so may be associated with inbreeding.

There is little doubt that many types of uniparental males are more likely to be viable and breed if they arise from inbred rather than outbred species. However, the evolution of male haploidy involves more than just the viability of uniparental versus biparental males, and inbreeding may have two negative effects on the evolution of male haploidy (Bull, 1979). (i) It was argued above that the advantage for a mother producing uniparental sons is that her grandchildren from these sons would inherit her alleles at twice the frequency they would if she produced biparental sons. Under inbreeding, the mating of close relatives increases homozygosity, increasing the probability that the two alleles within each individual are identical-by-descent (Crow and Kimura, 1970, Chaps. 3 and 4). Therefore, an inbred biparental male may inherit two copies of the maternal gene because his mother mated with a close relative who also carried genes identical-by-descent to hers. A biparental son with both alleles identical-by-descent to those of his mother is equivalent to a uniparental son in this respect. Therefore, inbreeding increases the probability of gene identity-by-descent between mother and grandchild through diploid sons and so reduces the advantage of uniparental sons. While this conclusion certainly holds for some systems of inbreeding, it must be emphasized that its application to systems of inbreeding in general remains conjecture.

(ii) A second complication from inbreeding concerns the possible deleterious effect of mating with close relatives. The initial uniparental males may face complications in meiosis causing them to produce aneuploid sperm (with extra or too few chromosomes). Aneuploid sperm can fertilize eggs in many species, so the progeny produced by these sperm would likely die. Under outbreeding, the two types of mothers—those producing uniparental sons, and those producing biparental sons—mate with uniparental males in proportion to their frequencies in the population. That is, each type of mother loses offspring to aneuploid sperm at the same rate. However, under inbreeding, uniparental males preferentially mate with sisters or other closely related females, and these are the females producing uniparental sons. The aneuploid sperm preferentially decrease the fecundity of these females, so the mothers of uniparental sons would be at a disadvantage.

There has been no thorough mathematical analysis of the interaction between inbreeding and the evolution of uniparental males. It seems unlikely that

complete sib-mating would usually enhance the evolution of uniparental males (models unpublished), but moderate degrees of inbreeding may be favorable. Systems with uniparental males are indeed often characterized by high degrees of inbreeding (Borgia, 1980), but it is difficult to determine whether inbreeding evolved before or after the appearance of uniparental males. The argument that the viability of haploid males is higher for an inbred than an outbred population may also be true in the reverse: male haploidy reduces the deleterious consequences of inbreeding. It is probably easier to evolve inbreeding under most forms of uniparental male systems than under diploid systems, because the haploid expression accompanying most types of uniparental males maintains recessive deleterious genes at low frequency. The phenomenon of inbreeding depression observed in most diploid populations may therefore be only slight in uniparental male populations (Hartl and Brown, 1970).

There are some uniparental male systems in which inbreeding is apparently absent, and there are others whose evolution would seem to have been precluded under extreme inbreeding. As noted by Hamilton (1967), the all-son/all-daughter mothers in *Sciara* with PGL preclude sib-mating (Sec. 11.E). Recall that *Sciara* males retain paternal chromosomes in the soma and thus presumably do not experience haploid gene expression. They might be adversely affected by inbreeding depression were they to inbreed. The sex determining mechanism of Hymenoptera, in which diploid homozygotes as well as haploids are male (Secs. 3.F, 11.C), could not have evolved arrhenotoky under extreme inbreeding, because nearly half the fertilized eggs would have become biparental males (Bull, 1981c; Sec. 13.B). However, aside from these few points, the importance of inbreeding in the evolution of uniparental male systems remains obscure.

E. Ecological and Sex Ratio Advantages of Arrhenotoky

Facultative parthenogenesis and other aspects of arrhenotoky permit certain behaviors not possible in most diploid or PGL species that may confer an advantage to arrhenotoky in special cases. As hypotheses, none of these has a general appeal equal to that of the "cost of meiosis," and it is hard to determine if any of these effects are as important.

Sex Ratio

In contrast to PGL, arrhenotoky allows the mother to control the sex of her offspring by influencing fertilization of each egg. Maternal control of offspring sex has been studied in several arrhenotokous hymenopterans, and there are many species whose life histories select for sex ratio modification in response

to the environment (i.e., a family sex ratio other than 1/2, Charnov, 1982). Selection of sex ratio control may provide an advantage for arrhenotoky in addition to the increased grandmother-grandchild gene identity (Sec. 12.A). Moreover, it is an advantage unique to arrhenotoky rather than to PGL, so that sex ratio control may constitute one advantage for the evolution of arrhenotoky from PGL.

Selection of sex ratio control commonly takes two forms in free-living hymenopterans: sex ratio modification in response to a patchy environment (Charnov et al., 1981; Charnov, 1982), and production of a female-biased sex ratio under local mate competition (Hamilton, 1967). In a patchy environment, with some patches relatively beneficial to males and others relatively beneficial to females, the mother is selected to adjust her sex ratio in each patch toward the sex experiencing the greatest relative benefit. This conclusion follows from the argument offered for nematodes under ESD (Sec. 10.B), except in this case the mother controls the sex ratio and is able to assess patch quality, but she is unable to freely choose patch type. There are in fact many examples of such life histories in solitary wasps, and the sex ratio corresponds to theoretical expectations (Charnov, 1982). In one well-studied parasite of grain weevils, host size varies: mother wasps preferentially put sons in small hosts and daughters in large hosts, since females benefit from large host size more than males do. The evolution of arrhenotoky is enhanced in such a situation because selection favors females that place sons (unfertilized eggs) in patches beneficial to males, and the presence of these uniparental males brings about a reduction in the frequency of biparental males. This particular advantage of arrhenotoky is perhaps weak for most plausible biological situations, although it supplements the advantage of producing *uniparental* sons (Sec. 12.A).

A second sex ratio advantage, as described by Borgia (1980) and in less detail by Hamilton (1967), is highly restrictive, but it is mentioned here as one of the few ways in which arrhenotoky may be advantageous under extreme inbreeding. The argument requires extreme local mate competition, such as would be accompanied by sib-mating. The population is substructured so that progeny are born in small groups of one or a few families. Mating occurs exclusively within these groups, and the inseminated females disperse to find new sites to lay eggs, completing the cycle. The model also requires male heterogamety, XX females/XY males and unfertilized eggs (X) developing into male, or an alternative sex determining mechanism in which biparental males can be lost abruptly. The sperm of XY males produce biparental sons in half the fertilizations, but sperm of uniparental males (X) produce only daughters. As long as a few eggs are always unfertilized, a few males will arise in broods of haploid sires, and they will be perpetuated.

The possible advantage here is that the sex ratio in broods from uniparental males can be highly female biased, while the sex ratio of biparental male (XY) broods is always at least 1/2 male. The extreme local mate competition structure assumed in this population selects a heavily female biased sex ratio

In this diagram,* females are restricted to the left of each pedigree, males to the right, and arrows indicate genetic transmission. The letters *m* and *p* in the parental generation represent the genomes of males and females, respectively, regardless of their origins in previous generations. In the filial generation, *m* and *p* are those parental genomes that have been inherited and will be transmitted to their offspring.

All of these systems have a similar advantage for their evolution under outbreeding: there is selection of one parent to produce "uniparental" offspring—those transmitting only his or her genome—provided these uniparentals are more than half as fit as their biparental counterparts. This conclusion stems from the gene-identity (cost of meiosis) advantage already described in this chapter. We now consider the four possible systems. In two systems the maternal genome is transmitted uniparentally, through sons or daughters, and in two systems the paternal genome is transmitted uniparentally. Why, then, are three of these systems essentially unknown? In the brief discussion that follows, it will be argued that biases in either (a) the *origin*, (b) evolutionary *stability*, or (c) the ability to *detect* the system renders PGL and arrhenotoky the most probable systems to be found.

System I

Maternal Sons: males transmit only the maternal genome. This system includes arrhenotoky and PGL. (a) Origin. Based on Chapters 11 and 12, this system can arise either by parthenogenetic production of sons or by PGL. (b) Stability. Both forms of this system are evolutionarily stable, because reproduction is sexual with a sex ratio equilibrium of 1/2 (in most cases, see Chapter 13); it also does not readily revert to diploidy. (c) Detectability. Many of these systems are readily detected because of the parthenogenetic production of sons and/or unusual cytological properties of males. The bases for these conclusions are to be found collectively in Chapters 11 and 12, Maynard Smith (1978), Hartl (1972), and Hamilton (1967).

System II

Paternal Daughters: females transmit only the paternal genome. This system is unknown. (a) Origin. Since only the paternal genome is transmitted by females, this system can evolve only with post-fertilization chromosome loss (maternal genome loss). This system is most easily selected if maternal

*From J.J. Bull. 1979 "An advantage for the evolution of male haploidy and systems with similar genetic transmission." *Heredity* 43:361-381, Figures on p. 375. Reprinted by permission of *Heredity*, published by Longman Group Limited, Harlow, U.K.

chromosome loss is caused by a paternal effect, rather than a zygotic effect (by analogy with system I, Fig. 12.C), but the feasibility of such mutations is unknown. It seems likely that such mutations would be susceptible to various maternal influences to avoid chromosome elimination. The origin and immediate persistence of this system are therefore in question. (b) Stability. Many of the dynamic properties of this system are the same as in system I, since both systems differ only in a change of the sexes, so given the necessary genetic basis for its existence, there are no necessary problems in the maintenance of this system. (c) Detectability. Only the female is unusual, and perhaps only in oogenesis, where the maternal set is eliminated. Oogenesis normally eliminates half the chromosomes, so markers would be required in order to determine if the maternal set was always eliminated. Hence, an observational bias renders this system unlikely to be detected, even if it exists.

System III

Paternal Sons: males transmit only the paternal genome. This system is unknown. (a) Origin. This system also requires mutations causing post-fertilization loss of the maternal genome, and its origin faces the same complications as system II. (b) Stability. The maintenance of this system has several problems not encountered above. Sons inherit only the paternal genome, so there is no mixing of genes in this line, and males are asexual. The female line is continually purged by genes from males. Such populations might be short-lived because of the lack of recombination (Maynard Smith, 1978). There is yet another problem from sex ratio selection. Under random mating there is selection to produce only sons, although with local mate competition any sex ratio could be selected, so the population need not become extinct from this effect alone. (These conclusions about sex ratio follow Hamilton's 1967 treatment of Y-linked sex ratio evolution.) (c) Detectability. This system would be detected readily because of the unusual cytological properties of males, and possibly an unusual sex ratio.

Examples. Although this exact system is unknown, males in some European frog populations (*Rana esculenta*) transmit only the paternal genome to sons. These males are actually two-species hybrids, and they mate only with females from the parental species (Uzzell et al., 1975, 1977; Uzzell and Berger, 1975; Uzzell, 1978).

System IV

Maternal Daughters: females transmit only the maternal genome. This system has fewer complications than the two "paternal" systems, II and III. (a) Origin.

A maternal daughter system may arise either with parthenogenetic production of daughters or the PGL in daughters. (b) Stability. The long-term persistence is problematic because the female line is asexual, and the male line is continually purged by genes from the female line. Selection favors elimination of males under random mating, but with parthenogenesis or if males from neighboring species could be used for fertilization, the population would not go extinct. Local mate competition may favor the production of some sons, but the sex ratio should always be female biased. (Sex ratio considerations follow from Hamilton, 1967, and Maynard Smith, 1978.) (c) Detectability. The discovery of this system is facilitated by the biased sex ratio and parthenogenesis. However, because of selection to eliminate males under random mating, these systems may be transformed into all-female populations.

Examples. There are many species in which females transmit only their mother's genome, but most of these do not produce males as well. They either reproduce parthenogenetically or they use males of sympatric species for sperm (gynogenesis, hydridogenesis; White, 1973; Schultz, 1977; Maynard Smith, 1978). There is no reason to suppose that these systems often or ever pass through an intermediate population similar to system IV, because the production of all-female broods can arise directly.

An example of system IV was described in the nematode *Rhabditis monohystera* (Belar, 1924). The sex ratio in this species was reported to be 15 females to one male. In a cytological study, the observed ova were of two types, differing in whether the second meiotic division was normal or suppressed. If meiosis was normal, then fertilization was also normal, and the sperm pronucleus fused with the egg pronucleus to produce a biparental male. If the second meiotic division was suppressed, the sperm degenerated upon entering the egg, and the individual became a uniparental female, inheriting only the maternal genome. A heavily female biased sex ratio is expected, as was observed, but it would be interesting to know why males were not completely eliminated. Nigon (1949b) studied the same or a similar species as Belar. Nigon found that about half the biparental offspring developed as females, suggesting male heterogametic sex determination, although chromosome numbers were the same in both sexes. If correct, this system represented a slight variation of system IV, due to the few biparental females.

13

Joint Evolution of Uniparental Males and Sex Determination

The preceding chapter described some possible advantages for the evolution of arrhenotoky and paternal genome loss, but those descriptions did not discuss the sex determining mechanism involved in this process. The reader will perhaps not be surprised to discover that the sex determining mechanism interacts with the evolution of uniparental males in some interesting ways. This chapter presents models for the evolution of arrhenotoky, followed by models for the evolution of paternal genome loss (PGL). Random mating will be assumed throughout the chapter.

A. Arrhenotoky

If the predecessor to arrhenotoky is assumed to be diploidy with biparental males, the origin of arrhenotoky is first constrained by the ability of eggs to develop without fertilization. Even once facultative parthenogenesis evolves, the evolution of arrhenotoky is further constrained by the sex determining mechanism: the young from unfertilized eggs will not necessarily be male; rather, their sex will depend on the ancestral sex determining mechanism. Unfortunately, the ancestral sex determining mechanism can no longer be

assessed for species that are now arrhenotokous, but the mechanisms capable of fostering arrhenotoky at least can be identified.

The two most common sex determining mechanisms in diploid animals are male and female heterogamety. Using the combinatorialist approach, it is readily determined that from the ten possible population systems derived from male and female heterogamety, there are just three that lead to all unfertilized eggs developing as male (offspring of unfertilized eggs indicated below as haploids)*:

System A		System B		System C	
♂	♀	♂	♀	♂	♀
XY	XX	ZZ	ZW	ZZ	ZW
X		Z		Z	
		W	WW	W	
				WW	.

Note that system C is a 2-factor version of the "complementary" hymenopteran mechanism (Sec. 3.F), also corresponding to $\phi(1.2.2)$ of Section 5.B, although the sex of uniparentals was not specified in these earlier phenotype systems. None of these three systems are accounted for by the additive-value model of sex determination (Sec. 4.E).

There are seven other distinct population systems possible, starting from male or female heterogamety, but all include the existence of at least one uniparental genotype that is female. Under many of these seven systems, arrhenotoky could not begin to evolve without introducing a major change in the sex determining mechanism. The very onset of arrhenotoky is therefore constrained by the pre-existing sex determining mechanism. It is not known whether systems A, B, and C represent plausible properties of sex determination in unfertilized eggs, and the extent to which heterogametic mechanisms found in animals behave accordingly dictates whether the requirement of an appropriate sex determining mechanism is a serious limitation to the evolution of arrhenotoky. In fact, only a few studies have been performed on male and female heterogamety which reveal the sex of uniparentals. Section 4.A reported that haploid tissue in *Drosophila* (XA) is female, so fruitflies are inconsistent with system A. However, Kawamura and Nishioka (1977) reported system A in a frog, where uniparental offspring were obtained after fertilization of normal eggs by irradiated sperm. The constraint of sex determination may therefore suggest why arrhenotoky is not more common, despite possible advantages found in producing uniparental sons.

The next question to consider is how arrhenotoky evolves under these three sex determining mechanisms. Hartl and Brown (1970) investigated system A in detail. In the explanation of their results, two parameters must be

*Based on J.J. Bull. 1981c. "Coevolution of haplo-diploidy and sex determination in the Hymenoptera." *Evolution* 35:568-580, Table on p. 576.

defined. As in Chapter 12, let w represent the fitness of uniparental males relative to biparental males (fertility times viability). Also, let u be the fraction of unfertilized eggs in the brood of a female and $1 - u$ the fraction fertilized. Here, u will be the same for matings of uniparental and biparental males, or it can be assumed that females mate many times so that sperm are not limiting the production of daughters.

Represent male frequencies as follows:

<i>Frequency in Population</i>	σ	φ		
p	XY	XX	.	
$1 - p$	X			(13.A.2)

Hartl and Brown showed that, under random mating, the frequency of biparental (XY) males adjusted in response to uniparental males, and they were lost if uniparental males were produced at sufficiently high levels. (Recall a parallel situation in the examples from polyfactorial sex determination, Sec. 8.F, and ESD, 10.C, in which XY males were lost if XX males were produced at sufficiently high levels.) Specifically, the frequency of biparental males in this model evolves to

$$\hat{p} = 1 - \frac{2uw}{1-u}, \quad (13.A.3)$$

or to zero if this quantity is not positive. The fraction of fertilized eggs producing biparental males is simply $\hat{p}/2$, since only half the fertilizations by XY males produce sons. Therefore, biparental males remain common (\hat{p} near 1) if u or w is near zero (and neither is large). But as u and w approach 1/2, for example, the equilibrium frequency of biparental males goes to zero, and arrhenotoky is established (Fig. 13.A; Hartl and Brown, 1970).

The loss of biparental males occurs if $1 - 2uw/(1-u) \leq 0$. These conditions could be satisfied if, for example, environmental influences caused the proportion of unfertilized eggs, u , to be especially high (e.g., extremely low population density). From the results of the last chapter, however, it can be anticipated that selection acts on u in relation to the fitness of uniparental males, w . It has been shown that if $w > 1/2$, selection favors mothers producing a higher than average proportion of unfertilized eggs, with the result that biparental males are eventually lost, whereas if $w < 1/2$ there is selection so that diploidy is established (Bull, 1979).

Sex Ratio. Conditions 13.A.3 defined \hat{p} as the equilibrium frequency of biparental males ($1 - \hat{p}$ being the frequency of uniparental males) for fixed u and w . The sex ratio under these conditions is 1/2 only if $w = 1/2$. If $w < 1/2$ the equilibrium sex ratio is male biased, and if $w > 1/2$ the sex ratio is female

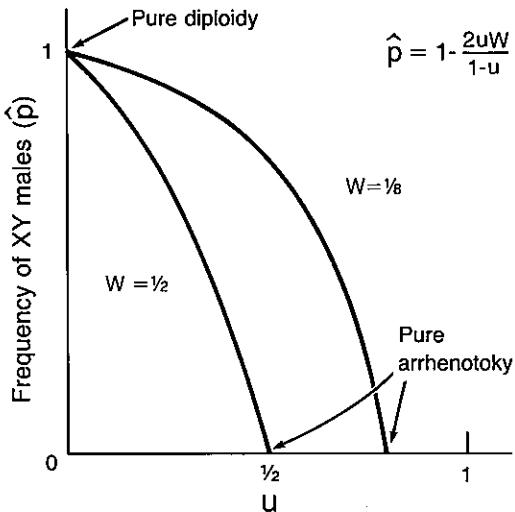


FIGURE 13.A. The possible equilibria between pure diploidy (all males XY, $\hat{p} = 1$) and arrhenotoky (all males X, $\hat{p} = 0$) in the Hartl-Brown model. As the fitness of uniparental males (w) and the fraction of unfertilized eggs (u) both increase, biparental males become less common and uniparental males more common at the equilibrium. Drawn for two different values of w .

biased. Once arrhenotoky is established selection favors a sex ratio of 1/2 through adjustment of the parameter u in females (Hartl and Brown, 1970; Bull, 1979).

As depicted here, the evolution of arrhenotoky occurs along an infinite path of equilibria (Fig. 13.A), similar to the paths of equilibria in the transitions between other forms of sex determination. Result 13.A.3 and Figure 13.A demonstrated continuous paths of equilibria from diploidy to arrhenotoky, allowing w and/or u to vary between 0 and 1. In comparison, the paths of equilibria between polyfactorial and major-factor sex determination (Sec. 8.F) and also between ESD and GSD (Sec. 10.C) were similar in this respect, although the equilibria in these earlier cases depended on just one parameter (k). However, in these earlier cases the equilibria were neutral with respect to selection of k if all males were equally fit. That is no longer the case with arrhenotoky. Arrhenotoky is neutral with respect to selection of u only if $w = 1/2$ —if uniparentals are half as fit as biparental males.

In the above model the establishment of arrhenotoky involved only minor changes in the zygotic sex determining mechanism. The loss of biparental males corresponded to the loss of the Y, or in the case of an XO system, the loss of sperm lacking an X. Two major characteristics of the ancestral mechanism were retained: (i) XX biparentals were female, and (ii) X uniparentals were male, although this second characteristic would not have been observed in the original diploid population.

Display 13.A.1 offered three population systems of male and female heterogamety which could possibly lead to the evolution of arrhenotoky from diploidy. The above paragraphs have discussed the evolution of arrhenotoky for system A. The evolution of arrhenotoky in system B is likely to be similar as that in system A, since the equilibrium proportion of biparental males is the same in both systems (results unpublished). In system B, arrhenotoky can evolve merely by loss of the sex factor Z. However, system C is different: all uniparentals are male, but so are all biparental homozygotes (ZZ and WW), so biparental males can never be eliminated. System C is relevant to the complementary sex determining mechanism in the Hymenoptera and will be discussed in the following section.

These models for the evolution of arrhenotoky apply equally to the evolution of PGL, if sex determination operates such that paternal chromosome loss *produces* males. (Recall the alternative type of PGL, as in *Sciara*, where chromosome loss depends on being male.) In this type of PGL, u is the fraction of inseminated eggs that eliminate the paternal genome. The formal equivalence in these models between the evolution of arrhenotoky and this type of PGL should not be construed as though all aspects of these evolutionary process are the same, however. Producing sons from unfertilized eggs has different consequences than eliminating paternal chromosomes from fertilized eggs, but these differences lie outside the scope of the models presented here.

B. A Model of Hymenopteran Arrhenotoky

The complementary sex determining mechanism of Hymenoptera presents a special problem in the study of the evolution of arrhenotoky. Since diploid homozygotes for sex factors are male, biparental males can never be eliminated because they always occur in fertilized eggs at roughly the square of the frequency of sex factors. Perhaps surprisingly however, the evolution of arrhenotoky with this form of sex determination differs only slightly from its evolution under the Hartl-Brown model, despite the complication that diploid males are never strictly eliminated. (The presentation here follows that of Bull, 1981c.)

Consider complementary sex determination in a diploid population as a possible ancestor to arrhenotoky. The restriction of two factors, as in system C, is removed in order to encompass more general circumstances. The possible genotypes in a diploid population with n sex factors are:

$$\text{♂} \quad \text{♀} \quad (13.B.1) \\ A_i A_i \quad A_i A_j \quad i \neq j, \quad i, j = 1, \dots, n .$$

There must be at least two sex factors, but there could be many more. System 13.B.1 is actually a phenotype system, and as in other multiple-factor phenotype systems, not all possible genotypes are maintained in the population. Under random mating, two types of population systems result* from 13.B.1 (Bull, 1981c; Scudo, 1964, for $n = 3$):

(i)		(ii)		
♂	♀	♂	♀	(13.B.2)
A_1A_1	A_1A_2	A_1A_1	A_1A_2	
A_2A_2			A_1A_3	
			•	
			•	
			A_1A_n .	

Both of these systems have an infinity of equilibria, constrained by the simple rule that the frequencies of genotypes within a sex add to unity. The sex ratio is 1/2 in *all* matings, and there is no selection of the relative frequencies of different genotypes within a sex. Consequently, regardless of starting point (i) or (ii), random fluctuations of gene frequency in a finite population would eventually lead to the loss of all but one male and one female genotype—female heterogamety, ZZ/ZW. The long-term maintenance of additional genotypes would therefore require recurrent mutation, and whether state (i) or (ii) was maintained would depend on whether mutations commonly generated just two types of sex factors [leading to system (i)] or generated many types [leading to system (ii)]. There seem to be many allelic states in hymenopterans with complementary sex determination (Sec. 11.C), so one might anticipate that state (ii) would have been present in a diploid ancestor.

Even with many genotypes present in females, system (ii) is difficult to distinguish from 2-factor female heterogamety. Furthermore, it is not evident in the context of this population system that all homozygotes are male. [In this respect, system (i) differs from system (ii).] That is, this possible ancestor of hymenopteran arrhenotoky is not readily distinguishable from ordinary female heterogamety. *One might therefore regard all known examples of female heterogamety in diploid populations as potentially similar to hymenopteran complementary sex determination, unless ZW and WW have been shown to be the same sex.* The reader may recall this same phenomenon from Chapter 5, in which it was noted that one population system could potentially represent different phenotype systems.

The onset of parthenogenesis in this population leads to a radical change

*From J.J. Bull. 1981c. "Coevolution of haplo-diploidy and sex determination in the Hymenoptera." *Evolution* 35:568–580, Figure on p. 570. Reprinted by permission of the Society for the Study of Evolution.

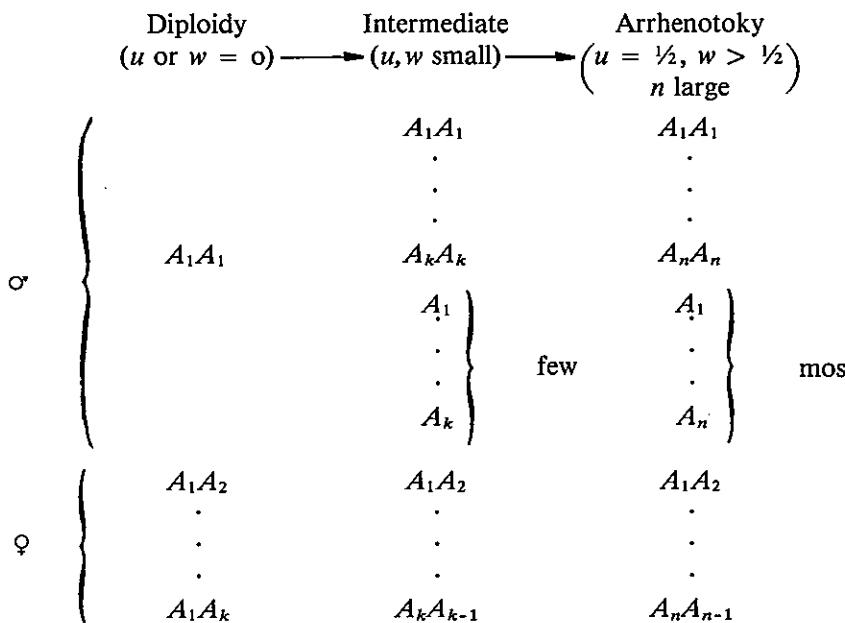
in the genotypic composition of sex factors (uniparental males again represented as haploids):

♂	♀	
A_1A_1	A_1A_2	
A_1	A_1A_3	(13.B.3)
A_2A_2	A_2A_3	
A_2		
.		
.		
.		

All factors are now present in both sexes because females produce unfertilized eggs that become males. Avoiding algebraic details, this system behaves much like the Hartl-Brown system, except for the constraint that biparental males are never lost, they merely become rare. In a previous analysis, the following results held:

- (i) The frequency of biparental males in fertilized eggs evolved to $\hat{p}/2$ (if this could be attained), where \hat{p} was given in the Hartl-Brown system as $1 - 2uw/(1 - u)$. Provided that $\hat{p}/2$ was positive (for large values of u and w it may be negative), there was some minimum number of sex factors needed to achieve this equilibrium value, but larger numbers of sex factors did not affect it. Apart from this constraint, then, the frequency of biparental males at equilibrium was the same in the Hartl-Brown system as in the hymenopteran system.
- (ii) If $\hat{p}/2 < 1/n$, where n is the number of sex factors, biparental males occupied a fraction $1/n$ of the fertilized eggs at equilibrium—they could not achieve the frequency $\hat{p}/2$. At this value all sex factors were equally common in both sexes, all at frequency $1/n$. In this case, new sex factors invading the population were selected. As the number of sex factors increased, biparental males decreased, and they ultimately equilibrated to a frequency of $\hat{p}/2$, if this number was positive. If $\hat{p}/2$ was zero or negative, rare sex factors were always selected, and as new factors continued to invade, biparental males became increasingly scarce, since their frequency in fertilized eggs ($1/n$) went to zero as n became large. (Of course, chance events in a finite population would cause the loss of rare sex factors so that an upper limit on their number would exist, cf. Yokoyama and Nei, 1979.) This process for the evolution of hymenopteran arrhenotoky is shown figuratively on p. 184* (from Bull, 1981c):

*From J.J. Bull. 1981c. "Coevolution of haplo-diploidy and sex determination in the Hymenoptera." *Evolution* 35:568-580, Figure on p. 574. Reprinted by permission of the Society for the Study of Evolution.



Here, as in the Hartl-Brown model, arrhenotoky eventually evolved if $\hat{p} = 1 - 2uw/(1 - u) < 0$, provided that enough new sex factors arose. It was shown, largely by numerical computation, that if $w < 1/2$, mothers were selected to fertilize all eggs, and the population remained diploid, but if $w > 1/2$, mothers were selected to leave enough eggs unfertilized such that arrhenotoky evolved (Bull, 1981c). If biparental males become sterile ($w = \infty$), as in Hymenoptera, there is selection for all rare sex factors, and the situation parallels self-incompatibility alleles in plants (Yokoyama and Nei, 1979; Wright, 1939).

Sex Ratio. In the hymenopteran model, a population with a primary sex ratio of 1/2 resulted under selection of u at the two extremes of complete diploidy or complete arrhenotoky (not strictly possible). The selected sex ratio in the transition was 1/2 only if $w = 1/2$. Recall that these results were also observed in the Hartl-Brown system.

In summary of these models, the transition from male or female heterogamety to arrhenotoky was accompanied by changes in the frequencies of different sex factors and perhaps by the incorporation of additional sex factors. The fundamental basis of sex determination (the phenotype system) was not altered, however. It should not be surprising that models for the evolution of arrhenotoky can be proposed in which the genetic basis of sex determination does change in fundamental ways, and the models here merely indicated that such changes are not essential. However, the evolution of arrhenotoky in these models did require specific phenotype systems of sex determination, and

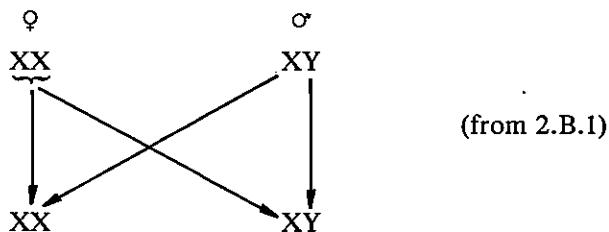
there is as yet a poor understanding of how commonly the appropriate phenotype systems occur.

C. Paternal Genome Loss

The evolution of PGL in males has some interesting effects on the sex determining mechanism and sex ratio that are quite distinct from those under arrhenotoky. One may recall the two distinct types of sex determination possible under PGL: the *Sciara*-type, in which sex is determined and paternal loss occurs in males; or the *unknown*-type, in which males result from chromosome loss. Although the evolution of uniparental males differs in these two systems (as noted above), once uniparental males have replaced the biparental males, sex ratio evolution is the same, although it occurs as the result of different types of genetic variation in each system. This section describes the evolution of sex determination and sex ratio from the perspective of a *Sciara*-type system, but the models assuming a strictly uniparental-male population apply equally to both types of PGL.

As described in Section 12.B, the evolution of PGL from diploidy has been modeled as a maternal-effect mutation causing paternal chromosome loss in sons (Brown, 1964; Bull, 1979). Uniparental males were selected if $w > 1/2$, eliminated if $w < 1/2$ (Bull, 1979). These models assumed that the sex ratio was unaffected by PGL, an assumption consistent with female heterogamety: under female heterogamety males are ZZ, so elimination of the paternal genome has no influence on the sex ratio.

A population consisting entirely of PGL cannot operate with male heterogamety, however. Under male heterogamety, the Y is transmitted father-to-son,



Paternal genome loss systems annihilate patrilineal transmission, so all sperm are X, and no male offspring would be produced. Yet male heterogamety does not preclude the invasion of PGL. The first few males eliminating the father's genome produce all daughters, but since the population sex ratio is nearly 1/2 when PGL is rare, there is only negligible selection against all-daughter broods. Consequently, selection of a rare gene causing PGL simply requires that $w > 1/2$, even under male heterogamety. However, as PGL

becomes more common, a balance is achieved where the increased number of grandchildren through uniparental sons is offset by the fact that these grandchildren are entirely female, the common sex. Biparental sons produce some grandsons and are maintained at a polymorphic equilibrium along with uniparental sons. This population can, however, be invaded by certain types of sex factors that increase male production, leading to complete PGL and a new sex determining mechanism.

If male heterogamety prevents the establishment of PGL, while female heterogamety does not pose any sex ratio complications, how is the sex ratio and sex determining mechanism selected under PGL? The answer is interesting. Under appropriate variation in *zygotic* sex factors, a sex ratio of 1/3 evolves, apparently through conversion of the major-factor mechanism into a polyfactorial one. It is difficult to explain this quantitative result on intuitive grounds, so an algebraic argument is provided in Appendix 13.I. The answer seems to involve two components: (i) when a gene is inherited from the father, it avoids elimination by producing female zygotes; however, (ii) when inherited from the mother, the gene benefits by causing male development, since it is the son's transmitted to all offspring. So from mothers, a gene benefits by producing males, but from fathers it benefits by producing females. These benefits are asymmetric: the gene from the father is either lost completely in a "son" or is transmitted to half of a daughter's progeny; the gene from the mother is transmitted to half of a daughter's progeny or all of a son's progeny.

This result is more than just a statement about sex ratio evolution under PGL. It also suggests an argument for the evolution of the *zygotic* sex determining mechanism. Starting from a system of female heterogamety and PGL, sex factors with a small female tendency can invade and shift the sex ratio toward 1/3. The major factors will be replaced, and a polyfactorial mechanism may evolve. Perhaps a similar final outcome applies to the evolution of PGL from male heterogamety despite the complication male heterogamety presents to the evolution of PGL.

If, within a PGL system, sex ratio variation exists as the result of different maternal effects, a sex ratio of 1/2 is selected instead of 1/3. This conclusion is obtained by analogy with sex ratio evolution under arrhenotoky for maternal control of fertilization. *The sex ratio of PGL species therefore evolves to different values depending on the sex determining mechanism (maternal or zygotic), and indeed the sex determining mechanism itself will be selected according to these sex ratio principles.* Maternal and zygotic mechanisms will be selected for their tendencies to produce sex ratios of 1/2 and 1/3, respectively, but the success of one type of mechanism (maternal or zygotic) in achieving its equilibrium sex ratio increases the potential for selection of the alternative type of mechanism. Consequently, there may be an evolutionary oscillation between maternal and zygotic sex determining mechanisms in PGL species. Although the course of evolutionary events in any particular PGL species will

be difficult to predict or reconstruct, two frequent outcomes can be anticipated when PGL species are considered as a group. First, PGL systems will often select the maternal influence of sex ratio. Second, mechanisms of maternal or zygotic control that are immune to sex ratio variation of the alternative type will evolve in place of more susceptible mechanisms.

Sciara. In view of these considerations, the sex ratios and sex determining mechanisms of PGL species are especially interesting. Much information is available on sex determination in fungal gnats of the genus *Sciara* (Metz, 1938; Sec. 11.E). At least six species are known to have the "monogenic" mechanism in which mothers produce only sons or only daughters. All the sex ratio variation, between families as well as between individuals, is accounted for by differences between mothers, so a strict maternal control of sex determination exists. If the inheritance of this monogenic condition is the same in all these species (as system 11.E.1), then the primary sex ratio is necessarily 1/2, since an equal number of daughter and son producing mothers occur. Not all *Sciara* species are strictly monogenic, but the sex ratio in these others has not been reported. Maternal determination of sex can nonetheless be anticipated in these other species because the embryonic loss of X in *Sciara* (which determines sex) occurs at such an early stage that, based on studies of other Diptera, the zygotic genome would not be expressed or would have contributed only a small fraction of the total RNA present in the embryo (Davidson, 1976; O'Brien and MacIntyre, 1978; Sawicki and MacIntyre, 1978; Anderson and Lengyel, 1979, 1981; Foe et al., 1982).

PGL in Mites and Scales. The inheritance of sex is not understood in these species, but indirect evidence is available for evaluating the role of maternal versus zygotic influences on sex determination. The cytological studies on chromosome loss in phytoseid mites have yielded ambiguous results, but the paternal genome is known to influence the fertility of males, so one might look for zygotic (paternal) effects on sex. In phytoseids, the sex ratios are nearly always female biased. (We must be cautious here, since PGL is definitely known in only one species.) Dyer (1975, Table 2) listed 19 studies on the adult sex ratio for ten species of phytoseid mites, and the sex ratios in 12 of these studies (nine species) ranged between .28 and .38. From her own studies on several phytoseids, Dyer observed sex ratios that were somewhat more female biased than in these previous reports. The evidence from these combined studies is therefore consistent with zygotic control of sex determination. However, little is presently known about whether sex is indeed influenced by the zygote: female biases such as these can evolve from selection of maternal variation in sex ratio under "local mate competition" (Hamilton, 1967; Charnov, 1982), or the female bias might simply exist as the result of greater male mortality from their haploidy (Smith and Shaw, 1980). To further investigate the possibility of a zygotic influence on sex determination, one might look for a

paternal effect on sex ratio, especially in crosses of different populations or species, where between-male genetic differences in sex ratio might be expected.

In scales, maternal control of sex ratio is anticipated both because chromosome loss in sons occurs early in embryogenesis and because progeny sex ratios are influenced by environmental effects on the mother. The embryological evidence was reviewed briefly in Section 11.F (from Nur, 1980; Brown and Chandra, 1977), and the sex ratio evidence will be presented here. As one example, the progeny sex ratio has been reported to depend on the mother's age and on other characteristics that vary with her age, ranging between .4 and .8 males (James, 1937; Brown and Bennett, 1957; Nelson-Rees, 1960). Nur's (1963) observations suggested that both males and females arose among genetically identical zygotes, indicating that sex was not determined by genotypic differences among zygotes, although not necessarily indicating a maternal influence. The natural primary sex ratio of scales is not subject to straightforward interpretation from these studies, partly because the environmental effects may differ between laboratory and field, and because there are difficulties in measuring the primary sex ratio. In the above studies, the sex ratio was never heavily female biased (without concomitant increased mortality), and the environmental perturbations produced a male excess, so these results from scales contrasted with the invariant female excesses of phytoseids. However, Brown and Chandra (1977) suggested that the sex ratio in scales was commonly around .4, so these different studies do not allow firm conclusions about population sex ratios. Sex ratio evolution in scales may be complicated by the various factors suggested for phytoseids, and scales also carry maternally-transmitted symbionts in the myctome (Nur, 1977). These symbionts are not known to influence the sex ratio, but symbionts in some other invertebrates cause a female bias (discussed in Chap. 14). So the interpretation of scale sex ratios from an evolutionary perspective will require a detailed understanding of many effects.

D. Summary of Chapters 11–13

(i) Various systems are known in which males transmit only the maternal genome, while females transmit the genomes from both the father and mother. These systems may be generally classified in two ways: arrhenotoky, in which males arise from unfertilized eggs, and paternal genome loss (PGL), in which males arise from fertilized eggs but eliminate paternal genes (Chap. 11).

(ii) A special advantage applies to the evolution of uniparental males from an outbred diploid ancestor (one with biparental males). Mothers of uniparental sons share an increased genetic identity with their grandchildren through sons in comparison to mothers of biparental sons. This increased genetic identity favors producing uniparental sons whenever they are more than half as fit as biparental sons. This advantage can account for the evolution of uniparen-

tal male systems, although the actual transitions in nature remain elusive. In view of this advantage, it cannot be explained why uniparental male systems have apparently arisen so infrequently, except to suggest that there must be many constraints preventing the realization of this advantage (Chap. 12).

(iii) The evolution of uniparental males is constrained by the sex determining mechanism. The present chapter considered only the evolution of uniparental males from a diploid, random mating population with male or female heterogamety. The origin of arrhenotoky requires a mechanism in which unfertilized eggs become male, and the extent to which this property applies to diploid species (as the possible ancestors to arrhenotoky) is unknown. However, given any of several appropriate ancestral sex determining mechanisms, there are paths of equilibria from pure diploidy to pure arrhenotoky, and the evolution of arrhenotoky is readily accomplished. A slight complication is found in the complementary sex determination of hymenopterans, in which biparental homozygotes are male, and the evolution of arrhenotoky in this system merely requires a large number of sex factors.

The evolution of PGL depends on the relationship between sex determination and chromosome loss. If paternal chromosome loss produces a male, the evolution of PGL is algebraically similar to the evolution of arrhenotoky. If instead, chromosome loss is limited to individuals already determined to be male, the evolution of PGL is different from the evolution of arrhenotoky; models of this process were studied specifically. The initial increase of PGL in a population is not affected by the sex determining mechanism (male or female heterogamety), but biparental males are not lost completely under male heterogamety. However, they will be lost under female heterogamety. Once present, PGL selects a *zygotic* polyfactorial sex determining mechanism with a sex ratio of 1/3, but selection also favors maternal control of sex determination to replace the zygotic mechanism and restore a sex ratio of 1/2. The outcome of these different selection processes is indeterminate until the genetic variation in sex determination is specified.

APPENDIX 13.I. Sex Ratio Evolution Under PGL: Zygotic Control

In the model for the evolution of sex ratio under paternal genome loss systems, assume that sex determination is a property of the zygote's genotype irrespective of which parent contributes the sex factors. The model will incorporate several simplifying assumptions, although it is supposed that the result reflects a more general set of circumstances.

We seek an evolutionarily stable sex ratio. Consider a locus for which nearly all members of the population are aa , and on average they become male

with probability M . Introduce at low frequency allele A ; zygotes inheriting A become male with probability r . For random mating and neglecting all matings with more than one A in the parents (i.e., ignoring "second and higher order" terms), the following matings are considered.

<i>Approximate Frequency</i>	<i>Mating</i>		<i>Progeny</i>		
	♀	♂	♀	♂	
1	aa	$\bullet \quad a$	\rightarrow	$1 - M(aa)$	$M(a)$
ϵ_1	Aa	$\bullet \quad a$	\rightarrow	$\frac{1-r}{2}(Aa)$	$\frac{r}{2}(A)$
ϵ_2	aa	$\bullet \quad A$	\rightarrow	$1 - r(Aa)$	$0(A)$.

Although this model is presented as though A is a sex factor, one may equally suppose that A influences whether the zygote eliminates paternal chromosomes; in this case, it must also be assumed that males necessarily result from chromosome loss.

From these matings, the first-order recursions are derived:

$$\begin{aligned} \epsilon'_1 &\approx \frac{\epsilon_1 \frac{(1-r)}{2} + \epsilon_2 (1-r)}{1-M} \\ \epsilon'_2 &\approx \epsilon_1 \frac{r}{2M}. \end{aligned} \quad (13.I.2)$$

System 13.I.2 is now linear in the ϵ_i , since all higher order terms have been ignored, and the methods of matrix algebra may be used to find the characteristic equation of the transition matrix:

$$F(\lambda) = \lambda^2 - \lambda \frac{(1-r)}{2(1-M)} - \frac{r(1-r)}{2M(1-M)} = 0. \quad (13.I.3)$$

If the largest value of λ satisfying this equation exceeds unity, then the sex factor A increases, whereas if the largest λ is less than unity, A is selected against. Since $F(\lambda)$ goes to ∞ as λ goes to ∞ , if $F(\lambda)$ is less than zero at $\lambda = 1$, then there *must* be a $\lambda > 1$ which satisfies $F(\lambda) = 0$.

Defining $\delta = M - 1/3$, $d = r - 1/3$,

$$F(\lambda|\lambda = 1) = (d - \delta)(d + 2\delta). \quad (13.I.4)$$

$F(\lambda|\lambda = 1) < 0$ gives the conditions for the spread of A . These are shown graphically in Figure 13.I and explained as follows.

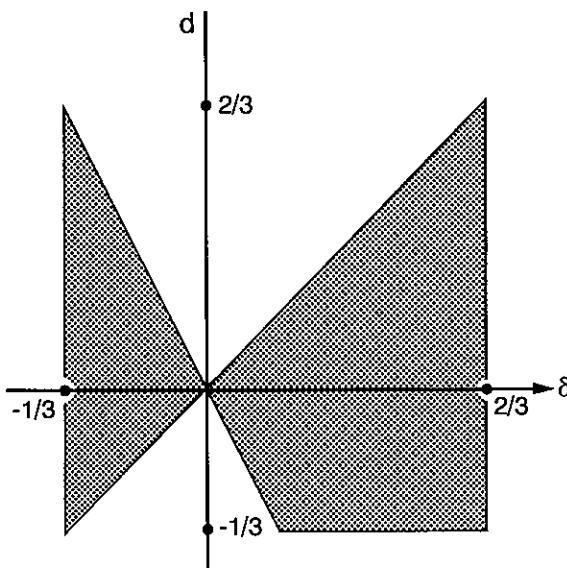


FIGURE 13.I. Sex ratio evolution under PGL. The model in the text considers selection of a rare allele A causing its bearers to develop as male with probability r , while other members of the population develop as male with probability M . Letting $\delta = M - 1/3$ and $d = r - 1/3$, the shaded area (inside the boundaries) provides the conditions under which A can invade. (The axes intersect at the origin.) The population cannot be invaded if the sex ratio is $1/3$, so $M = 1/3$ is an evolutionary stable sex ratio. However, even if M deviates slightly from $1/3$, the invading A will be selected for only if it produces a sex ratio sufficiently close to $1/3$ relative to M .

Given a $\delta (= M - 1/3)$, the slice at δ through the shaded range of $d (= r - 1/3)$ gives the values of d under which A can invade. As $M \rightarrow 1/3$, there is an increasingly narrow set of values of r about $1/3$ that enables A to invade. Selection not only favors a population sex ratio of $1/3$ but also favors the individual's probability of being male equalling $1/3$. Therefore, as $M \rightarrow 1/3$, major sex factors (those invariably producing males or females) cannot invade, and in fact one expects them to be eliminated from the population. It might be anticipated that this process leads to polyfactorial sex determination, with a narrow between-family sex ratio variance since other ways of achieving a zygotic sex ratio of $1/3$ (with a narrow variance) are difficult to imagine.

This analysis does not indicate how far A invades, nor whether the sex ratio moves closer to $1/3$. The complete dynamical process is complicated, and, without doing further numerical or analytical work, it must be regarded as conjecture that the sex ratio eventually evolves to $1/3$ (given arbitrary genetic variation).

14

Cytoplasmic Sex Determination

A. Introduction

In previous chapters it was assumed that sex factors were typical nuclear (chromosomal) genes transmitted to zygotes according to the usual rules of Mendelian, sexual populations. In contrast, there are cases in which sex is determined partly by factors inherited in the cytoplasm. The term *cytoplasmic sex factor* is used here for self replicating sex factors transmitted from mother to daughter but not transmitted through males. Since cytoplasmic factors are not transmitted in the same manner as nuclear factors, the evolution of sex determination is modified in some important ways. The major evolutionary difference between nuclear and cytoplasmic sex factors is that cytoplasmic factors are selected to produce a female bias rather than a sex ratio of 1/2. Although there are as yet few well-documented cases of cytoplasmic sex factors, if they prove to be widespread they will reduce in importance the theories that assume only nuclear factors.

There are several ways in which cytoplasmic factors may influence sex determination. (i) The factors may control sexual development in the embryo or juvenile, overriding the sex tendencies of nuclear genes. Under male heterogamety, for example, cytoplasmic sex determination of this sort would produce XX males or XY females. (ii) The factors may affect the segregation of sex chromosomes from the parents. The sex ratio would change because the frequency of XX and XY zygotes changes, but there would be no effect on sex-

ual development after conception. (iii) The factors may be lethal to zygotes of one sex. [Whether this third form is to be regarded as sex determination is disputable, but if the dead embryos were replaced by living ones so that brood sizes were not greatly influenced by sex ratio, then the distinction between classifications (ii) and (iii) would be slight in any quantitative description of the system.]

This chapter addresses cytoplasmic factors that influence sex development in the zygote [classification (i)]. Detailed case histories of cytoplasmic sex determination will first be described in three invertebrates (Sects. B, C and D), and models of populations with cytoplasmic sex factors will be presented at the end of this chapter (Sects. E and F). Although this chapter is restricted to cytoplasmic factors influencing sex development, it should be noted that male-lethal cytoplasmic factors are also known. Cytoplasmic male-lethal factors are well-established as the basis of some sex ratio conditions in *Drosophila* (Counce and Poulson, 1962; Poulson, 1963; Uyenoyama and Feldman, 1978). A single genus of maternally-transmitted protozoans, *Thelohania*, even exhibits two types of sex determining influences. In the amphipod *Gammarus* this protozoan produces females by overriding the effects of nuclear genes (Sec. 14.B), whereas in the mosquito *Culex* this protozoan kills males (Kellen et al., 1965). Models of sex ratio evolution for cytoplasmic control appropriate to either (ii) or (iii) were presented by Uyenoyama and Feldman (1978).

The following terminology will be used. From Vandel (1941), the word *thelygeny* denotes the regular production of highly female biased broods by one parent; *arrhenogeny* denotes highly male biased broods; and *amphogeny* denotes the regular production of sex ratios near 1/2. These terms may be applied either to the parent or to the brood.

B. Amphipods: *Gammarus*

An enlightening, comprehensive study of sex ratio and sex determination was conducted by Bulnheim in the brackish-water amphipod *Gammarus duebeni* (reviewed in Bulnheim 1975a,b, 1978a,b). The basic results were (i) a moderate proportion of the females in some populations produced nearly all daughters, (ii) this thelygeny was invariably associated with either of two microsporidians (intracellular protozoans) transmitted in the egg cytoplasm, and (iii) these microsporidians caused juveniles to develop as females.

Bulnheim suggested that *Gammarus* lacking cytoplasmic factors had polyfactorial sex determination because sex ratios were highly variable between families under any one photoperiod. Sex ratios also varied according to photoperiod (ESD): in the laboratory, light:dark intervals of 8:16 on average produced less than .25 male, and 16:8 usually produced an excess of males (see also Sec. 9.F). The effect of photoperiod in nature was unknown, so it was difficult to anticipate the natural zygotic sex ratio in the absence of the cytoplasmic factors.

The existence of cytoplasmic sex factors in *Gammarus* was anticipated by Traut (1962, and discussed by Bulnheim, 1978a), when he observed that some mothers produced only daughters and that these daughters inherited the thelygeny. Bulnheim subsequently observed that either of two parasitic microsporidians, *Octosporea effeminans* and *Thelohania herediteria*, were invariably associated with the thelygeny. The microsporidians harbored by the mother infected the oocytes and transmission to the young was achieved.

To indicate the extreme nature of the thelygeny, Bulnheim (1978a, his Table 2) listed 16 broods from 10 females infected with *Octosporea*. In this list there were 316 females but only 3 males, and thirteen of the broods were entirely female. Given the long-day photoperiod used; the sex ratio would have been male biased in the absence of the microsporidians. However, the sex ratio in broods of infected females varied between populations. *Octosporea*-infected females of some populations produced 99% daughters, and in other populations the value was closer to 90%. Furthermore, neither species of microsporidian consistently produced a greater fraction of daughters than the other. In some populations one species produced 99% daughters, and the other 90%, but these values were reversed in other populations. In most cases the males were uninfected, suggesting that sons resulted from eggs lacking microsporidians rather than from resistance to their influence on sexual development. However, in some populations one or both of the microsporidians were transmitted to many males as well as to females (Bulnheim, 1975a).

Bulnheim's work indicated that the microsporidians influenced sex determination by altering sexual development in immature amphipods. In addition to the basic observation that thelygeny was invariably associated with at least one of the microsporidians, females artificially infected with the microsporidian became thelygenic, and conversely, environmental factors inhibiting transmission of the microsporidian (high salinity, low temperature) led to mixed sex broods from mothers otherwise thelygenous. The number of surviving offspring was not sufficiently different between treatments to suppose that thelygeny resulted from increased male mortality (Bulnheim, 1978a, his Table 2). From this evidence alone, it could be argued that either the microsporidian controlled sex by influencing the genetic makeup of the zygote, or that it simply overrode any male tendency of the nuclear genes and produced females. The latter explanation seems more likely: post-hatching exposure to high salinity, impairing the microsporidian *Octosporea*, led to mixed sex broods. The microsporidian therefore did not influence the genetic composition of the zygote, since the exposure to high salinity occurred long after conception.

Two environmental factors influenced the expression of the thelygeny: salinity and temperature. Water temperatures as low as 3 ° to 4 °C seemed to inhibit microsporidian infection of the egg in the mother, but once the egg was infected, cold did not seem to interfere with the sex determining influence in the embryo. High salinity (in excess of 27 ‰) inhibited infection of the egg by *Octosporea* in the mother and inhibited its feminizing influence during post-

embryonic development. (*Thelohania* was not sensitive to salinity.) Bulnheim suggested that although the elevated salinity needed to achieve this effect was essentially unknown in natural populations, the influence of cold may have been realized in nature. Some females collected in winter in fact reverted to thelygeny after producing a few amphogenous broods, consistent with the laboratory suggestion that cold temperatures temporarily inactivated transfer of the microsporidian to eggs.

The fraction of females infected with the microsporidians in natural populations was variable, but rarely was significantly in excess of 1/2. According to Bulnheim, there were no obvious differences in fecundity or longevity between infected and uninfected individuals. In view of the extreme thelygeny caused by these protozoans, it is difficult to understand why essentially all females were not infected (Sec. 14.F will present the model behind this argument). Bulnheim's long-term study of one *Gammarus* population failed to note any dramatic increase in the frequency of infected females, so perhaps the populations were at equilibrium. He suggested that low temperatures in winter may have been partly responsible for the maintenance of uninfected females, but (as will be indicated in Sec. 14.F) this fact alone is probably not sufficient to maintain infected and uninfected females.

The adult sex ratios observed by Bulnheim in natural populations were often female-biased, although some were near 1/2. Unlike the situation with nuclear sex factors, a female biased sex ratio can be maintained at equilibrium in the presence of cytoplasmic sex factors, so a female excess is not unexpected (see Secs. 14.E and 14.F). Bulnheim suggested that *Gammarus* males lived longer, which could have led to an observational bias in favor of males among adults. It is also conceivable that seasonal shifts occurred in the sex ratio, both from the effects of photoperiod on uninfected broods, and the effect of temperature on infected broods, so the interpretation of population sex ratios is not straightforward.

C. Amphipods: *Orchestia*

Sex determination in another amphipod, *Orchestia gammarella*, is also influenced by cytoplasmic factors (Ginsburger-Vogel, 1975a; Ginsburger-Vogel, Carre-Lecuyer, and Fried-Montauzier, 1980; Ginsburger-Vogel and Magniette-Mergault, 1981a,b). This section considers the *Orchestia* results in detail, but at the outset it may be noted that the facts from *Orchestia* are similar to those from *Gammarus* in three important ways: (i) many females were thelygenous (in *Orchestia*, the few males from thelygenous broods were often intersexual); (ii) the thelygeny was associated with an internal parasitic protozoan transmitted maternally, in the egg cytoplasm; and (iii) the feminizing influence occurred in the juvenile. However, unlike *Gammarus*, sex determination in *Orchestia* lacking cytoplasmic factors appeared to be controlled by an XX/XY system.

Ginsburger-Vogel (1975a) distinguished two types of populations in *O. gammarella* based on habitat: beach populations and estuarine populations. Most beach populations had normal males and females (no intersexes), with the vast majority of sex ratios clustering at 1/2, and there was no reason to suspect cytoplasmic influences in the majority of these individuals. Estuarine populations, however, had lower overall sex ratios (.25) with many thelygenic females, and up to 15% of the males displayed intersexual phenotypes (Table 14.C). However, the sex ratios did not provide an absolute distinction between these two types of populations. One beach population was listed with a sex ratio of .39, and two estuarine populations had sex ratios in excess of .42 (Ginsburger-Vogel and Desportes, 1979). Furthermore, not all broods from thelygenous populations were female biased; some were even heavily male biased (Table 14.C).

Extensive laboratory studies marshalled three lines of evidence to suggest that the thelygeny/intersex-son syndrome observed in estuarine broods was characteristic of the mother and inherited maternally (Ginsburger-Vogel, 1975a). (i) Thelygenous females produced the same distribution of brood sex ratios and intersex sons regardless of whether they were mated to males from amphogenous or thelygenous strains. However, amphogenous females paired with males from thelygenous strains produced amphogenous sex ratios and normal sons. (ii) Thelygeny was transmitted from a mother to all her daughters, even in matings with amphogenous males (studied for three consecutive generations). Intersex sons from thelygenous mothers did not transmit the thelygeny. (iii) Amphogenous females were induced to become thelygenous

TABLE 14.C. Brood Compositions from
Orchestia Females of Thelygenic Populations

Males	Males ¹	Females
—	1	33
—	—	36
—	—	26
—	4	21
—	—	44
13	8	4
1	4	12
—	4	41
—	1	52
1	1	22
18	2	4
33	25	295

Based on T. Ginsburger-Vogel, 1975a. "Temperature-sensitive intersexuality and its determinism in *Orchestia gammarella* Pallas." In: *Intersexuality in the Animal Kingdom*, edited by R. Reinboth. Springer Verlag, Berlin, pp. 106-120, Table 1.

Note: Each row represents a separate brood.

Males¹—intersex males.

by tissue grafts from thelygenous females or intersex males. An intracellular protozoan (*Paramarteilia orchestiae*) was observed in the thelygenous females and intersex males of *Orchestia*. This protozoan perhaps represented the feminizing factor because of its association with the thelygeny and because tissue injections from thelygenous to amphogenous females failed to induce the thelygeny when these tissues were filtered through pores smaller than the diameter of this protozoan (Ginsburger-Vogel et al., 1980).

In the absence of the cytoplasmic factor's influence (e.g., in beach populations), sex was apparently determined by XX/XY male heterogamety, although a cytological heteromorphism was not evident. On this hypothesis, an infected female transmitted the cytoplasmic factor to offspring irrespective of their X/Y constitution, and XY and YY individuals were induced to become female, in opposition to their nuclear factors. The demonstration of this underlying male heterogamety would have perhaps not been possible except that the occurrence of thelygeny and intersex sons was temperature sensitive in most strains: exposure to 22 °C or above, either during oogenesis or during embryonic and early post-embryonic development, abolished the thelygeny and intersex sons; the inheritance of thelygeny had been studied at 17 °C (Ginsburger-Vogel, 1975a; Ginsburger-Vogel and Magniette-Mergault, 1981a,b). Abolishing the sex determining influence of the cytoplasmic factor thus enabled the study of nuclear sex factors in the same strains, as indicated in the following model.

Suppose a population initially contains primarily XX females and XY males, and some XX* infected females are introduced (infection designated as *). The first matings of infected females would be the following,

Parents		Progeny	
♀	♂	♀	♂
XX*	•	XY	→ XX, XX*, XY* XY,

with the proportions of different types of offspring depending on the rate of infection by the cytoplasmic factor. Further matings would generate YY individuals and the population would then contain the following genotypes (as in the progeny):

Parents		Progeny	
♀	♂	♀	♂
XY*	•	XY	→ XX, XX*, XY*, YY* XY, YY.

This population system would be difficult to ascertain in the absence of markers linked to X and Y or a chromosomal heteromorphism, unless some environmental influence could be used to annihilate the feminizing influence of

the cytoplasmic factor. If the cytoplasmic factor is annihilated in progeny, the sex ratios should cluster at 1/2, 3/4 and 1:

Mating		Progeny
♀	♂	Sex Ratio
XX, XX*	• XY	1/2
XX, XX*, XY*	• YY	1
YY*	• XY, YY	
XY*	• XY	3/4.

Returning to the results from *Orchestia*, the thelygenous strains raised at high temperatures (which annihilated the cytoplasmic influence) should have produced sex ratios near 1/2, 3/4, or 1. Early work on *Orchestia* (Ginsburger-Vogel, 1975a) indicated that family sex ratios from high temperatures were at least superficially consistent with these expectations. More recent work, especially the isolation of YY* female lines that produced all males at high temperature, provided further support of this model (Ginsburger-Vogel and Magniette-Mergault, 1981a,b). An additional and interesting observation was that YY seemed to be more resistant than XY to the feminizing influence of the cytoplasmic factor (Ginsburger-Vogel and Magniette-Mergault, 1981b).

Not all the observations on sex ratio in *Orchestia* were consistent with the above simple interpretation. Some puzzling results were observed in individuals from a beach population at the Bloscon locality (Ginsburger-Vogel, 1975b). While the vast majority of broods in the Bloscon population had sex ratios clustering near 1/2, a few were thelygenous and a few were arrhenogenous. The monogeny in this case was a property of the male: if the sire of a monogenic brood was crossed to a second female, the sex ratio was the same as in his first brood. The dam from a monogenic brood produced sex ratios in subsequent broods according to her sire. The thelygenous sires were perhaps XX, and on this interpretation, the occasional sons were also XX, their sex perhaps influenced by subtle environmental effects and/or background variation in weak sex factors. (Such genetic variation would be exhausted rapidly in these lines from the intense selection for males, unless the genetic effects were weak in comparison to the environmental effects.)

Arrhenogeny provides the most puzzling case of all. Approximately half the sons of an arrhenogenous sire were again arrhenogenous and half were amphogenous. This pattern continued through all 10 generations studied. Most sons from amphogenous males were themselves amphogenous, but some sons (1/4) were arrhenogenous. These results would suggest that a strain could be isolated in which the male bias was maintained, since amphogenous males have either amphogenous or arrhenogenous sons. These arrhenogenous males are without any plausible explanation in terms of the above model. While the arrhenogenous males comprise just a tiny fraction of males in this population, they may indicate that some important component of sex determination is not yet understood in *Orchestia*.

D. Isopods: *Armadillidium*

The sex ratios of terrestrial isopods (woodlice) have been extensively studied, originating with the work of Vandel (reviews of the early work are found in Vandel, 1941; Johnson, 1961). At least 10 isopod species have been studied to date, and monogeny has been observed in more than half of them, often in association with amphogeny. The most extensive investigations have been performed on *Armadillidium vulgare*, and the coverage here is limited to this species. The sex ratio in *A. vulgare* is influenced by cytoplasmic factors in some populations, and thelygenic as well as arrhenogenic broods are common occurrences in many wild populations. The inheritance of sex ratio in *A. vulgare* seems far more complicated than in *Gammarus* or *Orchestia*, and consequently, it is not well understood. In this section, some of the major sex ratio phenomena known in this isopod will be highlighted.

Stable Amphogeny with Female Heterogamety

Despite many examples of monogeny in *A. vulgare*, strains have been isolated and a population was discovered in which brood sex ratios were regularly amphogenic, clustering about 1/2 (Howard, 1958; Juchault and Legrand, 1972, 1981a). Female heterogamety was demonstrated in one such strain derived from Nice, France (Juchault and Legrand, 1972). When investigating the heterogametic sex, Juchault and Legrand utilized the well-known masculinizing property of the androgenic gland of male isopods. The androgenic gland is a testis-associated organ which, when implanted into genetic "females," causes them to develop as males. By implanting androgenic glands into several juveniles, Juchault and Legrand induced individuals of female genetic constitution to become males, and these "neo-males" produced 1/4 sons when crossed with normal females. A sex ratio of 1/4 is expected under female heterogamety:

<i>Neo-male</i>	<i>Female</i>	<i>Sons</i>	<i>Daughters</i>
ZW	ZW	→ 1/4 ZZ	1/2 ZW 1/4 WW.

The existence of WW females was subsequently indicated by their all-female progeny in crosses to ZZ males.

Monogeny

Various types of monogeny have been observed in *A. vulgare*, and their inheritances are so complicated as to defy a thorough explanation, despite many studies. It is now generally agreed that monogeny is not the result of differential mortality between male and female offspring (Vandel, 1938; Howard,

1942, 1958; see Table 14.D below). There are studies of monogeny in natural populations, but strains have also been isolated that breed true for arhenogeny or thelygeny, and these strains provide some hope for the eventual elucidation of the more complicated population phenomena. The presentation which follows will discuss the observations from laboratory strains first, and from wild populations second. The letter "T" will denote an abbreviation for "thelygenous."

Thelygeny and Cytoplasmic Factors

Several independent studies report the isolation of thelygenous strains (e.g., Howard, 1958; Legrand and Juchault, 1970; Juchault and Legrand, 1972, 1976). The cause of thelygeny in Howard's T line was not elucidated, but it was clear that the thelygeny was maternally inherited, because T females were nearly always mated to males from amphogenic origin, yet the thelygeny persisted. Two additional T lines were established from separate localities in France; one from Nice and the other from Niort (Legrand and Juchault, 1970; Juchault and Legrand, 1972, 1976). Although the thelygeny persisted within each line, the thelygeny was lost rapidly in at least some outcrosses of these lines (Juchault and Legrand, 1976). There were also some important differences in the nature of thelygeny between the two lines. In particular, the Niort T line had three characteristics absent from the Nice T line: (i) Niort T females were resistant to masculinization by androgenic gland implants; (ii) Niort T broods often contained intersexes; (iii) tissue from Niort T females induced thelygeny in amphogenic females of other strains (Table 14.D). On the basis of these criteria, the Niort thelygeny seemed to be stronger than the Nice thelygeny.

Martin, Juchault, and Legrand (1973) identified an intracellular microorganism present in thelygenous females and intersex males from the Niort T strain, but absent in amphogenic lines and the Nice T line. This microorganism was perhaps the cause of the thelygeny in the Niort line, but it could not have been the cause of thelygeny in the Nice line, because it was absent there (Juchault and Legrand, 1976). The fact that Niort intersex males possessed this factor suggested that it produced females by overriding the nuclear sex factors, rather than by controlling the segregation of Z and W (Legrand and Juchault, 1969a,b).

While thelygeny in these crustaceans has usually been associated with matrilineal inheritance, as though inherited in the egg cytoplasm, there are some intriguing observations suggesting that the thelygeny of the Nice line may have been transmitted in part through males. Individuals from the Nice T line were transformed into males by transplants of the androgenic gland. On the assumption of female heterogamety in the absence of T, these neo-males would have been either ZZ or ZW. When two such males were crossed with amphogenic females (ZW), both sires were unexpectedly thelygenic (6M:162F; 0M:18F; both sex ratios differ significantly from the expectations of 1/4 or

TABLE 14.D. Sex Ratios in Broods from *Armadillidium* Females of Amphogenous Origin Induced to Thelygeny by Tissue Transplants from Niort Thelygenous Females

	Progeny from Mothers Without Transplant		Progeny from Mothers With Transplant	
	♂	♀	♂	♀
Sire A	23	32		8
	43	38		3
Sire B	62	72		1
	42	43		0
	42	41		0
Sire C	59	66		0
	29	27		38
	16	17		21
Sire D	27	24		0
	27	25		73
	21	28		51

Based on J.-J. Legrand and P. Juchault. 1970. "Modification experimentale de la proportion des sexes chez les Crustaces Isopodes terrestres: induction de la thelygenie chez *Armadillidium vulgare* Latr." *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences* (D) 270:706-708, Table on p. 207.

Note: Different broods were presumably from different mothers, but all mothers were derived from the same amphogenous strain. In addition to the sons and daughters, three intersexes were produced in the broods of infected mothers.

1/2; results in Juchault and Legrand, 1972). Male transmission of thelygeny was also observed in some recent descendants of wild-caught Nice animals (Juchault and Legrand, 1981b). When crossed to amphogenous females, some of these males produced a heavy excess of daughters. In turn, these daughters were apparently thelygenous. These results are intriguing and warrant careful repetition in order to thoroughly characterize the different ways in which Nice thelygeny may be transmitted.

It should be noted that the Z/W genotype in these T lines could not be readily assayed, so there was no direct evidence identifying the nuclear (chromosomal) genotype. The Niort T females were not masculinizable by the androgenic gland, so the cytoplasmic factor could not be abolished to allow an assay of the nuclear sex factors. Furthermore, by the above account, Nice females transformed into males may have transmitted the thelygenous factor, so again the nuclear genotype could not be assayed independently of the thelygenous factor. The inability to nullify feminizing factors in these lines presents a major obstacle in the attempt to provide a comprehensive analysis of sex determination in *A. vulgare*.

Arrhenogenic Strains

Two lines derived from the Niort population produced nearly all males (Legrand and Juchault, 1972). One line, designated *Arf*, was interpreted as ZZ

in both sexes. The occasional females were then also ZZ, presumably the result of environmental effects. Two additional observations supported the hypothesis that this line was ZZ in both sexes. First, males from the *Arf* line produced sex ratios of 1/2 when bred to ZW amphogenous females. Second, females from this line were arrhenogenous when bred to ZZ amphogenous males.

A second arrhenogenous line, designated *Arm*, had a considerably different interpretation (Legrand and Juchault, 1972). Some of the males in this line were partly intersexual. When these intersex males were crossed with amphogenous females, an excess of males was produced (again, with some intersexes), but as many as 1/4 of the offspring were female (F_1 generation). When these F_1 intersex males were again crossed to amphogenic females, an even larger fraction of the progeny were female, perhaps up to 1/2 (F_2 generation). This pattern was repeated in subsequent crosses of F_2 intersex males and amphogenic females. Some of the F_2 females bred only daughters, as if they were WW (Legrand and Juchault, 1972). These results are not consistent with the hypothesis that intersex males were simply ZZ; other sex factors were apparently present, perhaps at other loci, but a detailed understanding of the inheritance of sex is not possible from only these experiments.

Wild Populations

Many of the studies of monogeny in *A. vulgare* concern individuals taken from wild populations, or the immediate descendants of these individuals. There are many interesting observations from this work, but the inheritance of sex ratio in wild populations is largely unexplained. Several of the major phenomena in the inheritance of sex ratio were reported by Vandel (1938, 1939) and Howard (1940, 1942). Vandel's 1938 study was on *Trichoniscus* rather than *Armadillidium*, but his discoveries have since been shown to apply to *A. vulgare* as well. These discoveries were:

- (i) The sex ratio of a brood was usually a property of the mother, since her sex ratio did not change with different sires, whereas a male's sex ratio varied according to that of his mate (e.g., Vandel, 1938; Howard, 1942).
- (ii) The sex ratio of some females changed in time. Vandel (1938) offered the term "allelogeny" for the change from one type of monogeny to the other (changing between thelygeny and arrhenogeny). Sequential sex ratio changes were also reported by Howard (1942) and Juchault and Legrand (1976, 1981a,b). Often, but not always, the sex ratio became increasingly male biased.
- (iii) Unlike the strains described above, daughters of wild-caught females did not necessarily inherit the sex ratio of their mother. Some T females had various combinations of T daughters, arrhenogenic daughters, and amphogenic daughters (Vandel, 1938; Howard, 1942; Juchault et al., 1980). Howard (1942) reported that in a brood of 1 male and 36 females, no females were strongly thelygenic, 3 were strongly arrhenogenic, 4 were weakly ar-

rhenogenic, 3 were amphogenic, and 2 were weakly thelygenic. ("Weak" indicates a sex ratio bias intermediate between amphogeny and unisexual broods.) Also, from 7 daughters of a strongly arrhenogenic female, 3 were strongly arrhenogenic, 3 were strongly thelygenic, and 1 was amphogenic.

These results, in conjunction with those from stable strains, indicate that a comprehensive understanding of the sex ratio in *A. vulgare* will prove to be exceedingly difficult. Many of the necessary steps have been performed by Juchault and Legrand, but the variety of phenomena, as well as the inability to knowingly abolish the feminizing influence of any cytoplasmic factors, introduces a complexity far greater than that indicated for *Gammarus* or *Orchestia*.

Although the inheritance of sex in wild populations may not be fully understood, it is nonetheless interesting to note the sex ratios in these populations. Johnson (1977) suggested that populations experienced male/female differential mortality, so that adult sex ratios of wild animals did not necessarily reflect primary sex ratios. However, several studies have avoided this complication by reporting the sex ratios among laboratory-reared broods of wild-caught females. The interpretation of results from lab-reared broods necessarily assumes that the laboratory is free of environmental effects on sex determination.

The overall sex ratios obtained from the lab-reared broods of parents caught in the wild (and in some cases their immediate descendants) were female biased for some populations but were near 1/2 for others. There were usually many monogenous broods observed in these studies, irrespective of the overall sex ratio. The most thorough (and indeed delightfully complete) data of this sort are from Juchault et al. (1980) and Juchault and Legrand (1981a,b). Most populations were characterized either by an excess of females, or by no significant deviation from 1/2. A test for statistical significance on total sex ratio should account for the wide between-family sex ratio variance, and when this point is considered, only 3 of 11 populations reported in one study had an appreciable female excess (Juchault and Legrand, 1981b). Detailed work is again available from the Niort population. A collection from 1963, maintained three years in the laboratory, yielded a heavy female bias. Collections from 1973 yielded nearly 50% males among broods born in that year, but the few broods in 1974 from the same parents yielded a strong male bias. It would be satisfying if the 1963–1973 comparison could be regarded as an evolution toward a sex ratio of 1/2, but the effects of captivity on sex ratios are not known, and the 1973–1974 comparison even suggests that the laboratory conditions may have influenced the sex ratio.

Conclusions

The possibilities suggested by the studies of *Armadillidium* are some of the most interesting in sex determination. There are different causes of arrhenogeny

and thelygeny, and these two sex ratio types have an unresolved inheritance in natural populations. There is an especially interesting possibility that one form of thelygeny may be transmitted through males. Many of these interesting observations require further documentation, a task that does not promise to be easy. But the work may be inspired by the hope of finding novel mechanisms for the inheritance of sex.

E. Evolution of Sex Ratio Modification by Cytoplasmic Factors (Models)

Essentially all well-documented examples of maternal (cytoplasmic) sex ratio inheritance, including the preceding cases, have a cytoplasmic factor that causes an overproduction of daughters rather than an overproduction of sons (other literature is reviewed in Uyenoyama and Feldman, 1978). Cases of male-biased cytoplasmic inheritance are unknown, although the extra-chromosomal father-to-son transmission of a daughterless trait is known in a wasp (Werren et al., 1981)*. It is hard to imagine that male-tendency cytoplasmic factors fail to arise; rather they are apparently selected against. This conclusion also emerges from the following algebraic argument.

Cytoplasmic factors are selected according to their sex ratio, and those that produce females are favored. The extreme case is obvious: a maternally inherited trait that produced only sons would be lost in the first generation. This argument may be developed more fully, as follows. Suppose that a population contains some females infected with a cytoplasmic particle that influences the sex of its carriers. These females are at frequency p in the population, while uninfected females are at frequency $1 - p$. Both types of females are equally likely to be mated. The sex ratio in broods of uninfected females is m . Infected females produce a fraction Q of their offspring as infected daughters, $(1 - Q)(1 - r)$ as uninfected daughters, and $(1 - Q)r$ as sons. It does not matter if sons are infected, since by definition cytoplasmic factors are not transmitted through males. There is no contagious infection between broods of different mothers.

The structure of the model is represented as follows:

<i>Maternal</i>		<i>Offspring</i>			
<i>Frequency</i>	<i>type</i>	<i>Infected</i>	φ	<i>Uninfected</i>	φ
p	Infected	\rightarrow	Q	$(1 - Q)(1 - r)$	$(1 - Q)r$
$1 - p$	Uninfected	\rightarrow	0	$1 - m$	m

(14.E.1)

*In hermaphroditic plants the case of inheritance through seeds but not pollen is analogous to cytoplasmic inheritance; cytoplasmic factors are known which cause pollen suppression; e.g., Lewis, 1941.

Note that with respect to the cytoplasmic factor, the type of male in the mating is irrelevant, and the fraction of infected daughters (Q) under this formulation admits the possibility of cytoplasmic control of sex determination. If $Q > 1 - m$, it is implied that the cytoplasmic factor causes an overproduction of daughters.

To obtain the conditions under which cytoplasmic factors spread, assume that p is small and that population size is so large that random influences on frequency p can be ignored. The frequency of infected females one generation later may be approximated by

$$p' \approx p \frac{Q}{(1-m)} \quad \text{for } p \ll 1. \quad (14.E.2)$$

The cytoplasmic factor increases when rare only if $Q > 1 - m$; i.e., the number of infected daughters in broods of infected mothers exceeds the average number of daughters in broods of uninfected mothers. In the special case where the initial sex ratio is 1/2, the cytoplasmic factor must produce an excess of females among its progeny in order to be selected. Here we are interested in cytoplasmic factors that override nuclear factors in the zygote (e.g., cause XY to be female). However, result 14.E.2 applies equally to additional cases of cytoplasmic factors causing segregation distortion (or differential fertilization) by sex chromosomes, or influencing the fitness of infected daughters. (In this latter case, Q is fitness times the fraction of daughters, and the terms in 14.E.1 involving $(1 - Q)$ are no longer valid.)

I wish to acknowledge that the conclusion drawn from 14.E.2 was pointed out by Lewis (1941) for the evolution of cytoplasmic male sterility in plants, and by Howard (1942) for the evolution of thelygeny (see also Hamilton, 1967), long before these ideas gained the prominence they now hold. This result accounts for the observation that cytoplasmic sex factors in natural populations always produce females, although it also does not preclude evolution of a cytoplasmic factor that increases female fitness without influencing the sex ratio. Note that the rate of evolution of the cytoplasmic sex factor is highest with $Q = 1$, when all progeny from infected mothers are infected daughters.

Equilibrium is reached in this model when

$$p' = p \frac{Q}{(1-M)} = p \quad (14.E.3)$$

where M is the population primary sex ratio. Equilibrium therefore requires that $Q = 1 - M$, which means that the fraction of daughters inheriting the cytoplasmic factor in broods from infected mothers equals the fraction of daughters from a random brood in the population. This equilibrium could be achieved if all females were infected ($p = 1$), or it could be satisfied in other ways, such as with polymorphism for infected and uninfected females. The inheritances of all sex factors must be specified before it can be concluded

whether uninfected females are maintained at equilibrium, and these details lie outside the scope of this discussion.

Even though 14.E.3 represents equilibrium in the above model, there is continued selection of cytoplasmic factors producing an even greater female bias if males remain in the population. Suppose, for example, that a new cytoplasmic variant arose and was transmitted to Q^* daughters. Following essentially the same argument that led to 14.E.2, and from (14.E.3), the evolution of this new variant when rare (frequency ϵ) would be given by

$$\epsilon' \approx \epsilon \frac{Q^*}{Q} \quad (14.E.4)$$

(since $Q = 1 - M$ at the equilibrium 14.E.3). Clearly, the new variant increases only if $Q^* > Q$ —if it produces even more infected daughters. In the absence of Mendelian variation to suppress the cytoplasmic influence, populations with cytoplasmic sex factors should evolve toward an ever-increasing female bias, balanced only by group extinction, or by males discriminating against mating with infected females.

F. Joint Evolution of Cytoplasmic and Nuclear Sex Factors (Models)

The spread of a cytoplasmic factor in a population necessarily leads to a female excess. We can expect, from the results of earlier chapters, that the female excess influences selection of nuclear factors. Indeed, under a wide variety of conditions, the female bias ultimately selects an increase in male tendency (nuclear) factors so that all non-infected individuals become male.

This result may be established with a minimum of effort if we assume the following: (i) In broods of infected mothers, the cytoplasmic sex factor infects a proportion Q of the offspring and causes them to become females. (ii) There are two nuclear sex factors at one locus (A, a); A is at frequency z in zygotes, frequency x in females, and frequency y in males. Also, the frequency of A is always higher in one sex than in the other ($x - y$ is nonzero and always the same sign). The population sex ratio is M . Now recall Nur's formula (6.A.1)

$$\Delta z = (x - y)[1/2 - (1 - M)],$$

and recall formula 14.E.3 for the evolution of the cytoplasmic factor,

$$p' = p \frac{Q}{1 - M}.$$

Starting from a population sex ratio of 1/2, the cytoplasmic factor increases only if $Q > 1/2$, and therefore causes a female bias as demonstrated in 14.E.2. The spread of the cytoplasmic factor causes a female bias in the population's primary sex ratio. From Nur's result, assuming random mating between males and females, the female bias selects the nuclear factor with a higher frequency in males. There is no point at which both the cytoplasmic factor ceases to spread (which would imply $1 - M = Q > 1/2$) and the male tendency factor ceases to increase (which would imply $1 - M \leq 1/2$). Equilibrium is therefore attained with fixation of factor A or a , whichever has the male tendency. At this point all uninfected offspring become male, all females are infected, and the sex ratio is Q .

The example of female heterogamety provides a simple illustration. Let A from the above paragraph be represented as the Z, and a as W. In the absence of the cytoplasmic factor, all females are ZW and all males are ZZ. With a cytoplasmic factor producing females [labeled (*)], there are two other types of females, as shown:

♀	♂
ZW	ZZ
ZW*	
ZZ*	

Provided that more than half the offspring from infected mothers are infected daughters, this system rapidly loses ZW* since only half her infected offspring are also ZW*. With only ZZ* and ZW present, the female excess selects an increase in Z (again, from Nur's result), and the population eventually consists of ZZ* females and ZZ males. Under male heterogamety, the population eventually becomes entirely YY and YY*, assuming the fitness of YY is normal. Of course, this result applies only if the cytoplasmic factor controls sex determination by influencing sex development in the zygote or embryo. Cytoplasmic-induced segregation distortion of nuclear factors or differential mortality does not alter the sex of XX and XY individuals and therefore does not lead to these changes.

If these models represent natural populations, we should observe that (i) there are no uninfected females, and (ii) all broods are female biased. However, these characteristics are not observed in *Gammarus* or *Orchestia*, because there are uninfected females in the populations of both species. (The evidence that uninfected females exist in *Orchestia* is simply that YY is not fixed.) It might instead be supposed that the cytoplasmic factors are spreading in these populations, except that Bulnheim stated the frequency of infected females did not markedly increase in his most thoroughly studied *Gammarus* population. Comparable data for *Orchestia* are not available, although it should be noted that a wide range of sex ratios has been observed among different estuarine populations (Ginsburger-Vogel and Desportes, 1979). This information would suggest that equilibrium has not been reached, unless the

equilibrium depended on peculiarities in the different populations (i.e., different genetic variation) or on different environments. Regarding *Armadillidium*, Juchault et al. (1980) and Juchault and Legrand (1981b) stated that some populations were entirely ZZ, with females produced only by "epigenetic" factors. Even if true, this conclusion was based on circumstantial evidence, since there was no direct means of assaying the Z/W genotype in thelygenic females. It is therefore not clear if *Armadillidium* is consistent with this prediction, although *Armadillidium* populations are clearly far more complicated than the above model.

To explain the observations from *Gammarus* and *Orchestia* requires modifications of this basic model, but even so, I have been unable to satisfactorily account for all the discrepancies. The primary problem is one of accounting for the coexistence of infected and uninfected females in the populations. I have considered alternative models similar to those above (unpublished), where these alternative models allowed variation in three parameters: female fitness, transmission fraction of the cytoplasmic factor (Q), and resistance to the cytoplasmic influence. Briefly, my conclusions were the following, based mostly on rather limited numerical results.

(i) Above, *fitness* was assumed equal between infected and uninfected females. Even if infected females were assumed to be inferior, with a constant fitness w , the cytoplasmic factor evolved only if a sufficient fraction of the brood became infected daughters, but the cytoplasmic factor was usually either fixed or lost, rather than retained polymorphic in the population. If the fitness of infected females was frequency-dependent, decreasing as the frequency of infected females increased, it was relatively easy to generate a stable polymorphism for infected and uninfected females. However, this supposition is implausible, since it is unsupported by observations from the amphipods.

(ii) Allowing the *transmission fraction* of the cytoplasmic factor (Q) to vary, as if from winter to summer, also did not generate a stable polymorphism. It seemed that the cytoplasmic factor increased to fixation if the long-term geometric mean of Q exceeded 1/2, but was lost if the geometric mean was less than 1/2. If the per-year geometric mean was near 1/2, high in one season but low in another, only gradual changes occurred in the frequency of infected females from year to year, but major seasonal changes occurred. Since major seasonal changes in the frequency of infected females were not reported in the amphipods, this model also does not seem to account for the maintenance of uninfected females.

(iii) *Resistance* to the feminizing influence of the cytoplasmic factor might enable the maintenance of infected and uninfected females in the population. Two forms of resistance are plausible. Resistance might be a property of the mother, so that all her offspring escape influence by the cytoplasmic factor. Resistance might also be a property of the zygote. In either case, nuclear genes that abolish the feminizing, cytoplasmic influence would be favored in these populations because these factors will occur at higher frequencies in males

than females (recall Nur's result 6.A.1). In my models for the joint evolution of a cytoplasmic factor and Mendelian resistance factors, the population invariably evolved to a sex ratio of 1/2, provided that resistance had no deleterious side effects (agreeing with Uyenoyama and Feldman's 1978 results for the alternative forms of cytoplasmic sex determination). The population sex ratios observed in amphipods, which were female biased, are therefore not consistent with the results of these models either. Also, in my numerical studies, resistance evolved slowly enough that the population was essentially fixed for male-tendency factors once the resistance genes became common. A high frequency of male-tendency factors is also inconsistent with the amphipod data.

In contrast to the amphipod results, the observations from *Armadillidium* are perhaps consistent with genetic resistance to cytoplasmic factors (Juchault and Legrand, 1976, 1981b). (However, it should be recalled that cytoplasmic inheritance of thelygeny was demonstrated or suggested only in a few laboratory strains, so thelygeny may not necessarily be caused by cytoplasmic factors in most *Armadillidium* populations.) First, the sex ratio observed in many populations was near 1/2, despite abundant thelygeny. Second, the thelygeny of wild-caught females was not regularly transmitted to most daughters. The existence of resistance is also consistent with the observed decay of thelygeny when the Nice and Niort T strains were outcrossed. Again, however, it must be stated that the *Armadillidium* results were so complicated as to preclude any firm conclusion about the inheritance of sex ratio in wild populations. The most useful data in this context are those of population sex ratios and of matings between strains breeding true for sex ratio.

G. The Interpretation of Sex Factors: Another Caution

Before completing this chapter, a few interesting points emerge from these models for the evolution of resistance. In a population with a widespread cytoplasmic sex factor, so widespread that the population sex ratio is female biased, nuclear genes for resistance evolve because their frequency is higher in males than in females (as above). These resistance genes therefore become sex factors, since they provide part of the inherited basis of sex. In extreme cases, the resistance locus can become almost the entire inherited basis of sex determination. Consider a population of female heterogamety, with two additional factors initially at low frequency: (i) a cytoplasmic factor (indicated by *) transmitted to the entire brood ($Q = 1$), and (ii) a dominant resistance allele, *A*. The population evolves from an initial state of predominantly

$$\begin{array}{ccc} \text{♀} & & \text{♂} \\ aa\ ZW & & aa\ ZZ \end{array}$$

to a final state of predominantly

$$\begin{array}{c} \text{♀} \\ \text{♂} \\ aa ZZ^* \quad Aa ZZ^*. \end{array}$$

This final state is essentially male heterogamety at the *A*-locus. Under the appropriate dominance relationships at the *A*-locus, this system would also be interpreted as a dominant-Y system, since *aO ZZ** would be female and *Aaa ZZ** would be male.

The point to be made here is that, while the inherited basis of sex determination is now the *A*-locus, these sex factors may have no direct participation in the biochemical process of sex differentiation—*A* might do nothing other than inhibit growth of the cytoplasmic factor. Thus the inherited basis of sex determination would be quite independent of the underlying physiological machinery of sex differentiation. Therefore, as suggested in earlier chapters, attempts to ascribe biochemical properties to sex factors merely on the basis of their inheritance are indeed precarious.

H. Summary

Cytoplasmic sex factors are thoroughly documented in a few species and suspected in others. This chapter described results from two amphipods, *Gammarus* and *Orchestia*, and from the isopod *Armadillidium*, which indicate that sex determination is influenced by maternally transmitted micro-organisms. These cytoplasmic factors cause an infected mother to produce essentially all daughters. The inheritance of sex seems relatively simple in the two amphipods, but it is remarkably complicated in *Armadillidium*.

Models were introduced to study the evolution of cytoplasmic and nuclear sex factors. Because of their unique inheritance, there is selection of cytoplasmic factors that produce an ever-increasing female bias. Cytoplasmic factors that cause extreme thelygeny (with *Q* near 1, as in these invertebrates) are expected to evolve rapidly to fixation. The female bias caused by a cytoplasmic factor in turn selects nuclear factors that produce males, and the population evolves toward a state in which all uninfected zygotes become male. The observations from natural populations of amphipods are discordant with the results of the above models, because uninfected females coexist with extreme thelygenic females—cytoplasmic factors are expected to evolve rapidly to fixation if they cause extreme thelygeny (*Q* = 1). Observations from *Armadillidium* are perhaps consistent with some of the anticipated characteristics of natural populations, but the complexity of sex ratio inheritance in this isopod is not well understood, hindering an analysis within the framework of the simple models presented here.

15

A Parental Mechanism of Sex Determination: Maternal Monogeny

A. Examples

The previous chapters emphasized sex determining mechanisms at the level of the zygote or embryo, but parental sex determining mechanisms are also included in the definition of the classical mechanism—the earliest elements in ontogeny common to one sex that distinguish it from the other sex. Any form of parental sex ratio variation can be regarded as a parental effect on sex determination under this definition, but there are only a few types of parental effects on sex ratio that are pronounced enough to be regarded as sex determining *mechanisms*, (in the sense that arrhenotoky, heterogamety, or ESD are regarded as zygotic or larval mechanisms). Parental effects on sex ratio are reviewed and discussed comprehensively in Charnov (1982), so this general topic will not be considered here.

This chapter briefly addresses maternal monogeny, one extreme form of a parental effect on sex determination. Maternal monogeny refers to systems in which some mothers regularly produce only sons and the others produce only daughters. This mechanism is distinguished from the more encompassing definition of monogeny used in the preceding chapter, which allowed paternal causes of monogeny and also did not imply that all broods in the population were monogenous. Maternal monogeny can operate under various zygotic sex

determining mechanisms: (i) arrhenotoky, if some females are mated upon maturing and produce only daughters (fertilized eggs), while the other females are never mated and produce only sons (unfertilized eggs); (ii) ESD, if mothers place eggs in either male or female producing environments; (iii) cytoplasmic sex determination, causing infected mothers to produce only daughters, and uninfected mothers to produce only sons (as in Sec. 14.F).

Examples of maternal monogeny are thoroughly documented in three genera of distantly related invertebrates. Species from two genera of flies, *Chrysomya* and *Sciara*, and a barnacle, *Peltogasterella*, all show the regular production of arrhenogenous and thelygenous broods in the population. In all three systems, the condition is inherited according to a simple, 2-factor system as follows (here, they are parental sex factors):

♀_T	♀_A	σ	
<i>Ff</i>	<i>ff</i>	<i>ff</i> .	(15.A.1)

The subscript T or A indicates a thelygenous or arrhenogenous female, respectively. Thelygenous females are heterozygous, *Ff*, while arrhenogenous females and males are homozygous, *ff*. Thelygenous females produce an equal number of thelygenous and arrhenogenous daughters, so the sex ratio is 1/2. The following paragraphs provide details of these systems. Maternal monogeny is also known in some aphids and possibly in cynipid wasps, but these systems involve cyclical parthenogenesis—generations of all-female parthenogenesis alternating with generations of sexual reproduction (Chap. 20 in White, 1973). These cyclical systems are not addressed below, although they could be studied along similar lines, with appropriate modifications to account for the alternating parthenogenesis.

Sciara. As described in Metz (1938) and in Section 11.E, maternal monogeny is present in several species of *Sciara*, and the system 15.A.1 has been demonstrated in *S. coprophila*. Sex determination in *Sciara* is mediated through differential loss of X chromosomes in embryonic somatic tissues: females have an XX soma, males have an XO soma, even though all zygotes are initially XXX. Thelygenous mothers cause all offspring to lose just one X, arrhenogenous mothers cause all offspring to lose two X's. The sex factors, *F* and *f*, are located on the X.

Chrysomya. In a study of sex determination in several blowflies, Ullerich (1963) demonstrated maternal monogeny in two species, *Chrysomya rufifacies* and *C. albiceps*. The inheritance of sex followed system 15.A.1, and by using induced translocations, Ullerich (1975) showed that the parental sex factors were inherited on chromosome 5. Other species of *Chrysomya* have male heterogamety, and in these pair 6 is usually heteromorphic, so the sex factor pair presumably changed in the evolution of maternal monogeny.

Peltogasterella. The parasitic barnacle *P. gracilis* is the most interesting of the three cases of monogeny presented here. Its life cycle is unusual, although typical among this group of barnacles. Female barnacles parasitize crabs. As larvae they attach to the crab and grow into it as roots into soil. Male barnacles are "parasitic" on the female barnacle. As larvae, the males attach to the external portion of the female barnacle, and they inject a clump of cells which migrate to her reproductive tract and later produce sperm.

Yanagimachi (1961) observed that there were two types of female barnacles in *P. gracilis*, differing in chromosome number and in the size of their eggs. Small-egg females had $2n = 31$ chromosomes, large-egg females had $2n = 30$ chromosomes, with essentially no overlap in egg size between the two types. Based on the behavior of larvae, whether they attached to a crab or to an adult female barnacle, Yanagimachi concluded that barnacles became females if they developed from small eggs and became males from large eggs. Although the inheritance of this condition was not studied further, it can be concluded that this system was 15.A.1, with *F* representing the extra chromosome of the thelygenous females (small egg producers), and *f* representing the absence of *F*.

B. Monogenic Houseflies

A dominant factor was discovered on chromosome I of houseflies, called *arrhenogenic* (*Ag*), that caused an XX mother to produce all sons if she mated with a standard XY male (Vanossi Este, 1971; Vanossi Este et al., 1972; Rubini et al., 1972; Vanossi Este et al., 1974; Milani, 1975). The males of arrhenogenous broods were either XX or XY, and those that inherited *Ag* transmitted it to daughters, so that arrhenogeny reappeared in alternate generations. (*Ag* had no sex determining effect when transmitted by the male.)

Strains of XX males and females were isolated in which *Ag* and its wild-type allele were the only sex factors (Vanossi Este, 1971; Rubini et al., 1972; Milani, 1975). There was some environmental variability in the effect of *Ag*, and these lines usually had an excess of females, with the sex ratio varying through time. If a line could be selected in which *Ag* showed stable and complete arrhenogeny, presumably it would be characterized by the following population system, which is distinct from 15.A.1:

♀_T	♀_A	♂	
+	+	+ <i>Ag</i>	
		+	+
		+ <i>Ag</i>	(15.B.1)
		<i>Ag Ag</i> .	

The "+" indicates the wild-type alternative allele to *Ag*, and the subscripts "T" and "A" again indicate thelygenous and arrhenogenous females. The male

does not influence the sex of his progeny, but he does influence the sex of his grandchildren.

C. Evolution of Monogeny (Models)

The classification of monogeny may be treated in the same framework as presented in earlier chapters. This chapter has been restricted to monogenous systems in which all broods are unisexual, whereas a presentation of the broader scope of monogeny would allow some mixed-sex broods. Even within this restriction, it is possible to classify monogeny according to whether the sex ratio is a property of the mother, the father, or both, or perhaps is a function of zygotic genotypes within a brood. If there is a genotypic basis for monogeny, the phenotype and population systems may then be derived.

The evidence described above indicated that maternal monogeny was a property of the mother, according to her genotype. Two different population systems were suggested,

$$\begin{array}{ccc} \text{♀}_T & \text{♀}_A & \sigma \\ Ff & ff & ff, \end{array} \quad (15.A.1)$$

$$\begin{array}{ccc} \text{♀}_T & \text{♀}_A & \sigma \\ FF & Ff & FF, Ff, ff. \end{array} \quad (15.B.1)$$

Under Mendelian segregation of sex factors, both systems equilibrate to a sex ratio of 1/2, with an equal number of thelygenous and arrhenogenous females. In 15.B.1, the three male genotypes, FF , Ff , and ff , equilibrate to frequencies of 1/4, 1/2, and 1/4, respectively.

The evolution of maternal monogeny from amphogeny may be no more complicated than transitions between other mechanisms of sex determination considered in this book. In both *Chrysomya* and *Sciara*, some species are monogenic and others amphogenic, suggesting recent transitions to or from monogeny. Furthermore, the *Ag* mutant of houseflies provides insight to the nature of mutations conferring monogeny in a female's brood. There are in fact several plausible transitions to monogeny. From Section 14.F, one possibility might begin with male or female heterogamety, followed by the invasion of a cytoplasmic sex factor producing all daughters. If this process were to be followed by the evolution of a dominant (or recessive) gene conferring resistance to the cytoplasmic factor in all offspring of the mother, monogeny would result. If monogeny arose by this route, there would necessarily be a cytoplasmic factor transmitted to all females.

A second model for the evolution of maternal monogeny follows the lines of the multiple-factor systems described in Chapters 3, 5 and 6. Consider the following set of genotypes,

♀	♂
<i>ff</i> XX	<i>ff</i> XY
<i>ff</i> XY	
<i>ff</i> YY	<i>ff</i> YY
produce all daughters	$\left\{ \begin{array}{l} Ff \text{ XX} \\ Ff \text{ XY} \\ Ff \text{ YY} \end{array} \right.$

It is assumed here that, in progeny from *ff* mothers, sex is determined according to the zygotic X/Y constitution so that an individual with one or more Y's is male. Male heterogamety is represented in the absence of *F*, since XY females and YY individuals would disappear after one generation, and all females would be *ff* XX, all males *ff* XY. *Ff* mothers are assumed to produce all daughters, thus giving rise to the *ff* XY females and *ff* YY males and females. Under random mating and equal fitness within a sex, there is an infinite path of neutral equilibria from male heterogamety, with *F* absent, to monogeny with YY fixed, again illustrating a simple transition between two sex determining mechanisms. Of course, monogeny may just as easily be lost as brought into existence by this route.

Consider now the evolutionary stability of monogeny. Are there any advantages of monogeny over amphogeny? Howard (1942) proposed that monogeny may be advantageous (in isopods) because it precludes sib mating—sibs are never the same sex, so they cannot mate. Sib mating often has the undesirable effect of generating inbreeding depression, so a sex determining mechanism that substantially reduced sib mating could indeed have an advantage. Johnson (1977) regarded this advantage as negligible in the monogenous isopods *Armadillidium* and *Venezillo*, since sibs dispersed so widely before maturing that sib mating was effectively prevented even in the absence of monogeny. Whether Howard's hypothesis can account for the evolution of monogeny in other species has not been studied.

A second possible advantage of monogeny is that mothers can readily produce eggs destined to become sons with different resources than eggs destined to become daughters. Amphogeny invariably complicates producing sons and daughters from different types of eggs, because sex is not determined when the egg is provisioned in most systems. Monogeny enables mothers of sons to produce different types of eggs than mothers of daughters, as observed in *Peltogasterella*. Once an egg dimorphism of this sort evolves, amphogeny is at an obvious disadvantage.

D. Summary

This chapter described one of the more striking parental mechanisms of sex determination, maternal monogeny, known in two flies and a barnacle. In these

systems, half the mothers produce only sons, and the other half produce only daughters. Maternal monogeny can in principle evolve from various alternative sex determining mechanisms and for various selective advantages, but the paths of this transition are unknown in nature. How mothers produce offspring entirely of one sex is unknown, but a mutation of houseflies indicates that monogeny can arise in systems with zygotic sex factors.

PART TWO

Sex Chromosome Evolution

INTRODUCTION

The term "sex chromosome" usually implies that sex factors are inherited within a large chromosome segment that has a low incidence of crossing-over in the heterogametic sex. Thus males and females differ not only in the inheritance of sex factors, but also in many loci linked to the sex factors. Sex chromosome evolution represents the expansion of these linkages, and the changes which subsequently occur within these linkages.

I regard sex chromosome evolution as a process distinct from the evolution of sex determination. To be sure, these two processes are not always independent, because the sex chromosomes must incorporate the sex factors, and the evolution of sex determination may sometimes require the tight linkage of two or more loci (cf. plants, Sec. 7.C). Yet, as the preceding chapters have shown, the evolution of sex determination may be studied quite apart from a detailed understanding of the chromosomal structure of sex factors. Furthermore, most aspects of sex chromosome evolution do not involve changes in the inheritance of sex. To regard sex chromosome evolution synonymous with the evolution of sex determination would have the undesirable effect of obscuring their many differences.

The treatment of sex chromosome evolution in this book consists of three chapters. The first chapter (16) will describe characteristics of highly differentiated sex chromosomes. The following chapter (17) will describe systems in which sex chromosome differences are slight, and it will also

review evidence for the generally accepted view that sex chromosome differences evolve from an initial state of X-Y similarity. The final chapter (18) will present a conceptual framework for understanding the process of sex chromosome differentiation. There are two important messages in these chapters: (i) the majority of observations on sex chromosomes fall into a single evolutionary process, and (ii) this process consists of two major stages, the suppression of X-Y crossing-over, followed by degeneration of the Y.

Sex chromosomes have been studied from two perspectives: genetics and cytology. The majority of work has been cytological—descriptions of the sizes and shapes of sex chromosomes, their staining characteristics, and their behavior in meiosis. In contrast, studies on the genetics of sex chromosomes have considered X- and Y-linked mutations, the dissimilarity of genetic functions on the X and Y, and recessive lethals on the Y. The two approaches of genetics and cytology have evolved somewhat independently of each other, such that the genetical implications of various cytological phenomena have remained obscure, and vice versa.

The present gap between cytological and genetic approaches renders it difficult to provide a comprehensive theory of sex chromosome evolution. However, the descriptions here of sex chromosome characteristics include both perspectives. The evolutionary framework presented in Chapter 18 centers on the genetical aspects of sex chromosome evolution, because evolutionary implications of many of the cytological aspects are unknown. Advances have been made at the molecular level relating the cytological phenomena to genetical phenomena (e.g., the DNA composition of the Y), and this work offers hope of an improved understanding of sex chromosome evolution beyond that which can be offered at present.

Note: In Part I boldface letters **X** and **Y** were used to indicate heteromorphic sex chromosomes, while lightface X and Y were often used to represent just the sex factors. This distinction is no longer necessary in Part II, because the emphasis will be on the *chromosomes* with the sex factors. Thus, the boldface symbols are omitted, and the lightface X and Y refers to the sex chromosomes. The extent and nature of X-Y heteromorphism in each discussion will be evident from the context.

16

Characteristics of Sex Chromosomes: Extreme X-Y Heteromorphism

This chapter will describe the major characteristics of heteromorphic sex chromosomes that distinguish them from autosomes, emphasizing characteristics of sex chromosomes with extreme heteromorphism. While heteromorphic sex chromosomes seem to have arisen independently in many groups, their cytological and genetical characteristics are often similar, so only those "generic" characteristics will be described here, without reference to taxonomic groups. This chapter represents an overview of many studies (see reviews in White, 1945, 1954, 1973; Darlington, 1937, 1965). The first section (A) briefly describes the discovery of sex chromosomes, followed by a detailed description of the nature of X-Y differences (B). Later sections will describe the meiotic behavior of sex chromosomes (C), multiple sex chromosomes (D), dosage compensation (E), and degenerate X chromosomes (F).

A. Historical Background

The first cytological study describing sex chromosomes is thought to have been by Henking (1891, reviewed in McClung, 1902a,b; Crew, 1965; Austin et al.,

1981). Henking studied an insect now known to have an XX/XO system. He observed that one "chromosome" of males failed to undergo normal meiosis, so that only half the sperm received it. This element was labelled "x" for "unknown," as it was not clear to Henking that this element was indeed a chromosome. Similar observations from other invertebrates followed, and in 1902, McClung suggested that the "X" chromosome was the inherited basis of sex (McClung, 1902a, b).

This era was undoubtedly one of great excitement in the field of sex determination, and there were rapid changes in the acceptance and rejection of theories on the role of sex chromosomes in the inheritance of sex. Two quotations from E. B. Wilson, both published in 1905, indicate the rapidity with which ideas about sex chromosomes changed:

The foregoing facts irresistibly lead to the conclusion that a causal connection of some kind exists between the chromosomes and the determination of sex; Analysis will show, however, that great, if not insuperable, difficulties are encountered by any form of the assumption that these chromosomes are specifically male or female sex determinants.

(Wilson, 1905a, p. 501)

I believe that the conclusion can hardly be escaped that the chromosome combination, established at the time of fertilization, is, in these insects, the determining cause of sex.

(Wilson, 1905b, p. 543)

The view expressed in the second quotation appears to be a reversal of the view expressed in the first.

It is interesting that McClung (1902a,b) proposed that the X existed only in males and thus produced males (i.e., an OO female/OX male system), but this error was soon corrected (Wilson, 1905a, b, 1906). It was also clear from these studies that the XX/XO systems was not universal: some species had XX/XY sex chromosomes in which the X and Y differed in size (Wilson, 1905b).

The hypothesis that sex chromosomes controlled sex determination was strengthened by Bridges' (1916, 1925) analyses of *Drosophila* with atypical sex chromosome constitutions (XXX, XXY, XO, Sec. 4.A). Bridges showed that sex varied according to the ratio of X chromosomes to autosomes in these fruitflies. As was described in Chapter 2, the cytological work on sex determination has grown immensely from these early studies, so that sex chromosome differences between males and females are now known in many plants and animals, and the type of experiments performed by Bridges have since been repeated on several species in addition to *Drosophila* (Sec. 2.D).

B. The Nature of Extreme Heteromorphisms

Sex chromosome heteromorphism is nearly always limited to species with male or female heterogamety (XX/XY), although male and female heterogamety

are not always accompanied by heteromorphic sex chromosomes. "Heteromorphism" simply refers to a difference in the constitution of the X and Y chromosomes. The X and Y are commonly observed to differ in three characteristics: size (shape), gene content, and chromatin/DNA content. Not only do the X and Y differ from each other, but sex chromosomes may also differ from the autosomes. Usually, the X (Z) is typical of autosomes, but the Y (W) is unusual both because it is depauperate of typical genes and is heterochromatic. If only part of the X and Y are dissimilar, the dissimilar parts are referred to as the "differential" segments.

Size and Shape

In animals, the X is usually longer than the Y; but even when these chromosome are the same length, they may differ in shape (Plates 16.B.1, 16.B.2, pp. 236-8; other examples in Table 2.C.1-5 and in White, 1973, Chaps. 16, 17; Darlington, 1937). In the extreme case the Y is absent, as in XX/XO systems. A difference in size and shape is commonly the sole criterion used to diagnose X and Y chromosomes (referenced as above).

Only a few angiosperms (flowering plants) have well-documented sex chromosome heteromorphism (*Rumex*, *Humulus*, *Cannabis*, *Silene*; Westergaard, 1958). This paucity of heteromorphic sex chromosomes is not surprising, since most plants are hermaphroditic, and heteromorphic sex chromosomes are not expected to evolve in hermaphrodites (Chap. 18). The Y is usually longer than the X in angiosperms, or if multiple sex chromosomes are present, the total length of the Y's exceeds that of the X's (Love, 1944; Westergaard, 1958). In hops (*Humulus*) the Y is smaller than the X (Jacobsen, 1957). Several bryophytes (mosses and liverworts) also have heteromorphic sex chromosomes, and the X is often larger than the Y. (Sex chromosome systems in bryophytes are special and will be considered more specifically in Sec. 18.C.)

Gene Content

It is a widespread conclusion that when the X and Y are grossly dissimilar, the X contains many functional genes absent from the Y (Muller, 1914, 1918; Muller and Gershenson, 1935; Darlington, 1937; Berg, 1942; White, 1945, 1973; Ohno, 1967). This conclusion is based on three lines of evidence. First, XX/XO species lack a Y altogether. Thus whatever functions exist on the X certainly do not also exist on a Y, although this evidence does not indicate that the X itself carries any functions. Second, in many XX/XY systems, combinations of YY and OY are never observed, so it seems they are inviable. The failure to observe OY may be contrasted to the observation of XO individuals in many species that usually have a Y (Sec. 2.D). YY inviability has been inferred from experiments in *Drosophila* (Bridges, 1916), guppies (Winge, 1934; Haskins et al., 1971), medakas (Yamamoto, 1959), the papaya (Westergaard,

1958), sorrell (*Rumex*, Smith, 1963), and lemmings (recall that the Y is absent in varying lemmings, and OO is presumed inviable, Sec. 3.C). In the mouse, the OY constitution is lethal but XO is not (Morris, 1968). And in the plant *Mercurialis*, YY is viable but sterile (Westergaard, 1958).

The third observation suggesting that the Y lacks many of the genes on the X is that many more X-linked than Y-linked genes are known in species with heteromorphic sex chromosomes, although an abundance of sex-linked markers is known for only a few species. However, it should be realized that the usual methods of detecting sex-linked genes are biased toward observing X-linked rather than Y-linked genes, since genes can be detected on the Y only if they have a (partially) dominant effect, whereas both recessive and dominant traits can be detected on the X. (It would be surprising, however, if this bias could account for the overwhelming preponderance of X-linked genes described below.)

More sex-linked genes are known in *Drosophila melanogaster* than in any other species. Lindsley and Grell (1968) listed over 450 mutations mapped to the X; many of these genes were undoubtedly allelic, so the number of loci represented by these would be much less than 450. There have also been some attempts to estimate the number of X-linked loci without assigning phenotypes to individual genes. The simplest of these approaches is achieved by counting the number of bands on the polytene X, which exceeds 1000. A current theory proposes that each band represents one functioning gene (reviewed by Lefevre, 1974). Alternatively, the number of viability loci on the X has been estimated to be between 800 and 1000 from studies of radiation-induced, sex-linked lethals (Lefevre, 1974).

In contrast to X-linked functions, only a few functions have been assigned to the Y of *Drosophila melanogaster*. The Y is heterochromatic and therefore does not develop into a banded polytene chromosome in salivary gland nuclei (Dobzhansky, 1957). The absence of a banded, polytene Y may reflect a paucity of Y-linked genes, but it also thwarts any attempt to count the number of genes from bands, and Y-linked genes have been identified by more specific methods. Males require a Y in order to produce motile sperm, and several sites on the Y seem to be important in this respect; the Y also carries the *bobbed* locus (Dronamraju, 1965; Hess and Meyer, 1968). By employing a special method of analysis, Lindsley et al. (1960) showed that the Y suppressed various X-linked lethals of males, but these lethals seemed to be a special type, since they were associated chiefly with the heterochromatin of the X. The Y also seemed to influence the pattern of variegation of certain autosomal genes; variegation is a phenomenon commonly associated with heterochromatin whereby a gene is expressed in some but not all cells of the same tissue (Dronamraju, 1965; Hartmann-Goldstein and Koliantz, 1981).

In man, there is good evidence for X-linkage of 107 traits, and X-linkage is suggested for another 98 (McKusick, 1978). Y-linkage is reported only for some functions essential to sperm production, one form of hairy ears, and a male tendency effect (Dronamraju, 1965; McKusick, 1978; Ohno, 1979). The

Y also affects stature, but this effect need not result from the influence of a specific locus (McKusick, 1978). In the laboratory mouse, 18 genes have been mapped to the X, but none to the Y. In the silk moth (*Bombyx*), Doira (1978) listed eight Z-linked markers but no W-linked markers.

It has often been emphasized that the Y is not totally inert (e.g., Dronamraju, 1965; Hess and Meyer, 1968; Voelker and Kojima, 1971), and the above evidence supports this view. A further example of Y-associated functions was observed in *Drosophila affinis*, with the coexistence of XO and XY males in a single population; the difference between these two types of males resulted from the presence or absence of a "degenerate" Y rather than from an X-autosome translocation (Voelker, 1970; Voelker and Kojima, 1971). XY males were reproductively more successful than XO males, so that the XY condition replaced the XO condition in population cage experiments, an effect clearly from the Y chromosome. However, although many studies have identified functions on the Y, there can be no doubt that these functions are often vastly different and much fewer in number than those on the X. Therefore, I will continue to refer to the Y as "degenerate" whenever it manifests signs of extreme heteromorphism from the X, even though it may perform several essential functions.

The above comparisons apply only to sex chromosome regions that are tightly linked with the sex factors (the differential segments). The X and Y chromosomes of a species may also have a common segment which recombines freely. Recombination will necessarily render genes similar on the X and Y within this segment; recombination will have the additional effect of generating genetic evidence consistent with autosomal inheritance of these loci. Consequently, demonstrating that these genes occur on the sex chromosomes requires a combination of genetic and cytological evidence. The extent of X-Y genetic similarity resulting from segments that recombine is largely unknown except in *Drosophila*: the *Drosophila* Y lacks the euchromatic part of the X—the segment in which nearly all X-borne functions have been mapped (Muller and Painter, 1932).

Heterochromatin

Chromatin is the protein-DNA complex that comprises the chromosomes. Present terminology distinguishes two major classes of chromatin: euchromatin and heterochromatin (terms proposed by Heitz, 1928; reviewed in Brown, 1966; John and Miklos, 1979). In most animals studied, the bulk of chromatin is euchromatic, remaining in a diffuse state during most of the cell cycle except prior to and during cell division. In contrast, heterochromatin is condensed throughout most of the cell cycle. Heterochromatin is often associated with Y chromosomes, and more rarely with the X. However, there are some outstanding differences in the types of heterochromatin associated with sex chromosomes, and it is consequently necessary to consider these

varieties before discussing heteromorphic sex chromosomes. (See Mittwoch, 1973 for a complementary discussion.)

Two general classes of heterochromatin are recognized: *facultative* and *constitutive* (Brown, 1966). Facultative heterochromatin is functionally altered euchromatin. Heterochromatin is classified as facultative if only one member of a homologous pair becomes heterochromatic, or if the heterochromatin is descended from a euchromatic state in previous generations. Two famous illustrations of facultative heterochromatin are (i) the heterochromatic paternal genome in male scale insects (recall Sec. 11.F), and (ii) the inactive X chromosome in female mammals (see below and Sec. 16.E). Constitutive heterochromatin is instead a more permanent state of heterochromatin and behaves identically on homologous chromosomes. For a long time it seemed as if constitutive heterochromatin was fundamentally different from facultative heterochromatin, but a study of mosquitoes revealed one case in which a region of constitutive heterochromatin was differentially euchromatic according to its genetic background (Motara and Rai, 1977).

The distinction between euchromatin and constitutive heterochromatin is historically cytological, but there have been attempts to characterize this distinction on genetic and molecular grounds. These studies have led to the recognition that there are many varieties of constitutive heterochromatin, and that no extant genetic or molecular criteria distinguish it from euchromatin. The property most commonly attributed to constitutive heterochromatin is genetic inertness, and there are four observations that have led to this conclusion: (i) constitutive heterochromatin can often be deleted from the genome without deleterious effects, (ii) relatively few genes are known in constitutive heterochromatin, (iii) radioactive uridine is not incorporated in heterochromatin (constitutive or facultative) at levels comparable to that of euchromatin, and (iv) the juxtaposition of euchromatin to heterochromatin (partially) suppresses expression of genes located in the euchromatin (reviewed in Brown, 1966; Brown and Chandra, 1977; John and Miklos, 1979). In addition, constitutive heterochromatin is often late replicating and consists of short, repeated sequences of DNA, quite unlike the DNA in most functional genes. Yet, there are known exceptions to most of these rules. A general problem here is that it has been difficult to resolve heterochromatin to a fine level in light microscopes, and so heterochromatin may often be interspersed with short euchromatic regions, which may also account for some of its genetic activities.

The advent of special chromosome staining techniques has permitted recognition of a type of constitutive (but not facultative) heterochromatin known as C-band heterochromatin (Arrighi and Hsu, 1971). The technical basis for the identification of C-bands involves two major treatments of chromosome preparations prior to staining. First, the chromosomes are exposed to a basic solution that denatures the chromosomes (commonly barium hydroxide). The chromosomes are then exposed to a warm salt solution and later stained. The resulting chromosomes are pale with regions of dark stain, and the dark regions are C-band heterochromatin (Plates 16.B.1, 16.B.2).

The Y (W) chromosome in mitotic and/or meiotic preparations has commonly been observed to be constitutively heterochromatic, as it stains heavily for C-bands in mammals (Sharma et al., 1981; Sharma and Raman, 1973; Pathak and Stock, 1974), birds (Stefos and Arrighi, 1971; Stock et al., 1974; Ryttman et al., 1979; Mengden, 1981), reptiles (Mengden, 1981; King, 1977), Diptera (Jan and Shu, 1972; Hsu, 1971), amphibians (Sessions, 1980; Schmid, 1980), and fish (Park and Grimm, 1981). The fraction of the Y that stains for C-band heterochromatin varies between species, and there are also different intensities of C-bands (above references). In some groups, the Y chromosome is also visible as a condensed body in interphase nuclei, a phenomenon known as "sex chromatin." This characteristic is sometimes employed as a method of diagnosing sex (Cock, 1964; Ray-Chaudhuri et al., 1970; Traut and Mosbacher, 1968; Clarke and Ford, 1980). (A different form of sex chromatin is known in mammals, however; see Sec. 16.E.) In angiosperms, heterochromatic Y's have been reported in *Rumex* and hops, but the heterochromatin was identified by methods other than C-banding (Jacobsen, 1957; Zuk, 1970a, b).

Not uncommonly in animals, part of the X may also be constitutively heterochromatic (e.g., mammals, Pathak and Stock, 1974; Plate 16.B.1; *Drosophila*, Hsu, 1971; grasshoppers, Gallagher et al., 1973; Rao and Arora, 1979). In mammals, many species with a large, heterochromatic Y (not necessarily larger than the X) also have an X chromosome with a heterochromatic addition (Sharma et al., 1981; Sharma and Raman, 1973). The X of the housefly and some other dipterans is unusual because it consists almost entirely of constitutive heterochromatin (Boyes, 1967; Ullerich, 1963; White, 1973; Jan and Shu, 1972; Plate 16.B.1).

In some species the X chromosomes are facultatively heterochromatic. The most famous example is the X in placental mammals. In females (XX), one X is inactivated in each somatic cell and is heterochromatic during interphase, but this X does not C-band differently from the other X (Arrighi and Hsu, 1971; Brown and Chandra, 1977; VandeBerg, 1983; VandeBerg et al., 1983; Sec. 16.E). In grasshoppers and *Drosophila*, the single X in males is facultatively heterochromatic in early spermatogenesis (John and Lewis, 1965; Brown and Chandra, 1977).

Y-DNA

Some recent and exciting work on sex chromosomes has employed techniques from molecular genetics to explore DNA sequences in the Y chromosome. From the few studies available, this field of investigation offers promise toward understanding the nature of X-Y differences at the genetic level, and it complements the observations from cytology. Four separate studies have reported the isolation of a DNA fraction concentrated on the Y but not the X, or only at the centromere of the X (Jones et al., 1973; Singh et al., 1980; Kunkel and Smith, 1982; Steinemann, 1982). In all cases, this Y-DNA shares homology with DNA

from the autosomes, although perhaps just in specific autosomal sites. These Y-DNA fractions consist in part of "repetitive" sequences—sequences of DNA that occur in many copies throughout the genome.

In their study of a snake with heteromorphic sex chromosomes (female heterogamety), Singh et al. (1976, 1980) isolated a DNA "satellite" from the female that was absent from the male. (A DNA satellite is a subset of the total DNA which has a different density than most of the DNA, and it is usually identified after the total DNA is centrifuged in a Cesium salt gradient.) When compared to the DNA of males and other females by a method known as "hybridization," this DNA satellite hybridized heavily to the W chromosome, and also hybridized to the autosomes and perhaps the Z, but the only areas of heavy hybridization occurred on the W. This W chromosome DNA was then used as a probe for other species, and it hybridized to the W chromosome of other snakes, to part of the mouse Y, and to a short region of the *Drosophila* X (Singh et al., 1981; Jones and Singh, 1982). The nucleotide sequence of part of this probe has since been shown to contain a small region of tandem repeats of the sequences GATA and GACA (26 and 12 repeats, respectively), and this probe led to the identification of a male-specific RNA in mice (Epplen et al., 1982).

Kunkel and Smith (1982) analyzed a long DNA segment specific to the human Y (3.4 kilobases) that was present in multiple copies and accounted for perhaps 40% of the Y DNA. This long segment was fragmented and its components were further classified into two major categories: subfragments specific to the Y (Y-specific fragments) and subfragments that hybridized to the autosomes (non-Y-specific fragments). (A further distinction within each of these two categories was identified, but the findings of interest here do not require enumeration of this additional classification.) In hybridizing the Y-DNA of humans to the DNA of great apes, there was no detectable homology with the Y chromosomes in the apes. However, the non-Y-specific subfragments of human Y-DNA hybridized to the ape autosomal DNA, just as they did to human autosomal DNA. Upon further investigation, these non-Y-specific fragments of human Y-DNA proved to be almost identical to the homologous autosomal sequences in apes and humans (i.e., these sequences were highly conserved in different primates).

The important conclusion from this work is that the human Y chromosome is composed, in part, of many copies of a DNA fragment absent from the Y's in apes, while present in an almost unchanged form in ape and human *autosomes*. Thus it appears that the human Y chromosome has evolved, at least in part, by the incorporation or loss of specific fragments, rather than by the gradual modification of DNA that has long been present in the Y (Kunkel and Smith, 1982). The lack of homology between Y-DNA from humans and apes contrasts with the findings of Singh et al. (1980), but both results are compatible if Y chromosomes contain different families of repeated sequences.

Another study considered the Y-DNA of *Drosophila pseudoobscura* and *D. miranda* (Steinemann, 1982). An RNA probe was prepared from unfrac-

tionated DNA of *miranda* and was hybridized to chromosomes of both *miranda* and *pseudoobscura*. (Based on technical details, it was supposed that the RNA was transcribed chiefly from repeated sequences of DNA.) The RNA probe hybridized heavily to the Y chromosome in both species, whereas hybridization to the X was negligible or localized at the centromere. The interesting part of Steinemann's findings concerned *D. miranda*, however. The Y of *D. miranda* is the union of an ancestral, "degenerate" Y and a former autosome (generating a multiple sex chromosome system). Steinemann found that the RNA probe hybridized throughout both ancestral and autosomal parts of the Y, although only at the centromere of one of the X's. Thus, as in Kunkel and Smith's study, it seemed that the Y was invaded by sequences of DNA found in multiple copies elsewhere in the genome.

C. Meiosis and Crossing-Over

In systems with extreme X-Y heteromorphism, the X and Y are usually free from crossing-over, at least along much of their lengths. In fact, extreme X-Y differences could not be maintained in chromosome segments undergoing free recombination, except under extreme selection against crossover products. The evidence for the absence of X-Y recombination is both genetic and cytological. Genetic evidence is provided from the strict X-linkage of the known sex-linked mutations in species with heteromorphic sex chromosomes. However, sex-linked markers are unknown in most species with heteromorphic sex chromosomes, and most evidence on the absence of X-Y crossing-over has been obtained from cytological studies, as explained below.

In meiosis, structures known as *chiasmata* are observed between homologous chromosomes, and these structures are thought to represent recombinations within the chromosome (White, 1973, his Chap. 6). Sex chromosomes have been the particular interest of many cytological studies, and there are several lengthy discussions about the different types of X-Y pairing and separation in meiosis (Darlington, 1937; John and Lewis, 1965; White, 1973; Solari, 1974). Cytological studies of meiosis in the heterogametic sex often reveal a lack of chiasmata along much of the X-Y bivalent, so it is presumed that X-Y recombination is absent in these segments (e.g., Darlington, 1937; White, 1973). In several cases, it appears that the X and Y pair (synapse) and perhaps recombine in a short segment. In most circumstances, such recombining segments must lie outside the differential segments so that recombination does not subdivide the differential segments between the X and Y.

The interpretation of recombination from cytological observations requires caution, however, because crossing-over occurs in meiosis prior to meiotic stages that facilitate observation of the chromosomes. Two complications are encountered when equating the presence (or absence) of chiasmata with the existence (absence) of recombination. First, there is not necessarily a

strict correspondence between the observed sites of chiasmata and the positions of crossovers, because the apparent positions of chiasmata change as the meiotic cycle proceeds. Second, chiasmata within the sex bivalent are not always easily observed when the Y and/or X are heterochromatic, because the heterochromatin may be too condensed for easy observation. In mammals, for example, the sex chromosomes are condensed early in meiosis, and hence the analysis of meiosis according to conventional methods is obscured (Plate 16.B.1). Some recent improvements in the analysis of early meiosis have greatly facilitated the study of X-Y behavior, at least in mammals (e.g., Moses et al., 1975; Tres, 1979; Plate 16.B.1).

In some invertebrate groups one sex completely lacks crossing-over or chiasmata (e.g., many Diptera, perhaps all Lepidoptera, several other invertebrates; Eloff, 1932; Tazima, 1964; John and Lewis, 1968, p. 21; White, 1973, pp. 476-490; Serrano, 1981; Bell, 1982, pp. 419-424). Haldane (1922), and especially Huxley (1928) noted that the sex with an absence of crossing-over was also the heterogametic sex (e.g., the male in Diptera, female in Lepidoptera). There is indeed a statistically significant association between the heterogametic sex and the crossover-free sex, but there are also cases that do not fit this rule. For example, crossing-over was reported to be low or absent in male houseflies, but some populations had multiple-factor sex determination with females heterozygous for sex factors (Sec. 3.D). Baker and Rabbani (1970) reported the possible absence of recombination in females of a mosquito species with male heterogamety. Some hermaphrodites lack chiasmata, so the absence of crossing-over is independent of heterogamety in these species (e.g., White, 1973; Bell, 1982). In addition, crossing-over has been reported in both sexes of many species with heteromorphic sex chromosomes. Dunn and Bennett (1967) reviewed evidence for various animals, especially mice, and they noted that when crossing-over occurred in both sexes there was no tendency for the rate of crossing-over to be lower in the heterogametic sex.

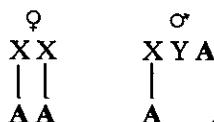
D. Multiple Sex Chromosomes

Sex chromosome differences between males and females commonly involve just one chromosome pair, the X and Y, or just the X in XX/XO species. However, there are numerous examples in which sex chromosome differences involve more than just an X and Y (recall Sec. 2.A). The male may contain two Y chromosomes (XX female/X₁Y₁ male), or two chromosomes may assort in the X-linked manner (X₁X₁, X₂X₂ female/X₁X₂ Y male). There are also more complicated systems. Multiple sex chromosomes are usually detected from differences in chromosome number between males and females, although this characteristic is neither indicative of multiple sex chromosomes nor a necessary consequence of their existence. The best criterion for diagnosing multiple sex chromosomes is found in the analysis of meiosis in the hetero-

gametic sex, which will reveal the multiple sex chromosomes associated during the first metaphase.

Systems of multiple sex chromosomes have been extensively studied and were reviewed by White (1945, 1954, 1973, Chap. 17) and others. The majority of these examples have such simple explanations that only the basic conclusions warrant description here. Multiple sex chromosome systems are usually derivatives of the simple XX/XY (or XX/XO) systems. An XX/XY system may generate multiple sex chromosomes either through translocation of an autosome to the X or Y, or less commonly, fission of the X or Y if all parts retain centromeric activity (recall p. 12).

Consider an autosome translocated to the X in a basic XX/XY system. Also suppose that there are no meiotic or other problems associated with the translocation. If this X-autosome translocation (the neo-X) eventually replaces all single X's, the sex chromosomes then become



(from p. 12)

where A represents the translocated autosome.

At this stage the sex chromosome difference between males and females is cytologically observable because males are heterozygous for the translocation. The ancestral Y remains free of the autosome as long as no X-Y recombination occurs between the sex factor region and the position of translocation. Note that if the Y is absent in the ancestral system, this translocation produces a superficially orthodox X-Y system.

Even though one may regard the autosomes involved in sex chromosome translocations as fundamentally distinct from the ancestral X and Y, the establishment of a multiple sex chromosome system may subsequently lead to the "degeneration" of the Y-linked autosome. This degeneration of a former autosome in fact has been observed (Swanson, 1957; John and Lewis, 1968; White, 1973, pp. 610, 646; Lucchesi, 1978; Steinemann, 1982), and these examples are of special interest in understanding the process of sex chromosome evolution (Sec. 17.C).

E. Dosage Compensation

If the Y is largely degenerate, an XX individual has two copies of every X-linked gene, while the XY individual has only one copy. In animals, a single copy of an autosome (a condition known as "aneuploidy") represents a highly deleterious condition, so it seems that there must be some accommodation for the two-fold difference of X-linked genes between males and females. In mammals, *Drosophila*, and possibly some crickets, the level of activity of most

X-linked genes is equalized between the two sexes. This phenomenon is known as *dosage compensation*, and there are two distinct ways in which compensation is achieved, as illustrated below by mammals and *Drosophila*.

The common method of assaying dosage compensation is to compare some measure of X activity between normal males and females. If the activities are equal between the sexes, then dosage compensation is thought to operate. However, comparison of XX females with XY males confounds gender with the number of X's present: is X activity regulated according to the number of X's present in the individual, or is it regulated according to the sex of the individual, or both (cf. Muller, 1950; Cock, 1964)? These alternative interpretations are addressed by some of the experiments discussed below.

Mammals (XX ♀/XY ♂)

Dosage compensation is achieved through the inactivation of one X in the female. Therefore, even though a female has two X's, only one is active, at least in somatic cells (Lyon, 1961; reviewed in Cattanach, 1975; Brown and Chandra, 1977; Cooper et al., 1977; Gartler and Cole, 1981; VandeBerg, 1983; VandeBerg et al., 1983). Inactivity of one X has been inferred chiefly from two types of observations. (i) One of the X's is facultatively heterochromatic, as it is condensed on the nuclear membrane during interphase. This condensed X is known as a Barr body (Barr and Bertram, 1949; Barr, 1959), and it replicates DNA at a later stage in the cell cycle than does the active X. (ii) With a few exceptions, females heterozygous for X-linked markers display the phenotype of just one X in any particular cell, and in placental mammals, different cells may display either of the two phenotypes. A third inference of dosage compensation, observed in cells of marsupials, is based on work with radioactive uridine (which is preferentially associated with genes transcribing RNA)—the radioactive uridine induced breaks in just one of the two X's (Donald and Cooper, 1977). However, a few X-linked loci, and perhaps all genes in a short segment of the X, are not compensated (Cattanach, 1975; Therman et al., 1976; Ropers and Wiberg, 1982; VandeBerg, 1983). In marsupials, the level of inactivation varies between loci and even between tissues for the same locus (VandeBerg et al., 1983). These observations apply to somatic cells, whereas it seems that both X's are active in oocytes (Brown and Chandra, 1977; Gartler and Cole, 1981; VandeBerg, 1983).

Placental and marsupial mammals differ fundamentally in one aspect of X-inactivation (Cattanach, 1975; Brown and Chandra, 1977; VandeBerg, 1983; VandeBerg et al., 1983). As originally proposed by Lyon (1961), the embryonic tissue of placental mammals inactivates the paternal X in some cells and the maternal X in others, so the adult female becomes a mosaic for patches of cells with an active paternal X and other patches with an active maternal X. In contrast, only the paternal X is inactive in somatic tissues of

marsupials. Even in placental mammals, however, extra-embryonic tissues inactivate the paternal X (Takagi et al., 1982; Brown and Chandra, 1977; VandeBerg, 1983).

X inactivation depends on the number of X chromosomes in the cell rather than gender. In humans, the single X of XO females is active, while one X of XXY males is inactive (Brown and Chandra, 1977). In humans with more than two X's, only one X is active (or they probably would not survive). A further detail of the dosage compensation mechanism in humans at least is that discrete inactivation centers occur on the X, and X chromosomes with deletions of these crucial sites fail to become completely inactive (Cattanach, 1975; Therman et al., 1979; Nakogomi, 1982). In the mouse, the probability that a particular X is inactivated depends on which allele it carries at the inactivation locus (Rastan, 1982).

Fruitflies (XX ♀/XY ♂)

Dosage compensation in *Drosophila melanogaster* operates through adjustment of X expression, equally for all X's (reviewed in Brown and Chandra, 1977; Lucchesi, 1977, 1978). This form of dosage compensation has been documented in three ways. (i) The width of polytene chromosomes in salivary gland nuclei is thought to reflect their level of RNA transcription, and the single X in males is approximately twice as wide as each X in females (Dobzhansky, 1957; Belote and Lucchesi, 1980a). (ii) The rate of radioactive uridine incorporation on polytene X chromosomes is half per X in an XX female what it is in an XY male. (iii) Observed levels of enzyme activity and other gene products have been the same in males and females for the few X-linked loci studied (although this observation does not preclude the mammalian system of dosage compensation).

Again, some interesting details have been resolved. Diploid XXX flies showed an even lower rate of transcription per X than XX flies, so that the total rate of RNA transcription for X chromosome genes was independent of the number of X's. However, flies with three sets of autosomes showed an elevated level of X products over that in flies with a diploid set of autosomes—regardless of the number of X's (Lucchesi, 1977, 1978). The study of translocations further showed that parts of the X translocated to autosomes underwent dosage compensation, whereas autosomes attached to the X were not regulated by dosage compensation. However, there does not seem to be a locus-specific mechanism of dosage compensation. In flies with separate parts of the X present in different numbers, transcription levels per individual copy of a locus were the same, regardless of the number of copies of the locus. Loci present in three copies, for example, had three times the total activity as loci present only once (Maroni and Lucchesi, 1980). Finally, several autosomal and X-linked mutants have been discovered with a major influence on dosage compensation (Belote and Lucchesi, 1980a, b; Lucchesi and Skripsky, 1981).

Nematodes (XX ♀/XO ♂)

An X-linked enzyme, *acetylcholinesterase-1* (*Ace-1*), was assayed in the nematode, *Caenorhabditis elegans* (Duckett, 1979). Recall from Sec. 4.B that these worms are normally XX and hermaphroditic, but they develop as male if they are XO. Since males occur only rarely in natural populations, there is no reason to expect dosage compensation, except perhaps as a mechanism retained from an ancestor with separate sexes. However, the results of this work are illuminating. Duckett observed that levels of *Ace-1* activity were nearly the same in XO wild-type males and in XX wild-type hermaphrodites, so full dosage compensation appeared to operate (Table 16.E). As suggested above, however, the comparison of XX hermaphrodites to XO males confounds the effect of sex with the number of X chromosomes. Was *Ace-1* activity dosage compensated, or was its activity merely higher in males than females? Duckett's experiments suggested that both effects operated (Table 16.E). When investigating these two possibilities, Duckett made use of several sex transforming mutations (recall Table 4.B), and he compared *Ace-1* activity in XX males and XX hermaphrodites (varying sex while holding the number of X's constant) and in XO males and XX males (varying the number of X's and holding sex constant). An elevated level of *Ace-1* activity was observed in XX males over XX hermaphrodites, thereby indicating that activity depended upon sex. But dosage compensation was also indicated because XX males had less than twice the level of activity as XO males.

Duckett's experiments illustrate the importance of distinguishing between sex-limited expression and dosage compensation of X-linked genes. However, his demonstration that both effects can be important is not necessarily fatal to all assays of X-activity that fail to investigate this distinction. It may be significant that Duckett assayed a single locus, while most methods have assayed the entire X, although at a more superficial level. If most loci do not experience large magnitudes of sex-limited expression, then assays of the entire X should provide valid indications of the extent of dosage compensation. These assays of the entire X of course should distinguish active segments present on both the X and Y from segments restricted to the X.

Crickets (XX ♀/XO ♂)

Two species of crickets have been investigated for dosage compensation by an ingenious method involving the incorporation of radioactive uridine by chromosomes transcribing RNA. In *Drosophila*, radioactive uridine provides a straightforward assay for determining the rate of RNA transcription, because polytene chromosomes actively transcribe RNA, and they incorporate radioactive uridine when they are amenable to cytological observation. The level of radioactivity—hence uridine incorporation—can be directly measured over individual chromosomes. In most organisms, however, the chromosomes

TABLE 16.E. X-Linked *Ace-1* Activity in a Nematode

Genotypes	Normalized Activity
Males	
XO (wild type)	1.14
XX <i>tra-2/tra-2</i>	1.73
XX <i>tra-3/tra-3</i>	1.41
Hermaphrodites	
XX (wild type)	1.00
XX <i>tra-2, +/+</i> , <i>dpy-10</i>	1.04
XX <i>tra-3, +/+</i> , <i>dpy-14</i>	}
XX <i>tra-3/tra-3</i>	0.95

Source: Duckett, 1979.

Note: The recessive *tra* mutations transform sex so that XX zygotes develop as males (Table 4.B). The mutation *tra-3* is a recessive maternal effect mutation, so that homozygous females and males can both be obtained. The *dpy* mutations are linked to the *tra* mutations and merely serve to distinguish the *tra* heterozygotes. The absolute activity, to which all activities here were standardized, was $.25 \pm .01$; standard errors on the other activities were also .01.

can be identified only in meiosis or mitosis, when they are transcriptionally inactive. Uridine is not actively incorporated into mitotic or meiotic chromosomes, so the *Drosophila* assay is not feasible. Rao and Ali (1982) are Rao and Arora (1979) utilized the fact that incorporation of radioactive uridine into RNA during interphase (when the chromosomes are too diffuse for identification) induces breaks in the chromosomes that can be assayed when the chromosomes enter metaphase (Klevecz and Hsu, 1964). By counting the number of breaks in the X, they obtained crude measures of X activity that enabled them to distinguish between the hypotheses of no dosage compensation versus complete dosage compensation.

Two species of crickets with male heterogamety were studied with these methods, and both species revealed evidence of dosage compensation for the X chromosome, although the type of dosage compensation differed. Evidence from the mole cricket (*Gryllotalpa fossor*) suggested a mammalian form of dosage compensation. (One arm of the X in this species was constitutively heterochromatic, so I will refer only to the euchromatic arm of the X.) Rao and Arora (1979) found that only one of the X's in the female was broken by the treatment, as if only one X was active (Donald and Cooper, 1977, reported similar observations from marsupials). The total number of X-breaks per cell in females was not significantly different from the number of X-breaks per cell in males, but the female value was significantly lower than twice as high as the male value. Evidence also indicated that the two X's in females replicated at different times, which was again consistent with a single active X.

The study of a second cricket, *Acheta domesticus*, revealed evidence of a *Drosophila* form of dosage compensation (Rao and Ali, 1982). The radioactive uridine induced breaks in both X's of the female, but the total number of

X-breaks per female was not significantly different from that found for males; the value for females was significantly less than twice the value found for males. There was also no indication that the two X's of females differed in the timing of replication. A useful addition to these studies would have been a comparison of the number of breaks in the X versus the number of breaks in a comparable length of autosomes.

Absence of Dosage Compensation

Dosage compensation may not be a universal phenomenon among highly differentiated sex chromosomes. Observations on the few known Z-linked traits in birds and lepidopterans are consistent with the absence of dosage compensation (Cock, 1964; Johnson and Turner, 1979; Baverstock et al., 1982). The possibility of dosage compensation in these groups has been assayed only for individual Z-linked loci, rather than for the entire Z.

F. Degenerate X's

The basic observation from studies of sex chromosomes is that the Y is largely degenerate but the X is functional and necessary for viability. Observations from a few species, however, suggest that the X is largely degenerate. As mentioned in Sec. 3.D, both the X and Y in the housefly are highly heterochromatic (Plate 16.B.1), and several extra X's are compatible with viability and fertility. No X-linked traits are known in houseflies, despite several traits known for each of the autosomes. It has also been noted that the X-Y chromosome pair of houseflies has no counterpart in some closely related flies whose karyotype is otherwise the same. Possibly, the X and Y of houseflies were lost or were never acquired in these other species. Some other animals were also reported to have highly variable numbers of X chromosomes (e.g., bed bugs, White, 1973, p. 664), as if the X had no function other than in the inheritance of sex. These examples seem distinct from and may have a different type of evolutionary history than most other sex chromosomes (Sec. 17.C, Chap. 18).

G. Summary

Sex chromosomes occur in a wide range of plants and animals with heterogametic sex determination. Many species have a single X and Y chromosome, but some species have multiple sex chromosomes (more than just one X and Y), a condition resulting from the translocation of an autosome to a sex

chromosome or from fission of a sex chromosome. Sex chromosomes are distinguished by various cytological and genetic phenomena in addition to controlling the inheritance of sex. The X and Y are often "heteromorphic," differing from each other in size and shape, a fact that led to their discovery in cytological studies around 1900. The X chromosomes of most species are typical of autosomes in staining properties and gene content, but the Y is often heterochromatic and lacks most or all of the X-linked genes. Consequently, the DNA constitution differs between the X and Y, although preliminary work has suggested that some segments of Y-DNA are homologous with sequences found in the autosomes. These X-Y differences are maintained because the X-Y differential segments do not recombine.

When the Y lacks some X-linked functions, the XX sex carries twice as many copies of these loci as does the XY sex. Dosage compensation is a phenomenon observed in some species with heteromorphic sex chromosomes (mammals, fruitflies, and possibly nematodes and crickets) whereby the activity of X chromosomes is regulated so that the total activity of X-linked loci is the same in both sexes regardless of the number of X's present.

The examples described in this chapter illustrate characteristics typical of sex chromosomes in many species. However, less extreme forms of sex chromosomes heteromorphism are known, as described in the following chapter.

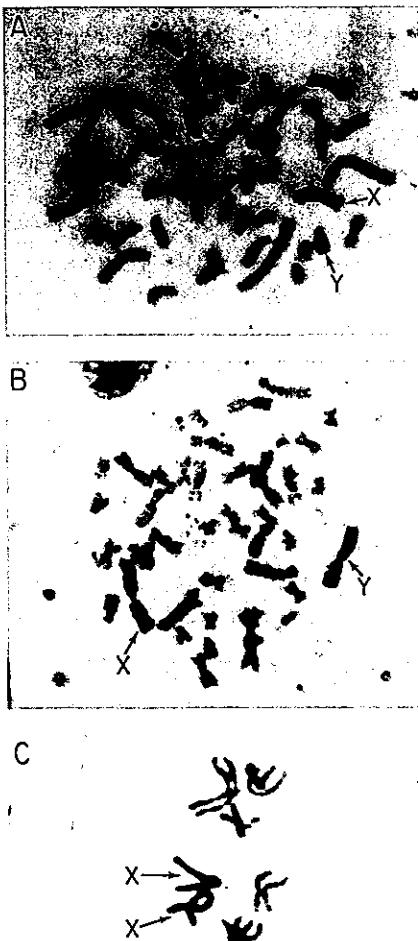
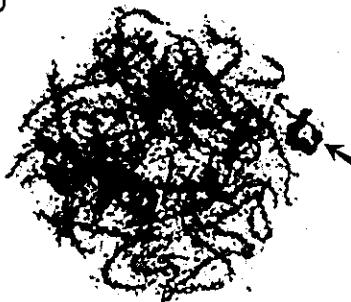


PLATE 16.B.1. Sex chromosomes in rodents and a fly. (A) A C-banded mitotic metaphase of the rodent *Oryzomys macconnelli* indicating the Y and the possible X chromosome ($2n = 54$). (The identity of the X is ambiguous among five chromosomes of similar size and shape.) The Y is smaller than the X and it also differs from all other chromosomes by staining positively for heterochromatin throughout its length. (See Sec. 16.B.) (Provided by M. Haiduk and R.J. Baker.)

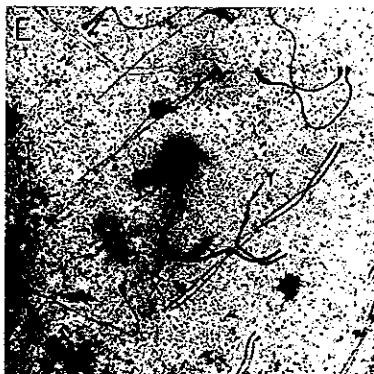
(B) A C-banded mitotic metaphase from the rodent *Ototylomys phyllotis* indicating the X and smaller Y ($2n = 48$). The entire Y and one arm of the X are heterochromatic. (See Sec. 16.B.) (Provided by J. Bickham, P. Tucker, and M. Engstrom.)

(C) A C-banded mitotic metaphase from an XX male housefly, *Musca domestica* ($2n = 12$). The X in this species consists almost entirely of constitutive heterochromatin, while only the centromeres of the autosomes are heterochromatic. (See Secs. 3.D, 16.F.)

D



E



(D) Silver stained chromosomes from early meiosis (pachytene) in a pocket gopher, *Geomys bursarius* ($2n = 70$). As is typical for mammals, the X-Y bivalent (arrowed) is highly condensed and is not amenable to detailed analysis of chromosome pairing, unlike the autosomes. (See Sec. 16.C.) (Provided by J. Bickham.)

(E) An electron micrograph of the X-Y bivalent from pachytene in the mouse, *Mus musculus* ($2n = 40$) (silver stain). The X and Y are paired along approximately half the length of the Y. Some of the autosomes also appear in the figure. (See Sec. 16.C.) (Provided by J. Bickham, P. Tucker, and M. Engstrom.)

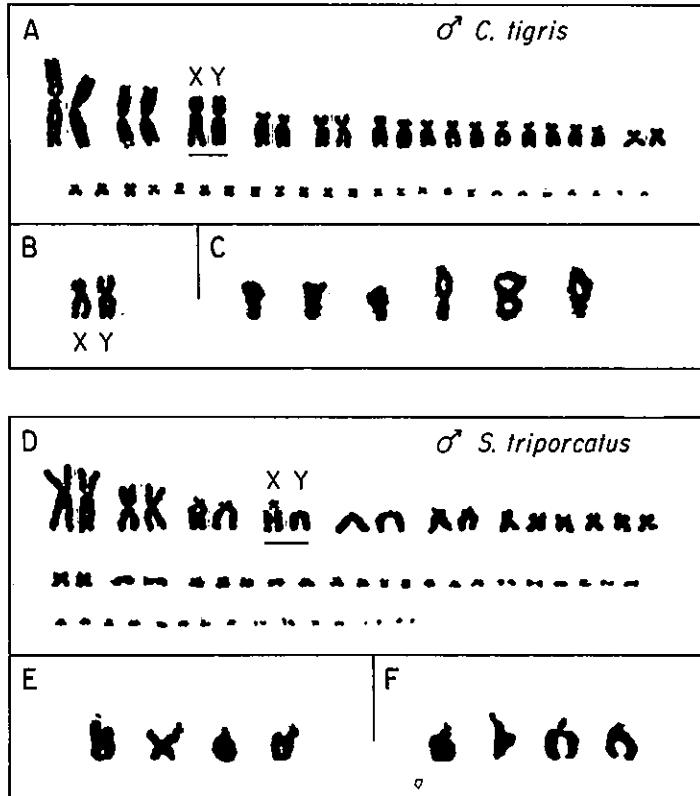


PLATE 16.B.2. Sex chromosomes in two reptiles with slight X-Y heteromorphism. (A) Karyotype of a male whiptail lizard (*Cnemidophorus tigris*) ($2n = 46$). The heteromorphic sex chromosomes are recognized from a slight difference in centromere position between the X and Y. (Standard Giemsa stain). (B) When stained for C-bands, the X's centromere bands strongly, but the Y either lacks a C-band or has only a faint one. (C) When stained for C-bands, the X-Y bivalent in male meiosis shows chiasmata in both arms. (The stage here is diakinesis, just prior to the first metaphase division.) The unpaired C-band of the X is evident in these bivalents. (Each of these X-Y bivalents was taken from a different cell.) (Based on J.J. Bull. 1978. "Sex chromosome differentiation: An intermediate stage in a lizard." *Canadian Journal of Genetics and Cytology* 20:205-209, Figures 1 and 3.

(D) Karyotype of a male mud turtle (*Staurotypus triporcatus*) ($2n = 54$). The X-Y heteromorphism is indicated because the Y lacks a short arm and secondary constriction (gap) observed on the X. (Standard Giemsa stain.) (E and F) X-Y bivalents from the first meiotic division (diakinesis) in *S. triporcatus* (E) and *S. salvini* (F), as identified by the longer X and its secondary constriction. Chiasmata appear throughout the bivalent. (Each bivalent was taken from a different cell.) (Based on J.J. Bull, R.G. Moon, and J.M. Legler. 1974. "Male heterogamety in kinosternid turtles (genus *Staurotypus*)." *Cytogenetics and Cell Genetics* 13:419-425, Figures 1 and 2. Reprinted by permission of S. Karger, A.G., Basel, Switzerland.

17

Slight X-Y Heteromorphism and Evidence of a Transition

Various species are known in which the sex chromosomes are indistinguishable or only slightly heteromorphic, as indicated by X-Y morphological similarity, X-Y recombination, and YY viability. Section A will describe some case histories of slightly differentiated sex chromosomes. The existence of extreme X-Y heteromorphism in some species as well as slight heteromorphism in other species raises the question of whether the different degrees of heteromorphism resulted from different processes of sex chromosome evolution or instead represent different stages in a single process. Section B will consider evidence for the generally accepted view that sex chromosome heteromorphism evolved from an initial state of X-Y similarity, hence that cases of slight heteromorphism are early stages in sex chromosome evolution. Section C will propose that highly conserved systems of male or female heterogamety are usually accompanied by extreme sex chromosome heteromorphism.

A. Examples of Slightly Heteromorphic Sex Chromosomes

This section will describe several examples of slightly differentiated sex chromosomes, drawing upon reptiles, amphibians, fish, and flies (summarized

in Table 17.A). Documented examples of X-Y similarity are uncommon in comparison to the many examples of extreme heteromorphism, but their scarcity may result partly from an observational bias, since discovering examples of X-Y similarity is complicated by the fact that similar X and Y chromosomes are difficult to identify cytologically or genetically. Many vertebrates and invertebrates karyotyped have not displayed heteromorphic sex chromosomes, but it seems unjustified to conclude that sex chromosomes are similar in these species without knowing whether heterogametic sex determination operates or without knowing the positions of sex factors. It is expected that with increasing frequency these species will provide additional examples of demonstrated X-Y similarity, as techniques for chromosome study improve.

Reptilia: whiptail lizards (*Cnemidophorus tigris*); Plate 16.B.2. *Cnemidophorus tigris* is the only lizard from the family Teiidae in which heteromorphic sex chromosomes have been identified. The X and Y are nearly alike in size and shape (both have centromeres near the middle of the chromosome), but they differ slightly in centromere position (Cole et al., 1969). The difference in centromere position appears to be the result of either an inversion or a transposition of the centromere. In meiosis, chiasmata (indicating crossing-over) were observed in both arms of the X and Y except in the short region between the centromeres (Bull, 1978a). A short differential segment therefore exists. The Y does not manifest signs of extreme degeneration in this short region, although the Y lacks the centric C-band present on the X, and there is a faint C-band on the Y within the short differential segment.

Reptilia: mud turtles (*Staurotypus triporcatus*, *S. salvini*); Plate 16.B.2. *Staurotypus* is one of the two turtle genera known to have heteromorphic sex chromosomes (Table 9.D). The X and Y in these mud turtles are slightly more heteromorphic than in whiptail lizards, but they are nonetheless similar over much of their lengths (Bull et al., 1974; Sites et al., 1979). The X has a short arm and a long arm, and the long arm contains a secondary constriction (gap) adjacent to the centromere. The Y has just one arm, which seems equivalent to the long arm of the X except that it lacks the secondary constriction. In meiosis, chiasmata occur throughout the entire Y with the long arm of the X. In conclusion, there is a short differential segment in these turtles, but the Y is smaller than the X (Bull et al., 1974; Sites et al., 1979).

Amphibia: newts (*Triturus alpestris*, *T. vulgaris*, *T. helveticus*). The karyotypes of these three salamanders are indistinguishable in the numbers, sizes, and shapes of chromosomes (Schmid et al., 1979). The X and Y are morphologically similar in all species, and in the first two species, the X and Y have been distinguished only by a terminal C-band present in the Y and absent in the X. The X and Y have not yet been distinguished in *helveticus*, and the karyotypes of males and females in this species seem identical to the karyotypes of females in *alpestris* and *vulgaris*. In spermatogenesis, chiasmata

TABLE 17.A. Examples of Slight X-Y Differentiation (Described in the Text)

Taxon	YY Viable	XY Size and Shape	Heterochromatin	X-Y Crossing Over
FLIES				
<i>Aedes</i>	?	=	two C-bands on X, absent from Y	on both sides of differential segment (C,G)
Chironomids	?	=, or differ by inversions	rarely	extensive (G)
<i>Musca*</i>	+	=	=	absent or uncommon in all chromosomes of males (G)
REPTILES				
<i>Cnemidophorus</i>	?	slight difference in centromere positions	centric C-band on X, not Y, slight C-band in differential segment of Y	extensive in both arms (C)
<i>Staurotypus</i>	?	Y lacks short arm and 2° constriction of X	?	extensive (C)
FISH				
<i>Poecilia</i>	+ / -	cytologically unidentified	?	+ (G)
AMPHIBIANS				
<i>Triturus</i>	?	=	C-band on Y in 2 of 3 species	restricted to one arm in 2 of 3 species (C)

Note: (+) the characteristic is observed; (+ / -) YY is viable in some cases but not others; (?) indicates the characteristic has not been studied; (=) indicates that observations have not detected X-Y differences; (C) — the evidence of crossing-over is cytological (chiasmata in meiosis); (G) — the evidence of recombination is genetical (the inheritance of sex-linked markers). * — refers to strains and populations of houseflies in which both sexes are chromosomally XX, and males are produced as the result of an M factor; in this table, the Y therefore refers to the M factor (cf. Sec. 3.D).

have been observed in the autosomes of all species. Chiasmata were also observed in both arms of the XY pair of *alpestris*, but in just one arm of the XY pair in *vulgaris*; the C-banded arm of the Y was free of crossing-over. The XY pair could not be identified with certainty in *helveticus*, but one pair in males conspicuously lacked crossing-over in one arm, and this pair was the same size as the XY pair in *vulgaris* and *alpestris* (Schmid et al., 1979). This evidence suggests that sex chromosomes are homologous in all three species, and that the X and Y in *helveticus* have restricted crossing-over, even though they are without observed morphological differences.

Fish: guppy (*Poecilia reticulata*). Winge (1934) was unable to observe any cytological evidence of X-Y heteromorphism, but genetic evidence indicated male heterogamety. There was also genetic evidence of X-Y recombination for pigment genes at five different loci on the X and Y, although several pigment genes were strictly Y- or X-linked. Winge suggested that the X and Y were largely similar because of the genetic evidence of X-Y recombination.

Some interesting observations on Y-linked recessive lethals have been obtained that suggest the Y is in an early stage of degeneration. Winge and Ditlevson (1947) and Haskins et al. (1970) observed that YY individuals were viable and fertile if the two Y's were derived from different strains, but YY was inviable if both Y's were from the same strain. From the inviability it seemed that each Y may have had one or a few recessive lethals, but Y's from different strains carried different lethals and thus sheltered each other. Similar, though less extensive, observations were reported for the medaka (Aida, 1921; Yamamoto, 1959, 1969).

Farr (1981) further suggested that Y chromosomes from different guppy strains differed in the degree to which they had accumulated deleterious genes. Strains maintained the longest in captivity produced the most significantly female biased sex ratios, and the sex ratio was inherited according to the Y. Farr proposed that the extent of the female-bias reflected the degeneration of the Y, so that sperm with a degenerate Y were less efficient or successful in fertilization than sperm with an X or sperm with a less degenerate Y. This finding is surprising, because the Y is not highly degenerate in guppies, and yet these Y's supposedly contain enough deleterious mutations to impair sperm function in the gametic (haploid) phase. Gene expression in the gametic phase of higher animals is supposedly negligible (Muller and Settles, 1927; McCloskey, 1966; but see Hecht and Williams, 1978).

Diptera: midges (*Chironomidae*) and blackflies (*Simuliidae*). Sex determination has been studied in many of these flies because their polytene chromosomes permit construction of cytological maps, and a variety of inversions within their populations may be used as markers. Nearly all these species lack highly differentiated sex chromosomes, but in some species an inversion or short heterochromatic segment has been observed to be invariably sex-linked. In other species the sex locus has been located approximately (from inversions closely but not strictly linked to the sex locus), and no consistent structural differences between the X and Y have been observed (Beermann, 1955; Rosin and Fischer, 1972; Martin et al., 1980; Rothfels, 1980; Post, 1982).

Diptera: housefly (*Musca domestica*); Plate 16.B.1. Although the recent common ancestor to all living houseflies may have possessed extreme X-Y heteromorphism, as still observed in many populations, various populations homozygous in males and females for the ancestral X now exist, while males are heterozygous (*Mm*) for sex factors at a locus on a former autosome (Sects.

3.A, D). No cytological evidence for heteromorphism has been observed in many of these new systems of male heterogamety. Furthermore, following the introduction of still other sex factors, the new YY combination (*MM*) has been fully fertile (Table 2.E). It is of course expected that these new systems of heterogamety are initially without significant X-Y differences.

Diptera: mosquito (*Aedes aegypti*). Both cytological and genetical evidence is available on the nature of sex chromosomes in this well-studied mosquito. Newton et al. (1974) and Motara (1982) reported that the X and Y were the same size and shape but that the Y usually lacked two C-bands found on the X. In meiosis, chiasmata were observed on both arms outside the region distinguished by the C-band differences (Newton et al., 1974).

The genetic evidence was also interesting. The eye color mutations *red* and *rust* were located on one side of the sex locus about 6-7 and 27 crossover units from the sex factors respectively. A parasite-resistance gene resided about 4 crossover units on the other side of the sex locus (McDonald and Sheppard, 1965). The fact that none of these loci was completely linked to the sex factors indicated that recombination occurred on both sides of the sex factors. A particularly interesting result from this study was that crossing-over occurred more frequently between these markers in XX individuals (females) than in XY (males). For one type of X, the crossover distance in females from *red* to the resistance locus was 34 units, whereas in males (XY) this value was 10 units (for another X these values were 16 and 6, respectively). The cytological basis for the low rate of crossing-over in XY individuals was not discovered.

B. From Homomorphism to Heteromorphism

The extent of X-Y differences clearly varies widely among species. The question addressed here is whether these variations represent different stages in one evolutionary process moving from homomorphism toward extreme heteromorphism, or whether they represent different processes of sex chromosome evolution. The former view—that extreme sex chromosome heteromorphism evolves from homomorphism—has considerable antiquity. An early hypothesis on the nature of sex chromosome evolution was offered by Wilson (1905b), who suggested that XX/XO systems were derived from XX/XY systems, hence the Y could be lost. Muller and Sturtevant, however, developed the first clear theory that sex chromosomes evolved from an initial state of similarity to one of a “degenerate” Y (published in Muller, 1914; Sturtevant was credited in Muller and Painter, 1932; this theory was elaborated by Muller, 1918, 1932; Muller and Painter, 1932; Muller and Gershenson, 1935). This theory was possibly developed independently by Darlington (1937, 1939) and Haldane (1933), and it has been accepted widely (e.g., White, 1945, 1973; Darlington, 1937, 1958; Beermann, 1955; Ohno, 1967; Lewis and John, 1968; Lucchesi,

1978), although not unanimously or in all respects (Brosseau, 1960; Voelker, 1970). This section evaluates three lines of evidence bearing on the origin of sex chromosomes and their evolution from homomorphism to heteromorphism.

The Origin of New Heterogametic Systems

Based on the ideas and evidence presented in Chapters 2-7, it appears that one system of heterogamety may evolve from another through a multiple-factor intermediate. The new heterogametic system (2-factor) need not, and does not always occur on the same chromosome as the ancestral system, but instead it often resides on a former autosome. Since it seems that sex factors are often no more complicated than single genes, cytological heteromorphism will not usually accompany the origin of the new 2-factor system. Sex chromosome heteromorphism seems to have been lost in houseflies through this process (Sects. 3.A, 3.D, 6.D, 17.A). If this theory for the origin of heterogametic sex determination is valid, then these newly arisen systems will usually be characterized by sex chromosome homomorphism, and the changes must therefore be toward heteromorphism.

Autosomal Translocations to the Sex Chromosomes

The various degrees of sex chromosome heteromorphism may be arranged as if they represent different stages in a progressive evolution toward heteromorphism, but these examples do not provide direct evidence of such a transition. Sex chromosome change is too slow for direct observation, so indirect evidence must be obtained indicating that a formerly functional chromosome experienced a progressive loss of function after becoming coupled to a Y chromosome. This indirect evidence may be obtained by studying the translocation of an autosome to the sex chromosomes in multiple sex chromosomes (e.g., White, 1954, 1973; Swanson, 1957; Lewis and John, 1968). Several cases are known in which a Y-linked chromosome of autosomal ancestry degenerated (White, 1973, pp. 610, 646). The clearest examples have been described from *Drosophila* (Patterson and Stone, 1952; reviewed in White, 1973, pp. 349-50). The ancestral karyotype for *Drosophila* apparently contained a heteromorphic X and Y and five autosomal pairs. In most species from the *Drosophila obscura* group, one of the ancestral autosomes was translocated to the X, while the Y-linked counterpart was either lost or became part of a highly degenerate Y, since it no longer exists in its ancestral state. Further indication that the Y-translocated autosome degenerated was provided by Lucchesi's (1978) observation that the autosomal part of *D. obscura*'s X underwent complete dosage compensation in males.

A second illustration that a Y-linked autosome has degenerated was obtained from *Drosophila miranda*. In this species, an autosome was translocated to the Y, and its homologue now assortes in an X-linked manner as

part of a multiple sex chromosome system (X_2). Although the autosomal part of the Y showed some characteristics of functional euchromatin, Steinemann (1982) observed that this part of the Y was interspersed with repetitive sequences, while the X_2 lacked these elements (Sec. 16.B). In addition, Lucchesi (1978) stated that the X_2 showed partial dosage compensation. Both observations again indicate that a former autosome acquired characteristics similar to those of differentiated Y chromosomes.

Phylogenetic Evidence

Within some groups, taxonomic evidence may suggest that evolution occurred from homomorphism to heteromorphism. The most renowned example is observed in snakes (Becak et al., 1964; Ohno, 1967). The four snake families discussed here are often assigned phylogenetic rank according to the extent they differ in skeletal characteristics from the oldest fossilized snakes. Snakes from the family Viperidae (vipers, rattlesnakes) and the family elapidae (cobras, mambas) are highly derived. The Colubridae (mostly non-venomous, garden-variety snakes) are morphologically intermediate, and the Boidae (pythons, boas) retain the characteristics of primitive snakes. The sex chromosomes follow a similar pattern. Female heterogamety obtains when sex chromosomes are apparent. Viperids and elapids have highly differentiated Z and W chromosomes, while colubrids have moderate to extreme heteromorphism. Heteromorphic sex chromosomes are known from only one boid, although several species have been studied (Baker et al., 1972; Singh, 1972; Gorman, 1973; Singh et al., 1976, 1980; Mengden and Stock, 1980). A nearly similar karyotype is found in all these families, as if inherited from a common ancestor, and the sex chromosomes invariably correspond to the fourth pair of this karyotype. It therefore appears that all heteromorphic sex chromosomes are retentions of the same ancestral mechanism of female heterogamety in early snakes (Ohno, 1967; Gorman, 1973).

Ohno (1967) argued that the various degrees of sex chromosome differentiation in snakes represented steps in the actual transition from homomorphism to heteromorphism. The evidence from boids suggested that sex chromosome heteromorphism was *perhaps* lacking in the earliest snakes. In further support of this conclusion, the existence of heteromorphism in the fourth pair of one boid has since suggested that the same basic mechanism of female heterogamety (or a capacity for it) is present in all snakes and was likely present in their common ancestor. Heteromorphism in the fourth pair of colubrids, viperids, and elapids therefore suggests that this ancestral pair underwent a transition to heteromorphism.

The three lines of evidence presented here support the hypothesis that sex chromosomes often evolve from an initial state of identity toward extreme heteromorphism. Although this process may be the most common route of sex chromosome evolution, there are examples of sex chromosomes that may have

evolved in other ways, such as degenerate X chromosomes (Sec. 16.F). Swanson (1957) suggested that X-degeneration would succeed loss of the Y, so that degenerate X's would also have evolved from an initial state of X-Y similarity. But extreme X-degeneration is too rare a phenomenon to have occurred in most sex chromosome systems. Rather, degenerate X's and their associated degenerate Y chromosomes may be descended from chromosomes other than typical autosomes, such as supernumerary or other chromosomes not vital to the individual. This hypothesis is certainly plausible for the X and Y of houseflies (Secs. 3.D, 16.F). Similarly, the frequent occurrence of X-heterochromatin is better explained as the addition of heterochromatin rather than degeneration of the X (Muller and Painter, 1932; Pathak and Stock, 1974; Sharma et al., 1981).

C. Conserved Systems

Not uncommonly, most species in a large group of animals possess the same sex chromosome pair, as if this sex chromosome system existed in their common ancestor and was retained. (In several cases a multiple sex chromosome system may have evolved, incorporating the original pair.) As described earlier and as noted by Ohno (1967), sex chromosome systems have been conserved in snakes and in mammals. Sex chromosomes are also apparently conserved in birds (Ohno, 1967; Baverstock et al., 1982). Furthermore, the widespread occurrence of XX/XO systems in large groups of insects, arachnids, and nematodes suggests a common ancestry, at least within these individual groups (Table 2.C.2). All these examples involve extreme heteromorphism. However, it is not always true that if heteromorphic sex chromosomes are observed, most species in the group are characterized by the same system. Sex chromosomes are common in lizards (King, 1977) and there are a few extreme heteromorphisms in amphibians (Schmid, 1980; Sessions, 1980), and fish (references from Table 2.C.4), but each sex chromosome system is apparently common to only a few species. Thus, systems of highly differentiated sex chromosomes are sometimes, but not always, common to many members of a group, as if preserved from a common ancestor.

Conversely, however, there are no known systems of male or female heterogamety conserved in the absence of extreme heteromorphism. Unfortunately, it is difficult to demonstrate whether this pattern is widespread, because diagnosing the heterogametic sex requires great effort if sex chromosome heteromorphism is absent. Only the data from chironomids and simulids indicate that highly heteromorphic sex chromosomes are uncommon in groups with varied sex determining mechanisms. (Arrhenotoky is preserved in some major groups without heteromorphic sex chromosomes, but as the next chapter will indicate, sex chromosome heteromorphism is not expected to evolve under arrhenotoky.)

There are two reasons for anticipating sex determining mechanisms to be conserved in groups with extreme sex chromosome heteromorphism. (i) De-

generate Y chromosomes preclude the evolution of certain multiple-factor systems and thus interfere with the evolution of new mechanisms. Complications with XX maleness have a similar effect (recall Sec. 6.D). Therefore, the sex determining mechanism is more capable of changing before, rather than after, sex chromosome heteromorphism evolves. (ii) If for whatever reason the sex determining mechanism fails to change, perhaps from a paucity of new sex factors, heteromorphism is likely to evolve. While the first argument proposes that heteromorphism precludes change, the second argument proposes that the absence of change invites heteromorphism. Both hypotheses may be true—sex chromosome heteromorphism could evolve when no genetic variation is available to change the sex determining mechanism, but once heteromorphism evolves, further change is precluded.

In mammals, the demonstrated sterility of XX males and inviability of YY embryos prevents change to a new heterogametic system (cf. Secs. 4.C, 6.D). Therefore the first argument helps to explain the continued conservation of sex linked genes in mammals. YY inviability is undoubtedly a constraint in many other systems, but XX males may or may not be impaired, as described in Section 6.D. Heteromorphic sex chromosomes do not always interfere with changes in the sex determining mechanism, as exemplified by houseflies (although the degenerate X in houseflies is highly unusual for sex chromosomes). Unfortunately there are as yet few examples indicating the extent to which heteromorphic sex chromosomes inhibit the evolution of new sex determining mechanisms, but the simple taxonomic patterns and examples presented here suggest that heteromorphic sex chromosomes are conserved in some groups.

D. Summary

In contrast to the extreme sex chromosome heteromorphisms common in plants and animals, the X and Y chromosomes of some species differ from each other only slightly and recombine along much of their lengths. Examples were described from reptiles, amphibians, fish, and flies. There appears to be a common process of sex chromosome evolution in which the X and Y originate from autosomes but undergo a gradual accumulation of differences until they become extremely heteromorphic. The slightly differentiated sex chromosomes discussed here therefore represent early stages in this process.

Once extreme sex chromosome differences evolve, the evolution of new sex determining mechanisms may be prevented, because YY individuals no longer survive and XX males may be less successful than XY males. This process will stabilize sex chromosome systems, such that species descended from a single ancestor will share the same sex chromosome system. Conserved sex chromosome systems are in fact observed in mammals, birds, snakes, and possibly many invertebrate groups, but for comparison, it is difficult to know whether sex determining mechanisms are conserved in groups without heteromorphic sex chromosomes.

18

Evolution of Sex Chromosome Differences: Models and Theory

The evidence cited in Section 17.B suggested that sex chromosome heteromorphism may evolve from homomorphic chromosomes with an autosomal ancestry, an idea first developed by Muller and Sturtevant (Muller, 1914, 1918). This chapter will present models that provide a quantitative justification for this theory of sex chromosome evolution, chiefly with respect to the genetics of sex chromosomes. Two basic processes are thought to occur in the evolution of X-Y differences: the suppression of crossing-over between the X and Y, followed by the loss of gene function at many Y-loci (Y degeneration). Mathematical models of these processes will be discussed in the first two sections (A, B), although so little is known about the early stages of X-Y differentiation that these models have little empirical support. Section C will consider sex chromosome systems in plants that may provide unique tests of these theories.

Under the theories presented here, sex chromosome differentiation is a process limited to certain types of sex determining mechanisms: 2-factor systems without environmental influences (male and female heterogamety, maternal monogeny), and the few multiple-factor systems in which YY does not arise. Sex chromosome heteromorphism is not observed under environmental sex determination, arrhenotoky, polyfactorial sex determination, and hermaphroditism, as may be anticipated from the arguments in this chapter.

A. Crossover Suppression

Before any absolute differences can exist between the X and Y, crossing-over must be virtually eliminated between the sex factor region and the site of the difference. Occasional crossovers distribute material to both the X and Y, and only opposing selection of sex-linked traits in males and females could maintain differences between the X and Y chromosomes in these crossover regions. The suppression of X-Y crossing-over must therefore precede or at least coincide with the evolution of extreme X-Y heteromorphism.

Sex Differences in Fitness

One can do little more than speculate why X-Y crossover suppression evolves. Perhaps the most plausible hypothesis derives from the fact that recombination is disadvantageous for sex-linked alleles with opposite effects in the two sexes; if these alleles begin to accumulate when the X and Y are subject to recombination, tighter sex linkage may be favored to reduce their transmission to the sex placed at a disadvantage by their presence (cf. Fisher, 1931). A central element in this argument is that genes with different effects in males and females do exist, and that their evolution is influenced by sex linkage, an idea implied or stated in several papers on sex chromosome evolution (Fisher, 1931; Muller, 1932; Haldane, 1933; Darlington, 1939, 1958; Lewis, 1941; Brosseau, 1960; Ohno, 1967; Lewis and John, 1968). To illustrate that sex linkage influences the evolution of such genes, consider a mutation with a slightly beneficial dominant effect in males, but a highly deleterious dominant effect in females. Such a mutation could not increase if it was inherited autosomally (irrespective of sex) because the large disadvantage in females would outweigh the small advantage in males. However, if the mutation was closely linked to the sex determining region on the Y, it could increase in frequency by virtue of the superior benefit conferred nearly exclusively on males (e.g., Fisher, 1931). This advantage of sex linkage applies even though the gene is not a sex factor. Beyond these specific cases, it can be shown that sex linkage always enhances the evolution of genes with different effects in males and females (App. 18.I).

The evolution of X-Y linkage will be considered more formally below, but two points regarding this argument may be noted here. First, the argument is valid only if these genes are not sex limited in expression. Sex linkage offers no advantage to genes expressed only in the sex they benefit, except perhaps while they are spreading to fixation. Although sex-limited expression may apply to some genes, it is not likely to be a property of all genes. Second, it must be considered whether or not sex differences in fitness are common enough to be important in selecting X-Y crossover suppression. At present, few examples of such effects are evident.

Solid evidence suggests that pigment genes in poeciliid fishes are beneficial in males but not in females (Kallman, 1970; Endler, 1978, 1980). Fisher (1931)

in fact offered an explanation for selection of X-Y crossover suppression based on this example. Bright colors are disadvantageous to females because of increased predation. Brightly colored males also experience increased predation, but this disadvantage is offset by female preference for bright males. There are varying degrees of sex limited expression for color genes in poeciliid fish. Both male and female platyfish (*Xiphophorus maculatus*) express many of the color genes, while female guppies (*Poecilia*) express only a few of the known color genes. Nevertheless, the vast majority of color genes in guppies are sex linked. Haskins et al. (1970) further noted that color genes in guppies were almost completely Y-linked in areas of high predation, but were often also on the X in areas of low predation. This sex-linked association of color genes in guppies is puzzling since most of these genes were sex-limited in expression, although the sex limitation may have evolved secondarily.

A second possible form of sex difference in fitness is reflected in the popular idea that sex chromosomes evolve by accumulating many sex factors in tight linkages (Haldane, 1922; Ohno, 1967; Mittwoch, 1973). Although some major sex factors assort as single loci or short chromosome regions and are not comprised of many tightly linked loci (Chapters 3 and 4), other sex factors are indeed comprised by many loci. The X's of *Drosophila* and *Caenorhabditis* do not have a major sex factor locus; rather they consist of many genes with weak female tendencies (Sects. 4.A, B). Angiosperm plants provide a better example of compound sex factors (Sec. 7.C). Based on empirical observations and models, it seems that dioecy often evolved in two steps, with the first step a mutation suppressing pollen production, and the second step a mutation suppressing seed production. Individuals with genes for both ovule and pollen suppression are sterile, representing a strong interaction between sex and fitness at the two loci. Dioecy evolves only if the two mutations are so tightly linked that male-sterility is rarely inherited with female-sterility, so X-Y crossover suppression coincides with the evolution of dioecy (Westergaard, 1958; Charlesworth and Charlesworth, 1978).

Beyond these examples, one may speculate about the possible nature of sex-specific fitness effects, but there are few examples so obvious as those presented above. A further example of sex differences in fitness was provided by observations of autosomal or partially sex-linked inversions maintained at different frequencies in the two sexes (Levitin, 1951; Post, 1982). The maintenance of these inversions at different frequencies in males and females indicated they experienced opposing selection in males and females (assuming that the observations were from populations at equilibrium). In addition, several autosomal mutations impair fertility or viability in one sex but not the other (e.g., Berg 1937a, b, 1938; Lindsley and Grell, 1968; Lindsley et al., 1960; Uyenoyama et al., 1982). These mutations indicate sex differences in fitness, although they are not necessarily beneficial to one sex; the evolution of tighter X-Y linkage in the model on page 251 requires alleles that are selected in opposite directions in males and females.

Evolution of Tight X-Y Linkage

Although sex linkage enhances the evolution of genes or gene combinations with different effects in males and females, this fact cannot stand alone as an argument for the evolution of crossover suppression. Models for the evolution of linkage generally incorporate at least three loci, with one locus modifying recombination between the other two. A model of X-Y crossover suppression therefore incorporates the sex factor locus (region), with a second locus whose alleles have possibly different effects in males and females. The third locus segregates for different degrees of recombination between the other two loci in the heterogametic sex (Fig. 18.A). Such models were proposed by Nei (1969) and Charlesworth and Charlesworth (1980). In the Charlesworths' model, sex was determined according to male or female heterogamety. Two alleles at a second, unlinked locus (A_1, A_2) were present at a polymorphic equilibrium, perhaps at different frequencies in males and females, and a third locus decreased recombination between the sex locus and the A -locus. The modifier was completely linked to one of the sex factors. With the A -locus at equilibrium, the Charlesworths observed that tighter X-Y linkage evolved when the equilibrium frequency at the A -locus differed for males and females.

Nei's model (1969) was somewhat different, and while his results revealed a different aspect of linkage evolution, they complemented the Charlesworths' results. Again the model assumed the presence of a sex locus and a second locus with alleles A_1 and A_2 . Nei assumed a strong fitness interaction between

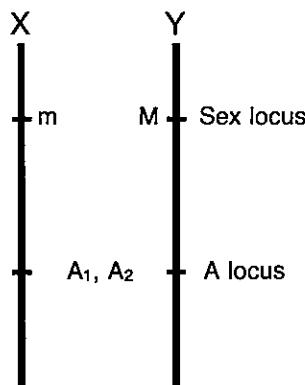


FIGURE 18.A. Model for the evolution of X-Y crossover suppression. M and m are the sex factors on the undifferentiated Y and X chromosomes respectively. A second locus on these chromosomes has two alleles with possibly different effects in males and females (A_1, A_2). The conditions are sought under which selection favors a modifier at a third locus (not shown) which reduces crossing-over between the sex locus and the A -locus in the heterogametic (XY) sex.

the sex factors and the *A*-locus, with some combinations sterile. This assumption was more severe than the assumptions made in the Charlesworths' model. However, Nei's model did not require the recombination modifier to be tightly linked with the sex factors, and it allowed arbitrary recombination between the sex locus and *A*-locus in the absence of the modifier. Nei observed, as did the Charlesworths, that selection favored reduced X-Y recombination. He also observed that selection was largely indifferent to the linkage between the sex factors and the recombination modifier. The results from both models were therefore consistent, and they strengthened the intuitive argument that cross-over suppression is favored between the sex locus and loci whose alleles experience different effects in males and females.

The evolution of X-Y crossover suppression requires a stable polymorphism at the *A*-locus, with the two alleles maintained at different frequencies in males and females. Whether the two alleles, A_1 and A_2 , satisfy this criterion depends on their fitnesses *and on their linkage to the sex factor region*. Tighter linkage between the *A*-locus and the sex factors enhances the maintenance of existing polymorphisms at the *A*-locus and *increases* the set of fitness values under which polymorphism at the *A*-locus may be maintained (Appendix 18.I). (The Charlesworths denoted this evolutionary phenomenon as a "linkage constraint," in which alleles with given properties cannot evolve unless sufficiently linked to a particular second locus.) This result is especially satisfying because it indicates that the loci closest to the sex factors are also the loci most likely to generate a favorable condition for the evolution of tighter X-Y linkage. It is presumably much easier to select tighter linkage between two loci on the same chromosome than it is if they are on different chromosomes. Although these models demonstrated how X-Y crossover suppression may have evolved, the importance of these processes also depends on an abundance of alleles with different effects in males and females, for which there is yet only meager evidence.

Mechanisms of Crossover Suppression

As noted by Darlington (1937, p. 390), X-Y crossing-over may be suppressed through genetic mechanisms or chromosomal rearrangements (structural changes). However, even now there is little evidence demonstrating the importance of each mechanism in the evolution of X-Y crossover suppression. Rearrangement differences are commonly observed between the X and Y, but they may have evolved as a consequence rather than a cause of crossover suppression.

It is difficult to evaluate which source of crossover suppression, genetic or structural, presents the most plausible case for its role in the evolution of tight X-Y linkage. The existence of genetic variation in recombination rates has been reported in several studies (reviewed in Bell, 1982, p. 410), so X-Y linkage could in principle be modified from genetic effects. However, much of the observed variation for reduced recombination influences several chromo-

somes, rather than a single pair, and the evolution of X-Y recombination from these particular genes would depend on the fitness effects accompanying the modification of recombination among other chromosomes.

Chromosome rearrangements offer a second possible mechanism to suppress crossing-over, but again the effects are not entirely beneficial. Chromosome rearrangements, such as inversions and translocations, may have two effects. First, a rearrangement may interfere with the synapsis of homologous chromosome regions and thereby inhibit crossing-over in these segments (Martin, 1967; White, 1973; an interesting, high-resolution study of the effect of an inversion is Moses et al., 1982). Consequently, sex chromosome rearrangements may be selected for suppression of X-Y recombination, and the effect on recombination would be local, limited to the segments involved in the rearrangement. Charlesworth and Charlesworth (1980) considered the possible advantage of certain types of sex chromosome-autosome translocations from this effect (advantages for the evolution of multiple sex chromosome systems). Ohno (1967) argued that sex-linked inversions may be advantageous through selection of crossover suppression (but see below for a qualification of his hypothesis). Of course, the evolution of a sex chromosome rearrangement does not imply that it was selected to reduce X-Y recombination—it may have evolved from other effects or by chance.

A second possible consequence of rearrangements is a deleterious one, because they often complicate meiosis and lead to aneuploid gametes (White, 1973, pp. 215–30). Consider inversions: inversions do not necessarily inhibit crossing-over, and the recombinant gametes resulting from a single crossover within the inversion contain duplications and deletions. Progeny inheriting unbalanced chromosomes do not usually survive. Therefore, an inversion that does not suppress crossing-over is likely to be eliminated, because its carriers leave fewer offspring than individuals not heterozygous for the inversion (contrary to a misleading statement of Ohno, 1967, p. 19). However, in *Drosophila* and some other Diptera a special mechanism in oogenesis reduces or eliminates crossover products resulting from paracentric inversions (inversions that do not overlap the centromere); crossing-over is rare or absent in the male, so inversions are without deleterious effects in either sex (White, 1973). Consequently, in this special case, paracentric inversions act as crossover suppressors without deleterious effects even though they do not necessarily inhibit the formation of crossovers.

Rearrangements other than inversions may also occur in sex chromosomes, such as translocations, and these other rearrangements may cause meiotic irregularities (White, 1973). However, whereas all the meiotic complications of an inversion result from crossing-over, such that an inversion free from crossing-over has no deleterious effect in meiosis (and might therefore drift to fixation), translocations may produce unbalanced gametes even when crossing-over is absent. This difference suggests one reason why inversions are expected to evolve on the Y more frequently than translocations, even if rearrangements have no role in suppressing crossing-over.

It is commonly observed that, prior to the evolution of extreme X-Y differences, the X and Y differ in shape as the result of rearrangement (Ohno, 1967; Sec. 17.A). The establishment of a structural difference between the X and Y indicates that X-Y crossing-over has been effectively suppressed, but it is not often known if rearrangements caused crossover suppression, or if they merely evolved after crossing-over was suppressed. This dilemma stems from an observational bias: it is difficult to identify the X and Y in the absence of some structural difference. Therefore the status of X-Y crossing-over prior to the evolution of a rearrangement difference is generally not known. Schmid et al.'s (1979) observations from the newt *Triturus helveticus* suggested that crossover suppression evolved in the absence of major rearrangements, since the X and Y were morphologically alike (Sec. 17.A). Similar observations on other species will be difficult to accumulate. It is equally difficult to find cases in which the reverse can be concluded—that an inversion (or other rearrangement) abolished crossing-over (excluding the special mechanism of some Diptera, in which paracentric inversions do indeed suppress crossing-over).

Recall that in some groups crossing-over is entirely absent in the heterogametic sex (Sec. 16.C). One hypothesis to explain the evolution of this phenomenon would be that crossing-over was abolished in heterogametic sex merely to suppress X-Y recombination, with the suppression of crossing-over in other chromosomes operating as a pleiotropic effect of X-Y crossover suppression. The evolution of crossover suppression in all chromosomes of the heterogametic sex would then presumably depend on the genetic variation available for X-Y crossover suppression; genes with such extreme effects on crossing-over are known (Dunn and Bennett, 1967; Bell, 1982, p. 410). However, Bell (1982) noted that since some species with achiasmate meiosis in the heterogametic sex have XX/XO systems, the lack of crossing-over can no longer be operating to maintain a large sex linkage. An alternative explanation for the concordance between the heterogametic sex and the crossover-free sex is that the absence of crossing-over in one sex may initially have existed independent of the heterogametic sex, but the sex determining mechanism in different species gradually evolved so that the heterogametic sex coincided with the sex lacking crossing-over. A correlation between heterogamety and the crossover-free sex could have resulted because Y-degeneration should occur faster for mechanisms in which the heterogametic sex lacks crossing-over than for those with crossing-over in the heterogametic sex. Recalling from Section 6.D that sex chromosome degeneration inhibits change in the sex determining mechanism, systems that hasten Y degeneration should also experience the smallest number of changes in the heterogametic sex. The process could thereby accumulate systems in which the sex without crossing-over eventually becomes the heterogametic sex.

B. Degeneration of the Y

Once X-Y recombination has been suppressed, differences may begin to evolve between the X and Y. Beginning with Muller and Sturtevant (Muller, 1914,

1918), this problem has been treated as the "accumulation of lethals"—the loss of gene function on the Y but not on the X. Muller and Sturtevant noted that in the absence of crossing-over, the Y was permanently heterozygous and was sheltered by the X, but the X was homozygous in one sex:



Consequently, non-functional alleles resulting from the loss of gene function could not be fixed on the X because they would be expressed as lethals in XX individuals, but non-functional alleles could be fixed on the Y, since the X would have a functional locus to mask the loss on the Y (assuming that the effects of gene loss were largely recessive). It was proposed that recessive lethals would accumulate on the Y owing to the lack of opposing selection (Muller, 1914).

Fisher (1935) criticized the Muller-Sturtevant theory on the following grounds. If lethal mutations arose on the Y, they would also arise on the X. A Y-linked deleterious mutation would be eliminated when it encountered an X-linked deleterious mutation at this locus. Hence, functional Y genes were always advantageous over non-functional genes. Fisher showed that the equilibrium level of recessive lethals was very low and was identical for the X and Y, if X- and Y- mutation rates to non-functional alleles were equal.

Frota-Pessoa and Aratangy (1968) realized that under inbreeding the level of X-linked non-functional alleles would be kept lower than under outcrossing, and that the Y locus would thereby acquire deleterious mutations at a higher frequency than the X. (Since the Y was never homozygous, it was not subject to the effects of inbreeding.) However, this theory does not seem to account for the degeneration of the Y because the Y does not accumulate deleterious mutations at high frequency in this model, even though it accumulates more deleterious mutations than the X.

Nei (1970) noted that a Y-linked non-functional gene might by chance become fixed in a finite population despite a selective disadvantage. He showed that for truly recessive lethals and plausible mutation rates, the Y was likely to accumulate recessive lethals in effective population sizes of 4,000 or less, but not in populations of 10,000 or more. If the lethal had a slight deleterious effect when heterozygous (e.g., .02 of its homozygous effect), the probability of fixation dropped dramatically. B. Charlesworth (1978) raised two objections to Nei's hypothesis. First, the population size relevant to degeneration of the Y was the species size, not deme size, since these lethals were fixed throughout the species. A total number of 4,000 individuals or less did not seem to apply to many species. Second, many recessive lethals (non-functional genes) apparently had small but significant deleterious effects when heterozygous. The deleterious heterozygous effects had been measured directly (Mukai et al., 1972; Simmons and Crow, 1977), and the existence of dosage compensation also suggested that genes present in one dose were mildly deleterious.

Thus, the accumulation of non-functional genes through chance fixation seemed implausible under this model.

The most recent development in this theory has been proposed by Charlesworth (1978). His theory assumes that many genes are completely linked on the Y and that mutations occur at different loci. At the outset in a large population, there may be some Y chromosomes without any deleterious mutations, others with only one, two, and so forth. Even among those chromosomes with the same number of mutations, there may be differences in which loci are mutant.

If the effect of each deleterious mutation is small, then only a slight selective difference exists between chromosomes with no mutations and those with one, and there is an equally slight fitness difference between Y chromosomes with two mutations and those with only one, and so forth. In a finite population with a sufficient rate of mutation to deleterious alleles, there is an appreciable chance that the class of Y chromosomes with the lowest number of mutations will be lost (beginning with the zero class). Loss of the lowest class can occur with a moderately large probability if the mutation rate is sufficiently high relative to population size. Once this lowest class is lost, it is not likely to reappear, since it cannot regenerate by recombination (the Y does not recombine), and the probability of reverse mutation restoring it is infinitesimal (Fig. 18.B).

This process was originally recognized by Muller (1964) in the more general context as an evolutionary advantage for recombination and was named Muller's "ratchet" by Felsenstein (1974). The ratchet works because each loss of the class with fewest mutations is irreversible. A perpetually increasing accumulation of deleterious genes therefore occurs in the population. Only a few quantitative studies have investigated this process, and it seems to be the most plausible explanation for the degeneration of the Y, but additional models and experimental investigation of the ratchet process are needed for a rigorous evaluation of Charlesworth's theory.

Charlesworth (1978) suggested that the ratchet process would not usually lead to fixation of lethals at particular loci on the Y because different Y chromosomes would have different compositions of lethals—even for Y chromosomes with the same total number of deleterious genes. However, J.F. Crow (pers. comm.) provided an interesting insight to this part of the theory. Selection and random drift may occur within the population, periodically leading to the fixation of certain ancestral Y chromosomes (or modified descendants). For example, if the fewest number of mutations per Y was 10, selection would favor these Y chromosomes over those with more than 10 mutations. There would also be random changes in the relative frequencies of different Y chromosomes with the same fitness. Eventually all Y chromosomes in the population would be descended from one of the Y chromosomes with 10 or more deleterious mutations. All Y chromosomes would then be fixed for the 10 mutations present in this ancestor, some descendants having acquired other mutations as well.

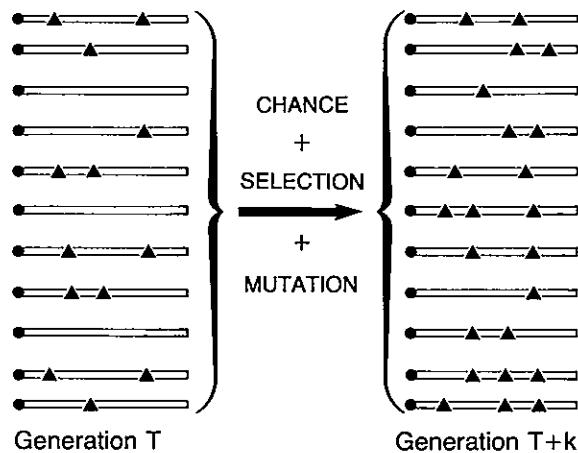


FIGURE 18.B. Muller's ratchet and the degeneration of the Y chromosome. In a population of Y chromosomes free of recombination, some Y's will have one or more mutations to non-functional genes, with different Y's mutated at different loci (indicated by a triangle). If the selective effect per locus is small, and population size is small enough relative to mutation rates, the class of Y chromosomes with zero mutations may be lost by chance. In the absence of recombination, the zero class is not regenerated. Repetition of this process continues to eliminate the class with the lowest number of mutations in the population, gradually leading to a population of Y chromosomes with many non-functional genes.

Charlesworth also suggested the Y may reach such a degenerate state that two effects would be selected: X dosage compensation for non-functional Y-linked genes, and suppression of gene activity on the Y (preventing the expression of loci that produce harmful products). Thus, deterioration of the Y may select dosage compensation, and dosage compensation may accelerate further deterioration of the Y by removing its loci from the effects of selection. Of course, the Y in many cases is not truly inert, although in comparison to the X, it has lost or greatly modified most of its original loci.

Y-Linked Segregation Distortion. A distinct alternative to these theories for the degeneration of the Y was offered by Hamilton (1967). He noted that the Y was especially responsive to selection for segregation distortion, leading to an overabundance of the heterogametic sex. Hamilton proposed that selection consequently would favor inactivation of the Y in order to suppress segregation distortion (from the advantage gained by overproducing the rare sex), and that this process might have occurred often enough in the history of species to account for the general degeneration of the Y. As discussed briefly by Charlesworth (1978), this hypothesis is difficult to entertain as a general account of Y degeneration, since known examples of segregation distortion are the result of highly specialized genes, and these would not necessarily occur on

the Y. Less drastic types of suppression would also be expected to evolve (e.g., Lyttle, 1982).

It is a challenge to evolutionary biologists that a common observation such as degenerate Y chromosomes is still so far from being understood. Except for the original observation that the Y degenerates and the realization that most recessive deleterious genes have slight effects when heterozygous, theories on the evolution of Y degeneration have been formulated largely in the absence of empirical support. Furthermore, the theories have been rejected on mathematical rather than empirical grounds. If Charlesworth is correct and the ratchet process does account for Y degeneration, then the process will be difficult to verify, since the ratchet process is difficult to study empirically as well as mathematically.

This section emphasized the accumulation of deleterious functions on the Y. The results in Section 18.A indicated that beneficial functions are also selected on sex chromosomes, and following the suppression of X-Y crossing-over, the X and Y may accumulate sex-specific functions that would not have evolved under free X-Y recombination. Additionally, *sex-limited* functions may be lost from the crossover-free regions of the X or Y, whereas they would have been maintained on both chromosomes under free recombination (cf. Neuhaus, 1939; Walker, 1971). Since the Y occurs only in males, but the W occurs only in females, these arguments also suggest that Y chromosomes may accumulate some systematic differences from W chromosomes (and vice versa), although no evidence indicates the existence of consistent Y-W differences.

Heterochromatin and Y-DNA

There is no common consensus explaining why the Y becomes heterochromatic, but heterochromatic Y chromosomes are so common that a solution to this problem should be of general importance. Two questions are of interest here. First, what is the nature of the heterochromatin on the Y? Second, why does the heterochromatin concentrate on the Y? With respect to the first question, the evidence cited above on Y-DNA indicates that the Y is not simply an array of inactivated genes homologous to those on the X, although this conclusion was also reached from a classical genetic study of sex chromosomes in *Drosophila* (Muller and Painter, 1932). Thus, the heterochromatization of the Y is not merely a shutdown of formerly active genes. Instead, major changes have occurred in the composition of Y-DNA, and those changes were perhaps associated with its heterochromatization. Some Y-DNA segments are homologous with autosomal segments, a fact that seems to rule out the accumulation of heterochromatin through a process confined to the Y, such as unequal sister chromatid exchange.

The function of Y-heterochromatin is mysterious. From the many functions proposed for autosomal heterochromatin (John and Miklos, 1979), one

might consider similar possibilities for Y heterochromatin: it may have a beneficial role in suppressing X-Y crossing-over or in suppressing gene activity at loci whose products have become deleterious. Yet the dense concentration of heterochromatin on the Y in systems with extreme X-Y differences renders these hypotheses implausible as general explanations, simply because the Y-DNA is apparently too altered to suppose that the differential segments cross over or that much of the Y still has functions similar to those on the X. Instead, a "selfish" or "parasitic" role of much of the Y-DNA might be considered (cf. Doolittle and Sapienza, 1980; Orgel and Crick, 1980). The Y may accumulate DNA whose function is merely to propagate itself. The disadvantage to the Y chromosome in acquiring selfish DNA (and hence the disadvantage to selfish DNA on the Y) appears to be slight because the loss of gene function on the Y would be sheltered by the X. The accumulation of heterochromatin and selfish DNA on the Y may also be facilitated by the purely mechanical consequences of being free from recombination. Resolving the problem of Y-heterochromatin will have important consequences for the interpretation of heterochromatin in general, and it may further lead to a better understanding of why the Y degenerates.

C. Haploid Expression and Haploid Sexes: Plants

The arguments in the preceding section assumed a small effect per individual deleterious mutation on the Y. The fact that these mutations may be recessive lethals is largely unimportant because they are sheltered by the X. However, the effect of an exposed mutation becomes a major consideration for genes expressed in haploid organisms, as in the gametic phase of higher plants (see below for lower plants). The inheritance of sex chromosomes in dioecious higher plants is identical to that in animals—males are XY, females XX (assuming male heterogamety)—so nearly the same theory can be applied to the degeneration of the Y in plants as in animals. The interesting difference between plants and animals with respect to sex chromosome evolution is that plants may experience considerable gene expression in the haploid (gametophyte) stage. The gametic phase in higher plants, while brief, is somewhat more elaborate than the gametic phase in animals. The gametophyte arises from a spore (pollen or gynospore), and then produces gametes that join in fertilization to form the sporophyte. For example, a pollen grain is a spore that produces male gametes (sperm) but also produces nuclei that do not form sperm. Therefore, there may be extensive haploid gene expression, at least in pollen. In contrast, essential haploid gene expression is apparently minor in animals (Muller and Settles, 1927; McCloskey, 1966; Hecht and Williams, 1978).

Anticipation of haploid gene expression in plants led Haldane (1933) to propose that extreme Y chromosome degeneration might be inhibited in higher

plants. [It is interesting to note that Haldane also proposed that haploid expression was greater in pollen than ova, so that a W chromosome (female heterogamety) might degenerate more than a Y (male heterogamety). Unfortunately, the scarcity of known female heterogamety in plants does not permit an evaluation of this hypothesis.] It is indeed the case that under all the above models of Y degeneration, Y-linked loci important in the haploid phase are not expected to degenerate (unless the deleterious mutation has only a small effect). However, in order to predict the extent of Y-degeneration in plants, an estimate is needed for the fraction of loci that function in the gametophyte. One such study was provided by Tanksley et al. (1981), who investigated the expression of enzymes in both the pollen and sporophytes of tomatoes. Of the 30 loci expressed in the sporophyte, 18 were also detected in pollen. However, this observation alone did not indicate whether the appearance of the enzyme in pollen was the result of expression in the haploid state, or whether it resulted from previous expression in the diploid state. Seven of these 18 loci were studied specifically to detect expression in the haploid gametophyte, and all seven showed haploid expression. Only one of the 31 loci studied had no detectable sporophytic expression, although there may have been a bias against the observation of such enzymes. Thus, if these loci are generally representative of other loci in the genome, it suggests that perhaps half the loci may be expressed during the haploid phase. According to Haldane, therefore, degeneration should have been precluded at many of the Y-linked loci in plants, although many others may degenerate.

In a strict sense, these theories of Y degeneration do not preclude the deterioration of genes functioning in the haploid. Instead, they put a limit on the magnitude of deleterious effects that may evolve in a short period of time. If a gene essential to the haploid state can deteriorate in a series of small steps, then these loci may gradually degenerate as well, even if the population gradually becomes extinct. The progressive deterioration of such loci would select the transfer of these functions to autosomes. However, it is unknown if genes can deteriorate in small steps, and even if they can, the degeneration of genes essential to the haploid might occur slowly enough to warrant the assumption that they remain functional.

At a superficial level, the data on sex chromosome heteromorphism in angiosperms (flowering plants) are not different from those in animals. Westergaard (1958) and Smith (1963) reported that YY was inviable in the sporophyte of some dioecious species. The Y was also highly heterochromatic in *Rumex* (Zuk, 1970a, b; Smith, 1963) and less so in *Humulus* (Jacobsen, 1957). Smith (1963) also reported an apparent deficiency in the X (which arose somatically) that was not masked by the Y.

Yet, upon closer examination, there are some aspects in which the Y in plants may be regarded as less degenerate than the Y in animals. Several indirect lines of evidence suggest that many loci on the Y are important to at least the gametophyte. First, the Y chromosome is usually larger than the X, or the combined length of the Y's exceeds that of the X's in multiple sex

chromosome systems (Love, 1944; Westergaard, 1958). While the Y's large size may indeed reflect the importance of many of its loci, it is also possible that the origins of dioecy in these species are so recent that the Y has not been present long enough to degenerate substantially.

The hypothesis that many X- and Y-linked loci are essential to the gametophyte is strengthened by several studies of sex chromosome aneuploids in plants that have either failed to detect individuals without at least one copy of each sex chromosome, or demonstrated that these individuals occur at extremely low frequency (i.e., few or no XO and OY individuals: Westergaard, 1946, 1958; Zuk, 1970a,b; Love, 1944). In contrast, XO individuals are frequently observed in animals with a Y (Table 2.D). The studies of sex chromosome deletions in plants also yielded results consistent with the hypothesis that these chromosomes play a vital gametophytic role. The deleted chromosomes were studied in polyploid individuals, so they were always potentially transmitted through a gametophyte with a copy of the missing segment (Westergaard, 1946, 1958). Since plants are especially tolerant of extra chromosomes (see the above references), the failure to observe individuals with less than two normal sex chromosomes may reflect the vital role played by the X/Y in the gametophyte. However, a few individuals with only one X have been observed, and they may have resulted, for example, from chromosome loss after fertilization. A final but isolated observation supporting the hypothesis of an essential role for the X and Y in pollen was an X chromosome deficiency that arose somatically in an individual of *Rumex* (Smith, 1963). Only the Y was transmitted through pollen produced in the part of the plant with this deficient X.

Despite the greater deleterious effects of mutations expressed in haploid stages over those in diploid stages, Y degeneration may affect some genes expressed in the haploid. Progeny sex ratios were female biased in some plants with heteromorphic sex chromosomes, as though pollen with a Y were impaired in competition with X-bearing pollen, and it was suggested that the reduced competitive ability of the Y versus the X may have resulted from its degeneration (Smith, 1963; Zuk, 1970a, b; Lloyd, 1974). Recall that a similar hypothesis was proposed for guppies (Sec. 17.A; Farr, 1981).

In conclusion, therefore, the few instances of heteromorphic sex chromosomes studied in higher plants do not clearly suggest fundamental differences with sex chromosomes in animals. Small Y chromosomes relative to the X are uncommon in plants, possibly suggesting that Y chromosomes are not as degenerate in plants as in animals, but even so, it is not clear whether the Y is prevented from degenerating substantially in plants by extensive haploid gene expression, or whether the sex chromosomes arose so recently that they have not existed long enough to degenerate. Some other observations suggest that sex chromosomes play essential roles in the gametophyte, however.

Haploid Sexes

The evolution of Y degeneration is different in plants with *haploid sexes*, such as bryophytes (haploid dioecy, Fig. 18.C). There are two important

consequences of haploid dioecy in this context. First, the dominant phase in life is haploid, so most genes may be expressed in the haploid. As argued above for angiosperms, the loss of sex-linked genes vital to the haploid is not expected, so sex chromosome degeneration under haploid dioecy should be minor, although as Charlesworth (1978) noted, the ratchet process may accumulate deleterious mutations even under these conditions. (*Note:* Again it should be noted that mutations with only a slight deleterious effect can accumulate on the sex chromosomes, even if they are vital to the haploid stage, and the ultimate degeneration depends on whether essential genes can deteriorate gradually. I adopt the position that the degeneration of loci is effectively prevented if they are important in the haploid phase.) Second, the inheritance of X and Y is symmetrical under haploid dioecy (Fig. 18.C; Lewis and Benson-Evans, 1960; Lewis, 1961; Lewis and John, 1968). In fact, it is merely convention to refer to the female sex chromosome as the X and the male sex chromosome as the Y, because there is no longer a heterogametic and a homogametic sex (Fig. 18.C). The symmetrical inheritance of the X and Y means that, whatever deleterious mutations do accumulate, they should not preferentially accumulate on the X or Y.

In summarizing the above points, it becomes clear that the theory for sex chromosome evolution under haploid dioecy is substantially different from the above theory for diploid dioecy (Bull, 1978b):

- (i) Given their symmetrical inheritance, the X and Y should show similar characteristics. The extent of degeneration should be similar on both chromosomes.
- (ii) From the presumed high proportion of genes functioning in the haploid phase, degeneration of the ancestral segments should be minor and should not seriously impair genes whose expression is essential to the haploid.

Despite these somewhat straightforward predictions, the cytological pattern of sex chromosome differences in bryophytes is not grossly different from that found in animals: the X is larger than the Y in 34 of 36 species listed by Allen (1945). Therefore, a third prediction may be offered (Bull, 1978b):

- (iii) Changes in size of the X and Y are due to additions rather than losses, such as aneuploid translocations.

There is no obvious reason to expect the X to accumulate more additions than the Y, so the preponderance of larger X's remains mysterious (see Bull, 1978b, for some suggestions).

Few data are available for testing these predictions. Both X and Y chromosomes show similar characteristics in that they are often reported to be heterochromatic (Allen, 1945; Berrie, 1963), but the implications of this heterochromatin are unclear. Allen observed that the X was more commonly reported to be (partly) heterochromatic than the Y. Using the C-band technique, Newton (1977) studied three liverworts with heteromorphic sex

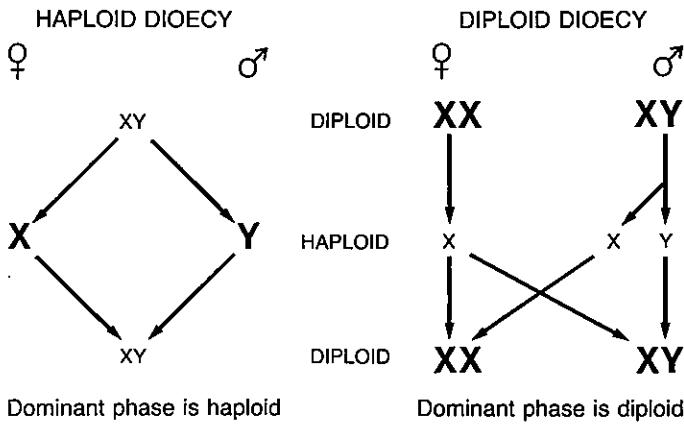


FIGURE 18.C. Sex chromosome inheritance in haploid dioecy versus diploid dioecy. The inheritance of sex chromosomes in species with haploid sexes, such as mosses and liverworts, differs from their inheritance in diploid dioecy, as in most animals and angiosperm plants. Under haploid dioecy, the X and Y have symmetric inheritances, and no distinction between a heterogametic and homogametic sex is found, in contrast to diploid dioecy. Furthermore, the dominant phase of the life cycle is haploid in mosses and liverworts (although not in all species with haploid dioecy), so most genes are expected to function in the haploid phase. Under diploid dioecy, most or all gene expression occurs in the diploid phase (indicated by the relative sizes of the X's and Y's). As a consequence of these two features, the sex chromosomes under haploid dioecy are expected to show only minor degeneration and of equal magnitude on the X and Y, in contrast to the expected major degeneration of the Y under diploid dioecy. (Based on J.J. Bull, 1978. "Sex chromosomes in haploid dioecy: A unique contrast to Muller's theory for diploid dioecy." *The American Naturalist*. 112:245-250, Figure 1.)

chromosomes. In two species the euchromatic parts of the X and Y were the same size, but the X had more heterochromatin. In a third species, the sex chromosomes contained little heterochromatin, and the euchromatic part of the X was larger than the euchromatic part of the Y. It is unfortunately difficult to reach firm conclusions from these cytological observations, because the genetic functions of these different types of chromatin are unknown.

However, one set of observations is available to test prediction (iii), and the observations are consistent with the prediction, in striking contrast to the characteristics of sex chromosomes in animals. In a study of the liverwort *Sphaerocarpus donnellii* (Knapp, 1936; discussed by Allen, 1945), the X was much larger than the Y. Knapp presumed that both the X and Y carried an equivalent set of genes vital to the gametophyte. Prediction (iii) proposes that much of the X has been added and is non-essential. Through the identification of sex-linked mutations, Knapp showed that nine non-essential functions could be attributed to the X, but only seven could be attributed to the

autosomes, and none to the Y. Thus the X carried more non-essential functions than the remainder of the genome in this sample. In addition, Knapp observed viable females missing large portions of the X. So it was clear in this species that the X was composed of a large portion of non-essential material, quite unlike the X in most animals.

Despite the fact that bryophytes comprise only a small spectrum of species, they provide a critical test for theories of sex chromosome degeneration, because some of the key assumptions of the diploid dioecy theory (inheritance, haploid expression) are violated in the bryophytes. Such critical tests have an important place in the testing of a theory. Since there are only a few critical tests for sex chromosome evolution, the bryophytes are worth extensive, careful study, and it is unfortunate that they are not more amenable to genetic and cytological analysis.

D. Summary

Two major processes are involved in the evolution of X-Y differences: suppression of X-Y crossing-over, and loss of gene function from the Y. The evolution of genes with different effects in males and females is enhanced by sex linkage, and X-Y crossover suppression will be favored if these genes are sufficiently common on the undifferentiated sex chromosomes. There is little evidence, however, to suggest whether crossover suppression evolves for this reason. There is also little evidence to indicate whether X-Y crossover suppression evolves initially from genetic modifiers of recombination or from sex-linked chromosome rearrangements. The X and Y frequently have different shapes, indicating that rearrangement differences have evolved, but the rearrangements may have evolved subsequent to X-Y crossover suppression, rather than operating as the initiators of crossover suppression.

Beginning with Muller and Sturtevant, various theories have been proposed to explain the degeneration of Y chromosomes. Perhaps the most plausible theory is Charlesworth's (1978), which suggests that Y chromosomes should accumulate mutations through a process known as "Muller's ratchet". This process depends on the Y never recombining and its containing many loci capable of mutating to non-functional genes with only small effects. Tests of this and other theories for the degeneration of the Y are limited by an absence of genetic data on early stages of Y chromosome degeneration.

Sex chromosome evolution has been intensively studied in animals, and animals are characterized by negligible gene function in the haploid gametic phase. Plants offer systems with considerable haploid gene expression. Consequently, Y chromosomes are expected to degenerate at fewer loci in plants than in animals, although available evidence does not clearly indicate whether this prediction is supported. Mosses and liverworts have haploid sexes, and their sex chromosomes are expected to evolve under rules that do not apply to

sex chromosomes in animals and angiosperm plants. Some predictions pursuant to the theory for haploid dioecy were supported in a test case, but the X is larger than the Y in most mosses and liverworts, a pattern that remains unexplained.

APPENDIX 18.I. Evolution of Genes with Sex-Specific Fitnesses as a Function of Linkage to Sex Factors

Let sex be determined by male heterogamety, and consider a second locus with two alleles, A and a , perhaps linked to the sex factors. Assign fitnesses as follows:

σ	<i>Fitness</i>	φ	<i>Fitness</i>
XY <i>AA</i>	1	XX <i>AA</i>	1
XY <i>Aa</i>	U	XX <i>Aa</i>	V
XY <i>aa</i>	S	XX <i>aa</i>	T
$0 < U, S, V, T.$			

One further restriction is of interest: $U \neq V$, or $S \neq T$, implying that A has different effects in males and females. In heterozygous males, Aa , the recombination fraction between the sex locus and A -locus is r . For example, the genotype Xa/YA produces gametes (Xa) and (YA) with probability $1-r$, and gametes (XA) and (Ya) with probability r . In this model, recombination is irrelevant in homozygous males and in all females.

The conditions are investigated under which a can increase when rare, and also those for which A can increase when rare. These two sets of conditions guarantee that a stable polymorphism exists globally. Stable polymorphism may possibly exist even if these conditions are not met, but there would not be global attraction to internal equilibria in these cases, and they are therefore of less interest. The methodology used in determining the conditions for invasion by A and a involves two steps. First, the general recursions are written for change in the frequencies of the four gametic types in sperm and the two in ova. Second, they are rewritten to linear approximations in the frequencies of all gametes with the rare A or a allele. These linear recursions are valid approximations for selection of the rare allele, except in one special case described below. Methods of matrix algebra are then used to determine whether the rare

allele increases in an infinitely large population, or is instead selected against. The results from such an analysis are as follows:

1. Allele α necessarily increases when rare if the largest λ solving

$$F_1(\lambda) = \lambda^3 - \lambda^2 \left[\frac{V}{2} + U(1-r) \right] + \frac{VU^2}{2}(1/2 - r) = 0$$

exceeds unity.

2. Allele A necessarily increases when rare if the largest λ solving

$$F_2(\lambda) = \lambda^3 - \lambda^2 \left[\frac{V}{2T} + \frac{U}{S}(1-r) \right] + \frac{VU^2}{TS^2}(1/2 - r) = 0$$

exceeds unity.

For each of these cases, if the largest λ solving the equation is less than unity, the rare allele is eliminated. If the largest λ is unity, this analysis does not indicate how selection acts, but these conditions comprise such a small set of parameter values that generality is not lost by omitting them from consideration (as below).

These conditions may now be used to understand whether tighter X-Y linkage (decreasing r) inhibits or enhances the evolution of stable polymorphism—whether tighter linkage enlarges or shrinks the set of (U, V, S, T) satisfying (1) and (2) simultaneously. The following analysis suggests that *decreased X-Y recombination always enhances the evolution of polymorphism*, and never leads to selection against alleles retained in the absence of sex linkage. A complete analytical proof has not been obtained, but the effect of sex linkage is evident in comparing the results for $r = 1/2$ (free recombination) to those for $r = 0$ (completely sex linked). Only the analysis of $F_1(\lambda)$ is presented, and it may be readily observed that the analysis of $F_2(\lambda)$ is identical after transformation of U into U/S and V into V/T .

$$(i) r = 1/2. \quad F_1(\lambda) = \lambda^2 \left[\lambda - \frac{V}{2} - \frac{U}{2} \right] = 0.$$

Thus,

$$\lambda_{\max} = \frac{V}{2} + \frac{U}{2}$$

If $\lambda_{\max} > 1$, allele α increases when rare, but if $\lambda_{\max} < 1$, allele α is selected against. This result simply shows that a rare autosomal gene is selected according to the average of its effects in males and females, as expected. The (U, V) plane is thus divided by a line into regions of which α is selected versus eliminated (Fig. 18.I.1, again neglecting the effect of selection if $\lambda_{\max} = 1$).

$$(ii) r = 0. \quad F_1(\lambda) = \lambda^3 - \lambda^2 \left[\frac{V}{2} + U \right] + \frac{VU^2}{2} = 0$$

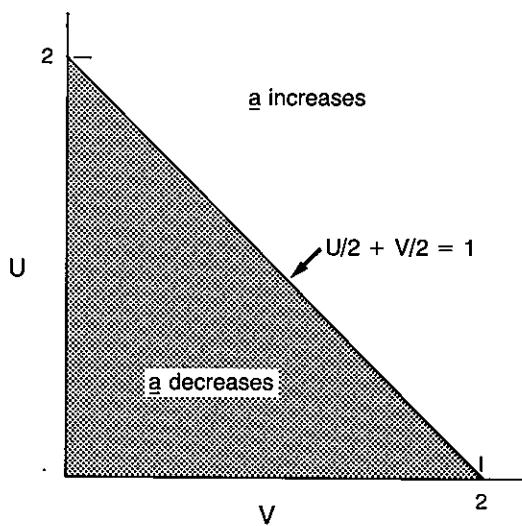


FIGURE 18.I.1. The evolution of allele a when unlinked to the sex factors. The shaded region indicates the fitness values for which a is selected against when rare. U and V are the fitnesses of the Aa genotype in males and females, respectively, relative to the fitness of the AA genotype within the respective sex.

This equation is difficult to factor, so the following approach is used. First, all roots can be shown to be real. To find the set of (U, V) for which λ_{\max} exceeds unity, note that this region is necessarily bounded by the set of (U, V) for which $\lambda_{\max} = 1$, since $F_1(\lambda)$ is continuous. These regions may be obtained by noting that if $\lambda_{\max} = 1$, $F(\lambda) = 0$, requiring the following:

$$F_1(\lambda|\lambda = 1) = 1 - U - \frac{V}{2} + \frac{VU^2}{2} = 0,$$

$$\Rightarrow \frac{V}{2}(1 - U)\left(\frac{2 - V}{V} - U\right) = 0,$$

with solutions

$$U = 1,$$

$$U = \frac{2 - V}{V}.$$

The (U, V) plane is subdivided by this as shown in Figure 18.I.2. There are four regions to consider, as indicated in the figure. $F_1(\lambda|\lambda = 1)$ is positive in R_1 and R_4 , negative in R_2 and R_3 . The implications of these results are indicated by the following. Since $F_1(\lambda|\lambda = -\infty) < 0$ but $F_1(\lambda|\lambda = 0) > 0$, there must be at

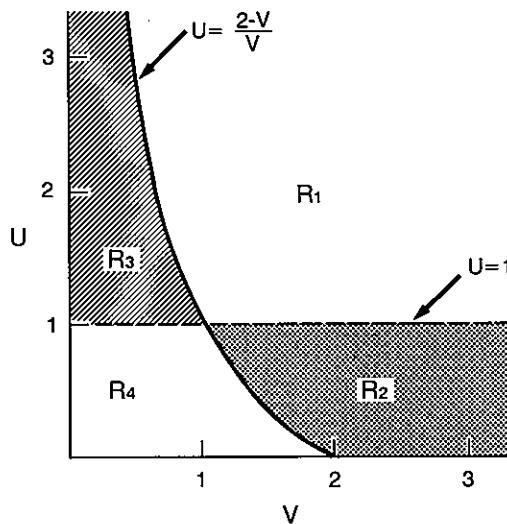


FIGURE 18.I.2. The evolution of allele a when completely linked to the sex factors ($r = 0$). The right quadrant is divided into four regions according to the rules governing selection of a when rare. See text for explanation.

least one negative root. Thus if $F_1(\lambda|\lambda = 1) < 0$, there is both a real root less than and one greater than unity. Therefore:

in R_2, R_3 ; $\lambda_{\max} > 1$, so allele a increases.

If instead, $F_1(\lambda|\lambda = 1) > 0$, as in R_1 and R_4 , either of two situations may obtain: two λ may exceed unity, or all three λ are less than unity. Inspection of eigenvalues from an arbitrary point in each of R_1 and R_4 indicates which of these alternatives obtain—if it were true for some but not other points in the region, then $F_1(\lambda|\lambda = 1)$ would be zero at some points. Yet all points for $F_1(\lambda|\lambda = 1) = 0$ have been found as the partial boundaries for the four regions; thus all points within a region have the same number of eigenvalues greater than unity. Therefore the following also applies, noting that $\lambda_{\min} > -1$ in R_4 :

in R_1 : two $\lambda > 1$, so a increases;

in R_4 : all $\lambda < 1$, so a is eliminated.

Combining the analyses for $r = 1/2$ and 0 leads to the set for which a cannot spread if autosomal ($r = 1/2$) but can spread if sex linked ($r = 0$) (Fig. 18.I.3, shaded area). Furthermore, there is no region in this positive quadrant of the (U, V) plane for which a can increase for $r = 1/2$ yet cannot increase for $r = 0$. Thus, $r = 0$ invariably enlarges the set (U, V) for which a can invade.

Comparison of selection under $r = 0$ and $r = 1/2$ may be criticized because these are two extremes of r , possibly not representative of the effects of selection under small changes in r within the interval $(0, 1/2)$. I cannot address this criticism generally but it can be shown that decreasing r in the neighborhood of $r = 1/2$ has the same qualitative effect as decreasing it to zero. From $F_1(\lambda) = 0$ at $r = 1/2$, for λ_{\max} ,

$$\frac{\delta \lambda}{\delta r} = -\frac{U(U-V)^2}{(U+V)^2} < 0, \quad \frac{\delta^2 \lambda}{\delta r^2} > 0 \quad 0 < U, V; U \neq V$$

indicating that λ_{\max} increases with decreasing r , more so as r decreases. Therefore at $r = 1/2$, decreasing r enlarges the set of (U, V) which enables a to invade.

The analysis of (2) is the same as for (1) if U and V are replaced by U/S and V/T , respectively. The same conclusions apply, now to the $(U/S, V/T)$ plane. Since positive values of U and V do not determine the values of U/S and V/T [hence values in the right quadrant of the (U, V) plane do not exclude values in the $(U/S, V/T)$ plane], the set of (U, V, S, T) that permits stable polymorphism at the A -locus is unequivocally increased by sex linkage. Polymorphism does not necessarily guarantee that the frequency of A will differ in males and females, but there can be little doubt that only a trivial subset of these points will lead to equal frequencies in both sexes at equilibrium.

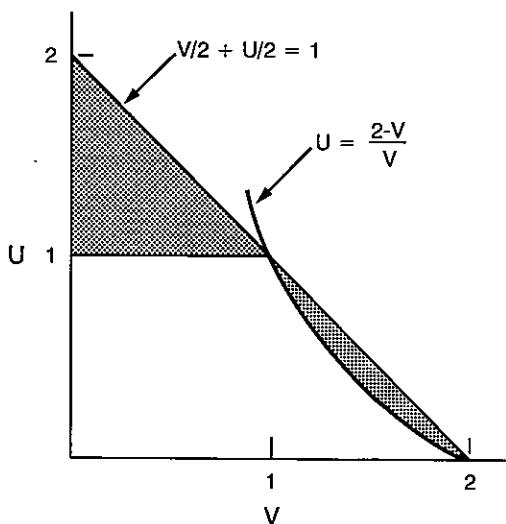
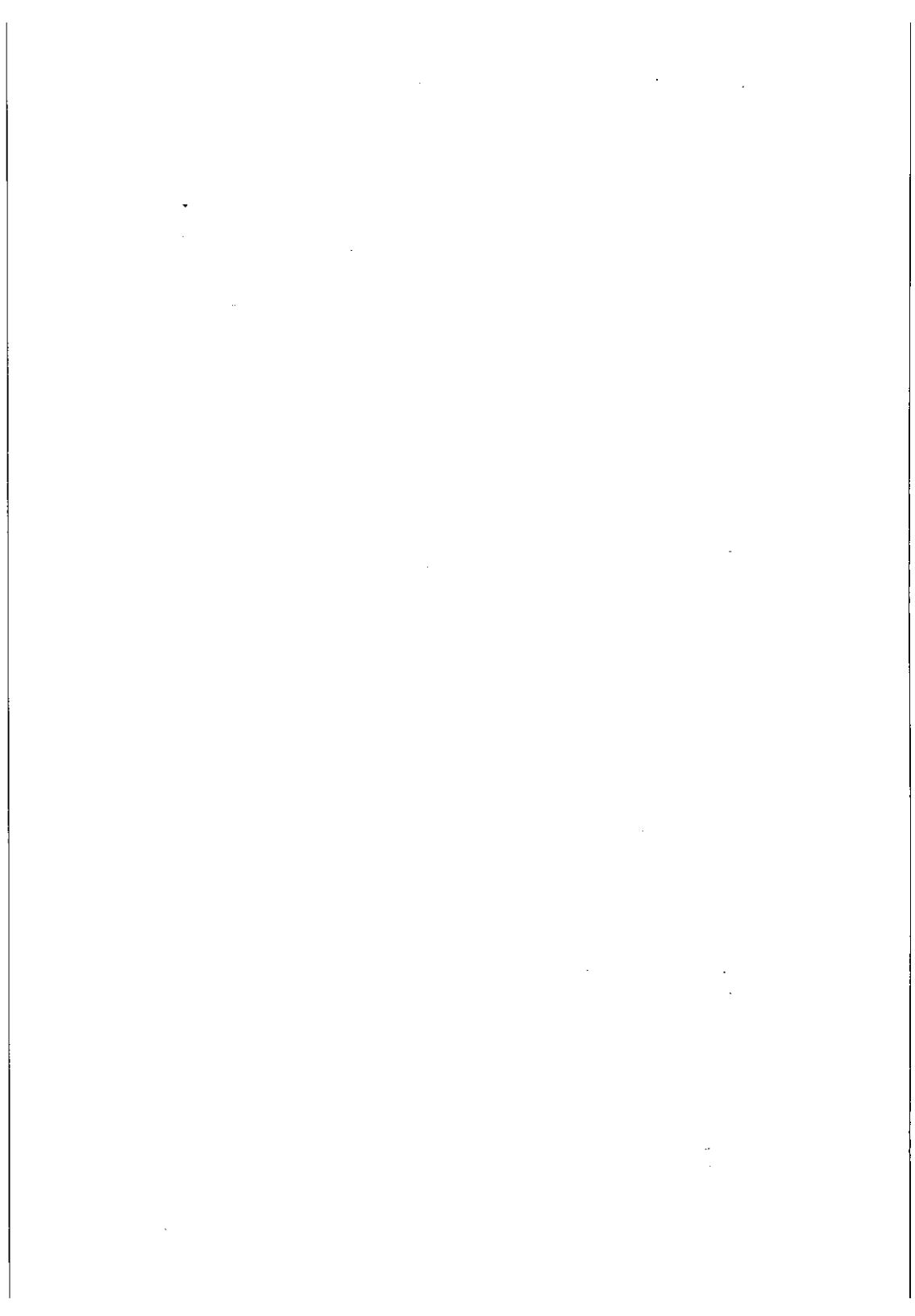


FIGURE 18.I.3. The set of fitness values are shown for which a can increase when completely linked to the sex factors but not when unlinked (shaded).



References

- Adkins-Regan, E. 1981. Early organizational effects of hormones. In *Neuroendocrinology of Reproduction: Physiology and Behavior*, ed. N. T. Adler, pp. 159-228. Plenum Press, New York.
- Aida, T. 1921. On the inheritance of color in a fresh-water fish, *Aplocheilus latipes* Temminck and Schlegel, with special reference to sex linked inheritance. *Genetics* 6:554-573.
- Aida, T. 1936. Sex reversal in *Aplocheilus latipes* and a new explanation of sex differentiation. *Genetics* 21:136-153.
- Allen, C.E. 1945. The genetics of bryophytes II. *Bot. Rev.* 11:260-287.
- Anderson, K.V., and J.A. Lengyel. 1979. Rates of synthesis of major classes of RNA in *Drosophila* embryos. *Dev. Biol.* 70:217-231.
- Anderson, K.V., and J.A. Lengyel. 1981. Changing rates of DNA and RNA synthesis in *Drosophila* embryos. *Dev. Biol.* 82:127-138.
- Aoki, K. 1980. A criterion for the establishment of a stable polymorphism of higher order with an application to the evolution of polymorphism. *J. Math. Biol.* 9:133-146.
- Arrighi, F.E., and T.C. Hsu. 1971. Localization of heterochromatin in human chromosomes. *Cytogenetics* 10:81-86.
- Atz, J.W. 1964. Intersexuality in fishes. In *Intersexuality in Vertebrates Including Man*, ed. C.N. Armstrong and A.J. Marshall, pp. 145-232. Academic Press, New York.
- Austin, C.R., and R.G. Edwards (eds.). 1981. *Mechanisms of Sex Differentiation in Animals and Man*. Academic Press, New York, London.
- Austin, C.R., R.G. Edwards, and U. Mittwoch. 1981. Introduction. In *Mechanisms of Sex Differentiation in Animals and Man*, ed. C.R. Austin and R.G. Edwards, pp. 1-54. Academic Press, New York, London.
- Avtalion, R.R., and I.S. Hammerman. 1978. Sex determination in *Sarotherodon* (Tilapia) I. Introduction to a theory of autosomal influence. *Bamidgeh* 30:110-115.
- Bacci, G. 1965. *Sex Determination*. Pergamon Press, Oxford, New York.
- Baker, B.S., and J.C. Hall. 1976. Meiotic mutants: Genetic control of meiotic recombination and chromosome segregation. In *The Genetics and Biology of Drosophila*, ed. M. Ashburner and E. Novitski, vol. 1a. Academic Press, New York.

- Baker, B.S., and D.L. Lindsley. 1983. The genetic control of sex determination and male fertility in *Drosophila melanogaster*. In *Genetic Control of Gamete Production and Function*. No. 3. ed. P.G. Crosignani and B.L. Rubin, Sorrenso Symposium, Academic Press, New York.
- Baker, B.S., and K.A. Ridge. 1980. Sex and the single cell. I. On the action of major loci affecting sex determination in *Drosophila melanogaster*. *Genetics* 94:383-423.
- Baker, R.H., and M.G. Rabbani. 1970. Complete linkage in females of *Culex tritaeniorhynchus* mosquitoes. *Heredity* 61:59-61.
- Baker, R.H., U.T. Saifuddin, and R.K. Sakai. 1977. Variations in the linkage of the sex allele in laboratory colonies of the mosquito *Culex tritaeniorhynchus*. *Jap. J. Genet.* 52:425-430.
- Baker, R.J., G.A. Mengden, and J.J. Bull. 1972. Karyotypic studies of thirty-eight species of North American snakes. *Copeia* 1972:257-265.
- Baltzer, F. 1912. Über die Entwicklungsgeschichte von *Bonellia*. *Verh. Dtsch. Zool. Ges.* 22:252-261. (Cited from Leutert, 1975.)
- Baltzer, F. 1914. Die Bestimmung und der Dimorphismus des Geschlechtes bei *Bonellia*. *Sitz.-Ber. Physikal.-med. Ges.* (Wurzburg) 43:1-4. (Cited from Leutert, 1975.)
- Barr, M.L. 1959. Sex-chromatin and phenotype in man. *Science* 130:679-685.
- Barr, M.L., and L.F. Bertram. 1949. A morphological distinction between neurones of the male and female and the behavior of the nucleolar satellite during accelerated nucleoprotein synthesis. *Nature* 163:676-677.
- Baverstock, P.R., M. Adams, R.W. Polkinghorne, and M. Gelder. 1982. A sex-linked enzyme in birds—Z-chromosome conservation but no dosage compensation. *Nature* 296:763-766.
- Becak, W., M.L. Becak, H.R.S. Nazareth, and S. Ohno. 1964. Close karyological kinship between the reptilian suborder Serpentes and the class Aves. *Chromosoma* 15:606-617.
- Becker, P., H. Roland, and R. Reinboth. 1975. An unusual approach to experimental sex inversion in the teleost fish, *Betta* and *Macropodus*. In *Intersexuality in the Animal Kingdom*, ed. R. Reinboth, pp. 236-242. Springer-Verlag, Berlin, New York.
- Beermann, W. 1955. Geschlechtsbestimmung und evolution der genetischen Y-Chromosomen bei *Chironomus*. *Biol. Zentr.* 74:525-544.
- Belar, K. 1924. Die cytologie der merospermie bei freilebenden *Rhabditis*-arten. *Z. Zellen -u. Gewebelehre*. 1:1-24.
- Bell, G. 1982. *The Masterpiece of Nature. The Evolution and Genetics of Sexuality*. Univ. of Calif. Press, Los Angeles.
- Belote, J.M., and B.S. Baker. 1982. Sex determination in *Drosophila melanogaster*: Analysis of *transformer-2*, a sex-transforming locus. *Proc. Nat. Acad. Sci. USA* 79: 1568-1572.
- Belote, J.M., and J.C. Lucchesi. 1980a. Control of X chromosome transcription by the *maleless* gene in *Drosophila*. *Nature* 285:573-575.
- Belote, J.M., and J.C. Lucchesi. 1980b. Male-specific lethal mutations of *Drosophila melanogaster*. *Genetics* 196:165-186.
- Bengtsson, B.O. 1977. Evolution of the sex ratio in the wood lemming, *Myopus schisticolor*. In *Measuring Selection in Natural Populations*, ed. T.M. Fenchel and F.B. Christiansen, pp. 333-343. Springer-Verlag, Berlin.
- Berg, R.L. 1937a. The relative frequency of mutations in different chromosomes of *Drosophila melanogaster*. I. Lethal mutations, and II. Sterility mutations. *Genetics* 22:225-248.

- Berg, R.L. 1937b. The relative roles of stabilization and redifferentiation of the gene in the evolution of the hereditary substance. *Genetics* 22:402-405.
- Berg, R.L. 1938. Sterility mutations in *Drosophila melanogaster*. Distribution of sterility mutations in the chromosomes of *Drosophila melanogaster* (in Russian, with English summary). *Reports Leningrad Soc. Nat.* 67:96-108.
- Berg, R.L. 1942. Evolution of the mechanism of sex determination (in Russian). *J. General Biology* 3:171-189.
- Bernstein, R., G.C. Koo, and S.S. Wachtel. 1980. Abnormality of the X chromosome in human 46, XY female siblings with dysgenetic ovaries. *Science* 207:768-769.
- Berrie, G.K. 1963. Cytology and phylogeny of liverworts. *Evolution* 17:347-357.
- Berry, J.F., and R. Shine. 1980. Sexual size dimorphism and sexual selection in turtles (order Testudines). *Oecologia* 44:185-191.
- Bickham, J.W. 1982. Patterns and modes of chromosomal evolution in reptiles. In *Chromosomes in Evolution of Eukaryotic Groups*, ed. A.K. Sharma and A. Sharma, vol. 2. CRC Press, Boca Raton, Fla.
- Bickham, J.W., and J.L. Carr. 1983. Taxonomy and phylogeny of the higher categories of cryptodiran turtles based on a cladistic analysis of chromosomal data. *Copeia*. In press.
- Borgia, G. 1980. Evolution of haplodiploidy: Models for inbred and outbred systems. *Theor. Pop. Biol.* 17:103-128.
- Boyes, J.W. 1967. The cytology of muscoid flies. In *Genetics of Insect Vectors of Disease*, ed. J.W. Wright and R. Pal. Elsevier Publ. Co., London, New York, pp. 371-384.
- Breider, H. 1935. Über Aussenfaktoren die das Geschlechtsverhältnis bei *Xiphophorus helleri* Heckel kontrollieren sollen. *Z. wiss. Zool.* 146:383-416.
- Bridges, C.B. 1916. Non-disjunction as proof of the chromosome theory of heredity. *Genetics* 1:1-52 and 107-163.
- Bridges, C.B. 1922. The origin of variations in sexual and sex-limited characters. *Am. Nat.* 56:51-63.
- Bridges, C.B. 1925. Sex in relation to genes and chromosomes. *Am. Nat.* 59:127-137.
- Bridges, C.B. 1939. Cytological and genetic basis of sex. In *Sex and Internal Secretions*, 2d ed., ed. C. Allen et al., pp. 15-63. Williams and Wilkins Co., Baltimore.
- Brosseau, G.E. 1960. Genetic analysis of the male fertility factors on the Y chromosome of *Drosophila melanogaster*. *Genetics* 45:257-274.
- Brown, S.W. 1963. The Comstockiella system of chromosome behavior in the armored scale insects (Coccoidea: Diaspididae). *Chromosoma* 14:360-406.
- Brown, S.W. 1964. Automatic frequency response in the evolution of male haploidy and other coccid chromosome systems. *Genetics* 49:797-817.
- Brown, S.W. 1966. Heterochromatin. *Science* 151:417-425.
- Brown, S.W., and F.D. Bennett. 1957. On sex determination in the diaspine scale *Pseudaulacaspis pentagona* (Targ.) (Coccoidea). *Genetics* 42:510-523.
- Brown, S.W., and H.S. Chandra. 1977. Chromosome imprinting and their differential regulation of homologous chromosomes. In *Cell Biology*, ed. L. Goldstein and D.M. Prescott, vol. 1, pp. 109-189. Academic Press, New York.
- Brown, S.W., and W.A. Nelson-Rees. 1961. Radiation analysis of a lecanoid genetic system. *Genetics* 46:983-1007.
- Bull, J.J. 1978a. Sex chromosome differentiation: An intermediate stage in a lizard. *Can. J. Genet. Cytol.* 20:205-209.
- Bull, J.J. 1978b. Sex chromosomes in haploid dioecy: A unique contrast to Muller's theory for diploid dioecy. *Am. Nat.* 112:245-250.

- Bull, J.J. 1979. An advantage for the evolution of male haploidy and systems with similar genetic transmission. *Heredity* 43:361-381.
- Bull, J.J. 1980. Sex determination in reptiles. *Quart. Rev. Biol.* 55:3-21.
- Bull, J.J. 1981a. Evolution of environmental sex determination from genotypic sex determination. *Heredity* 47:173-184.
- Bull, J.J. 1981b. Sex ratio evolution when fitness varies. *Heredity* 46:9-26.
- Bull, J.J. 1981c. Coevolution of haplo-diploidy and sex determination in the Hymenoptera. *Evolution* 35:568-580.
- Bull, J.J., and M.G. Bulmer. 1981. The evolution of XY females in mammals. *Heredity* 47:347-365.
- Bull, J.J., and E.L. Charnov. 1977. Changes in the heterogametic mechanism of sex determination. *Heredity* 39:1-14.
- Bull, J.J., and J.M. Legler. 1980. Karyotypes of side-necked turtles (Testudines: Pleurodira). *Can. J. Zool.* 58:828-841.
- Bull, J.J., R.G. Moon, and J.M. Legler. 1974. Male heterogamety in kinosternid turtles (genus *Staurotypus*). *Cytogenet. Cell Genet.* 13:419-425.
- Bull, J.J., and R.C. Vogt. 1979. Temperature-dependent sex determination in turtles. *Science* 206:1186-1188.
- Bull, J.J., and R.C. Vogt. 1981. Temperature-sensitive periods of sex determination in emydid turtles. *J. Exp. Zool.* 218:435-440.
- Bull, J.J., R.C. Vogt, and M.G. Bulmer. 1982. Heritability of sex ratio in turtles with environmental sex determination. *Evolution* 36:333-341.
- Bull, J.J., R.C. Vogt, and C.J. McCoy. 1982. Sex determining temperatures in emydid turtles: A geographic comparison. *Evolution* 36:326-332.
- Bulmer, M.G., and J.J. Bull. 1982. Models of polygenic sex determination and sex ratio evolution. *Evolution* 36:13-26.
- Bulnheim, H-P. 1967. Über den einfluss der photoperiode auf die geschlechtsrealisation bei *Gammarus duebeni*. *Helgoländer wiss. Meeresunters* 16:69-83.
- Bulnheim, H-P. 1969. Zur Analyse geschlechtesbestimmender Faktoren bei *Gammarus duebeni* (Crustacea, Amphipoda). *Zool. Anz. Suppl.* 32 (Verh. Dtsch. Zool. Ges. 1968):244-260.
- Bulnheim, H-P. 1975a. Microsporidian infections of amphipods with special reference to host-parasite relationships: A review. *Marine Fisheries Review* 37:39-45.
- Bulnheim, H-P. 1975b. Intersexuality in Gammaridae and its conditions. *Pubbl. Staz. Zool. Napoli* 39:399-416.
- Bulnheim, H-P. 1978a. Interaction between genetic, external and parasitic factors in sex determination of the crustacean amphipod *Gammarus duebeni*. *Helgolander wiss. Meeresunters* 31:1-33.
- Bulnheim, H-P. 1978b. Variability of the modes of sex determination in littoral amphipods. In *Marine Organisms*, ed. B. Battaglia and J. Beardmore, pp. 529-548. Plenum Publ. Corp., New York.
- Burgoyne, P.S. 1978. The role of the sex chromosomes in mammalian germ cell differentiation. *Ann. Biol. Anim. Bioch. Biophys.* 18:317-325.
- Burns, R.K. 1961. Hormones and differentiation of sex. In *Sex and Internal Secretions*, ed. W.C. Young, vol. 1, 3d ed., pp. 76-158. Williams and Wilkins Co., Baltimore.
- Bush, G.L. 1966. Female heterogamety in the family Tephritidae (Acalytratae, Diptera). *Am. Nat.* 100:119-126.
- Cattanach, B.M. 1961. XXY mice. *Gen. Res.* 2:156-158.
- Cattanach, B.M. 1975. Control of chromosome inactivation. *Ann. Rev. Gen.* 9:1-18.

- Caullery, M., and M. Comas. 1928. Le determinisme du sexe chez un nematode (*Paracermis contorta*), parasite des larves des *Chironomus*. *C.R. Acad. Sci.* 186:646-648.
- Charlesworth, B. 1978. Model for evolution of Y chromosomes and dosage compensation. *Proc. Nat. Acad. Sci. USA* 75:5618-5622.
- Charlesworth, B., and D. Charlesworth. 1978. A model for the evolution of dioecy and gynodioecy. *Am. Nat.* 112:975-997.
- Charlesworth, D., and B. Charlesworth. 1980. Sex differences in fitness and selection for centric fusions between sex-chromosomes and autosomes. *Gen. Res.* 35:205-214.
- Charnier, M. 1966. Action de la température sur la sex-ratio chez l'embryon d'*Agama agama* (Agamidae, Lacertilien). *Soc. Biol. Ouest Af.* 160:620-622.
- Charnov, E.L. 1979. The genetical evolution of patterns of sexuality: Darwinian fitness. *Am. Nat.* 113:465-480.
- Charnov, E.L. 1982. *The Theory of Sex Allocation*. Princeton Univ. Press, Princeton, N.J.
- Charnov, E.L., and J.J. Bull. 1977. When is sex environmentally determined? *Nature* 266:828-830.
- Charnov, E.L., R.L. Los-Den Hartogh, T. Jones, and J. van den Assem. 1981. Sex ratio evolution in a variable environment. *Nature* 289:27-33.
- Chitwood, B.G., and M.G. Chitwood. 1974. *An Introduction to Nematology* (revised). University Park Press, Baltimore.
- Christie, J.R. 1929. Some observations on sex in the Mermithidae. *J. Exp. Zool.* 53:59-76.
- Clarke, C., and E.B. Ford. 1980. Intersexuality in *Lymantria dispar* (L.). A reassessment. *Proc. Roy. Soc. Lond.* 206:381-394.
- Cline, T.W. 1978. Two closely linked mutations in *Drosophila melanogaster* that are lethal to opposite sexes and interact with daughterless. *Genetics* 90:683-698.
- Cline, T.W. 1979a. A male-specific lethal mutation in *Drosophila melanogaster* that transforms sex. *Dev. Biol.* 72:266-275.
- Cline, T.W. 1979b. A product of maternally-influenced sex-lethal gene determines sex in *Drosophila melanogaster*. *Genetics* 91:s22.
- Cock, A.G. 1964. Dosage compensation and sex-chromatin in non-mammals. *Gen. Res.* 5:354-365.
- Cohen, M.M., and C. Gans. 1970. The chromosomes of the order Crocodilia. *Cytogenetics* 9:81-105.
- Cole, C.J. 1975. Evolution of parthenogenetic species of reptiles. In *Intersexuality in the Animal Kingdom*, ed. R. Reinboth, pp. 340-355. Springer-Verlag, Berlin.
- Cole, C.J., C.H. Lowe, and J.W. Wright. 1969. Sex chromosomes in teiid whiptail lizards (genus *Cnemidophorus*). *Amer. Mus. Nov.* 2395.
- Collenot, A. 1975. Unisexual female offsprings in the salamander *Pleurodeles waltlii* Michah. In *Intersexuality in the Animal Kingdom*, ed. R. Reinboth, pp. 311-317. Springer-Verlag, Berlin.
- Conover, D.O. 1983. Adaptive significance of temperature-dependent sex determination in a fish. *Am. Nat.* (Submitted.)
- Conover, D.O., and B.E. Kynard. 1981. Environmental sex determination: Interaction of temperature and genotype in a fish. *Science* 213:577-579.
- Cooper, D.W., P.G. Johnston, G.B. Sharman, and J.L. VandeBerg. 1977. The control of gene activity on eutherian and metatherian X chromosomes: A comparison. In

- Reproduction and Evolution, Proc. 4th Int. Symposium on Comparative Biology of Reproduction*, pp. 81-87. Australian Acad. Sci., Canberra.
- Cotterman, C.W. 1953. Regular two-allele and three-allele phenotype systems. *Am. J. Hum. Genet.* 5:193-235.
- Counce, S.J., and D.F. Poulson. 1962. Developmental effects of the sex-ratio agent in embryos of *Drosophila willistoni*. *J. Exp. Zool.* 151:17-31.
- Couturier, A. 1963. Recherches sur des mermithidae, nematodes parasites du hanneton commun (*Melolontha melolontha* L. Coléopt. Scarab.) *Ann. Epiphyties* 14:203-267.
- Craig, G.B. 1965. Genetic control of thermally-induced sex reversal in *Aedes aegypti*. In *Proc. XIIth Int. Cong. of Entom.*, London, ed. P. Freeman, p. 263. Roy. Ent. Soc., London.
- Crew, F.A.E. 1965. *Sex Determination*. 4th ed. Menthuen & Co. Ltd. Reprinted: Dover, New York.
- Crouse, H.V. 1943. Translocations in *Sciara*; Their bearing on chromosome behavior and sex determination. *Univ. of Missouri Research Bulletin* #379.
- Crouse, H.V. 1960. The nature of the influence of X-translocations on sex of progeny in *Sciara coprophila*. *Chromosoma* 11:146-166.
- Crow, J.F. 1946. The absence of a primary sex factor on the X-chromosome of *Drosophila*. *Am. Nat.* 80:663-665.
- Crow, J.F., and M. Kimura. 1970. *Introduction to Population Genetics Theory*. Harper and Row, New York.
- Crozier, R.H. 1971. Heterozygosity and sex determination in haplo-diploidy. *Am. Nat.* 105:399-412.
- Crozier, R.H. 1977. Evolutionary genetics of the Hymenoptera. *Ann. Rev. Ent.* 22:263-288.
- Darlington, C.D. 1937. *Recent Advances in Cytology*. 2d ed. Churchill, London.
- Darlington, C.D. 1939. *The Evolution of Genetic Systems*. 1st ed. Cambridge Univ. Press, Cambridge, U.K.
- Darlington, C.D. 1958. *The Evolution of Genetic Systems*. 2d ed. Oliver and Boyd, Edinburgh and London.
- Darlington, C.D. 1965. *Recent Advances in Cytology 1937-1964*. Churchill, London.
- Davidson, E.H. 1976. *Gene Activity in Early Development*. 2d ed. Academic Press, New York.
- Dobzhansky, Th. 1957. The X-chromosome in the larval salivary glands of hybrids *Drosophila insularis* x *Drosophila tropicalis*. *Chromosoma* 8:691-698.
- Dobzhansky, Th., and J. Schultz. 1931. Evidence for multiple sex factors in the X-chromosome of *Drosophila melanogaster*. *Proc. Nat. Acad. Sci. USA* 17:513-518.
- Dobzhansky, Th., and J. Schultz. 1934. The distribution of sex factors in the X-chromosome of *Drosophila melanogaster*. *J. Genet.* 28:349-386.
- Doira, H. 1978. Genetic stocks of the silkworm. In *The silkworm: An important laboratory tool*, ed. Y. Tazima, pp. 53-81. Kodanasha Ltd., Tokyo.
- Donald, J.A., and D.W. Cooper. 1977. Studies on metatherian sex chromosomes. III. The use of tritiated uridine-induced chromosome aberrations to distinguish active and inactive X chromosomes. *Aust. J. Biol. Sci.* 30:103-114.
- Doolittle, W.F., and C. Sapienza. 1980. Selfish genes, the phenotype paradigm, and genome evolution. *Nature* 284:601-603.

- Dronamraju, K.R. 1965. The function of the Y-chromosome in man, animals and plants. *Adv. Genet.* 13:227-310.
- Duckett, J. 1979. The genetic control and localization of the multiple molecular forms of acetylcholinesterase in *Caenorhabditis elegans*. Master's thesis, U. of Pittsburgh.
- Dunn, L.C., and D. Bennett. 1967. Sex differences in recombination of linked genes in animals. *Gen. Res.* 9:211-220.
- Dyer, J.G. 1975. Sex ratio and arrhenotokous reproduction in phytoseiid mites (Acarina: Mesostigmata). Ph.D. thesis, Rutgers University.
- Dzierzon, J. 1845. Eichstadte Bienenzzeitung 1:113. (Cited by Whiting, 1945.)
- Ebeling, A.W., and T.R. Chen. 1970. Heterogamety in teleostean fishes. *Trans. Amer. Fish. Soc.* 99:131-138.
- Eddington, A.S. 1929. *The Nature of the Physical World*. Macmillan Co., New York.
- Eicher, E.M., L.L. Washburn, J.B. Whitney III, and K.E. Morrow. 1982. *Mus poschiavinus* Y chromosome in the C57B1/6J murine genome causes sex reversal. *Science* 217:535-537.
- Eichwald, E.J., C.R. Silmser, and I. Weissman. 1958. Sex-linked rejection of normal and neoplastic tissue. I. Distribution and specificity. *J. Nat. Cancer Inst.* 20:563-575.
- Ellenby, C. 1954. Environmental determination of the sex ratio of a plant parasitic nematode. *Nature* 174:1016-1017.
- Eloff, G. 1932. A theoretical and experimental study on the changes in the crossing-over value, their causes and meaning. *Genetica* 14:1-116.
- Endler, J.A. 1978. A predator's view of animal color patterns. *Evol. Biol.* 11:319-364.
- Endler, J.A. 1980. Natural selection on color patterns in *Poecilia reticulata*. *Evolution* 34:76-91.
- Engel, W., B. Klemme, and M. Schmid. 1981. H-Y antigen and sex determination in turtles. *Differentiation* 20:152-156.
- Epplen, J.T., J.R. McCarrey, S. Sutou, and S. Ohno. 1982. Base sequence of a cloned snake W-chromosome DNA fragment and identification of a male-specific putative mRNA in the mouse. *Proc. Nat. Acad. Sci. USA* 79:3798-3802.
- Evans, E.P., M.D. Burtenshaw, and B.M. Cattanach. 1982. Meiotic crossing-over between the X and Y chromosomes of male mice carrying the sex-reversing (sxr) factor. *Nature* 300:443-445.
- Ezenwa, A.O., and N.E. Carter. 1975. Influence of multiple infections on sex ratios of mermithid parasites of blackflies. *Environ. Entom.* 4:142-144.
- Falconer, D.S. 1981. *Introduction to Quantitative Genetics*. 2d ed. Longman Group Ltd. Essex, U.K.
- Farr, J.A. 1981. Biased sex ratios in laboratory strains of guppies, *Poecilia reticulata*. *Heredity* 47:237-248.
- Felsenstein, J. 1974. The evolutionary advantage of recombination. *Genetics* 78:737-756.
- Ferguson, M.W.J., and T. Joosten. 1982. Temperature of egg incubation determines sex in *Alligator mississippiensis*. *Nature* 296:850-853.
- Fisher, R.A. 1930. *The Genetical Theory of Natural Selection*. Dover Reprint (1958), New York.
- Fisher, R.A. 1931. The evolution of dominance. *Biol. Rev.* 6:345-368.
- Fisher, R.A. 1935. The sheltering of lethals. *Am. Nat.* 69:446-455.
- Foe, V., H. Forrest, L. Wilkinson, and C. Laird. 1982. Morphological analysis of

- transcription in insect embryos. In *Insect Ultrastructure*, ed. R.C. King and H. Akai, pp. 222-246. Plenum Press, New York.
- Foote, C.L. 1964. Intersexuality in Amphibians. In *Intersexuality in Vertebrates Including Man*, ed. C.N. Armstrong and A.J. Marshall, pp. 233-372. Academic Press, London, New York.
- Franco, M.G., P.G. Rubini, and M. Vecchi. 1982. Sex-determinants and their distribution in various populations of *Musca domestica* L. of Western Europe. *Gen. Res.* 40:279-293.
- Fredga, K., A. Gropp, H. Winking, and F. Frank. 1976. Fertile XX- and XY-type females in the wood lemming *Myopus schistocolor*. *Nature* 261:225-227.
- Fredga, K., A. Gropp, H. Winking, and F. Frank. 1977. A hypothesis explaining the exceptional sex ratio in the wood lemming (*Myopus schistocolor*). *Hereditas* 85:101-104.
- Friedler, G., and D.T. Ray. 1951. Androgenesis and mutation in the wasp *Mormoniella*. *Anat. Rec.* 111:475. (Abst.)
- Frota-Pessoa, O., and L.R. Aratangy. 1968. The degeneration of the Y chromosome. *Rev. Brasileira de Pesquisas Med. Biol.* 1:241-244.
- Gallagher, A., G. Hewitt, and I. Gibson. 1973. Differential giemsa staining of heterochromatic B-chromosomes in *Myrmeleotettix maculatus* (Thumb.). (Orthoptera: Acrididae). *Chromosoma* 40:167-172.
- Gallien, L.G. 1959. Sex Determination. In *The Cell*, ed. J. Brachet and A.E. Mirsky, vol. 1, pp. 399-436. Academic Press, New York.
- Gartler, S.M., and R.E. Cole. 1981. Recent developments in the study of mammalian X-chromosome inactivation. In *Mechanisms of Sex Differentiation in Animals and Man*, ed. C.R. Austin and R.G. Edwards. Academic Press, New York, London.
- German, J., J.L. Simpson, R.S.K. Chaganti, R.L. Summitt, L.B. Reid, and I.R. Merkatz. 1978. Genetically determined sex-reversal in 46, XY humans. *Science* 202:53-56.
- Ghiselin, M.T. 1969. The evolution of hermaphroditism among animals. *Quart. Rev. Biol.* 44:189-208.
- Gibbons, J.W. 1970. Sex ratios in turtles. *Res. Pop. Ecology* 12:252-254.
- Gilchrist, B.M., and J.B.S. Haldane. 1947. Sex linkage and sex determination in a mosquito, *Culex molestus*. *Hereditas* 33:175-189.
- Gileva, E.A. 1980. Chromosomal diversity and an aberrant genetic system of sex determination in the Arctic lemming, *Dicrostonyx torquatus* Pallas (1779). *Genetica* 52/53:99-103.
- Gileva, E.A., and N.A. Chebotar. 1979. Fertile XO males and females in the varying lemming, *Dicrostonyx torquatus* Pall. (1779). *Heredity* 42:67-77.
- Gileva, E.A., I.E. Benenson, L.A. Konopistseva, V.F. Puchkov, and I.A. Makaranets. 1982. XO females in the varying lemming, *Dicrostonyx torquatus*: Reproductive performance and its evolutionary significance. *Evolution* 36:601-609.
- Gillespie, J. 1973. Polymorphism in random environments. *Theor. Pop. Biol.* 4:193-195.
- Ginsburger-Vogel, T. 1975a. Temperature-sensitive intersexuality and its determinism in *Orchestia gammarella* Pallas. In *Intersexuality in the Animal Kingdom*, ed. R. Reinboth, pp. 106-120. Springer-Verlag, Berlin.
- Ginsburger-Vogel, T. 1975b. Determination génétique du sexe, mongénie et intersexualité chez *Orchestia gammarella* Pallas (Crustace Amphipode Talitridae) III. Étude des phénomènes de monogénie indépendants de l'intersexualité. *Arch. Zool. Exp. Gen.* 116:615-647.

- Ginsburger-Vogel, T., M.C. Carre-Lecuyer, and M.C. Fried-Montauzier. 1980. Transmission expérimentale de la thélygénie liée à l'intersexualité chez *Orchestia gammarellus* (Pallas); Analyse des génotypes sexuels dans la descendance des femelles normales transformées en femelles thélygenes. *Arch. Zool. Exp. Gen.* 122:261-270.
- Ginsburger-Vogel, T., and I. Desportes. 1979. Structure and biology of *Marteilia sp.* in the amphipod, *Orchestia gammarellus*. *Marine Fish. Rev.* 41:3-7.
- Ginsburger-Vogel, T., and F. Magniette-Mergault. 1981a. The effects of temperature on sexual differentiation in the temperature sensitive thelygenic-intersexual offspring of *Orchestia gammarellus* (Pallas) (Amphipoda; Crustacea). I. Effects of temperature on pubescent females. *Int. J. Invert. Reprod.* 4:39-50.
- Ginsburger-Vogel, T., and F. Magniette-Mergault. 1981b. The effects of temperature on sexual differentiation in the temperature sensitive thelygenic-intersexual offspring of *Orchestia gammarellus* (Pallas) (Amphipoda; Crustacea). II. Effects of temperature during embryonic and post-embryonic development. *Int. J. Invert. Reprod.* 4:51-65.
- Gold, J.R. 1979. Cytogenetics. In *Fish Physiology*, vol. 8. Academic Press, New York, pp. 353-405.
- Goldschmidt, R.B. 1920a. *The Mechanism and Physiology of Sex Determination*. London, Methuen & Co. Ltd.; New York, G.H. Doran Co. Translation by W.J. Dakin (1923).
- Goldschmidt, R.B. 1920b. Untersuchungen über Intersexualität I.Z. indukt. *Abstammung. Vererb.* 23:1-199.
- Goldschmidt, R.B. 1931. *Die Sexuellen Zwischenstufen*. Mong. Gesamtgeb. Pflanzen, Tiere, 23. J. Springer, Berlin.
- Goldschmidt, R.B. 1934. *Lymmantria. Bibliog. Genetica* 11:1-186.
- Goldschmidt, R.B. 1955. *Theoretical Genetics*. Univ. of California Press, Berkeley, Los Angeles.
- Gordon, M. 1946. Interchanging genetic mechanisms for sex determination for fishes under domestication. *J. Heredity* 37:307-320.
- Gordon, M. 1954. Two opposing sex determining mechanisms, one XX-XY and the other WY-YY in different natural populations of the platyfish, *Xiphophorus maculatus*. *Proc. 9th Int. Cong. Gen.* 2:960-964. (Supplement to *Caryologia* v. 6.)
- Gorman, G. 1973. The chromosomes of the Reptilia, a cytotaxonomic interpretation. In *Cytotaxonomy and Vertebrate Evolution*, ed. A.B. Chiarelli and E. Capanna, pp. 349-424. Academic Press, New York.
- Green, M.M. 1980. Transposable elements in *Drosophila* and other Diptera. *Ann. Rev. Genet.* 14:109-120.
- Gropp, A., H. Winking, F. Frank, G. Noack, and K. Fredga. 1976. Sex-chromosome aberrations in wood lemmings (*Myopus schistocolor*). *Cytogenet. Cell Genet.* 17:343-358.
- Grossman, A.I., R.B. Short, and G.D. Cain. 1981. Karyotypic evolution and sex chromosome differentiation in schistosomes (Trematoda, Schistosomatidae). *Chromosoma* 84:413-430.
- Gutzke, W.H.N., and G.L. Paukstis. 1983a. A low temperature threshold for sexual differentiation in the painted turtle, *Chrysemys picta*. *Copeia*. In press.
- Gutzke, W.H.N., and G.L. Paukstis. 1983b. Influence of the hydric environment on sexual differentiation of turtles. *J. Exp. Zool.* In press.
- Haldane, J.B.S. 1922. Sex ratio and unisexual sterility in hybrid animals. *J. Genet.* 12:101-109.

- Haldane, J.B.S. 1933. The part played by recurrent mutation in evolution. *Am. Nat.* 67:5-19.
- Haldane, J.B.S. 1957. Sex determination in Metazoa. *Proc. Zool. Soc. Calcutta, Mookerjee Memor.* Vol.:13-28.
- Hall, J.C., W.M. Gelbart, and D.R. Kankel. 1976. Mosaic systems. In *The Genetics and Biology of Drosophila*, ed. M. Ashburner and E. Novitski, vol. 1a. Academic Press, New York.
- Hamilton, W.D. 1967. Extraordinary sex ratios. *Science* 156:477-488.
- Hamilton, W.D. 1979. Wingless and fighting males in fig wasps and other insects. In *Reproductive Competition and Sexual Selection in Insects*, ed. M.S. Blum and N.A. Blum. Academic Press, New York.
- Hansmann, I. 1982. Sex reversal in the mouse. *Cell* 30:331-332.
- Harlos, J., R.A. Brost, and T.D. Galloway. 1980. Observations on a nematode parasite of *Aedes vexans* (Diptera: Culicidae) in Manitoba. *Can. J. Zool.* 58:215-220.
- Harrington, R.W. Jr. 1967. Environmentally controlled induction of primary male gonochorists from eggs of the self-fertilizing hermaphroditic fish, *Rivulus marmoratus* Poey. *Biol. Bull.* 132:174-199.
- Harrington, R.W. Jr. 1968. Delimitation of the thermolabile phenocritical period of sex determination and differentiation in the ontogeny of the normally hermaphroditic fish, *Rivulus marmoratus* Poey. *Physiol. Zool.* 41:447-460.
- Hartl, D.L. 1972. A fundamental theorem of natural selection for sex linkage or arrhenotoky. *Am. Nat.* 106:516-524.
- Hartl, D.L., and S.W. Brown. 1970. The origin of male haploid genetic systems and their expected sex ratio. *Theor. Pop. Biol.* 1:165-190.
- Hartl, D.L., and Y. Hiraizumi. 1976. Segregation distortion. In *The Genetics and Biology of Drosophila*, ed M. Ashburner and Novitski, vol. 1b. Academic Press, New York.
- Hartmann, M. 1956. Die Sexualität. 2d ed. Fischer, Stuttgart.
- Hartmann-Goldstein, I., and G. Koliantz. 1981. Modification of gene suppression in *Drosophila melanogaster* by sex chromosomes. I. Effect of the Y chromosome on variegation in malpighian tubules of W^{m4} larvae. *Heredity* 47:337-345.
- Haseltine, F., K. DePonte, W.R. Breg, M. Genel. 1982. Presence of H-Y antigen in patients with Ullrich-Turner Syndrome and X-chromosome rearrangements. *Am. J. Med. Gen.* 11:97-107.
- Haskins, C.P., P. Young, R.E. Hewitt, and E.F. Haskins. 1970. Stabilised heterozygosis of supergenes mediating certain Y-linked colour patterns in populations of *Lebistes reticulatus*. *Heredity* 25:575-589.
- Hécht, N.B., and J.L. Williams. 1978. Synthesis of RNA by separated heads and tails from bovine spermatozoa. *Biol. Reprod.* 19:573-579.
- Heitz, E. 1928. Das Heterochromatin der Moose. *Jb. wiss. Bot.* 69:762-818.
- Henking, H. 1891. Untersuchungen über die ersten Entwicklungsvorgänge in die Eiern der Insecten. II. Über spermatogenese und deren Beziehung Zur Entwicklung bei *Pyrrochoris apterus*. *Zeit. wiss. Zool.* 51:685-786. (Cited from Austin et al., 1981.)
- Herbst, E.W., K. Fredga, F. Frank, H. Winking, and A. Gropp. 1978. Cytological identification of two X-chromosome types in the wood lemming (*Myopus schisticolor*). *Chromosoma* 69:185-191.
- Heslop-Harrison, J.W. 1919. Studies in the hybrid Bistoninae. IV. Concerning the sex and related problems. *J. Gen.* 9:1-38.
- Hess, O., and G.F. Meyer. 1968. Genetic activities of the Y chromosome during spermatogenesis. *Adv. Genet.* 14:171-223.

- Hiroyoshi, T. 1964. Sex limited inheritance and abnormal sex ratio in strains of the housefly. *Genetics* 50:373-385.
- Hodgkin, J. 1980. More sex determination mutants of *Caenorhabditis elegans*. *Genetics* 96:649-664.
- Hoshiba, H., I. Okada, and A. Kusanagi. 1981. The diploid drone of *Apis cerana japonica* and its chromosomes. *J. Apic. Res.* 20:143-147.
- Houllion, C., and C. Dournon. 1978. Inversion du phénotype sexuel femelle sous l'action d'une température élevée chez l'Amphibian Urodéle *Pleurodeles waltlili* Michah. *C.R. Acad. Ac. Paris (D)* 286:1475-1478.
- Howard, H.W. 1940. The genetics of *Armadillidium vulgare*. I. A general survey of the problems. *J. Gen.* 40:83-108.
- Howard, H.W. 1942. The genetics of *Armadillidium vulgare* Latr. II. Studies on the inheritance of monogeny and amphogeny. *J. Gen.* 44:143-159.
- Howard, H.W. 1958. The genetics of *Armadillidium vulgare*. IV. Lines breeding true for amphogeny and thelygeny. *J. Gen.* 56:1-10.
- Hsu, T.C. 1971. Heterochromatin pattern in metaphase chromosomes of *Drosophila melanogaster*. *J. Hered.* 62:285-287.
- Hubbs, C. 1964. Interaction between a bisexual fish species and its gynogenetic sexual parasite. *Texas Mem. Mus. Bull.* 8:1-72.
- Huey, R.B. 1982. Temperature, physiology, and the ecology of reptiles. In *Biology of the Reptilia*, ed. C. Gans and F.H. Pough, vol. 12, pp. 25-91.
- Humphrey, R.R. 1945. Sex determination in ambystomid salamanders: A study of the progeny of females experimentally converted into males. *Am. J. Anat.* 76:33-66.
- Humphrey, R.R. 1948. Reversal of sex in females of genotype WW in the axolotle (*Siredon* or *Ambystoma mexicanum*) and its bearing upon the role of the Z chromosome in the development of the testis. *J. Exp. Zool.* 109:171-185.
- Huxley, J.S. 1928. Sexual differences of linkage in *Gammarus chevreuxi*. *J. Gen.* 20:145-156.
- Iturra, P., and A. Veloso. 1981. Evidence for heteromorphic sex chromosomes in male amphibians (Anura: Leptodactylidae). *Cytogenet. Cell Genet.* 31:108-110.
- Jacobsen, P. 1957. The sex chromosomes in *Humulus L.* *Hereditas* 43:357-370.
- James, H.C. 1937. Sex ratios and the status of the male in Pseudococcinae (Hem. Coccoidea). *Bull. Ent. Res.* 28:429-461.
- Jan, K.Y., and A.-P. Shu. 1972. Localization of repetitive DNA in house fly chromosomes with a modified Giemsa stain. *Bull. Inst. Zool., Acad. Sinica* 11:29-33.
- John, B., and K.R. Lewis. 1965. *The Meiotic System. Protoplasmatologia VI, F1*, Springer-Verlag, Vienna, pp. 1-335.
- John, B., and K.R. Lewis. 1968. *The Chromosome Complement. Protoplasmatologia VI, A*, Springer-Verlag, Vienna, pp. 1-206.
- John, B., and G.L.G. Miklos. 1979. Functional aspects of satellite DNA and heterochromatin. *Int. Rev. Cytol.* 58:1-114.
- Johnson, A.A. 1955. Life history studies on *Hydromermis contorta* Kohn, a nematode parasite of *Chironomus plumosus*. Ph.D. thesis, Univ. of Illinois.
- Johnson, C. 1977. Evolution of sex ratios in the isopod, *Venezillo evergladensis*. *Evolution* 31:603-610.
- Johnson, G. 1961. Le sexe chez les oniscoïdes. II. Contribution à l'étude de la détermination du sexe chez les Oniscoïdes. *Bull. Biol. Fr. et Belg.* 95:117-267.
- Johnson, M.S. and J.R.G. Turner. 1979. Absence of dosage compensation for a sex-linked enzyme in butterflies (*Heliconius*). *Heredity* 43:71-77.

- Johnstone, R., T.H. Simpson, A.F. Youngson, and C. Whitehead. 1979. Sex reversal in salmonid culture. Part II. The progeny of sex reversed rainbow trout. *Aquaculture* 18:13-19.
- Jones, K.W., J. Prosser, G. Corneo, E. Ginelli, and M. Babrow. 1973. Satellite DNA, constitutive heterochromatin and human evolution. In Modern aspects of cytogenetics: Constitutive heterochromatin in man. Symp. Med. Hoechst 6:45-61. (Cited from Kunkel and Smith, 1982.)
- Jones, K.W., and L. Singh. 1982. Conserved sex-associated repeated DNA sequences in vertebrates. In *Genome Evolution*, ed. G.A. Dover and R.B. Flavell, pp. 135-154. Academic Press, New York, London.
- Jost, A. 1965. Gonadal hormones in the sex differentiation of the mammalian fetus. In *Organogenesis*, ed. R.L. DeHaan and H. Ursprung, pp. 611-628. Holt, Rinehart, & Winston, Inc., New York.
- Juchault, P., and J.-J. Legrand. 1972. Croisements de néo-mâles expérimentaux chez *Armadillidium vulgare* Latr. (Crustacé Isopodae Oniscoide). Mise en évidence d'une hétérogamétie femelle. *C.R. Acad. Sci. (D)* 274:1387-1389.
- Juchault, P., and J.-J. Legrand. 1976. Modification de la sex-ratio dans les croisements entre différentes populations du Crustacé Oniscoide *Armadillidium vulgare* Latr. Notion de déterminisme polygénique et épigénétique du sexe. *Arch. Zool. Exp. Gen.* 117:81-93.
- Juchault, P. and J.-J. Legrand. 1981a. Contribution à l'étude qualitative et quantitative des facteurs contrôlant le sexe dans les populations du Crustacé Isopode terrestre *Armadillidium vulgare* Latreille. II. Populations hébergeant le facteur féminisant F (Bacteroïde intracytoplasmique). *Arch. Zool. Exp. Gen.* 122:65-74.
- Juchault, P. and J.-J. Legrand. 1981b. Contribution à l'étude qualitative et quantitative des facteurs contrôlant le sexe dans les populations du Crustacé Isopode terrestre *Armadillidium vulgare* Latreille. III. Populations n'hébergeant pas le facteur féminisant F (Bacteroïde intracytoplasmique). *Arch. Zool. Exp. Gen.* 122: 117-131.
- Juchault, P., J.-J. Legrand, and J.-P. Mocquard. 1980. Contribution à l'étude qualitative et quantitative des facteurs contrôlant le sexe dans les populations du Crustacé Isopode terrestre *Armadillidium vulgare* Latreille. I. La population de Niort (Deux-Sèvres). *Arch. Zool. Exp. Gen.* 121:3-27.
- Kallman, K.D. 1965. Genetics and geography of sex determination in the poeciliid fish, *Xiphophorus maculatus*. *Zoologica* 50:151-190.
- Kallman, K.D. 1968. Evidence for the existence of transformer genes for sex in the teleost *Xiphophorus maculatus*. *Genetics* 60:811-828.
- Kallman, K.D. 1970. Sex determination and the restriction of sex-linked pigment patterns to the X and Y chromosomes in populations of a poeciliid fish, *Xiphophorus maculatus*, from the Belize and Sibun rivers of British Honduras. *Zoologica* 55:1-16.
- Kallman, K.D. 1973. The sex determining mechanism of the platyfish, *Xiphophorus maculatus*. In *Genetics and Mutagenesis of Fish*, ed. J.H. Schroder. Springer-Verlag, Berlin.
- Kallman, K.D. 1983. A new look at sex determination in poeciliid fishes. *Evolutionary Biology*. In press.
- Kallman, K.D., and J.W. Atz. 1967. Gene and chromosome homology in fishes of the genus *Xiphophorus*. *Zoologica* 51:107-135.
- Karlin, S., and U. Lieberman. 1974. Random temporal variation in selection intensities: Case of large population size. *Theor. Pop. Biol.* 6:355-382.

- Kawamura, T., and M. Nishioka. 1977. Aspects of the reproductive biology of Japanese anurans. In *The Reproductive Biology of Amphibians*, ed. D.H. Taylor and S.I. Guttman. Plenum Publ. Corp., New York.
- Kellen, W.R., H.C. Chapman, T.B. Clark, and J.E. Lindgren. 1965. Host-parasite relationships of some *Thelohania* from mosquitoes (Nosematidae: Microsporidia). *J. Invert. Pathol.* 7:161-166.
- Kerr, R.W. 1970. Inheritance of DDT resistance in a laboratory colony of the housefly, *Musca domestica*. *Aust. J. Biol. Sci.* 23:377-400.
- Kerr, W.E. 1974. Advances in cytology and genetics of bees. *Ann. Rev. Ent.* 19:253-268.
- Kezer, J., and S.K. Sessions. 1979. Chromosome variation in the plethodontid salamander, *Aneides ferreus*. *Chromosoma* 71:65-80.
- Kihara, H. 1953. Genetics of *Bombyx* and *Drosophila*: A comparison of materials, methods, and results. *Seiken Zihō, Rep. Kihara Inst. Biol. Res.* 6:15-29. (Cited in Goldschmidt, 1955, p. 434.)
- King, M. 1977. The evolution of sex chromosomes in lizards. In *Evolution and Reproduction*, ed. J. Calaby and H. Tyndale-Briscoe, pp. 55-60. Aust. Acad. Sci., Canberra.
- Kitchin, R.M. 1970. A radiation analysis of a Comstockiella chromosome system: Destruction of heterochromatic chromosomes during spermatogenesis in *Parlatoria oleae* (Coccoidea: Diaspididae). *Chromosoma* 31:165-197.
- Klass, M., N. Wolf, and D. Hirsh. 1976. Development of the male reproductive system and sexual transformation in the nematode *Caenorhabditis elegans*. *Dev. Biol.* 52:1-18.
- Klevecz, R.R., and T.C. Hsu. 1964. The differential capacity for RNA synthesis among chromosomes: A cytological approach. *Proc. Nat. Acad. Sci. USA* 52:811-817.
- Knapp, E. 1936. Zur genetik von *Sphaerocarpus* (tetradenanalytische Untersuchungen.) *Ber. Deut. Bot. Ges.* 54:58-69. (Cited from Allen, 1945.)
- Kosswig, C. 1964. Polygenic sex determination. *Experientia* 20:190-199.
- Kunkel, L.M., and K.D. Smith. 1982. Evolution of human Y-chromosome DNA. *Chromosoma* 86:209-228.
- Lande, R. 1981. The minimum number of genes contributing to quantitative variation between and within populations. *Genetics* 99:541-553.
- Lefevre, G., Jr. 1974. The relationship between genes and polytene chromosome bands. *Ann. Rev. Gen.* 8:51-62.
- Legrand, J.-J., and P. Juchault. 1969a. Le déterminisme de l'intersexualité chez les Crustaces Isopodes terrestres: Correlation entre intersexualité et monogenie. *C.R. Acad. Sci. (D)* 268:1647-1649.
- Legrand, J.-J., and P. Juchault. 1969b. Le déterminisme de la monogenie chez les Oniscoïdes. *C.R. Acad. Sci. (D)* 268:1774-1777.
- Legrand, J.-J., and P. Juchault. 1970. Modification experimentale de la proportion des sexes chez les Crustaces Isopodes terrestres: Induction de la thélygénie chez *Armadillidium vulgare* Latr. *C.R. Acad. Sci. (D)* 270:706-708.
- Legrand, J.-J., and P. Juchault. 1972. Mise en évidence dans une population d'*Armadillidium vulgare* Latr. (Crustacé Isopode Oniscoïde) de deux types de lignées arrhenogénès en relation avec des facteurs épigénétiques à effet respectivement masculinisant et feminisant. *C.R. Acad. Sci. (D)* 274:1554-1557.
- Lester, D.S., R.H. Crozier, and E. Shipp. 1979a. Recombination in the male housefly, *Musca domestica*. *Experientia* 35:175.
- Lester, D.S., R.H. Crozier, and E. Shipp. 1979b. Cytological and genetic localization

- of a Y-autosome translocation in an Australian strain of the housefly, *Musca domestica*. *Experientia* 35:172.
- Leutert, R. 1975. Sex determination in *Bonellia*. In *Intersexuality in the Animal Kingdom*, ed. R. Reinboth, pp. 84–90. Springer-Verlag, Berlin.
- Levitian, M. 1951. Selective differences between males and females in *Drosophila robusta*. *Am. Nat.* 85:385–388.
- Levitian, M. 1963. A maternal factor which breaks paternal chromosomes. *Nature* 200:437–438.
- Lewis, D. 1941. Male sterility in natural populations of hermaphrodite plants. *New Phytol.* 40:50–63.
- Lewis, K.R. 1961. The genetics of bryophytes. *Trans. Brit. Bryol. Soc.* 4:111–130.
- Lewis, K.R., and K. Benson-Evans. 1960. The chromosomes of *Cryptothallus mirabilis* (Hepaticae: Ricciaceae). *Phyton* 14:21–35.
- Lewis, K.R., and B. John. 1968. The chromosomal basis of sex determination. *Int. Rev. Cytol.* 17:277–379.
- Lewontin, R.C., L.R. Ginzburg, and S.D. Tuljapurkar. 1978. Heterosis as an explanation for large amounts of genic polymorphism. *Genetics* 88:149–170.
- Lindsley, D.L., C.W. Edington, and E.S. von Halle. 1960. Sex-linked recessive lethals in *Drosophila* whose expression is suppressed by the Y chromosome. *Genetics* 45:1649–1670.
- Lindsley, D.L., and E.H. Grell. 1968. *Genetic variations of Drosophila melanogaster*. *Carnegie Inst. Wash. Publ.* 627.
- Lizarralde, M.S., N.O. Bianchi, and M.S. Merani. 1982. Cytogenetics of South American akodont rodents (Cricetidae). VII. Origin of sex chromosome polymorphism in *Akodon azarae*. *Cytologia* 47:183–193.
- Lloyd, D.G. 1974. Theoretical sex ratios of dioecious and gynodioecious angiosperms. *Heredity* 32:11–34.
- Lobato, L., G. Cantos, B. Araujo, N.O. Bianchi, and S. Merani. 1982. Cytogenetics of the South American akodont rodents (Cricetidae) X. *Akodon mollis*: A species with XY females and B chromosomes. *Genetica* 57:199–205.
- Love, A. 1944. Cytogenetic studies on *Rumex* subgenus *acetosella*. *Hereditas* 30:1–136.
- Lucchesi, J.C. 1977. Dosage compensation: Transcription-level regulation of X-linked genes in *Drosophila*. *Amer. Zool.* 17:685–693.
- Lucchesi, J.C. 1978. Gene dosage compensation and the evolution of sex chromosomes. *Science* 202:711–716.
- Lucchesi, J.C., and T. Skripsky. 1981. The link between dosage compensation and sex differentiation in *Drosophila melanogaster*. *Chromosoma* 82:217–227.
- Lutz-Ostertag, L. 1966. Action de la chaleur sur le développement de l'appareil genital de l'embryon de Caille (*Coturnix coturnix japonica*). *C.R. Acad. Sci. (D)* 262:133–135.
- Lyon, M.F. 1961. Gene action in the X-chromosome of the mouse (*Mus musculus* L.). *Nature* 190:372–373.
- Lyon, M.F., B.M. Cattanach, and H.M. Charlton. 1981. Genes affecting sex differentiation in mammals. In *Mechanisms of Sex Differentiation in Animals and Man*, ed. C.R. Austin and R.G. Edwards, pp. 329–386. Academic Press, New York, London.
- Lyon, M.F., and S.G. Hawkes. 1970. An X-linked gene for testicular feminization of the mouse. *Nature* 227:1217–1219.
- Lytle, T.W. 1977. Experimental population genetics of meiotic drive systems. I.

- Pseudo-Y chromosomal drive as a means of eliminating cage populations of *Drosophila melanogaster*. *Genetics* 86:413-445.
- Lyttle, T.W. 1982. A theoretical analysis of the effect of sex chromosome aneuploidy on X and Y chromosome meiotic drive. *Evolution* 36:822-831.
- McCarrey, J.R., and U.K. Abbott. 1979. Mechanisms of genetic sex determination, gonadal sex differentiation, and germ-cell development in animals. *Adv. Gen.* 20:217-290.
- McCloskey, J.D. 1966. The problem of gene activity in the sperm of *Drosophila melanogaster*. *Am. Nat.* 100:211-218.
- McClung, C.E. 1902a. Notes on the accessory chromosome. *Anat. Anz.* 20:220-226.
- McClung, C.E. 1902b. The accessory chromosome—Sex-determinant? *Biol. Bull.* 3:43-84.
- McDonald, I. 1971. A male-producing strain of the house fly. *Science* 172:489.
- McDonald, I.C., P. Evenson, C.A. Nickel, and O.A. Johnson. 1978. House fly genetics: Isolation of a female determining factor on chromosome 4. *Ann. Entomol. Soc. Amer.* 71:692-694.
- McDonald, I.C., D.E. Overland, R.A. Leopold, M.E. Degrujiller, P.B. Morgan, and H.C. Hoffman. 1975. Genetics of houseflies. *J. Heredity* 66:137-140.
- MacDonald, W.W., and P.M. Sheppard. 1965. Cross-over values in the sex chromosomes of the mosquito *Aedes aegypti* and evidence of the presence of inversions. *Med. Parasit.* 59:74-87.
- McKusick, V.A. 1978. *Mendelian Inheritance in Man: Catalogs of Autosomal Dominant, Autosomal Recessive, and X-linked Phenotypes*. 5th ed. Johns Hopkins Univ. Press, Baltimore.
- McLaren, A. 1981. *Germ Cells and Soma: A New Look at an Old Problem*. Yale Univ. Press, New Haven, Conn., London.
- Madl, J.E., and R.K. Herman. 1979. Polyploids and sex determination in *Caenorhabditis elegans*. *Genetics* 93:393-402.
- Mainx, F. 1964. The genetics of *Megaselia scalaris* Loew (Phoridae): A new type of sex determination in Diptera. *Am. Nat.* 98:415-430.
- Maroni, G., and J.C. Lucchesi. 1980. X-chromosome transcription in *Drosophila*. *Chromosoma* 77:253-261.
- Marsh, J.L., and E. Wieschaus. 1978. Is sex determination in germ line and soma controlled by separate genetic mechanisms? *Nature* 272:249-251.
- Martin, G., P. Juchault, and J.-J. Legrand. 1973. Mise en évidence d'un microorganisme intracytoplasmique symbiose de l'oniscoïde *Armadillidium vulgare* Latr. dont la présence accompagné l'intersexualité ou la féminisation total des mâles génétiques de la lignée thélygène. *C.R. Acad. Sci. (D)* 276:2313-2316.
- Martin, J. 1967. Meiosis in inversion heterozygotes in Chironomidae. *Can. J. Gen. Cytol.* 9:255-268.
- Martin, J., C. Kuvangkadilok, D.H. Peart, and B.T.O. Lee. 1980. Multiple sex determining regions in a group of related *Chironomus* species (Diptera: Chironomidae). *Heredity* 44:367-382.
- Masui, K. 1967. *Sex Determination and Sexual Differentiation in the Fowl*. Univ. of Tokyo Press, Tokyo, Japan.
- Maynard Smith, J. 1978. *The Evolution of Sex*. Cambridge, Univ. Press, Cambridge, U.K.
- Maynard Smith, J. 1980. A new theory of sexual investment. *Behav. Ecol. Sociobiol.* 7:247-251.

- Maynard Smith, J. 1982. *Evolution and the Theory of Games*. Cambridge Univ. Press, Cambridge, U.K.
- Mengden, G.A. 1981. Linear differentiation of the C-band pattern of the W chromosome in snakes and birds. *Chromosoma* 83:275-287.
- Mengden, G.A., and A.D. Stock. 1980. Chromosomal evolution in serpentes: A comparison of G and C chromosome banding patterns of some colubrid and boid genera. *Chromosoma* 79:53-64.
- Metz, C.W. 1938. Chromosome behavior, inheritance and sex determination in *Sciara*. *Am. Nat.* 72:485-520.
- Mikamo, K., and E. Witschi. 1963. Functional sex reversal in genetic females of *Xenopus laevis*, induced by implanted testes. *Genetics* 48:1411-1421.
- Mikamo, K., and E. Witschi. 1964. Masculinization and breeding of WW *Xenopus*. *Experientia* 20:622-623.
- Milani, R. 1969. Le variazioni delle formule sessuali di *Musca domestica* L. come possibile esempio di coadattamenti genetici. *Bollettino di Zoologia* 36:372-373.
- Milani, R. 1971. Genetics of factors affecting fertility and of sex ratio distortions in the house fly. Sterility principle for insect control or eradication. In *Proceedings of a Symposium, Athens, 14-18 September 1970*. International Atomic Energy Agency Proceedings Series, Vienna, pp. 381-297.
- Milani, R. 1975. The house fly, *Musca domestica*. In *Handbook of Genetics. Vol. 3. Invertebrates of Genetic Interest*, ed. R.C. King, pp. 377-399. Plenum Press, New York.
- Milani, R., P.G. Rubini, and M.G. Franco. 1967. Sex determination in the housefly. *Genetica Agraria* 21:385-411.
- Miller, J.D., and C.J. Limpus. 1981. Incubation period and sexual differentiation in the green turtle, *Chelonia mydas* L. in *Proceedings of Melbourne Herp. Symposium*, ed. C. Banks and A. Martin, pp. 66-73. Zoological Board of Victoria, Australia.
- Miller, R.A. 1938. Spermatogenesis in a sex-reversed female and in normal males of the domestic fowl, *Gallus domesticus*. *Anat. Rec.* 70:155-189.
- Mittwoch, U. 1967. *Sex Chromosomes*. Academic Press, New York, London.
- Mittwoch, U. 1973. *Genetics of Sex Differentiation*. Academic Press, New York.
- Moreira-Filho, C.A., S.P.A. Toledo, V.R. Bagnolli, O. Frota-Pessoa, H. Bisi, and A. Wajntal. 1979. H-Y antigen in Swyer syndrome and the genetics of XY gonadal dysgenesis. *Hum. Genet.* 53:51-56.
- Moreira-Filho, O., L.A.C. Bertollo, and P.M. Galetti, Jr. 1980. Evidences for a multiple sex chromosome system with female heterogamety in *Apareiodon affinis* (Pisces, Parodontidae). *Caryologia* 33:83-91.
- Morreale, S.J., G.J. Ruiz, J.R. Spotila, and E.A. Standora. 1982. Temperature-dependent sex determination: Current practices threaten conservation of sea turtles. *Science* 216:1245-1247.
- Morris, T. 1968. The XO and OY chromosome constitutions in the mouse. *Gen. Res.* 12:125-137.
- Moses, M.J., S.J. Counce, and D.F. Paulson. 1975. Synaptonemal complex complement of man in the spreads of spermatocytes, with details of the sex chromosome pair. *Science* 187:363-365.
- Moses, M.J., P.A. Poorman, T.H. Roderick, and M.T. Davisson. 1982. Synaptonemal complex analysis of mouse chromosomal rearrangements. IV. Synapsis and synaptic adjustment in two paracentric inversions. *Chromosoma* 84:457-474.

- Motara, M.A. 1982. Giemsa C-banding in four species of mosquitoes. *Chromosoma* 86:319-323.
- Motara, M.A., and K.S. Rai. 1977. Chromosomal differentiation in two species of *Aedes* and their hybrids revealed by Giemsa C-banding. *Chromosoma* 64:125-132.
- Mrosovsky, N. 1980. Thermal biology of sea turtles. *Amer. Zool.* 20:531-547.
- Mukai, T., S.I. Chigusa, L.E. Mettler, and J.F. Crow. 1972. Mutation rate and dominance of genes affecting viability in *Drosophila melanogaster*. *Genetics* 72:335-355.
- Muller, H.J. 1914. A gene for the fourth chromosome of *Drosophila*. *J. Exp. Zool.* 17:325-336.
- Muller, H.J. 1918. Genetic variability, twin hybrids and constant hybrids, in a case of balanced lethal factors. *Genetics* 3:422-499.
- Muller, H.J. 1932. Some genetic aspects of sex. *Am. Nat.* 66:118-138.
- Muller, H.J. 1950. Evidence of the precision of genetic adaptation. *Harvey Lect.* 43:165-229.
- Muller, H.J. 1964. The relation of recombination to mutational advance. *Mutat. Res.* 1:2-9.
- Muller, H.J., and S.M. Gershenson. 1935. Inert regions of chromosomes as the temporary products of individual genes. *Proc. Nat. Acad. Sci. USA* 21:69-75.
- Muller, H.J., and T.S. Painter. 1932. The differentiation of the sex chromosomes of *Drosophila* into genetically active and inert regions. *Z. Ind. Abst. Vererbse.* 62:316-365.
- Muller, H.J., and F. Settles. 1927. The nonfunctioning of genes in spermatozoa. *Z. Indukt. Abstamm.-Vererbungsl.* 43:285-312.
- Muller, U. 1982. Identification and function of serologically detectable H-Y antigen. *Human Genet.* 61:91-94.
- Muller, U., and U. Wolf. 1979. Cross reactivity to mammalian anti-H-Y antiserum in teleostean fish. *Differentiation* 14:185-187.
- Muller, U., M.T. Zenzes, U. Wolf, W. Engel, and J.P. Weniger. 1979. Appearance of H-W (H-Y) antigen in the gonads of oestradiol sex reversed male chicken embryos. *Nature* 280:142-144.
- Murofushi, M., S. Oikawa, S. Nishikawa, and T.H. Yosida. 1980. Cytogenetical studies on fishes. III. Multiple sex chromosome mechanism in the filefish, *Stephanolepis cirrifer*. *Jap. J. Gen.* 55:127-132.
- Muth, A., and J.J. Bull. 1981. Sex determination in desert iguanas: Does incubation temperature make a difference? *Copeia* 1981:869-870.
- Nakagome, Y. 1982. Inactivation centers in the X chromosome of man. *Am. J. Hum. Gen.* 34:182-194.
- Nei, M. 1969. Linkage modification and sex difference in recombination. *Genetics* 63:681-699.
- Nei, M. 1970. Accumulation of nonfunctional genes on sheltered chromosomes. *Am. Nat.* 104:311-322.
- Nelson, G.A., K.K. Lew, and S. Ward. 1978. *Intersex*, a temperature-sensitive mutant of the nematode *Caenorhabditis elegans*. *Dev. Biol.* 66:386-409.
- Nelson-Rees, W.A. 1960. A study of sex predetermination in the mealy bug *Planococcus citri* (Risso). *J. Exp. Zool.* 144:111-137.
- Nelson-Rees, W.A., M.A. Hoy, and R.T. Roush. 1980. Heterochromatinization, chromatin elimination and haploidization in the parahaploid mite *Metaseiulus occidentalis* (Nesbitt) (Acarina:Phytoseiidae). *Chromosoma* 77:263-276.

- Neuhaus, M.J. 1939. A cytogenetic study of the Y chromosome of *Drosophila melanogaster*. *J. Genet.* 37:229-254.
- Newton, M.E. 1977. Heterochromatin as a cyto-taxonomic character in liverworts: *Pellia*, *Riccardia*, and *Cryptothallus*. *J. Bryol.* 9:327-342.
- Newton, M.E., D.I. Southern, and R.J. Wood. 1974. X and Y chromosomes of *Aedes aegypti* (L.) distinguished by Giemsa C-banding. *Chromosoma* 49:41-49.
- Nigon, V. 1949a. Effets de la polyploidie chez un nematode libre. *C.R. Acad. Sci.* 228:1161-1162. (Cited from Madl and Herman, 1979.)
- Nigon, V. 1949b. Les modalités de la reproduction et le déterminisme de sexe chez quelques nématodes libres. *Ann. Sci. Nat. Zool.* ser 11, 2:1-132. (Cited from Haldane, 1957; Madl and Herman, 1979.)
- Nigon, V. 1951a. La gamétogénèse d'un nématode tetraploïde obtenu par voie expérimentale. *Bull. Soc. Hist. Nat. Toulouse* 86:192-200. (Cited from Madl and Herman, 1979.)
- Nigon, V. 1951b. Polyplioïde expérimentale chez un nematode libre, *Rhabditis elegans* Maupas. *Bull. Biol. Fr. et Belg.* 85:187-225. (Cited from Madl and Herman, 1979.)
- Norris, D.M. 1979. The mutualistic fungi of Xyleborini beetles. In *Insect-fungus symbiosis*, ed. Batra. Allanheld, Osmun, Montclair, N.J.
- Nur, U. 1963. Meiotic parthenogenesis and heterochromatization in a soft scale, *Pulvinaria hydrangeae* (Coccoidea: Homoptera). *Chromosoma* 14:123-139.
- Nur, U. 1967. Reversal of heterochromatization in the activity of the paternal chromosome set in the male mealy bug. *Genetics* 56:375-389.
- Nur, U. 1971. Parthenogenesis in coccids (Homoptera). *Amer. Zool.* 11:301-308.
- Nur, U. 1974. The expected changes in the frequency of alleles affecting the sex ratio. *Theor. Pop. Biol.* 5:143-147.
- Nur, U. 1977. Maternal inheritance of enzymes in the mealybug *Pseudococcus obscurus* (Homoptera). *Genetics* 86:149-160.
- Nur, U. 1980. Evolution of unusual chromosome systems in scale insects (Coccoidea: Homoptera). In *Insect Cytogenetics*, ed. R.L. Blackman, G.M. Hewitt, and M. Ashburner, pp. 97-118. Blackwell Sci. Publ., Oxford, London.
- O'Brien, S.J., and R.J. MacIntyre. 1978. Genetics and biochemistry of enzymes and specific proteins of *Drosophila*. In *The Genetics and Biology of Drosophila*, ed. M. Ashburner and T.R.F. Wright, pp. 396-551. Academic Press, New York, London.
- Ohno, S. 1967. *Sex Chromosomes and Sex-Linked Genes*. Springer-Verlag, Berlin.
- Ohno, S. 1979. *Major Sex-Determining Genes*. Springer-Verlag, Berlin.
- Oktay, M. 1959a. Über Ausnahmemaenchen bei *Platypoecilus maculatus* und eine neue Sippe mit XX-Maennchen und XX-Weibchen. *Istanbul Universitesi fen Fakultesi Mecmuasi B.* 24:75-91.
- Oktay, M. 1959b. Weitere Untersuchungen über eine Ausnahme (XX-) Sippe des *Platypoecilus maculatus* mit polygene Geschlechtsbestimmung. *Rev. Fac. Sci. Istanbul. Ser. B.* 24:225-233.
- Oliver, J.H., Jr. 1971. Parthenogenesis in mites and ticks. *Am. Zool.* 11:283-299.
- Oliver, J.H., Jr. 1977. Cytogenetics of mites and ticks. *Ann. Rev. Ent.* 22:407-429.
- Oliver, J.H., Jr. 1983. Chromosomes, genetic variation, and reproductive strategies among mites and ticks. *Bull. Ent. Soc. Amer.* (June, in press).
- Orgel, L.E., and F.H.C. Crick. 1980. Selfish DNA: The ultimate parasite. *Nature* 284:604-607.
- Orzack, S.H., J.J. Sohn, K.D. Kallman, S.A. Levin, and R. Johnston. 1980. Maintenance of the three sex chromosome polymorphism in the platyfish, *Xiphophorus maculatus*. *Evolution* 34:663-672.

- Osgood, D. 1980. Sex ratio and incubation temperature in a watersnake. *Quart. Rev. Biol.* 55:21 (App).
- Packard, G.C., M.J. Packard, and T.J. Boardman. 1981b. Patterns and possible significance of water exchanges by flexible-shelled eggs of painted turtles (*Chrysemys picta*). *Physiol. Zool.* 54:165-178.
- Packard, G.C., M.J. Packard, T.J. Boardman, and M.D. Ashen. 1981a. Possible adaptive value of water exchanges in flexible-shelled eggs of turtles. *Science* 213:471-473.
- Packard, G.C., T.L. Taigen, T.J. Boardman, M.J. Packard, and C.R. Tracy. 1979. Changes in mass of softshell turtle (*Trionyx spiniferus*) eggs incubated on substrates differing in water potential. *Herpetologica* 35:78-86.
- Page, R.E., Jr., and R.A. Metcalf. 1982. Multiple mating, sperm utilization, and social evolution. *Am. Nat.* 119:263-281.
- Parenti, U. 1962. Ricerche sulla sessualità dei Mermitidi. I. Rapporto sessi in una popolazione di *Paramermis contorta*. *Archivio Zoologico Italiano* 47:209-224.
- Parenti, U. 1965. Male and female influence of adult individuals on undifferentiated larvae of the parasitic nematode *Paramermis contorta*. *Nature* 207:105-106.
- Park, E.-H., and H. Grimm. 1981. Distribution of C-band heterochromatin in the ZW sex chromosomes of European and American eels (Anguillidae, Teleostomi). *Cytogenet. Cell Genet.* 31:167-174.
- Park, E.-H., and Y.S. Kang. 1979. Karyological confirmation of conspicuous ZW sex chromosomes in two species of Pacific anguillloid fishes (Anguilliformes: Teleostomi). *Cytogenet. Cell Genet.* 23:33-38.
- Parker, G.A. 1982. Why are there so many tiny sperm? Sperm competition and the maintenance of two sexes. *J. Theor. Biol.* 96:281-294.
- Parker, G.A., R.R. Baker, and V.G.F. Smith. 1972. The origin and evolution of gamete dimorphism and the male-female phenomenon. *J. Theor. Biol.* 36:529-553.
- Pathak, S., and A.D. Stock. 1974. The X-chromosomes of mammals: Karyological homology as revealed by banding techniques. *Genetics* 78:703-714.
- Patterson, J.T. 1931. The production of gynandromorphs in *Drosophila melanogaster* by X-rays. *J. Exp. Zool.* 60:173-211.
- Patterson, J.T. 1938. Aberrant forms in *Drosophila* and sex differentiation. *Am. Nat.* 72:193-206.
- Patterson, J.T., and W.S. Stone. 1952. *Evolution in the genus Drosophila*. Macmillan, New York. (Cited from White, 1973.)
- Patterson, J.T., W.S. Stone, and S. Bedichek. 1937. Further studies on X-chromosome balance on *Drosophila*. *Genetics* 22:407-426.
- Paukstis, G.L., Gutzke, W.H.N., and G.C. Packard. 1983. Environmental sex determination of the turtle *Chrysemys picta*: Effects of fluctuating temperature and substrate water potential on hatchling sex ratios. Forthcoming.
- Peccinini-Seale, D. 1981. New developments in vertebrate cyt taxonomy. IV. Cytogenetic studies of reptiles. *Genetica* 56:123-148.
- Peters, G. 1964. Vergleichende Untersuchungen an drei Subspecies von *Xiphophorus helleri* Hechel (Pisces). *Z. Zool. Syst. Evolutionsforsch.* 2:185-271.
- Petersen, J.J. 1972. Factors affecting sex ratios of a mermithid parasite of mosquitoes. *J. Nematology* 4:83-87.
- Petersen, J.J. 1977. Effects of host size and parasite burden on sex ratio in the mosquito parasite *Octomymermis muspratti*. *J. Nemat.* 9:343-346.
- Pieau, C. 1971. Sur la proportion sexuelle chez les embryons de deux Cheloniens

- (*Testudo graeca* L. et *Emys orbicularis* L.) issus d'oeufs incubés artificiellement. *C.R. Acad. Sci. Paris (D)* 272:3071-3074.
- Pieau, C. 1972. Effets de la température sur le développement des glandes génitales chez les embryons de deux Cheloniens, *Emys orbicularis* L. et *Testudo graeca* L. *C.R. Acad. Sci. Paris (D)* 274:719-722.
- Pieau, C. 1973. Nouvelles données expérimentales concernant les effets de la température sur la différenciation sexuelle chez les embryons de Cheloniens. *C.R. Acad. Ac. Paris (D)* 277:2789-2792.
- Pieau, C. 1974. Sur la différenciation sexuelle chez des embryons d'*Emys orbicularis* L. (Chélonien) issus d'oeufs incubés dans le sol au cours de l'été 1973. *Bull. Soc. Zool. Fr.* 99:363-376.
- Pieau, C. 1975a. Temperature and sex differentiation in embryos of two chelonians, *Emys orbicularis* L. and *Testudo graeca* L. In *Intersexuality in the Animal Kingdom*, ed. R. Reinboth, pp. 332-339. Springer-Verlag, Berlin.
- Pieau, C. 1975b. Effets des variations thermiques sur la différenciation du sexe chez les vertébrés. *Bull. Soc. Zool. Fr.* 100:67-76.
- Pieau, C. 1976. Données récentes sur la différenciation sexuelle en fonction de la température chez les embryons d'*Emys orbicularis* (Chélonien). *Bull. Soc. Zool. Fr.* 101(suppl. 4):46-53.
- Pieau, C. 1978. Effets de températures d'incubation basses et élevées sur la différenciation sexuelle chez des embryons d'*Emys orbicularis* L. (Chélonien). *C.R. Acad. Sci. Paris (D)* 286:121-124.
- Pieau, C. 1982. Modalities of the action of temperature on sexual differentiation in field-developing embryos of the European pond turtle *Emys orbicularis* (Emydidae). *J. Exp. Zool.* 220:353-360.
- Pieau, C., and M. Dorizzi. 1981. Determination of temperature sensitive stages for sexual differentiation of the gonads in embryos of the turtle *Emys orbicularis* (Testudines, Emydidae). *J. Morph.* 170:373-382.
- Pipkin, S.D. 1960. Sex balance in *Drosophila melanogaster*: Aneuploidy of long regions of chromosome 3, using the triploid method. *Genetics* 45:1205-1216.
- Poinar, G.O. 1979. *Nematodes for Biological Control of Insects*. CRC Press, Boca Raton, Fla.
- Post, R.J. 1982. Sex-linked inversions in blackflies (Diptera: Simuliidae). *Heredity* 48:85-93.
- Poulson, D.F. 1963. Cytoplasmic inheritance and hereditary infections in *Drosophila*. In *Methodology in Basic Genetics*, ed. W.J. Burdette. Holden-Day, San Francisco.
- Rao, S.R.V., and S. Ali. 1982. Insect sex chromosomes. IV. A presumptive hyperactivation of the male X chromosome in *Acheta domesticus* (L.). *Chromosoma* 86:325-339.
- Rao, S.R.V., and P. Arora. 1979. Insect sex chromosomes. III. Differential susceptibility of homologous X chromosomes of *Gryllotalpa fossor* to ^3H -Urd-induced aberrations. *Chromosoma* 74:241-252.
- Rastan, S. 1982. Primary non-random X-inactivation caused by controlling elements in the mouse demonstrated at the cellular level. *Gen. Res.* 40:139-147.
- Ray-Chaudhuri, R. 1973. Cytotaxonomy and chromosome evolution in birds. In *Cytotaxonomy and Vertebrate Evolution*, ed. A.B. Chiarelli and E. Capanna, pp. 425-483. Academic Press, New York.
- Ray-Chaudhuri, S.P., L. Singh, and T. Sharma. 1970. Sexual dimorphism in somatic interphase nuclei of snakes. *Cytogenet.* 9:410-423.

- Raynaud, A., and C. Pieau. 1972. Effets de diverses températures d'incubation sur le développement somatique et sexuel des embryons de lézard vert (*Lacerta vividis* Laur.). *C.R. Acad. Sci. Paris (D)* 275:2259-2262.
- Richards, C.M., and G.W. Nace. 1978. Gynogenetic and hormonal sex reversal used in tests of the XX-XY hypothesis of sex determination in *Rana pipiens*. *Growth* 42:319-331.
- Ropers, H.-H., and U. Wiberg. 1982. Evidence for X-linkage and non-activation of steroid sulphatase locus in wood lemming. *Nature* 296:766-767.
- Rosin, S., and J. Fischer. 1972. Polymorphismus des realisators für männliches Geschlecht bei *Chironomus*. *Rev. Suisse Zool.* 79:119-141.
- Rothenbuhler, W.C. 1957. Diploid male tissue as new evidence on sex determination in honeybees. *J. Hered.* 48:160-168.
- Rothfels, K.H. 1980. Chromosomal variability and speciation in blackflies. In *Insect Cytogenetics*, ed. R.L. Blackman, G.M. Hewitt, and M. Ashburner, pp. 207-224. Blackwell Sci. Publ., Oxford, London.
- Royer, M. 1975. Hermaphroditism in insects. Studies on *Icerya purchasi*. In *Intersexuality in the Animal Kingdom*, ed. R. Reinboth, pp. 135-145. Springer-Verlag, Berlin.
- Rubin, D.A. 1984. Effect of pH on sex ratio in cichlids and poeciliids (Teleostei) *Copeia*. In press.
- Rubini, P.G., M.G. Franco, and S. Vanossi Este. 1972. Polymorphisms for heterochromosomes and autosomal sex-determinants in *Musca domestica* L. *Atti IX Congresso Italiano Ent.*:341-352.
- Rubini, P.G., M. Vecchi, and M.G. Franco. 1980. Mitotic recombination in *Musca domestica* L. and its influence on mosaicism, gynandromorphism and recombination in males. *Genet. Res.* 35:121-130.
- Rupes, V., and J. Pinterova. 1975. Genetic analysis of resistance to DDT, Methoxychlor and Fenitrothion in two strains of housefly (*Musca domestica*). *Ent. Exp. & Appl.* 18:480-491.
- Ryan, S.L., and G.B. Saul. 1968. Post-fertilization effect of incompatibility factors in *Mormonilla*. *Molec. Gen. Genet.* 103:29-36.
- Ryttman, H., H. Tegelstrom, and H. Jansson. 1979. G- and C-banding in four related *Larus* species (Aves). *Hereditas* 91:143-148.
- Sabour, M. 1972. RNA synthesis and heterochromatization in early development of a mealybug. *Genetics* 70:291-298.
- Sawicki, J.A., and R.J. MacIntyre. 1978. Localization at the ultrastructural level of maternally derived enzyme and determination of the time of paternal gene expression for acid phosphatase-1 in *Drosophila melanogaster*. *Dev. Biol.* 63:47-58.
- Schmid, M. 1980. Chromosome banding in Amphibia. V. Highly differentiated ZW/ZZ sex chromosomes and exceptional genome size in *Pyxicephalus adspersus* (Anura, Ranidae). *Chromosoma* 80:69-96.
- Schmid, M., J. Olert, and C. Klett. 1979. Chromosome banding in Amphibia. III. Sex chromosomes in *Triturus*. *Chromosoma* 71:29-55.
- Schrader, F., and S. Hughes-Schrader. 1931. Haploidy in metazoa. *Quart. Rev. Biol.* 6:411-438.
- Schreck, C.B. 1974. Hormonal treatment and sex manipulation in fishes. In *Control of sex in fishes*, ed. C.B. Schreck, pp. 84-106. Publ. of Virginia Polyt. Inst. and State Univ., Blacksburg, Va.
- Schultz, R.J. 1977. Evolution and ecology of unisexual fish. *Evol. Biol.* 10:277-331.

- Schupback, T. 1982. Autosomal mutations that interfere with sex determination in somatic cells of *Drosophila* have no direct effect on the germline. *Dev. Biol.* 89:117-127.
- Scott, C.D., P.W. Gregory. 1965. An XXY trisomic in an intersex of *Bos taurus*. *Genetics* 52:473-474 (Abstract).
- Scudo, F.M. 1964. Sex population genetics. *Ricerca Sci.* 34, II-B:93-146.
- Scudo, F.M. 1967. Criteria for the analysis of multifactorial sex determination. *Mon. Zool. Ital.* 1:1-21.
- Serrano, J. 1981. Male achiasmatic meiosis in *Caraboidea* (Coleoptera, Adephaga). *Genetica* 57:131-137.
- Sessions, S.K. 1980. Evidence for a highly differentiated sex chromosome heteromorphism in the salamander *Necturus maculosus* (Rafinesque). *Chromosoma* 77:157-168.
- Sessions, S.K. 1982. Cytogenetics of diploid and triploid salamanders of the *Ambystoma jeffersonianum* complex. *Chromosoma* 84:599-621.
- Sharma, T., I.K. Gadi, and R. Raman. 1981. Similarity in the G-band patterns of constitutive heterochromatin of the composite X and Y chromosomes of certain rodents. *Genetica* 54:281-284.
- Sharma, T., and R. Raman. 1973. Variation of constitutive heterochromatin in the sex chromosomes of the rodent *Bandicota bengalensis bengalensis* (Gray). *Chromosoma* 41:75-84.
- Sharman, G.B. 1970. Reproductive physiology of marsupials. *Science* 167:1221-1228.
- Shaw, R.F. 1958. The theoretical genetics of the sex ratio. *Genetics* 43:149-163.
- Shields, W.M. 1982. *Philopatry, Inbreeding and the Evolution of Sex*. SUNY Press, Albany, New York.
- Shine, R., and J.J. Bull. 1977. Skewed sex ratios in snakes. *Copeia* 1977: 228-234.
- Silvers, W.K., D.L. Gasser, and E.M. Eicher. 1982. H-Y antigen, serologically detectable male antigen and sex determination. *Cell* 28:439-440.
- Simmons, M.J., and J.F. Crow. 1977. Mutations affecting fitness in *Drosophila* populations. *Ann. Rev. Genet.* 11:49-78.
- Singh, L. 1972. Evolution of karyotypes in snakes. *Chromosoma* 38:185-236.
- Singh, L., and K.W. Jones. 1982. Sex reversal in the mouse (*Mus musculus*) is caused by a recurrent nonreciprocal crossover involving the X and an aberrant Y chromosome. *Cell* 28:205-216.
- Singh, L., I.F. Purdom, and K.W. Jones. 1976. Satellite DNA and evolution of sex chromosomes. *Chromosoma* 59:43-62.
- Singh, L., I.F. Purdom, and K.W. Jones. 1980. Sex chromosome associated satellite DNA: Evolution and conservation. *Chromosoma* 79:137-157.
- Singh, L., I.F. Purdom, and K.W. Jones. 1981. Conserved sex-chromosome-associated nucleotide sequences in eukaryotes. *Cold Spring Harbor Symp. Quant. Biol.* 45:805-814.
- Sites, J.W., Jr., J.W. Bickham, and M.W. Haiduk. 1979. A derived X chromosome in the turtle genus *Staurotypus*. *Science* 206:1410-1412.
- Skinner, S.W., and J.H. Werren. 1984. On the mechanism of sex determination in *Nasonia vitripennis*: A test of Crozier's hypothesis. Forthcoming.
- Smith, B.W. 1963. The mechanism of sex determination in *Rumex hastatulus*. *Genetics* 48:1265-1288.
- Smith, R.H., and M.R. Shaw. 1980. Haplo-diploid sex ratios and the mutation rate. *Nature* 287:728-729.

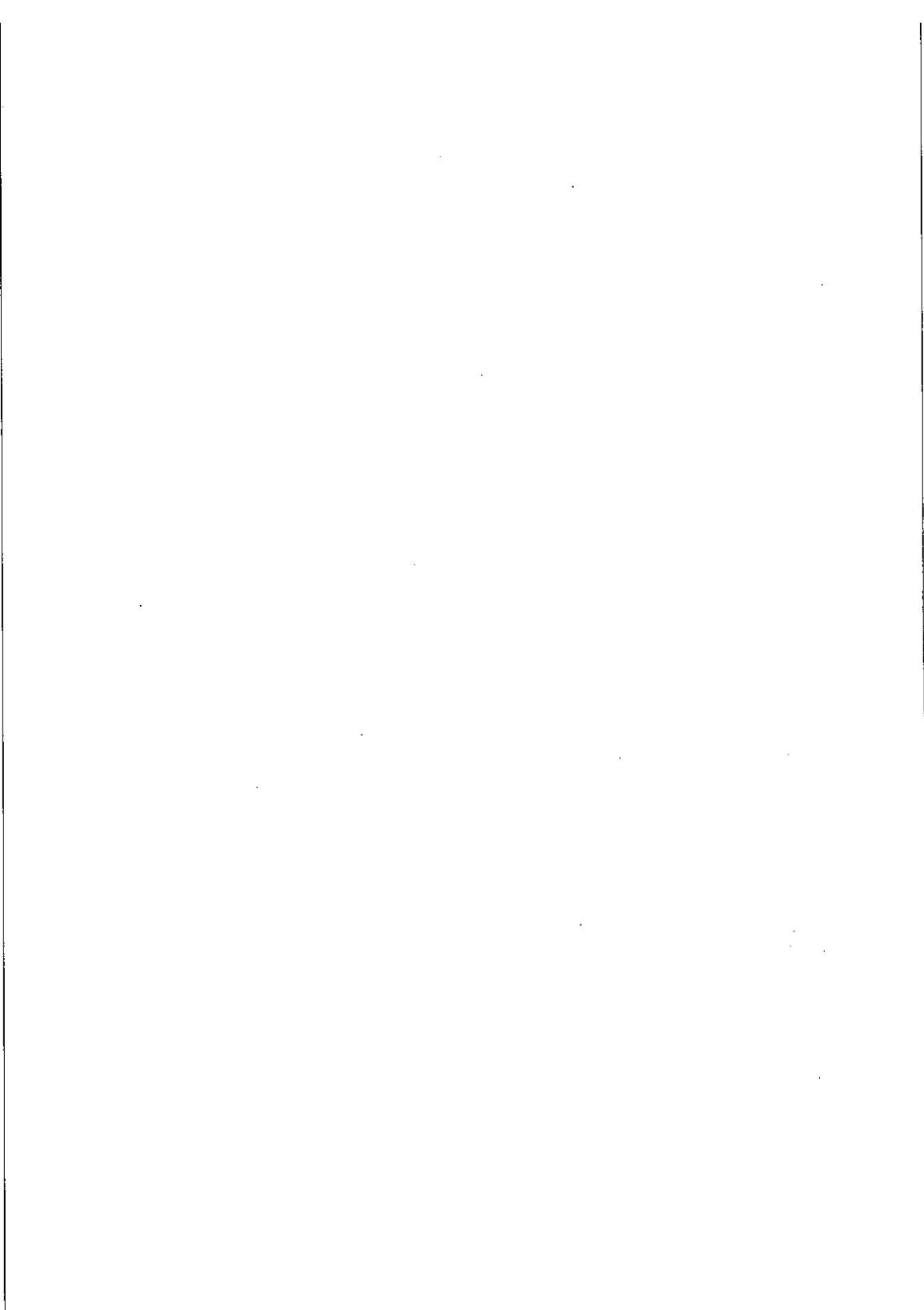
- Smith, S.G. 1960. Chromosome numbers of Coleoptera. II. *Can. J. Gen. Cytol.* 2:67-88.
- Sola, L., S. Cataudella, and E. Capanna. 1981. New developments in vertebrate cytotaxonomy. III. Karyology of bony fishes: A review. *Genetica* 54:285-328.
- Solari, A.J. 1974. The behavior of the XY pair in mammals. *Int. Rev. Cytol.* 38:273-317.
- Southern, D.I. 1980. Chromosome diversity in tsetse flies. In *Insect Cytogenetics*, ed. R.L. Blackman, G.M. Hewitt, and M. Ashburner, pp. 225-244. Blackwell Sci. Publ., Oxford, London.
- Stalker, H.D. 1954. Parthenogenesis in *Drosophila*. *Genetics* 39:4-34.
- Stefos, K., and F.E. Arrighi. 1971. Heterochromatic nature of W chromosomes in birds. *Exp. Cell Res.* 68:228-231.
- Steinemann, M. 1982. Multiple sex chromosomes in *Drosophila miranda*: A system to study the degeneration of a chromosome. *Chromosoma* 86:59-76.
- Stock, A.D., F.E. Arrighi, and K. Stefos. 1974. Chromosome homology in birds: Banding patterns of the chromosomes of the domestic chicken, ring-necked dove, and domestic pigeon. *Cytog. Cell Gen.* 13:410-418.
- Streisinger, G., C. Walker, N. Dower, D. Knäuber, and F. Singer. 1981. Production of clones of homozygous diploid zebra fish (*Brachydanio rerio*). *Nature* 291: 293-296.
- Sturtevant, A.H. 1920. Genetic studies on *Drosophila simulans*. I. Introduction. Hybrids with *Drosophila melanogaster*. *Genetics* 5:488-500.
- Swanson, C.P. 1957. *Cytology and Cytogenetics*. Prentice Hall, Englewood Cliffs, New Jersey.
- Taber, E. 1964. Intersexuality in birds. In *Intersexuality in Vertebrates Including Man*, ed. C.N. Armstrong and A.J. Marshall, pp. 285-310. Academic Press, London, New York.
- Takagi, N., and M. Sasaki. 1974. A phylogenetic study of bird karyotypes. *Chromosoma* 46:91-120.
- Takagi, N., O. Sugawara, and M. Sasaki. 1982. Regional and temporal changes in the pattern of X-chromosome replication during the early post-implantation development of the female mouse. *Chromosoma* 85:275-286.
- Tanksley, S.D., D. Zamir, and C.M. Rick. 1981. Evidence for extensive overlap of sporophytic and gametophytic gene expression in *Lycopersicum esculentum*. *Science* 213:453-455.
- Tazima, Y. 1964. *The Genetics of the Silkworm*. Logos Press, London.
- Templeton, A.R. 1982. The prophecies of parthenogenesis. In *Evolution and Genetics of Life Histories*, ed. H. Dingle and J.P. Hegmann pp. 75-101. Springer-Verlag, New York, Berlin.
- Therman, E., G.E. Sarto, C. Disteche, and C. Denniston. 1976. A possible active segment on the inactive human X chromosome. *Chromosoma* 59:137-145.
- Therman, E., G. Sarto, C.G. Palmer, H. Kallio, and C. Denniston. 1979. Position of the human X inactivation center on Xq. *Hum. Genet.* 50:59-64.
- Thompson, P.E., and J.S. Bowen. 1972. Interactions of differentiated primary sex factors in *Chironomus tentans*. *Genetics* 70:491-493.
- Thorgaard, G.H. 1978. Sex chromosomes in the sockeye salmon: A Y-autosome fusion. *Can. J. Genet. Cytol.* 20:349-354.
- Traut, W., and G.C. Mosbacher. 1968. Geschlechtschromatin bei Lepidopteren. *Chromosoma* 25:343-356.

- Tres, L.L. 1979. Side-by-side pairing of the XY bivalent in spermatocytes and the ubiquity of the H-Y locus. *Arch. Androl.* 2:101-108.
- Triantaphyllou, A.C. 1973. Environmental sex differentiation of nematodes in relation to pest management. *Ann. Rev. Phytopath.* 11:441-462.
- Triantaphyllou, A.C. 1976. Genetics and cytology. *Adv. Parasit.* 14:1-34.
- Trivers, R.L., and D.E. Willard. 1973. Natural selection of parental ability to vary the sex ratio of offspring. *Science* 179:90-92.
- Tsukamoto, M., T. Shono, and M. Horio. 1980. Autosomal sex-determining system of the housefly: Discovery of the first-chromosomal male factor in Kitakyushu, Japan. *J. Univ. Occup. Env. Health* 2:235-252.
- Ullerich, F.-H. 1963. Geschlechtschromosomen und Geschlechtsbestimmung bei einigen Calliphorinen (Calliphoridae, Diptera). *Chromosoma* 14:45-110.
- Ullerich, F.-H. 1975. Identifizierung der genetischen Geschlechtschromosomen bei der monogenen Schmeissfliege *Chrysomya rufifacies* (Calliphoridae, Diptera). *Chromosoma* 50:393-419.
- Ullerich, F.-H., H. Bauer, and R. Dietz. 1964. Geschlechtsbestimmung bei Tipuliden (Nematocera, Diptera). *Chromosoma* 15:591-605.
- Uyenoyama, M.K., and M.W. Feldman. 1978. The genetics of sex ratio distortion by cytoplasmic infection under maternal and contagious transmission: An epidemiological study. *Theor. Pop. Biol.* 14:471-497.
- Uyenoyama, T., A. Fukunaga, and K. Ioshi. 1982. Studies on the sex-specific lethals of *Drosophila melanogaster*. V. Sex transformation caused by interactions between a female-specific lethal *sxl^{f1}* and the male-specific lethals *mle* (3)132, *msl-2⁷*, and *mle*. *Genetics* 102:233-243.
- Uzzell, T. 1978. Immunological distances between the serum albumins of *Rana ridibunda* and *Rana lessonae*. *Proc. Acad. Nat. Sci. Phil.* 130:1-10.
- Uzzell, T., and L. Berger. 1975. Electrophoretic phenotypes of *Rana ridibunda*, *Rana lessonae*, and their hybridogenetic associate, *Rana esculenta*. *Proc. Acad. Nat. Sci. Phil.* 127:13-24.
- Uzzell, T., R. Gunther, and L. Berger. 1975. Diploid and triploid progeny from a diploid female of *Rana esculenta* (Amphibia: Salientia). *Proc. Acad. Nat. Sci. Phil.* 127:81-91.
- Uzzell, T., R. Gunther, and L. Berger. 1977. *Rana ridibunda* an *Rana esculenta*: A leaky hybridogenetic system (Amphibia: Salientia). *Proc. Acad. Nat. Sci. Phil.* 128:147-171.
- VandeBerg, J.L. 1983. Developmental aspects of X chromosome inactivation in eutherian and metatherian mammals. *J. Exp. Zool.* In press.
- VandeBerg, J.L., and D.W. Cooper. 1978. Possible autosomal inheritance of erythrocyte phosphoglycerate kinase-A in echidnas. *Bioch. Gen.* 16:1031-1034.
- VandeBerg, J.L., P.G. Johnston, D.W. Cooper, and E.S. Robinson. 1983. X-chromosome inactivation and evolution in marsupials and other mammals. *Isozymes Curr. Top. Biol. Med. Res.* 9. In press.
- Vandel, A. 1938. Recherches sur la sexualité des isopodes terrestres. III. Le déterminisme du sexe et de la monogénie chez *Trichoniscus (Spiloniscus) provisorius* Racovitza. *Bull. Biol. Fr. et Belg.* 72:147-168.
- Vandel, A. 1939. Sur le mode de répartition des sexes chez l'isopode terrestre, *Armadillidium vulgare* (Latr.) *C.R. Acad. Sci.* 208:1050-1052.
- Vandel, A. 1941. Recherches sur la génétique et la sexualité des isopodes terrestres. VI. Les phénomènes de monogénie chez les Oniscoïdes. *Bull. Biol. Fr. et Belg.* 75:316-363.

- Vanossi Este, S. 1971. Nuovi equilibri nella determinazione del sesso in *Musca domestica* L. *Boll. Zool.* 38:566 (Abs).
- Vanossi Este, S., C. Rovati, M.G. Franco, and P.G. Rubini. 1974. Localizzazione genetica del fattore arrenogeno *Ag* di *Musca domestica* L. *Boll. Zool.* 41 (Abs).
- Vanossi Este, S., P.G. Rubini, M.G. Franco, and C. Rovati. 1972. Arrenogenia in *Musca domestica* L. e sua hereditarietà. *Boll. Zool.* 39:669 (Abs).
- Voelker, R.A. 1970. Relative fitnesses of XO and XY males of *Drosophila affinis*. Ph.D. diss. Univ. of Texas, Austin.
- Voelker, R.A., and K. Kojima. 1971. Fertility and fitness of XO males in *Drosophila*. I. Qualitative study. *Evolution* 25:119-128.
- Vogt, R.C. 1980. Natural history of the map turtles *Graptemys pseudogeographica* and *G. ouachitensis* in Wisconsin. *Tulane Stud. Zool. Bot.* 22:17-48.
- Vogt, R.C., and J.J. Bull. 1982. Genetic sex determination in the spiny softshell (*Trionyx spiniferus*)? *Copeia* 1982:699-700.
- Vogt, R.C. and J.J. Bull. 1984. Ecology of hatchling sex ratio in map turtles. *Ecology*. In press.
- Vorontsov, N.N. 1973. The evolution of the sex chromosomes. In *Cytotaxonomy and Vertebrate Evolution*, ed. A.B. Chiarelli and E. Capanna, pp. 619-657. Academic Press, New York.
- Vorontsov, N.N., E.A. Lyapunova, Y.M. Borissov, and V.E. Dovgal. 1980. Variability of sex chromosomes in mammals. *Genetica* 52/53:361-372.
- Wachtel, S.S., P.A. Bresler, and S.S. Koide. 1980. Does H-Y antigen induce the heterogametic ovary? *Cell* 20:859-864.
- Wachtel, S.S., and G.C. Koo. 1981. Y-Y antigen in gonadal differentiation. In *Mechanisms of Sex Differentiation in Animals and Man*, ed. C.R. Austin, R.G. Edwards, pp. 255-299. Academic Press, New York, London.
- Wachtel, S.S., G.C. Koo, and E.A. Boyse. 1975a. Evolutionary conservation of H-Y (male) antigen. *Nature* 254:270-272.
- Wachtel, S.S., G.C. Koo, S. Ohno, A. Gropp, V.G. Dei, R. Tantravahi, D.A. Miller, and O.J. Miller. 1976. H-Y antigen and the origin of XY female wood lemmings (*Myopus schisticolor*). *Nature* 264:638-639.
- Wachtel, S.S., S. Ohno, G.C. Koo, and E.A. Boyse. 1975b. Possible role of H-Y antigen in primary sex determination. *Nature* 257:235-236.
- Wagner, E. 1980. Temperature-dependent sex determination in a gekko lizard. *Quart. Rev. Biol.* 55:21 (App).
- Wagoner, D.E. 1968. Linkage group-karyotype correlation in the housefly, *Musca domestica* L., confirmed by cytological analysis of X-ray induced Y-autosome translocations. *Genetics* 62:115-121.
- Wagoner, D.E. 1969. Presence of male determining factors found on three autosomes in the housefly, *Musca domestica*. *Nature* 223:187-188.
- Walker, P.M.B. 1971. Origin of satellite DNA. *Nature* 229:306-308.
- Webb, G.J.W., R. Buckworth, and S.C. Manolis. 1983. *Crocodylus johnstoni* in the McKinlay River area, N.T. V. Nesting biology. *Aust. Wildl. Res.* In press.
- Welch, H.E. 1965. Entomophilic nematodes. *Ann. Rev. Ent.* 10:275-302.
- Werren, J.H., S.W. Skinner, and E.L. Charnov. 1981. Paternal inheritance of a daughterless sex ratio factor. *Nature* 293:467-468.
- Westergaard, M. 1946. Aberrant Y chromosomes and sex expression in *Melandrium album*. *Hereditas* 32:419-443.
- Westergaard, M. 1958. The mechanism of sex determination in dioecious flowering plants. *Adv. Genet.* 9:217-281.

- White, M.J.D. 1945. *Animal Cytology and Evolution*. 1st ed. Cambridge Univ. Press, Cambridge, U.K.
- White, M.J.D. 1954. *Animal Cytology and Evolution*. 2d ed. Cambridge Univ. Press, Cambridge, U.K.
- White, M.J.D. 1973. *Animal Cytology and Evolution*. 3rd ed. Cambridge Univ. Press, Cambridge, U.K.
- Whiting, A.R. 1961. Genetics of *Habrobracon*. *Adv. Genet.* 10:295-348.
- Whiting, P.W. 1943. Multiple alleles in complementary sex determination of *Habrobracon*. *Genetics* 28:365-382.
- Whiting, P.W. 1945. The evolution of male haploidy. *Quart. Rev. Biol.* 20:231-260.
- Whiting, P.W. 1960. Polyploidy in *Mormoniella*. *Genetics* 45:949-970.
- Wiberg, U., A. Mayerova, U. Muller, K. Fredga, and U. Wolf. 1982. X-linked genes of the H-Y antigen system in the wood lemming (*Myopus schisticolor*). *Hum. Genet.* 60:163-166.
- Wilhoft, D.C., E. Hotaling, and P. Franks. 1983. Effects of temperature on sex determination in embryos of the snapping turtle, *Chelydra serpentina*. *J. Herpet.* 17:38-42.
- Williams, G.C. 1966. *Adaptation and Natural Selection*. Princeton Univ. Press. Princeton, N.J.
- Williams, G.C. 1975. *Sex and Evolution*. Princeton Univ. Press, Princeton, N.J.
- Williams, G.C. 1979. The question of adaptive sex ratio in outcrossed vertebrates. *Proc. Roy. Soc. London (B)* 205:567-580.
- Williams, G.C. 1980. Kin selection and the paradox of sexuality. In *Sociobiology: Beyond Nature/Nuture?*, ed. G.W. Barlow and J. Silverberg, pp. 371-384. Amer. Assoc. Adv. Sci., Westview Press, Boulder, Colo.
- Wilson, E.B. 1905a. The chromosomes in relation to the determination of sex in insects. *Science* 22:500-502.
- Wilson, E.B. 1905b. Studies on chromosomes. II. The paired microchromosome, idiochromosome and heterotropic chromosomes in Hemiptera. *J. Exp. Zool.* 2:507-545.
- Wilson, E.B. 1906. Studies on chromosomes. III. The sexual difference of the chromosome-groups in Hemiptera, with some consideration on the determination and inheritance of sex. *J. Exp. Zool.* 3:1-40.
- Winge, O. 1931. X- and Y-linked inheritance in *Melandrium*. *Hereditas* 15:127-165.
- Winge, O. 1932. The nature of sex chromosomes. *Proc. 6th Int. Congr. Genet.* 1:343-355.
- Winge, O. 1934. The experimental alteration of sex chromosomes into autosomes and vice versa, as illustrated by *Lebistes*. *Compt. Rend. Lab., Carlsburg. Ser. Physiol.* 21:1-49.
- Winge, O. 1937. Goldschmidt's theory of sex determination in *Lymantria*. *J. Genet.* 34:81-89.
- Winge, O., and E. Ditlevson. 1947. Colour inheritance and sex determination in *Lebistes*. *Heredity* 1:65-83.
- Witschi, T. 1929. Studies on sex differentiation and sex determination in amphibians. II. Sex reversal in female tadpoles of *Rana sylvatica* following the application of high temperature. *J. Exp. Zool.* 52:267-292.
- Witschi, E. 1951. Embryogenesis of the adrenal and the reproductive glands. I. Gonad development and function. pp. 1-27. In *Recent Progress in Hormone Research* Vol. VI.

- Wright, S. 1939. The distribution of self-sterility alleles in populations. *Genetics* 24:538-552.
- Wright, S. 1968. *Evolution and the Genetics of Populations*. Vol. 1. Univ. of Chicago Press, Chicago.
- Wurster, D.H., and K. Benirschke. 1970. Indian Muntjac, *Muntiacus muntjak*: A new deer with a low chromosome number. *Science* 168:1364-1366.
- Wylie, A.P., A.M.O. Veale, and V.E. Sands. 1968. The chromosomes of the tuatara. *Proc. Univ. Otago Med. Sch.* 46:22-23.
- Yamamoto, T. 1959. A further study on induction of functional sex reversal in genotypic males of the medaka (*Oryzias latipes*) and progenies of sex reversals. *Genetics* 44:739-757.
- Yamamoto, T. 1963. Induction of sex reversal in sex differentiation of YY zygotes in the medaka, *Oryzias latipes*. *Genetics* 48:293-306.
- Yamamoto, T. 1969. Sex differentiation. In *Fish Physiology*, ed. W.S. Hoar and D.J. Randall, vol. 3, pp. 117-175. Academic Press, New York, London.
- Yamamoto, T. 1975. A YY male goldfish from mating estrone-induced XY female and normal male. *J. Hered.* 66:2-4.
- Yanagimachi, R. 1961. Studies on the sexual organization of the rhizocephala. III. The mode of sex-determination in *Peltogasterella*. *Biol. Bull.* 120:272-283.
- Yntema, C.L. 1976. Effects of incubation temperatures on sexual differentiation in the turtle, *Chelydra serpentina*. *J. Morphol.* 150:453-462.
- Yntema, C.L. 1979. Temperature levels and periods of sex determination during incubation of eggs of *Chelydra serpentina*. *J. Morphol.* 159:17-27.
- Yntema, C.L. 1981. Characteristics of gonads and oviducts in hatchlings and young *Chelydra serpentina* resulting from three incubation temperatures. *J. Morphol.* 167:297-304.
- Yntema, C.L., and N. Mrosovsky. 1980. Sexual differentiation in hatchling loggerheads (*Caretta caretta*) incubated at different controlled temperatures. *Herpetologica* 36:33-36.
- Yntema, C.L., and N. Mrosovsky. 1982. Critical periods and pivotal temperatures for sexual differentiation in loggerhead sea turtles. *Can. J. Zool.* 60:1012-1016.
- Yokoyama, S., and M. Nei. 1979. Population dynamics of sex-determining alleles in honey bees and self-incompatibility alleles in plants. *Genetics* 91:609-626.
- Zaborski, P., A. Guichard, and M. Reyss-Brion. 1980. H-Y antigen in ovariectomized chicks: Disappearance of its expression during the transformation of the right gonad into a testis. *Biol. Cell* 39:291-294.
- Zaborski, P., A. Guichard, and D. Scheib. 1981. Transient expression of H-Y antigen in quail ovotestis following diethylstilbestrol (DES) treatment. *Biol. Cell* 41:113-122.
- Zuk, J. 1970a. Function of Y chromosomes in *Rumex thysiflorus*. *Theor. App. Gen.* 40:124-129.
- Zuk, J. 1970b. Structure and function of sex chromosomes in *Rumex thysiflorus*. *ACTA Soc. Bot. Poloniae* 39:539-564.



Name Index

- Adkins-Regan, 1981: 126
Aida, 1921: 242
Aida, 1936: 24, 36, 51, 96–97, 106, 125
Allen, 1945: 262–63
Anderson and Lengyel, 1979: 187
Anderson and Lengyel, 1981: 187
Aoki, 1980: 91
Arrighi and Hsu, 1971: 224–25
Atz, 1964: 15, 126, 134
Austin and Edwards, 1981: 42
Austin et al., 1981: 6, 219
Avtalion and Hammerman, 1978: 88
- Bacci, 1965: 10, 13, 15, 93, 97, 110–11,
124–26
Baker and Ridge, 1980: 37–39
Baker and Lindsley, 1983: 36, 52
Baker and Ridge, 1980: 37–9
Baker and Rabbani, 1970: 228
Baker et al., 1977: 27
Baker et al., 1972: 245
Baltzer, 1912: 110–11
Baltzer, 1914: 110–11
Barr, 1959: 230
Barr and Bertram, 1949: 230
Baverstock et al., 1982: 234, 246
Becak et al., 1964: 245
Becker et al., 1975: 126
Beermann, 1955: 21, 27, 35, 242–43
Belar, 1924: 176
Bell, 1982: 6, 147–49, 228, 252, 254
Belote and Baker, 1982: 37, 39
- Belote and Lucchesi, 1980a: 231
Belote and Lucchesi, 1980b: 231
Bengtsson, 1977: 79
Berg, 1937a: 52, 250
Berg, 1937b: 52, 250
Berg, 1938: 52, 250
Berg, 1942: 221
Berg, pers. comm.: 51
Bernstein et al., 1980: 45
Berrie, 1963: 262
Berry and Shine, 1980: 141
Bickham, 1982: 119
Bickham and Carr, 1983: 119
Bickham et al., pers. comm.: 236–37
Borgia, 1980: 169–72
Boyes, 1967: 30–31, 225
Breider, 1935: 95, 100–101
Bridges, 1916: 21, 49, 220–21
Bridges, 1922: 9, 49
Bridges, 1925: 10, 21, 23, 49, 51, 220
Bridges, 1939: 36, 51–52
Bridges (general): 48–52, 93, 107
Brosseau, 1960: 244, 249
Brown, 1963: 154, 158
Brown, 1964: 153–54, 158, 165, 167–
68, 185
Brown, 1966: 223–24
Brown and Bennett, 1957: 188
Brown and Chandra, 1977: 153–55,
158–59, 166, 188, 224–25, 230–31
Brown and Nelson-Rees, 1961: 158
Bull, 1978a: 238–40
Bull, 1978b: 262–63

- Bull, 1979: 153, 159, 161–65, 167, 169–70, 173–76, 179–80, 185
- Bull, 1980: 115–18, 120
- Bull, 1981a: 105–6, 114, 134
- Bull, 1981b: 129–32, 136–37
- Bull, 1981c: 164, 170, 178, 181–84
- Bull (unpub.): 69, 170
- Bull and Bulmer, 1981: 79–80
- Bull and Charnov, 1977: 69–76, 87
- Bull and Charnov (unpub.): 120, 122
- Bull and Legler, 1980: 119
- Bull and Legler (unpub.): 119
- Bull et al., 1974: 238, 240
- Bull and Vogt, 1979: 115–16, 121
- Bull and Vogt, 1981: 118
- Bull and Vogt (unpub.): 119
- Bull, Vogt, and Bulmer, 1982: 102
- Bull, Vogt, and McCoy, 1982: 115–16, 122, 143
- Bulmer and Bull, 1982: 49, 102–3, 116, 129, 131–32, 134, 137–38
- Bulnheim, 1967: 124
- Bulnheim, 1969: 124
- Bulnheim, 1975a: 193–95
- Bulnheim, 1975b: 193–95
- Bulnheim, 1978a: 124, 193–95
- Bulnheim, 1978b: 124, 193
- Bulnheim (general): 207
- Burgoyne, 1978: 45
- Burns, 1961: 126
- Bush, 1966: 21
- Cattanach, 1961: 23
- Cattanach, 1975: 166, 230–31
- Caulery and Comas, 1928: 112, 143
- Charlesworth, 1978: 255–57, 262, 264
- Charlesworth and Charlesworth, 1978: 16, 25, 42, 91–92, 250
- Charlesworth and Charlesworth, 1980: 251–53
- Charnier, 1966: 115, 117, 119
- Charnov, 1979: 129, 143
- Charnov, 1982: 6, 67–68, 83, 110–11, 129, 143, 171, 187, 211
- Charnov and Bull, 1977: 128–32, 134, 137, 141
- Charnov and Bull (unpub.): 132
- Charnov et al., 1981: 171
- Chitwood and Chitwood, 1974: 17, 39
- Christie, 1929: 111–12, 114, 139
- Clarke and Ford, 1980: 48, 225
- Cline, 1978: 38
- Cline, 1979a: 37–38
- Cline, 1979b: 37–39
- Cock, 1964: 15, 225, 230, 234
- Cohen and Gans, 1970: 119
- Cole, 1975: 118
- Cole et al., 1969: 240
- Collenot, 1975: 24
- Conover, 1983: 123, 139–40
- Conover and Kynard, 1981: 123
- Cooper et al., 1977: 44, 166, 230
- Cotterman, 1953: 55–56, 58–59
- Cotterman (unpub.): 4, 62–63
- Counce and Poulson, 1962: 192
- Couturier, 1963: 142
- Craig, 1965: 125
- Crew, 1965: 13, 15, 110–11, 125–26, 219
- Crouse, 1943: 158
- Crouse, 1960: 158
- Crow, 1946: 36
- Crow (pers. comm.): 82, 256
- Crow and Kimura, 1970: 103, 168–69
- Crozier, 1971: 152
- Crozier, 1977: 34, 151–52
- Darlington, 1937: 219, 221, 227, 243, 252
- Darlington, 1939: 243, 249
- Darlington, 1958: 243, 249
- Darlington, 1965: 219
- Davidson, 1976: 187
- Dobzhansky, 1957: 222, 231
- Dobzhansky and Schultz, 1931: 36
- Dobzhansky and Schultz, 1934: 36
- Doira, 1978: 223
- Donald and Cooper, 1977: 230, 233
- Doolittle and Sapienza, 1980: 155, 259
- Dronamraju, 1965: 222–23
- Duckett, 1979: 232–33
- Dunn and Bennett, 1967: 228, 254
- Dyer, 1975: 187
- Dzierzon, 1845: 148
- Ebeling and Chen, 1970: 19
- Eddington, 1929: 4
- Eicher et al., 1982: 45
- Eichwald et al., 1958: 43
- Ellenby, 1954: 115
- Eloff, 1932: 227
- Endler, 1978: 80, 249
- Endler, 1980: 80, 249
- Engel et al., 1981: 104
- Epplen et al., 1982: 226

- Evans et al., 1982: 46
 Ezenwa and Carter, 1975: 112
 Falconer, 1981: 98, 103, 168
 Farr, 1981, 242, 261
 Felsenstein, 1974: 256
 Ferguson and Joanan, 1982: 115,
 117–19, 122, 141–42
 Ferguson (pers. comm.): 122
 Fisher, 1930: 4, 67, 82–84
 Fisher, 1931: 249–50
 Fisher, 1935: 255
 Foe et al., 1982: 187
 Foote, 1964: 125–26
 Franco et al., 1982: 15, 24, 27,
 31–32, 78
 Fredga et al., 1976: 29, 79
 Fredga et al., 1977: 29, 79
 Friedler and Ray, 1951: 152
 Frota-Pessoa and Aratangy, 1968: 255
 Gallagher et al., 1973: 225
 Gallien, 1959: 13, 15, 19, 24
 Gartler and Cole, 1981: 230
 German et al., 1978: 45
 Ghiselin, 1969: 172
 Gibbons, 1970: 121
 Gilchrist and Haldane, 1947: 35
 Gileva, 1980: 29, 30, 79
 Gileva and Chebotar, 1979: 29
 Gileva et al., 1982: 29, 79, 80
 Gillespie, 1973: 136
 Ginsburger-Vogel, 1975a: 195–98
 Ginsburger-Vogel, 1975b: 198
 Ginsburger-Vogel et al., 1980: 195,
 197–98
 Ginsburger-Vogel and Desportes, 1979:
 196, 207
 Ginsburger-Vogel and Magniette-
 Mergault, 1981a: 24, 195, 197
 Ginsburger-Vogel and Magniette-
 Mergault, 1981b: 24, 195, 197–98
 Gold, 1979: 19
 Goldschmidt, 1920a: 46
 Goldschmidt, 1920b: 47–49
 Goldschmidt, 1931: 46
 Goldschmidt, 1934: 47–50
 Goldschmidt, 1955: 47
 Gordon, 1946: 28
 Gordon, 1954: 28
 Gorman, 1973: 119, 245
 Green, 1980: 28, 35
 Gropp et al., 1976: 79
 Grossman et al., 1981: 17
 Gutzke and Paukstis, 1983a: 117
 Gutzke and Paukstis, 1983b: 118, 141
 Haiduk and Baker (pers. comm.): 236
 Haldane, 1922: 228, 250
 Haldane, 1933: 243, 249, 259–60
 Haldane, 1957: 154
 Hall et al., 1976: 166
 Hamilton, 1967: 67, 79, 168–72, 174–
 76, 187, 205, 257
 Hamilton, 1979: 67
 Hansmann, 1982: 46
 Harlos et al., 1980: 112, 114
 Harrington, 1967: 125
 Harrington, 1968: 125
 Hartl, 1972: 174
 Hartl and Brown, 1970: 147, 163–64,
 168, 170, 172, 178–80, 181,
 183–84
 Hartl and Hiraizumi, 1976: 166
 Hartmann, 1956: 10
 Hartmann-Goldstein and Koliantz,
 1981: 222
 Haseltine et al., 1982: 44
 Haskins et al., 1970: 81, 221, 242, 250
 Hecht and Williams, 1978: 242, 259
 Heitz, 1928: 223
 Henking, 1891: 219–20
 Herbst et al., 1978: 30
 Heslop-Harrison, 1919: 49
 Hess and Meyer, 1968: 23, 222–23
 Hiroyoshi, 1964: 27, 32
 Hodgkin, 1980: 41–2
 Hoshiba et al., 1981: 151
 Houllion and Dournon, 1978: 125
 Howard, 1940: 202
 Howard, 1942: 79, 199, 202–3, 205,
 215
 Howard, 1958: 199, 200
 Hsu, 1971: 225
 Hubbs, 1964: 125
 Huey, 1982: 132
 Humphrey, 1945: 19, 24
 Humphrey, 1948: 24, 124
 Huxley, 1928: 228
 Iturra and Veloso, 1981: 19
 Jacobsen, 1957: 221, 225, 260

- James, 1937: 188
 Jan and Shu, 1972: 30, 225
 John and Lewis, 1965: 225
 John and Lewis, 1968: 227-29
 John and Miklos, 1979: 30, 223-24,
 258
 Johnson, 1955: 112
 Johnson, 1977: 203, 215
 Johnson, 1961: 199
 Johnson and Turner, 1979: 15, 234
 Johnstone et al., 1979: 19
 Jones et al., 1973: 225
 Jones and Singh, 1982: 226
 Jost, 1965: 43
 Juchault and Legrand, 1972: 24,
 199-201
 Juchault and Legrand, 1976: 200, 202
 Juchault and Legrand, 1981a: 202
 Juchault and Legrand, 1981b:
 201-3, 208-9
 Juchault et al., 1980: 202-3, 208

 Kallman, 1965: 28, 80, 97
 Kallman, 1968: 15, 28-29, 80
 Kallman, 1970: 28, 80-81, 249
 Kallman, 1973: 28
 Kallman, 1983: 24, 29, 80, 93, 95-97,
 102, 134
 Kallman and Atz, 1967: 29, 80-81,
 95, 101
 Kallman (pers. comm.): 80-81, 101
 Karlin and Lieberman, 1974: 136
 Kawamura and Nishioka, 1977: 19, 24,
 126, 178
 Kellen et al., 1965: 193
 Kerr, 1970: 77-78
 Kerr, 1974: 152
 Kezer and Sessions, 1979: 19
 Kihara, 1953: 23
 King, 1977: 20, 119, 225, 246
 Kitchin, 1970: 158, 167
 Klass et al., 1976: 40-41
 Klevecz and Hsu, 1964: 233
 Knapp, 1936: 263-64
 Kosswig, 1964: 93, 95-97, 102
 Kunkel and Smith, 1982: 225-26

 Lande, 1981: 100
 Lefevre, 1974: 222
 Legrand and Juchault, 1969a: 200
 Legrand and Juchault, 1969b: 200
 Legrand and Juchault, 1970: 200-202

 Legrand and Juchault, 1972: 201
 Lester et al., 1979a: 31
 Lester et al., 1979b: 31
 Leutert, 1975: 110-11
 Levitan, 1951: 250
 Levitan, 1963: 166
 Lewis, 1941: 203-4, 249
 Lewis, 1961: 262
 Lewis and Benson-Evans, 1960: 262
 Lewis and John, 1968: 243-44, 249,
 262
 Lewontin et al., 1978: 91
 Lindsley et al., 1960: 222, 250
 Lindsley and Grell, 1968: 222, 250
 Lizarralde et al., 1982: 30
 Lloyd, 1974: 16, 91, 261
 Lobato et al., 1982: 30
 Love, 1944: 23, 221, 261
 Lucchesi, 1977: 231
 Lucchesi, 1978: 229, 231, 243-45
 Lucchesi and Skripsky, 1981: 38, 231
 Lutz-Ostertag, 1966: 125
 Lyon, 1961: 46, 230
 Lyon et al., 1981: 23, 45-46
 Lyon and Hawkes, 1970: 45
 Lyttle, 1977: 79
 Lyttle, 1982: 258

 McCarrey and Abbott, 1979: 6
 McCloskey, 1966: 242, 259
 McClung, 1902a: 219-20
 McClung, 1902b: 219-20
 McDonald, 1971: 24
 McDonald et al., 1978: 31
 McDonald et al., 1975: 32
 MacDonald and Sheppard, 1965: 243
 McKusick, 1978: 44, 222-23
 McLaren, 1981: 46
 Madl and Herman, 1979: 40
 Mainx, 1964: 27-28, 35
 Maroni and Lucchesi, 1980: 231
 Marsh and Wieschaus, 1978: 38
 Martin et al., 1973: 200
 Martin, 1967: 253
 Martin et al., 1980: 27, 33, 35, 242
 Masui, 1967: 126
 Maynard Smith, 1978: 6, 7, 25, 76, 83,
 130, 147, 150, 160, 174-76
 Maynard Smith, 1980: 80
 Maynard Smith, 1982: 130
 Mengden, 1981: 225
 Mengden and Stock, 1980: 119, 245
 Metz, 1938: 153, 155-58, 187, 212

- Mikamo and Witschi, 1963: 24
 Mikamo and Witschi, 1964: 19, 24, 124
 Milani, 1969: 78
 Milani, 1971: 31-2, 78
 Milani, 1975: 27, 30, 78, 213
 Milani et al., 1967: 24, 27, 30-31
 Miller and Limpus, 1981: 115
 Miller, 1938: 126
 Mittwoch, 1967: 13
 Mittwoch, 1973: 13, 224, 250
 Moreira-Filho et al., 1979: 45
 Moreira Filho et al., 1980: 19
 Morreale et al., 1982: 115
 Morris, 1968: 222
 Moses et al., 1975: 228
 Moses et al., 1982: 253
 Motara, 1982: 243
 Motara and Rai, 1977: 225
 Mrosovsky, 1980: 116
 Mukai et al., 1972: 255
 Muller, 1914: 221, 243, 254-55
 Muller, 1918: 221, 243, 254-55
 Muller, 1932: 21, 36, 51, 86, 243, 249
 Muller, 1950: 230
 Muller, 1964: 256-57
 Muller and Gershenson, 1935: 221, 243
 Muller and Painter, 1932: 223, 243,
 246, 258
 Muller and Settles, 1927: 242, 259
 Muller, 1982: 43-44
 Muller and Wolf, 1979: 43
 Muller et al., 1979: 44, 126
 Murofushi et al., 1980: 19
 Muth and Bull, 1981: 118-19
- Nakogome, 1982: 231
 Nei, 1969: 251-52
 Nei, 1970: 255
 Nelson et al., 1978: 40-41
 Nelson-Rees, 1960: 159, 188
 Nelson-Rees et al., 1980: 149, 153-55
 Neuhaus, 1939: 258
 Newton, 1977: 262-63
 Newton et al., 1974: 243
 Nigon, 1949a: 40
 Nigon, 1949b: 40, 176
 Nigon, 1951a: 40
 Nigon, 1951b: 40
 Norris, 1979: 172
 Nur, 1963: 159, 188
 Nur, 1967: 159
 Nur, 1971: 147, 159
 Nur, 1974: 67-69, 77, 206-7, 209
- Nur, 1977: 188
 Nur, 1980: 147-49, 153-54, 158, 167,
 188
- O'Brien and MacIntyre, 1978: 187
 Ohno, 1967: (xix), 13, 15, 23, 44,
 119-20, 221, 243, 245-46, 250-
 51, 253-54
 Ohno, 1979: 36, 42-46, 222
 Oktay, 1959a: 96, 106
 Oktay, 1959b: 96, 106
 Oliver, 1971: 17, 148-49
 Oliver, 1977: 17, 148-49
 Oliver, 1983: 148-49
 Oliver (pers. comm.): 149
 Orgel and Crick, 1980: 155, 259
 Orzak et al., 1980: 74, 81
 Osgood, 1980: 118-19
- Packard et al., 1981b: 141
 Packard et al., 1981a: 141
 Packard et al., 1979: 141
 Page and Metcalf, 1982: 151
 Parenti, 1962: 143
 Parenti, 1965: 113
 Park and Grimm, 1981: 19, 225
 Park and Kang, 1979: 19
 Parker, 1982: 25
 Parker, et al., 1972: 25
 Pathak and Stock, 1974: 44, 225, 246
 Patterson, 1931: 36
 Patterson, 1938: 36
 Patterson and Stone, 1952: 244
 Patterson et al., 1937: 36
 Paukstis et al., 1983: 118-19, 141
 Peccinini-Seale, 1981: 118
 Peters, 1964: 95-96
 Petersen, 1972: 112-14
 Petersen, 1977: 112-13
 Pieau, 1971: 115
 Pieau, 1972: 115
 Pieau, 1973: 115
 Pieau, 1974: 115, 121
 Pieau, 1975a: 115
 Pieau, 1975b: 125
 Pieau, 1976: 115
 Pieau, 1978: 115
 Pieau, 1982: 115, 121
 Pieau and Dorizzi, 1981: 118
 Pipkin, 1960: 36, 51
 Poinar, 1979: 111
 Post, 1982: 242, 250
 Poulsom, 1963: 193

- Rao and Ali, 1982: 233–34
 Rao and Arora, 1979: 225, 233
 Rastan, 1982: 231
 Ray-Chaudhuri, 1973: 19, 120
 Ray-Chaudhuri et al., 1970: 225
 Raynaud and Pieau, 1972: 118–19
 Richards and Nace, 1978: 19, 125–26
 Ropers and Wiberg, 1982: 230
 Rosin and Fischer, 1972: 27, 242
 Rothenbuhler, 1957: 152
 Rothfels, 1980: 242
 Royer, 1975: 148
 Rubin, 1984: 124
 Rubini et al., 1972: 23, 30, 32, 78, 213
 Rubini et al., 1980: 31
 Rupes and Pinterova, 1975: 78
 Ryan and Saul, 1968: 152
 Ryttman et al., 1979: 225

 Sabour, 1972: 159
 Sawicki and MacIntyre, 1978: 187
 Schmid, 1980: 19, 225, 246
 Schmid et al., 1979: 19, 240–41, 254
 Schrader and Hughes-Schrader, 1931: 150
 Schreck, 1974: 126
 Schultz, 1977: 176
 Schupback, 1982: 38
 Scott and Gregory, 1965: 23
 Scudo, 1964: 55, 57–58, 60–61, 69, 70,
 72, 74, 76, 105, 133, 182
 Sudo, 1967: 27, 55, 60, 62–63, 65, 69,
 70, 72, 74
 Serrano, 1981: 228
 Sessions 1980: 19, 225, 246
 Sessions, 1982: 19
 Sharma et al., 1981: 225, 246
 Sharma and Raman, 1973: 225
 Sharman, 1970: 23
 Shaw, 1958: 79
 Shields, 1982: 6, 142
 Shine and Bull, 1977: 119
 Silvers et al., 1982: 43–44
 Simmons and Crow, 1977: 255
 Singh, 1972: 245
 Singh and Jones, 1982: 36, 46
 Singh et al., 1976: 226, 245
 Singh et al., 1980: 225–26, 245
 Singh et al., 1981: 226
 Sites et al., 1979: 240
 Skinner and Werren, 1984: 152
 Smith, 1963: 23, 222, 260–61
 Smith and Shaw, 1980: 187

 Smith, 1960: 149, 172
 Sola et al., 1981: 19
 Solari, 1974: 227
 Southern, 1980: 23
 Stalker, 1954: 164
 Stefos and Arrighi, 1971: 225
 Steinemann, 1982: 225–27, 229, 245
 Stock et al., 1974: 225
 Streisinger et al., 1981: 98, 101
 Streisinger (pers. comm.): 98
 Sturtevant, 1920: 48
 Swanson, 1957: 229, 244, 246

 Taber, 1964: 126
 Takagi and Sasaki, 1974: 19
 Tagaki et al., 1982: 231
 Tanksley et al., 1981: 260
 Tazima, 1964: 36, 228
 Templeton, 1982: 164–65
 Therman et al., 1976: 230
 Therman et al., 1979: 231
 Thompson and Bowen, 1972: 32–33
 Thorgaard, 1978: 19
 Tracy (pers. comm.): 143
 Traut and Mosbacher, 1968: 225
 Tres, 1979: 228
 Triantaphyllou, 1973: 17, 115
 Triantaphyllou, 1976: 17, 115
 Trivers and Willard, 1973: 129, 132
 Tsukamoto et al., 1980: 15, 27–28,
 30–31

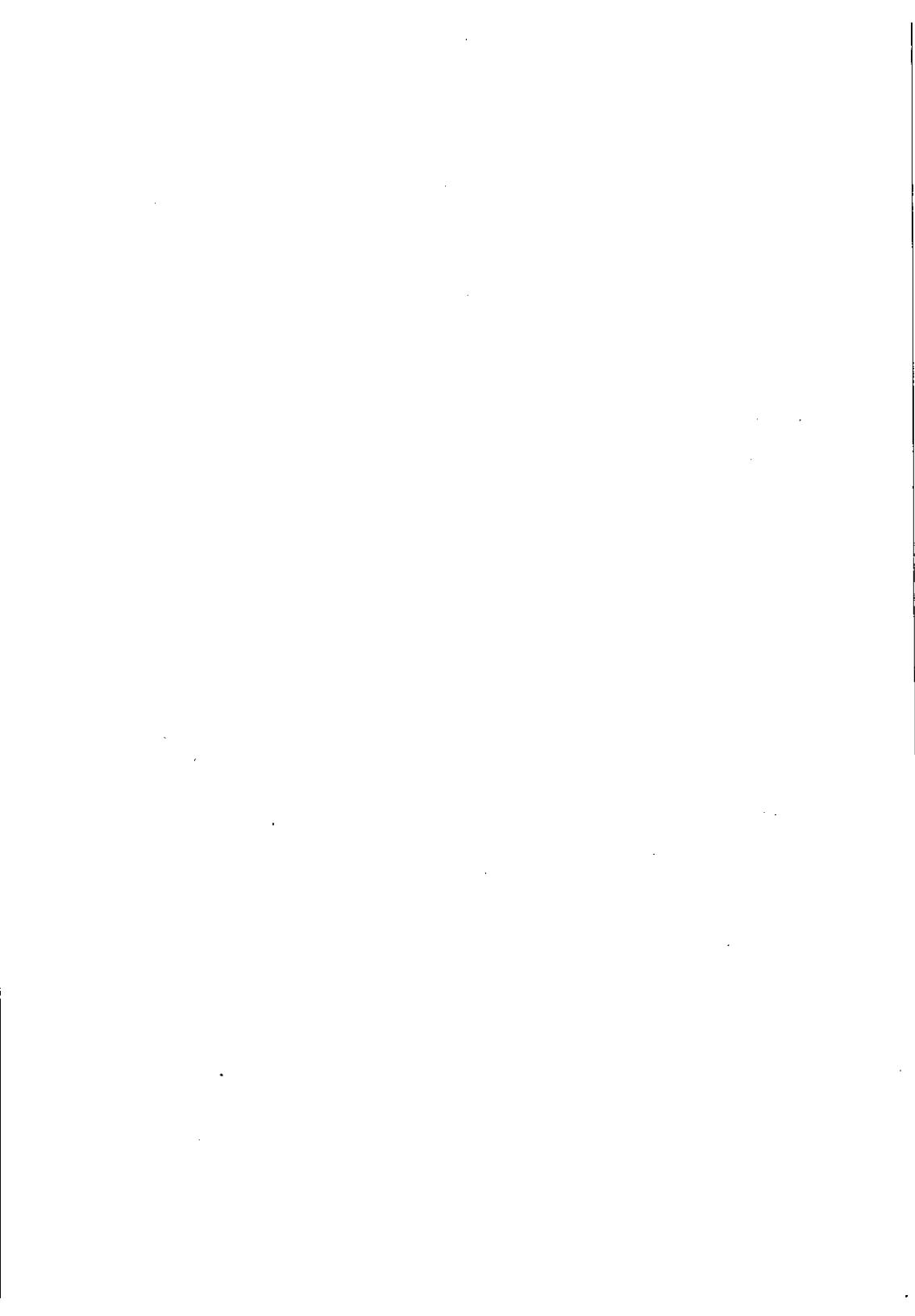
 Ullerich, 1963: 23, 212, 225
 Ullerich, 1975: 212
 Ullerich et al., 1964: 23
 Uyenoyama and Feldman, 1978: 193,
 204, 209
 Uyenoyama et al., 1982: 38, 250
 Uzzell, 1978: 175
 Uzzell and Berger, 1975: 175
 Uzzell et al., 1975: 175
 Uzzell et al., 1977: 175

 VandeBerg, 1983: 44–45, 166, 225,
 230–31
 VandeBerg and Cooper, 1978: 44
 VandeBerg et al., 1983: 166, 225, 230
 Vandel, 1938: 199, 202
 Vandel, 1939: 202
 Vandel, 1941: 193, 199
 Vanossi Este, 1971: 213

- Vanossi Este et al., 1974: 213
 Vanossi Este et al., 1972: 213
 Voelker, 1970: 223, 244
 Voelker and Kojima, 1971: 23, 223
 Vogt, 1980: 121
 Vogt and Bull, 1982: 118
 Vogt and Bull, 1984: 121–22
 Vogt et al., 1982: 115, 117
 Vorontsov, 1973: 44
 Vorontsov et al., 1980: 46

 Wachtel et al., 1980: 44
 Wachtel and Koo, 1981: 43–45
 Wachtel et al., 1975a: 43
 Wachtel et al., 1976: 44
 Wachtel et al., 1975b: 43
 Wagner, 1980: 116–17, 119
 Wagoner, 1968: 27
 Wagoner, 1969: 31
 Walker, 1971: 258
 Webb et al., 1983: 117, 119
 Welch, 1965: 111
 Werren et al., 1981: 204
 Westergaard, 1946: 261
 Westergaard, 1958: 13, 16, 23–25, 42,
 91, 221–22, 260–61
 White, 1945: 13, 164, 219, 221, 229,
 243
 White, 1954: 13, 154, 219, 229, 244
 White, 1973: 13, 17–18, 22, 147–50,
 152–54, 163, 176, 212, 219, 221,
 225, 227–29, 234, 243–44, 253
 Whiting, 1961: 151
 Whiting, 1943: 34, 151
 Whiting, 1945: 34, 151–52, 163, 168
 Whiting, 1960: 152
 Wiberg et al., 1982: 44–45
 Wilhoft et al., 1983: 121
 Williams, 1966: (xix)
- Williams, 1975: 5, 147, 160–61
 Williams, 1979: 83
 Williams, 1980: 160–61
 Wilson, 1905a: 220
 Wilson, 1905b: 220, 243
 Wilson, 1906: 220
 Winge, 1931: 16
 Winge, 1932: 10, 49, 86–87, 90, 93, 96,
 125
 Winge, 1934: 10, 49, 87, 93, 96, 102,
 104, 106–7, 125, 221, 242
 Winge, 1937: 10, 50
 Winge and Ditlevson, 1947: 24, 242
 Witschi, 1929: 10, 125
 Witschi, 1951: 126
 Wright, 1939: 184
 Wright, 1968: 98, 100
 Wurster and Benirschke, 1970: 14
 Wylie et al., 1968: 119

 Yamamoto, 1959: 221, 242
 Yamamoto, 1963: 24, 124
 Yamamoto, 1969: 10, 15, 18, 49, 93,
 96–97, 102, 104, 124–25, 242
 Yamamoto, 1975: 19, 24
 Yanagimachi, 1961: 213
 Yntema, 1976: 115–17
 Yntema, 1979: 117–18
 Yntema, 1981: 115
 Yntema and Mrosovsky, 1980: 115–16
 Yntema and Mrosovsky, 1982: 115, 118
 Yokoyama and Nei, 1979: 151, 183–84
- Zaborski et al., 1980: 126
 Zaborski et al., 1981: 44, 126
 Zuk, 1970a: 23, 225, 260–61
 Zuk, 1970b: 23, 225, 260–61



Subject Index*

- Acari: 148–49 (*see also* Mites; Ticks)
Acheta: 233; (*see also* Crickets)
Additive-value model: 9, 29, 57; description of, 49–50; example, 50; interpretation of, 50–51; relationship to genic balance, 51; incompatibility with arrhenotoky, 51, 145, 150, 178
Aedes: 243; (*see also* Mosquitoes)
Agamermis: 114 (*see also* Mermithids)
Akodon: 30
Akodont rodents: 44
Allelogeny: definition of, 202
Alligators: 116, 118, 122, 141–42 (*see also* Crocodilians)
Amphibians: 57, 125–26, 225, 246 (*see also* Frogs; *Triturus*)
Amphipods: *see* *Gammarus*; *Orchestia*
Amphogeny: definition of, 193; in *Orchestia*, 196–97; in *Armadillidium*, 199; table of, 201, in wild-caught females, 202–3
Androgenic gland: in *Armadillidium*, 199–201
Aneuploidy: 30, 229, 261; translocation, 262; sperm, 169
Angiosperms: 16, 25, 221, 250, 259–61 (*see also* Plants: higher)
Anisomorphic: 56–57, 59, 63
- Ants: 148, 151 (*see also* Hymenoptera)
Apes: 226
Apis: 148, 151–52 (*see also* Honeybees; Hymenoptera)
Aplocheilus (*see* *Oryzias*)
Arachnids: 16, 17, 149, 246 (*see also* Mites; Ticks)
Armadillidium: 199–204, 208–9, 215
Arrhenogenic factor in houseflies: 213–14
Arrhenogeny: 212–13; definition of, 193; in *Armadillidium*, 201–3; in *Orchestia*, 198
Arrhenotoky: general, 24, 34, 145–52, 159–60, 163–64, 170–74, 177–85, 189, 212, 248; definition and description of, 8, 145–48, 164; various taxa, enumerated, 148–49; origins, 149–50; possible ancestral systems, 150, 177–78, 189; constraints in evolution of, 164–65, 177–78; models for evolution of, 171–72, 179–85; advantages for evolution of, 161–63, 170–72, 180, 184; ecological advantages of, 170–72; detection of, 148–49; Hartl-Brown model, 179–80; diploid arrhenotoky with diploid males as normal, 147; diploid males as

*The subject index does not include entries from most of the tables. For information included in the tables, see the list of tables in the front of the book.

- abnormal, 151; sex determination in Hymenoptera, 150–52; see also uniparental males
- Asexual reproduction: 147, 175–76
- Autosomes, boldface notation: 10
- Bark beetles: 148, 172
- Barnacles: 213, 215
- Bed bugs: 234
- Bees: 148, 151; (*see also* Hymenoptera)
- Biparental females in *Rhabditis*: 176
- Biparental homozygotes, under *hymenopteran arrhenotoky*: 151; in models, 181–84
- Biparental males: 176–86, 188; during evolution of uniparental males, 160–66; reversion to biparental males from uniparental males, 166–68; in origin of PGL, 165, 185–86; in origin of arrhenotoky, 164, 177–85; equilibrium with uniparental males under arrhenotoky, 179, 183; examples of non-functional biparental males in Hymenoptera, 151
- Biparental reproduction: origin of, 6
- Birds: 15–16, 19, 43–44, 84, 125–26, 225, 234, 246
- Blackflies: 242
- Boidae: 245 (*see also* Snakes)
- Bombyx*: 223; silk moth, 36 (*see also* Lepidoptera)
- Bonellia*: 110–11, 132, 138–39
- Bracon*: 151–52 (*see also* Hymenoptera)
- Bridges, C.: X:autosome ratio in *Drosophila*, 21, 36, 50–51, 220; genic balance theory, 35, 48–53, 93, 107; model of regulation in sex development, 51–52
- Bryophytes: 261–64
- Bufo*: 126
- C-band heterochromatin: see under sex chromosomes, heterochromatin
- Caenorhabditis*: 35, 40–42, 89, 114, 232 (*see also* Nematodes)
- Cannabis*: 221
- Cattle: 45
- Cecidomyiid gnats: 148, 153
- Chiasmata: 227–28, 240–41, 243; changes in, during meiosis. 228; in sex bivalent, 228; illustrated, Plate 16.B.2, 238
- Chickens: 126 (*see also* Birds)
- Chironomus/chironomids*: 27, 32–33, 242 (*see also* Midges)
- Chromatin: description of, 223; euchromatin, 223; heterochromatin, 223–24; C-band heterochromatin, 224; constitutive heterochromatin, 224; facultative heterochromatin, 224 (*see* Sex chromosomes, heterochromatin)
- Chromosome inversions: as markers in midges, 27, 32, 242; role in sex chromosome evolution, 253–54
- Chrysemys*: 122 (*see also* Turtles, painted)
- Chrysomya*: 212, 214
- Cichlids: 124 (*see also* Fish)
- Cnemidophorus*: 238, 240
- Coccids (*see* Scale insects)
- Color genes: as indicators of sex linkages, 15; in platyfish, 29, 80–81; as examples of sex differences in fitness, 249–50
- Colubridae: 245 (*see also* Snakes)
- Combinatorialist perspective: 3–4, 54–65 (Chap. 5), 163; meaning of, 3–4, 54; for arrhenotoky, 178; for uniparental offspring, 163, 173–76
- Complementary sex-determination, Hymenoptera: 33–34, 150–52, 181–84; in *Apis* and *Bracon*, 151–52; molecular basis, 152; Crozier's multiple-locus hypothesis, 152; phenotype systems, 56–57, 59, 181–82; producing female heterogamety, 34, 181–82
- Comstockiella genetic system: 158–59 (*see also* Scale insects)
- Cost of meiosis (*see under* Uniparental males)
- Crickets: 232–35 (*see also* Grasshoppers)
- Crocodilians: 115, 118–20 (*see also* Alligators; Reptiles)
- Crossing-over: see chiasmata; sex chromosomes, general
- Crossover-free sex: 228; explanation of, 254
- Crustaceans: 57 (*see also* *Armadillidium*; *Gammarus*; *Orchestia*)
- Culex*: 193 (*see also* Mosquitoes)
- Culicimermis*: 114 (*see also* Mermithids)

Cytoplasmic sex factors/determination: definition of and types, 192–93; in *Armadillidium*, 200–202; in *Gammarus*, 193–95; in *Orchestia*, 195–98; model of evolution, 204–9; joint evolution with nuclear sex factors, models, 206–9; possibly the cause of a progressive female bias in houseflies, 79; parallel with cytoplasmic male sterility in plants, 204–5

Deleterious mutations, in degeneration of Y chromosomes: 254–64

Diaspidid genetic system: 158–59

Diaspididae: 158 (*see also* Scale insects)

Dicrostonyx: 29, 79–80 (*see also* Lemmings)

Dioecy: evolution of, 25, 91–92, 250; sex chromosomes in diploid dioecy, 254–61; sex chromosomes in haploid dioecy, 261–64

Diploid males: in Hymenoptera, as abnormalities, 151–52; from inbreeding in Hymenoptera, 151–52; in *Nasonia*, 152; in diploid arrhenotoky as normal males, 147; as defined in normal diploid genetic systems, 147 (*see also* Biparental males)

Diptera: 15, 18, 27–28, 35, 64, 91, 228, 253 (*see also* *Drosophila*; Gnats; Houseflies; Midges)

DNA (*see* specific types: Selfish; Satellite; Y-)

Dominant-Y systems: 20–22, 34, 210; in mammals, 35–36

Dosage compensation (*see under* Sex chromosomes, general)

Drosophila: 48–52, 89, 164–66, 178, 193, 220–21, 223, 225–26, 232, 244; *affinis*, 223; *melanogaster*, 21, 36–39, 48, 50–52, 91, 222, 231; *miranda*, 226–27, 244–45; *obscura*, 244; *pseudaobscura*, 226–27; *similans*, 48 (*see also* Diptera)

Elapidae: 245 (*see also* Snakes)

Ellobius: 46

Emys: 121 (*see also* Turtles, emydid)

Environmental sex determination:

109–44 (Chaps. 9 and 10): definition of, 8, 109–10; in marine worms (*Bonellia*), 110–11; in mermithid nematodes, 111–15; in reptiles 115–22; in fish, 123–24; in mermithids, host crowding, 112–13, host nutrition, 113–14, parthenogenetic reproduction, 114; temperature-dependent ESD, in reptiles, 115–22, in fish, 123; threshold temperatures in reptiles, 116–17; developmental sensitive stages in reptiles, 117–18; ecology of, in reptiles, 120–22; in *Gammarus*, 124; in *Ione*, 124; environmental influences on species with GSD, 124–26; advantages of, 128–30; Charnov-Bull model for evolution of ESD, 128–30; evolution from GSD to ESD model, 132–34; evolution of male heterogamety from ESD, 134–37; disadvantages of, 134–37; analysis of life histories in species with ESD, 137–41; population sex ratios under ESD, 131, 142–43; geographic variation of ESD, 143–44; possible estimation of the number of sex factors, 100

Epistasis, 31, 39, 41

ESD, defined as abbreviation for environmental sex determination: 109

Euchromatin: as contrasted to heterochromatin, 223; in houseflies, 30

Female heterogamety (*see* Heterogamety, female)

Fish: 15, 43, 57, 88, 125–26, 225, 246 (*see also* Cichlids; Medakas; Platypfish; Poeciliids; Swordtails; Zebra fish)

Flies (*see* Diptera)

Frogs: 43, 178 (*see also* Amphibians; *Rana*; *Xenopus*)

Fruitflies (*see* *Drosophila*)

Fungal gnats: 155–58 (*see also* *Sciara*)

Gammarus: 124, 193–95, 207–8

Genic balance theory: 48–52 (*see also* Additive-value model; Bridges)

- Genotypic sex determination: defined, 12; contrasted to environmental sex determination, 110; as alternative to ESD, 130, 132–37; environmental alterations of, 124–26 (see listing of specific mechanisms, such as Heterogamety; Polyfactorial; etc.)
- Geomys*: 237
- Gnats, cecidomyiid: 148, 153
- Gnats, fungal: 155–58 (see also *Sciara*)
- Goats: 46
- Goldschmidt, R.B.: work on sex determination in *Lymantria*, 35, 46–48; geographic variation in sex tendencies, 47–48
- Gonadectomy: 126
- Graptemys*: 121–22 (see also Turtles, map)
- Grasshopper: 225 (see also Crickets)
- Gryllotalpa*: 233 (see also Crickets)
- GSD, as abbreviation for genotypic sex determination: 110
- Guppy: 81, 96, 104, 125, 221 (see also *Poecilia*; Poeciliids)
- Gypsy moth (see *Lymantria*)
- H-Y antigen: 43–44
- Habrobracon* (see *Bracon*)
- Haploid gene expression (see under Sex chromosomes, general)
- Haploid males: in uniparental male systems, 147; low fitness of, 160, 168; effect of inbreeding on 169–70 (see also Uniparental males)
- Haploid sexes: 261–64 (see under Sex chromosomes, general)
- Haplodiploidy (see Arrhenotoky)
- Hermaphrodites: 6, 15, 25, 228, 248; in *Caenorhabditis*, 40, 232; in *Iceya*, 148; in origin of dioecy in plants, 25, 91–92
- Heterochromatin (see under Sex chromosomes, heterochromatin)
- Heterodera*: 115
- Heteroderidae: 115
- Heterogamety: 11–25 (Chap. 2); methods of diagnosis, 13–15; distinction from heteromorphic sex chromosomes, 10, 217; tables for plants, 16; tables for animals, 17–20; origins of, 24–25; equivalence of recurrent genotype pair, 70; phenotype systems, 55–57; population systems, 57–58; as endpoints of paths of equilibria in multiple-factor systems, 70–72; representation under the additive-value model, 50; evolution of in plants, 91–92; evolution of in animals from other mechanisms, see listing for the other mechanisms; evolution from resistance to cytoplasmic factors, 209–10; compatible with arrhenotoky, 171–72, 178; in model for evolution of sex linkage 251–52, 265–69 (see also Sex chromosomes, general; Two-factor systems; Heterogamety, female and male)
- Heterogamety, female: definition and symbols, 8, 12; boldface notation, 10; in *Armadillidium*, 199; in birds, 15–16, 234, 246; in flowering plants, 16, 91; in Lepidoptera, 16, 47, 234; in snakes, 245; in Trichoptera, 16; preponderance of versus male heterogamety, 90–92; equivalence with male heterogamety, 12, in phenotype and population systems 56; as possible ancestor to arrhenotoky, 178, hymenopteran, 181–82; in evolution of PGL, 185–86, 189; in model with cytoplasmic factor, 207
- Heterogamety, male: definition and symbols, 8, 11–12; boldface notation, 10; under multiple sex chromosomes, 12–13; in *Aedes*, 223; in arachnids, 16–17; in bark beetles, 172; in *Caenorhabditis*, 40–42; in *Drosophila*, 36–39; in *D. affinis*, 223; in *D. miranda*, 244–45; in *D. obscura*, 223; in *D. pseudoobscura*, 244; in flowering plants, 16, 91; in guppies, 96, 242; in insects, 16–17; in mammals, 16, 44, 246; in medakas, 96; in mud turtles, 238, 240; in *Orchestia* lacking cytoplasmic factors, 197–98; in nematodes, 16–17; in diploid scales, 158; possibly in *Rhabditis*, 176; in *Triturus*, 240; in whiptail lizards, 238, 240; apparent XX/XO system in *Sciara*, 157; preponderance over female heterogamety, 90–92; inheritance of sex

- factors illustrated, 14, 185, 261; with sex tendencies assigned, 21, 50; equivalence to female heterogamety in phenotype and population systems, 56; in evolution of arrhenotoky, 178–79; in evolution of PGL, 154, 185–86; evolution from resistance to cytoplasmic factors, 209–10
- Heteromorphism** (*see under Sex chromosomes, general*)
- Honeybees:** 148, 151 (*see also Apis; Hymenoptera*)
- Hops:** 225 (*see also Humulus*)
- Hormones:** 42–43, 45, 125–26
- Houseflies:** 27–28, 30–32, 77–79, 213, 216, 242–43, 247 (*see also Diptera; Musca*)
- Humans** (*see Man*)
- Humulus:** 221 (*see also Hops*)
- Hymenoptera:** 23–24, 33–34, 148, 150–52, 171, 181–85 (*see also Apis; Bracon; Wasps*)
- Icerya:** 148
- Inbreeding:** in evolution of uniparental males, 168–70; depression, 168–70; cause of biparental males in Hymenoptera, 151–52
- Insects:** 17, 148–49, 246 (*see also Diptera; Hymenoptera; Lepidoptera; and listings of specific genera*)
- Invertebrates:** 17, 228 (*see also Insects; and listings of specific groups and genera*)
- Ione:** 124
- Isogamy:** description of, 25
- Isopods:** 199 (*see also Armadillidium*)
- Klinefelter's Syndrome:** 46
- Lachnодиус:** 167 (*see also Scale insects*)
- Lebistes** (*see Poecilia*)
- Lecanoid genetic system:** 158–59
- Lecanoidae:** 158 (*see also Scale insects*)
- Lemmings:** 29–30, 44, 59, 61, 79–80, 222
- Lepidoptera:** 15–17, 222, 228, 234 (*see also Insects; Lymantria; Bombyx*)
- Leydig cells:** 43
- Limited chromosomes:** in *Sciara*, 155–57
- Linkage constraint:** 252
- Liverworts** (*see Bryophytes*)
- Lizards:** 20, 115–20, 246 (*see also Reptiles*)
- Local mate competition:** 169, 171–72, 176, 187
- Lymantria:** 46–48
- M factors:** in Diptera, 28, 31–32
- Mammals:** 15–16, 19, 35, 42–46, 84, 126, 224–25, 230–31, 246–47; marsupial, 166, 230–31; monotreme, 44; placental, 225, 230–31; dosage compensation in, 166, 230–31
- Man:** 35, 45–46, 222–23, 226
- Marsupials:** 166, 230–31 (*see also Mammals*)
- Maternal genome loss:** models of, 174–75
- Maternal monogeny:** 157; examples of, 212–13; inheritance of, 212, 214–15; mutation in houseflies, 213–14; advantages of, 215; transition to/from male heterogamety, 215
- Maternal sex ratio/determination:** 157, 211–15; in evolution of PGL systems, 186–88; under ESD, 132, 142; as definition of cytoplasmic sex factors, 192 (*see also Cytoplasmic sex determination*)
- Medakas:** 96–97, 125, 221, 242
- Megaselia:** 27–28
- Meiosis** (*see under Sex chromosomes, general*)
- Melandrium** (*see Silene*)
- Meloidogyne:** 115
- Mendelian genetics:** 3
- Mendelian populations/inheritance:** assumptions stated, 147, 192, 206, 209, 214; defined as basis of diploidy, 147; resistance factors, 209
- Menidia:** 123, 139–40
- Mermis:** 112, 114 (*see also Mermithids*)
- Mermithids:** 111–14, 131, 139, 142
- Metaseiulus:** 154–55 (*see also Mites, phytoseids*)
- Mice:** 35, 45–46, 222, 226, 228 (*see also Mammals; Mus*)
- Micromalthus:** 148

- Midges: 32–33, 242 (*see also Chironomus*)
 Mites: 148–50, 153–55, 187–88; phytoseids, 154–55, 187–88
Mollinesia: 125
 Monogeny: description of, 211; in *Armadillidium*, 199–203 (*see also* listings of specific types, maternal monogeny; Arrhenogeny; thelygeny)
 Monotremes: 44 (*see also* Mammals)
Mormoniella (*see* *Nasonia*)
 Mosaic haploid males, in *Apis* and *Bracon*: 152
 Mosquitoes: 224, 228, 243 (*see also* *Culex*)
 Mosses (*see* Bryophytes)
 Mullerian ducts: 43, 45
 Muller's ratchet: 256–58, 262, 264
 Multiple-factor systems: general, 26–34 (Chap. 3), 58–65, 66–85 (Chap. 6), 86–90, 181–82; in Diptera, 27–28; in houseflies, 27–28, 30–32, 77–78; in Hymenoptera, 33–34, 150–52, 181–84; in lemmings, 29–30, 79–80; in midges, 32–33; in platyfish, 28–29, 3-factor phenotype and population systems enumerated, 58–61; 2-locus/2-factor phenotype and population systems enumerated, 61–65; models of evolution in, 69–77; fitness in, 77–84; models, 73–77; stability of (models), 74, 76; maintenance from color genes, 80–1; as transitions between heterogametic mechanisms, 86–90, 181–82; inhibition by sex chromosomes, 82, 247; influence of son/daughter cost, 82–84; hybridization between two 2-factor systems generating a multiple-factor system, 88
Muntiacus: 14
 Muntjac: 14
Musca: 27, 30–32, 236, 242–43 (*see also* Diptera; Houseflies)
Mus: 45, 237 (*see also* Mice)
Myopus: 29, 79 (*see also* Lemmings)

Nasonia: 152 (*see also* Wasps)
 Nematodes: 16–17, 91, 232, 246 (*see also* *Caenorhabditis*, *Rhabditis*)

 Newts (*see* *Pleurodeles*; *Triturus*)
 Nur's sex ratio model: 67–68; under segregation distortion, 77; under cytoplasmic and nuclear sex factors, 206

Octosporea: 194
Orchestia: 195–98, 207–8
Oryzias: 96–97 (*see also* Medakas)
Oryzomys: 236
Ototylomys: 236

 Papaya: 221
 Parahaploidy: equivalent to paternal genome loss, 147
Paramarteilia: 197
Paramermis: 113, 143 (*see also* Mermitids)
 Parthenogenesis: 182; evolution of, 6; thelytoky, 147; facultative, considered for the evolution of arrhenotoky, 164–65, 170, 177; advantages of, 160; cyclical, 212; in mermitids, 114
 Paternal chromosomes/genome: in scales, 158–59, 166; heterochromatization of, 158–59, 168; retained in *Sciara* soma, 155, 170
 Paternal genome loss: general, 145–47, 159–60, 165–67, 173–74, 185–91; description of, 145, 152, 159, 188–89; various systems of, 153; in *Sciara*, 155–58; in scale insects, 158–59; in mites, 154–55; possibly in cecidomyiid gnats, 153; possible origins, 153–54; advantage for evolution of, 160–63; diploid PGL males, 147, 155, 170; constraints in evolution of, 165–66; evolution of sex determination under PGL, 186–87, 189–91; possible ancestry to arrhenotoky, 150
 Pedogenetic reproduction: 148
Peltogasterella: 213, 215
 PGL: as abbreviation for paternal genome loss, 145
 Phenotype systems: 55–59, 61–63; definition of, 55 (*see also* Multiple-factor systems; Two-factor systems)
 Phytoseid mites: 154–55, 187–88
 Pigs: 46

- Plants: higher, 42, 91–92, 259–61
 flowering (*see also* Angiosperms);
 lower (*see* Bryophytes)
 Platypus: 28–29, 59, 61, 80–84, 96;
 system of, 23, 28–29, 59, 61, 70,
 73–76, 80–81, 83–84, 94 (*see also*
 Poeciliids; *Xiphophorus*)
Pleurodeles: 125 (*see also* Amphibians)
Poecilia: 96, 242, 250 (*see also* Guppy)
 Poeciliids: 81, 88, 106, 124, 134, 249
 (*see also* Fish)
 Polyfactorial sex determination: 93–108
 (Chap. 8); definition of, 8, 93–94,
 107; in medakas, 96–97; in sword-
 tails, 95–96; species as examples
 of, 95–97; criteria for the diagno-
 sis of, 94–95; calculation of the
 number of sex factors, 100–101;
 additive-value model with minor
 sex factors, 102–4; coexistence
 with major sex factors, 104–7;
 evolutionary consequences of, 103,
 Winge model, 93, 107; possible
 disadvantages of, 107; model with
 just two sex factors, 97–99; envi-
 ronmental effect, 97–98, 102–3;
 heritability in model of, 102–3
 Polymorphisms, sex specific: 250–52;
 evolution of, sex-linked (model),
 265–69
 Polyploids: 22
 Population systems: 57–58, 60–61,
 64–65; definition of, 55 (*see*
 Multiple-factor systems; Two-
 factor systems)

 Quail: 125

Rana: 126, 175 (*see also* Frogs)
 Rats: 45
 Recessive-X systems: 20–22; in *Dro-
 sophila*, 21, 36; in *Caenorhabditis*,
 40
 Recurrent genotype pair: definition,
 70; in multiple-factor systems,
 70–76; connected by path of equil-
 ibria, 70–72 (*see also* Hetero-
 gamety)
 Reptiles: 43, 115–22, 126, 132,
 140–41, 143, 225 (*see also* Croco-
 dilians; Lizards; Snakes; Turtles;
 and listings of specific genera)
Rhabditis: 176 (*see also* Nematodes)
- Rivulus*: 125
Romanomermis: 113–14 (*see also*
 Mermithids)
Rumex: 221–22, 225, 261 (*see also*
 Angiosperms; Plants, higher)
- Salamanders (*see* *Pleurodeles*; *Triturus*)
 Satellite DNA: 226
 Scale insects: 148, 150, 153, 158–59,
 187–88, 224
Sciaridae: 153, 155–58, 170, 187,
 212
 Segregation distortion: 76–77, 257
 Selfish DNA: 155, 259
 Sertoli cells: 43, 45
 Sex allocation theory: 6, 67
 Sex chromosomes, general: 217–64
 Chaps. 16–18); description of, 10,
 13–14; boldface notation, 10, 218;
 distinction from sex determining
 mechanisms, 5, 10, 217; discovery
 of, 219–20; crossover suppression,
 227–28; dosage compensation,
 229–34; gene content, X-Y
 differences, 221–23; heteromor-
 phism, defined, 221, nature of,
 221–27; meiotic behavior, 227–29,
 240–43; recombination, 227–28,
 with slight X-Y heteromorphism,
 240–43; Y degeneration, evidence
 of, 221–23; Y-DNA, 225–27;
 X-inactivation, 166, 225, 230–31,
 233; slight X-Y differences, ex-
 amples, 239–42; Plates 16.B.1,
 16.B.2, 236–38; haploid gene ex-
 pression, diploid dioecy, 259–60,
 haploid dioecy, 261–64; haploid
 dioecy versus diploid dioecy,
 261–64; satellite DNA, 226–27;
 degenerate X, 234; age of hetero-
 morphisms in reptiles, 120;
 influence on evolution of multiple-
 factor systems, 82; linkage (*see*
 under this listing, crossover sup-
 pression, recombination)
- Sex chromosomes, evolution of: 91–92,
 249; conserved systems, 246;
 origins, 243–45; progression toward
 heteromorphism, 243–46; rear-
 rangements in, 252–54; X-Y dif-
 ferences, 243–46, 254–58; Y
 degeneration, animals, 243–46,
 249–52, 254–58, plants, 259–64;

- sex linkages, 91–92, 249, 251–52; models of, 251–52, 265–69; unexpected under arrhenotoky, hermaphroditism, polyfactorial sex determination, 15, 248
- Sex chromosomes, heterochromatin:** 223–24; on Y, 225; on X, 225; in houseflies, 30; in bryophytes, 262–63; constitutive, 224; facultative, 224, of X, 225, 230; evolution of, 258–59; C-band, 262, explained, 224–25, illustrated, Plates 16.B.1 and 16.B.2, 236–38, on Y, 225, on X, 225
- Sex chromosomes, multiple:** descriptions of and types, 12–13, 228–29; in *Drosophila miranda*, 227, 244–45; in *D. obscura*, 244; in muntjac deer, 14; in houseflies, 27, 31; evolution of, 12–13, 228–29, 253; as evidence of Y-degeneration, 229, 244–45
- Sex chromosomes, taxa considered:** amphibians, 240, 246; ancestors of PGL species, 154; barnacle, 213; birds, 84, 246; blackflies, 242; bryophytes, 261–64; *Caenorhabditis*, 40, 232; *Drosophila*, 21, 36, 223, 226–27, 231; fish, 242, 246; flowering plants, 91–92, 221; guppies, 242; houseflies, 27, 30–31, 242–43; lizards, 238 (Plate 16.B.2), 240, 246; *Lymantria*, 47–48; mammals, 29–30, 44, 84, 236–37 (Plate 16.B.1), 246, 230–31; midges, 32, 242; mosquitoes, 243; mud turtles, 238 (Plate 16.B.2), 240; muntjac, 14; reptiles, 118–20; scales, 158; *Sciara*, 155–58; snakes, 245–46; *Triturus*, 240 (*see also* under Sex chromosomes, multiple)
- Sex determining mechanism:** general definition, 6–8; classical, description of, 8, 211; variety of, 3–4, 54; contrasted to sex chromosomes, 5, 217; zygotic, 186–87, 189, definition of, 12; parental, definition of, 12, 211; maternal, 186–87 (*see* specific mechanisms: Arrhenotoky; Polyfactorial; Two-factor; Heterogamety; Multiple-factor; Environmental; Paternal genome loss; Cytoplasmic; and Maternal monogeny)
- Sex development:** 5, 12, 194; defined, 8; genetics of in *Drosophila*, 35–39; genetics of in *Caenorhabditis*, 35, 40–42
- Sex differences in fitness:** 249–52; in evolution of X-Y crossover suppression, 251–52
- Sex differences in recombination:** 228, 254
- Sex factors, nuclear (chromosomal):** definition of, 9; minor, 9, 11; major, 9, 11; zygotic, 9, 216; parental, 9, 212; cytoplasmic (*see* Cytoplasmic sex factors/determination); characterization, in heterogametic systems, 12–15; in multiple-factor systems, 26–34; in polyfactorial systems, 93–94, 100–101; in Hymenoptera, 33–34; 151–52; sex tendencies of, 22; physical size of, 35–36; relation of sex transformer mutations to, in *Drosophila*, 36–39, in *Caenorhabditis*, 40–42; in mammals, 42–46; as regulatory genes, 36; role in sex development, 42; caution, 209–10
- Sex linkage:** in diagnosis of sex factors, 14–15, 26–32, 100–101; advantages of, 249–50; evolution of 251–52, models, 265–69
- Sex ratio, general:** stability of 1/2, in Nur model, 67–68, under polyfactorial sex determination, 103, in multiple-factor systems, 69–70; as a dominating force in evolution of sex determination, 66–67; parental influence upon, 211, definition of, 9
- Sex ratio, under arrhenotoky:** stability of 1/2 under pure arrhenotoky, 180, 184; equilibria with biparental and uniparental males present, 179–80, 184; sex ratio selection in contemporary Hymenoptera, local mate competition, 171–72, a patchy environment, 171
- Sex ratio, with cytoplasmic factors:** in *Armadillidium*, 199–204; in *Gammareus*, 193–95; *Orchestia*, 195–98; evolution of female bias, 192, 205–6; evolution of, models, 204–6; joint evolution of nuclear and cytoplasmic factors, 206–9
- Sex ratio, under environmental sex determination:** in *Bonellia*, 110–11,

- in mermitid nematodes, 111–15; in reptiles, 115–18, 121–22; in fish, 123; other examples, 124; rate of evolution, 131; equilibrium according to patch type, 130; evolution of population primary sex ratio, 130–31; evolution of under choice of patch type, 132; population primary sex ratio, definition of, 130–31; examples discussed, 142–43; geographic comparison of, 142–43
- Sex ratio**, under maternal monogeny: control by the mother, 211; in houseflies with the mutation *Ag*, 213; equilibrium of 1/2, 214
- Sex ratio**, in multiple-factor systems: equilibrium of 1/2, 69–70; in lemmings, 80; in diagnosis of multiple-factor systems, 26–7; progressive female bias in houseflies, 78–79; Fisherian sex ratio with unequal son/daughter cost in the platyfish system, 83–84; implications of long-term maintenance of heterogamety, 84; use in testing models of multiple-factor systems, 88–89; relevance to Y degeneration, in plants, 261, in guppies, 242
- Sex ratio**, under paternal genome loss: in *Sciara*, 187; in scales and mites, 187–88; equilibrium under zygote control, 186, model of evolution, 189–91; equilibrium for maternal control, 186; maternal/zygote conflict, 186–87
- Sex reversal**: in birds, 44; in species with GSD, 124–26; as means of identifying the heterogametic sex, 15; inheritance of *Sxr* in mice, 46
- Sex tendency**: 57, 93; definition of, 9–10; use in additive-value model, 49–50, 182; alternative interpretations under male heterogamety, 21; of sex factors, 22; platyfish an exception, 29; incompatibility with arrhenotoky, 145, 178 (*see also* Additive-value model)
- Sex transforming mutations**: in *Aedes*, 125; in *Drosophila*, 37–39; in *Caenorhabditis*, 40–42; in hermaphroditic plants, 42, 91–92; in mammals, 45–46
- Sex-linked genes/markers**: 26–27; vari-
- ous examples of, 14–15, 222–23; in houseflies, 30; in *Sphaerocarpus*, 263–64; in multiple-factor systems, 26–29, 31–32, in poly-factorial systems, 100–101
- Silene*: 221
- Silk moth**: 223
- Silverside fish**: 123, 139–40
- Simuliidae**: 242
- Snakes**: 119–20, 226, 245–46 (*see also* Reptiles; Squamate reptiles)
- Sorrell** (*see Rumex*)
- Spermatogenesis**: complications to uniparental males, 160; complications to biparental males in Hymenoptera, 34, 152
- Sphaerocarpus*: 263–64 (*see also* Bryophytes)
- Sphenodon*: 120
- Squamate reptiles**: 119–20 (*see also* Lizards; Reptiles; Snakes)
- Staurotypus*: 238, 240
- Supergenes**: 9
- Supersexes**: 51
- Swordtails**: 95–96, 100–101 (*see also* Poeciliids; *Xiphophorus*)
- Temperature-sensitive developmental periods**: in reptiles, 117–18 (*see also* ESD); in *Drosophila*, 38–39; in *Caenorhabditis*, 40–41
- Temperature-sensitive mutations**: in *Aedes*, 125; in *Drosophila*, 37–8; in *Caenorhabditis*, 40–41
- Temperature-sensitive sex determination**: in reptiles, 115–22; in fish, 123 (*see* ESD)
- Testicular feminization**, mutation: 45
- Testosterone**: 43, 45
- Thelohania*: 193–95
- Thelygeny**: evolution of by cytoplasmic factors, 204–6; in *Armadillidium*, 200–203; in *Gammarus*, 193–95; in *Orchestia*, 195–96, 198; under maternal monogeny, 212–13; male transmission of, 200–201 (*see also* Cytoplasmic sex factors)
- Thelytoky**: evolution of, 147; definition of, 147
- Thrips**: 148
- Thysanoptera*: 148
- Ticks**: 148–50 (*see also* Arachnids; Mites)

- Tomatoes: 260
Trionyx: 141 (*see also* Turtles)
 Triploid females, in *Nasonia*: 152
Triturus: 240–41, 254 (*see also* Amphibians)
 Tuatara: 120
 Turtles: 115, 117–21, 141, 143; emydid, 117–18, 121–22, 143; map, 116, 121–22, 142; mud, 117; painted, 117, 122; sea, 118; snapping, 117; softshelled, 141 (*see also* Reptiles)
 Two-factor systems: 11–25 (Chap. 2)
 with environmental variance, 97–100; Nur model, 67–68; parental, 157, 212–14; phenotype, 55–57; population, 57–58 (*see* Heterogamety)

 Uniparental (offspring): 173–74; defined, 145, 147, 173
 Uniparental females: 174–76
 Uniparental males: 145–91 (Chaps. 11–13); definition of, 145, 159–60; basic systems of, arrhenotoky and paternal genome loss, 145–46; cost of meiosis as advantage for evolution of, 160–63, 170–74; disadvantages of, 166–68; inbreeding in evolution of, 168–70; fitness components in evolution of, 161 (*see also* Arrhenotoky; Paternal genome loss)

Venezillo: 215
 Vertebrates: 18–19 (*see also* amphibians; Birds; Fish; Mammals; Reptiles)

 Viperidae: 245 (*see also* Snakes)

 W-Y chromosome comparison: 258, 260
 Water potential: effect on sex determination in reptiles, 118, 141
 Wasps: 148, 151, 171, 204 (*see also* Hymenoptera)
 Whiptail lizards: 238, 240 (*see also* Lizards)

Xenopus: 44 (*see also* Amphibians; Frogs)
Xiphophorus: 28–29, 81, 95–96, 101, 250 (*see also* Fish; Platypfish; Poeciliids; Swordtails)
Xyleborus: 172 (*see also* Bark beetles)
 X-autosome ratio model: of Bridges, 21, 36, 50–51, 220 (*see also* Recessive-X systems)
 X chromosome characteristics (*see* listings under Sex chromosomes)

 Y chromosome characteristics (*see* listings under Sex chromosomes)
 Y-DNA: 218; in apes and man, 226; in *Drosophila*, 226–27; in snakes, 226
 Y-W chromosome comparison: 258, 260
 YY: sex of, 22–24; inviability of, 23, 29–30, 221–22; viability of, 24, 28, 30–32; sterility of, 222

 Zebra fish: 98, 101