Lecture handout 7

SELECTION: **Natural selection** is the process by which favorable heritable traits become more common in successive generations of a population.

-Selection is a dominant force shaping the course of evolution, but difficult to quantify

-genetic variation plus environment determine phenotypic variation of traits

-Phenotypic variation determines variation in survival, fecundity, mating ability, other factors

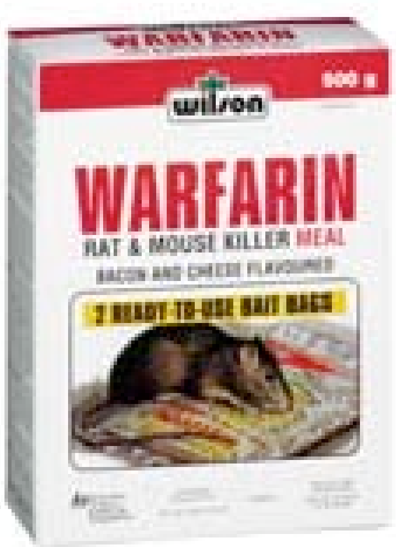
-Overall effect is called fitness

-Relative fitness is the relative ability of different genotypes to pass on their alleles to future generations

-Since selection is complex, a reductionist approach is adopted to studying it

-Simplifying approach, especialy for Basic Selection Model discussed in chapter 3.

Some examples of selection follow



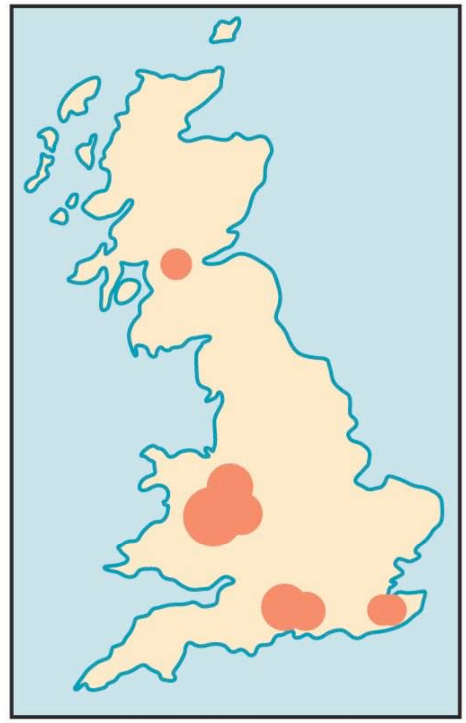
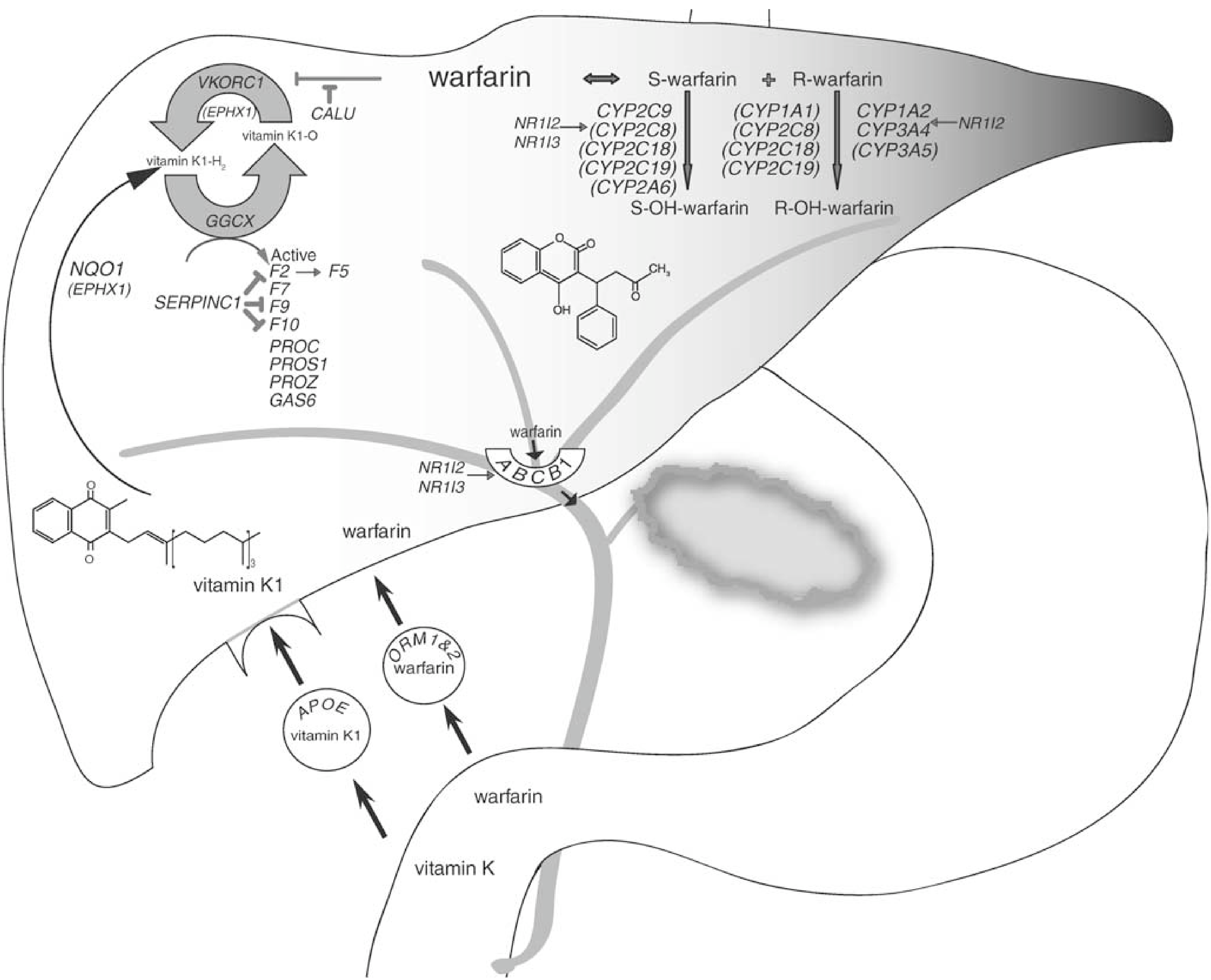


FIGURE 18.3. Resistance to the anticoagulant poison warfarin in rats (*Rattus norvegicus*) is due to multiple alleles. Areas where warfarin-resistant rats are found are in *red*. Here, resistant alleles are kept polymorphic by heterozygote advantage. The Scottish, Welsh, and English resistance outbreaks are due to different alleles.

18.3, Web source, no longer available



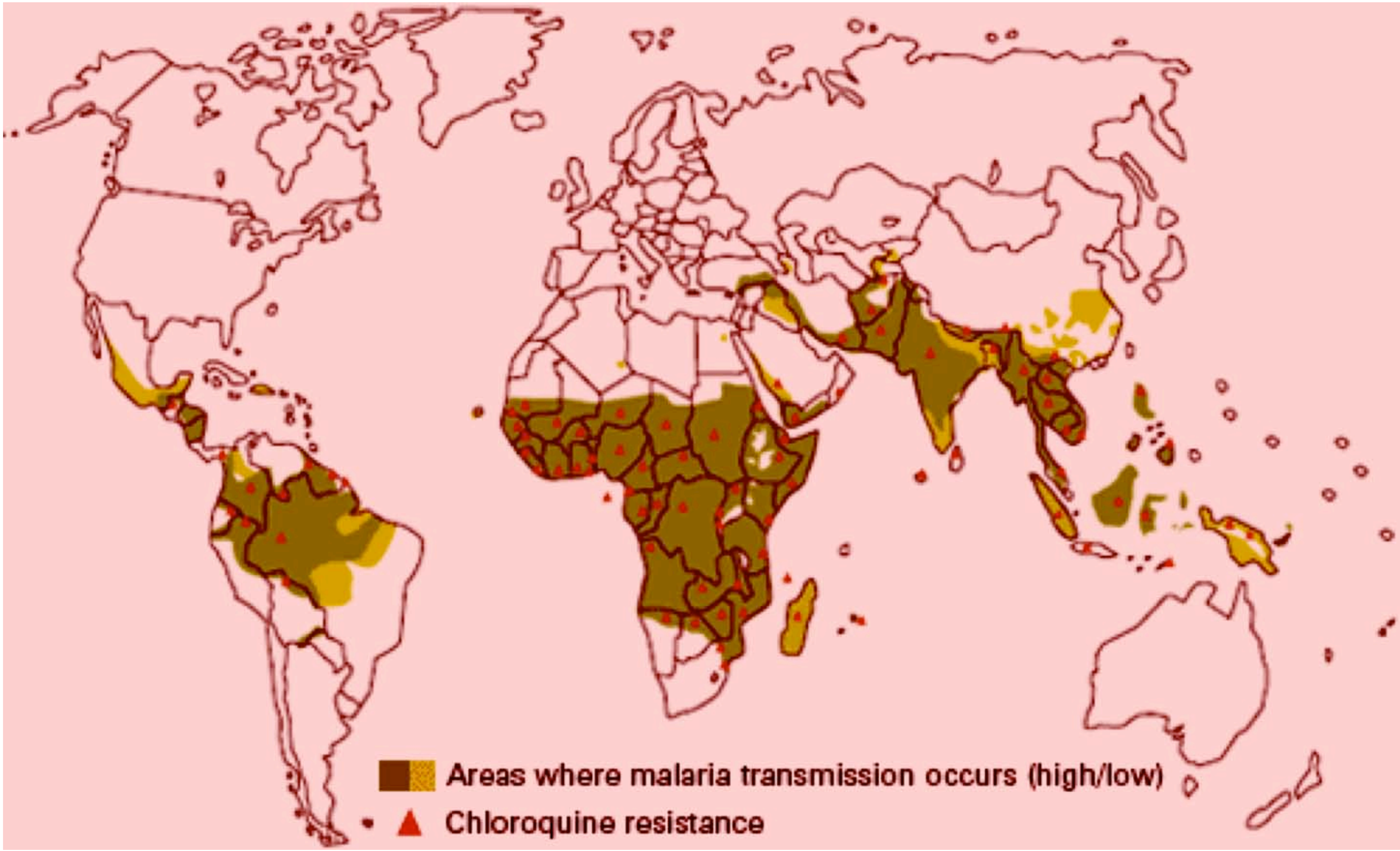
VKORC1
(EPHX1)
CALU
vitamin K1-O
vitamin K1-H2
GGCX
warfarin
S-warfarin
R-warfarin
CYP2C9
(CYP2C8)
(CYP2C18)
(CYP2C19)
(CYP2A6)
NR1I2
NR1I3
(CYP1A1)
(CYP2C8)
(CYP2C18)
(CYP2C19)
CYP1A2
CYP3A4
(CYP3A5)
NR1I2
S-OH-warfarin
R-OH-warfarin
NQO1
(EPHX1)
Active
F2
F5
F7
SERPINC1
F9
F10
PROC
PROS1
PROZ
GAS6
warfarin
ABCB1
NR1I2
NR1I3
warfarin
vitamin K1
ORM1&2
warfarin
APOE
vitamin K1
warfarin
vitamin K

Mosquito resistance to organophosphates

TABLE 3.2 Nucleotide polymorphism in exon 3 of gene *ace*-1 in *Culex pipiens* mosquitoes (Weill *et al.*, 2003). Samples are listed according to subspecies (*C. p. pipiens* and *C. p. quinquefasciatus*), presence of resistance (R) or susceptibility (S), and country of origin. Only polymorphic sites are indicated, and a dash indicates identity with the R consensus sequence for the subspecies (top line). The position of the G119S mutation at nucleotide position 739 is indicated by an asterisk.

			Nucleotide position																						
Subspecies	R or S	Country	450	453	471	498	528	564	573	603	651	691	696	714	732	739*	747	753	774	770	780	790	798	813	846
C. p. pipiens	R	Consensus	T	C	A	T	G	G	G	C	G	C	C	C	C	A	C	C	C	C	C	G	G	A	T
	R	Burkina Faso	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	R	Zimbabwe	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	R	Ivory Coast	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	R	Mali	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	R	Martinique	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	R	Brazil	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	S	United States	-	T	-	C	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	G
	S	United States	-	T	-	C	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	G
	S	United States	-	T	-	-	-	-	A	-	-	-	-	-	-	G	-	-	-	-	-	A	-	-	-
	S	United States	-	T	-	-	-	-	A	-	-	-	-	-	-	G	-	-	-	-	-	A	-	-	-
	S	China	-	T	C	C	-	-	-	-	-	-	-	-	-	G	-	-	T	-	-	-	-	-	-
	S	China	-	T	-	C	-	-	-	-	-	-	-	-	-	G	-	-	T	-	-	-	-	-	-
	S	Thailand	-	T	C	C	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	G
	S	India	-	T	-	C	-	A	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	G
	S	South Africa	-	T	C	C	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	G
	S	South Africa	-	T	-	-	-	-	A	-	-	-	-	-	-	G	-	-	T	-	-	-	-	-	-
	S	Ivory Coast	-	T	-	C	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	-
	S	Congo	-	T	C	C	-	-	-	-	-	-	-	-	-	G	-	-	T	-	-	-	-	-	G
	S	Brazil	-	T	-	C	-	-	-	-	-	-	-	-	-	G	T	-	-	-	-	-	-	-	G
	S	Polynesia	-	T	-	-	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	G
C. p. quinque	R	Consensus	A	T	A	C	G	G	A	C	C	A	G	T	T	A	C	T	C	T	T	G	G	G	T
	R	Tunisia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	R	Portugal	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	R	Italy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	R	France	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	S	Belgium	-	-	-	-	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	-
	S	Belgium	-	-	-	-	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	-
	S	Australia	-	-	-	-	-	-	-	A	-	-	-	-	-	G	-	-	-	-	-	-	-	-	-
	S	France	-	-	-	-	-	-	-	-	-	-	-	-	-	G	-	-	-	-	-	-	-	-	-
	S	Holland	-	-	-	-	A	-	-	A	-	-	-	-	C	G	-	-	-	C	-	-	A	-	-

Malaria resistance to chloroquine



Basic selection model: Uses simplifying assumptions to examine dynamics of genetic change caused by selection, and statics of genetic variation (where selection maintains variation).

TABLE 3.3 A categorized list of assumptions in the basic selection model.

Genetic system
- (a) Single, biallelic, autosomal locus
- (b) Diploidy
- (c) Random mating among individuals

Selection
- (a) Selection identical in both sexes
- (b) Selection occurs through differences in viability
- (c) Constant value in space and time for each genotype

Other factors
- (a) Nonoverlapping generations
- (b) No inbreeding
- (c) Infinite population size
- (d) No gene flow
- (e) No mutation

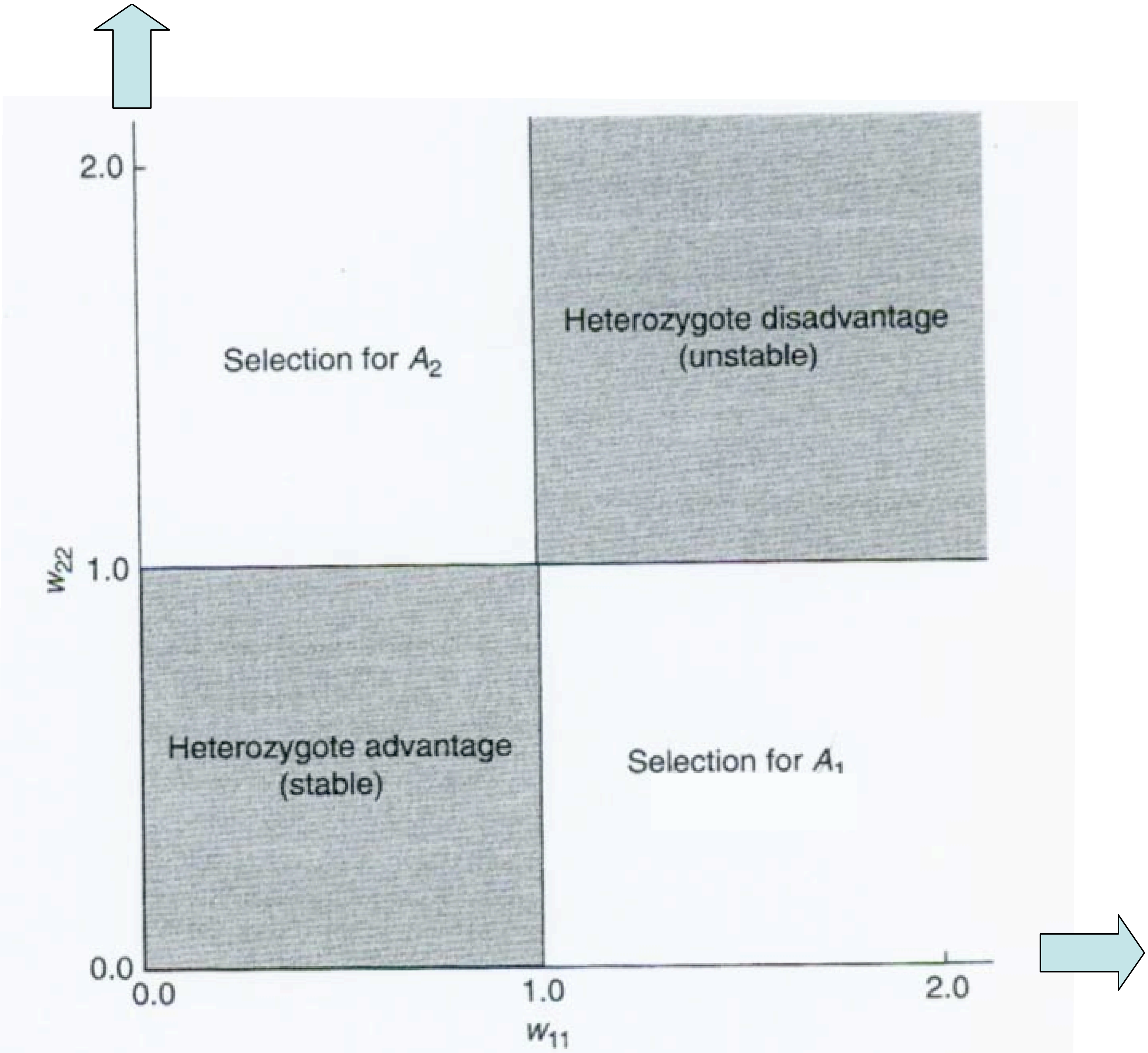
Relative fitness for three genotypes in a biallelic system is designated by the lower case Greek letter omega, ω.

TABLE 3.4 The frequency of genotypes before and after selection, assuming Hardy–Weinberg proportions before selection.

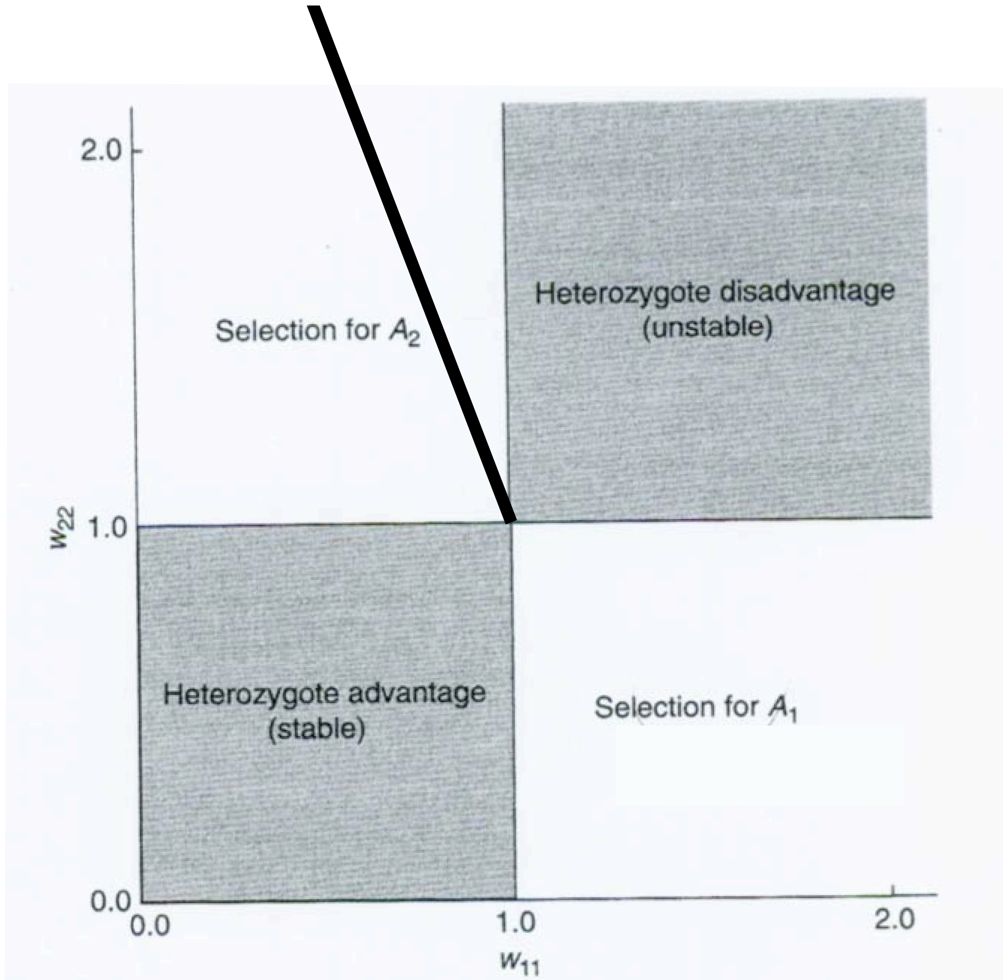
	Genotype			
	A_1A_1	A_1A_2	A_2A_2	*Total*
Relative fitness	w_{11}	w_{12}	w_{22}	—
Frequency before selection	p_0^2	$2p_0q_0$	q_0^2	1
Weighted contribution	$p_0^2w_{11}$	$2p_0q_0w_{12}$	$q_0^2w_{22}$	$\overline{w}$
Frequency after selection	$\frac{p_0^2w_{11}}{\overline{w}}$	$\frac{2p_0q_0w_{12}}{\overline{w}}$	$\frac{q_0^2w_{22}}{\overline{w}}$	1

The fitness of the heterozygous genotype, ω_{12}, is set as 1, while the fitness of the two homozygotes are each standardized relative to the heterozygote.

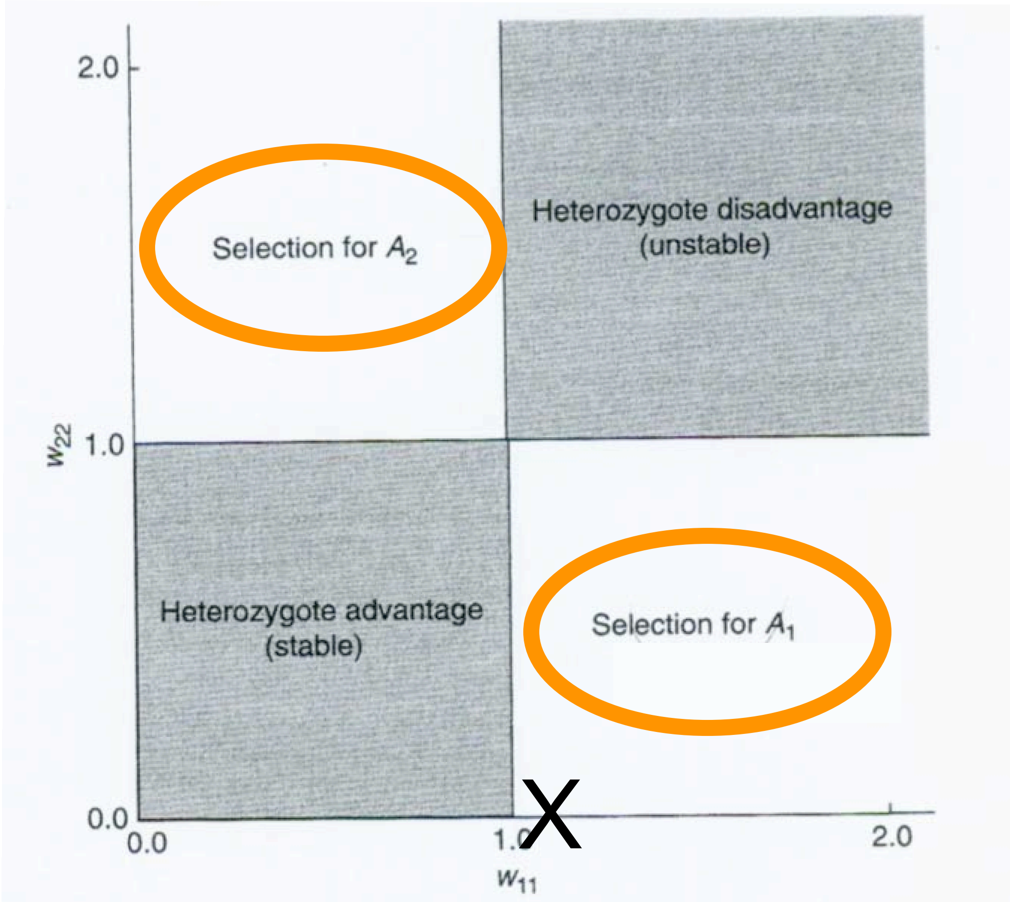
This makes it easier to see how different fitness values can affect genetic change or stability


2.0
1.0
0.0
w_{22}
Selection for A_2
Heterozygote disadvantage
(unstable)
Heterozygote advantage
(stable)
Selection for A_1
0.0
1.0
2.0
w_{11}

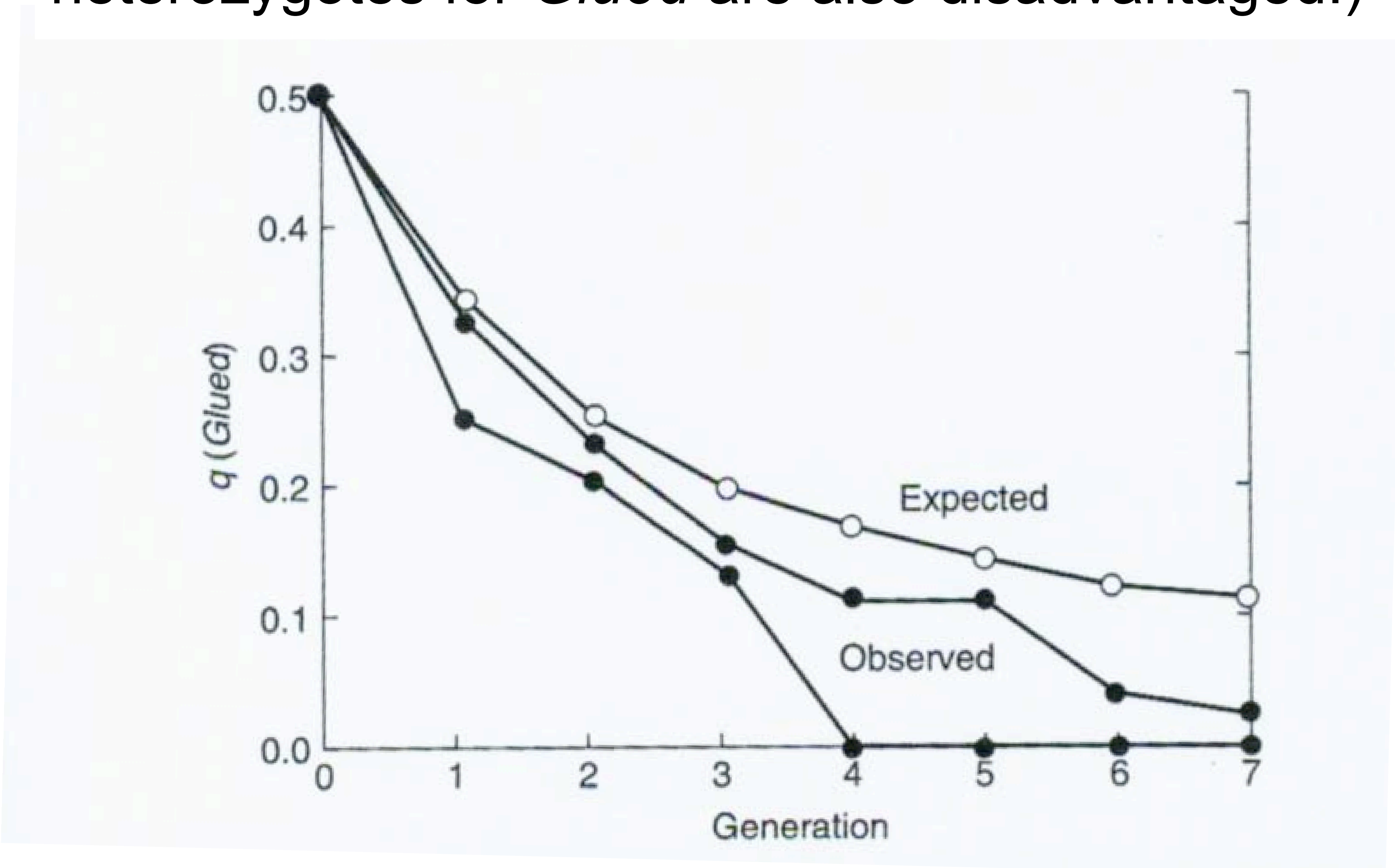
Point at which all genotypes (both homozygotes and the heterozygote) have the same relative fitness.



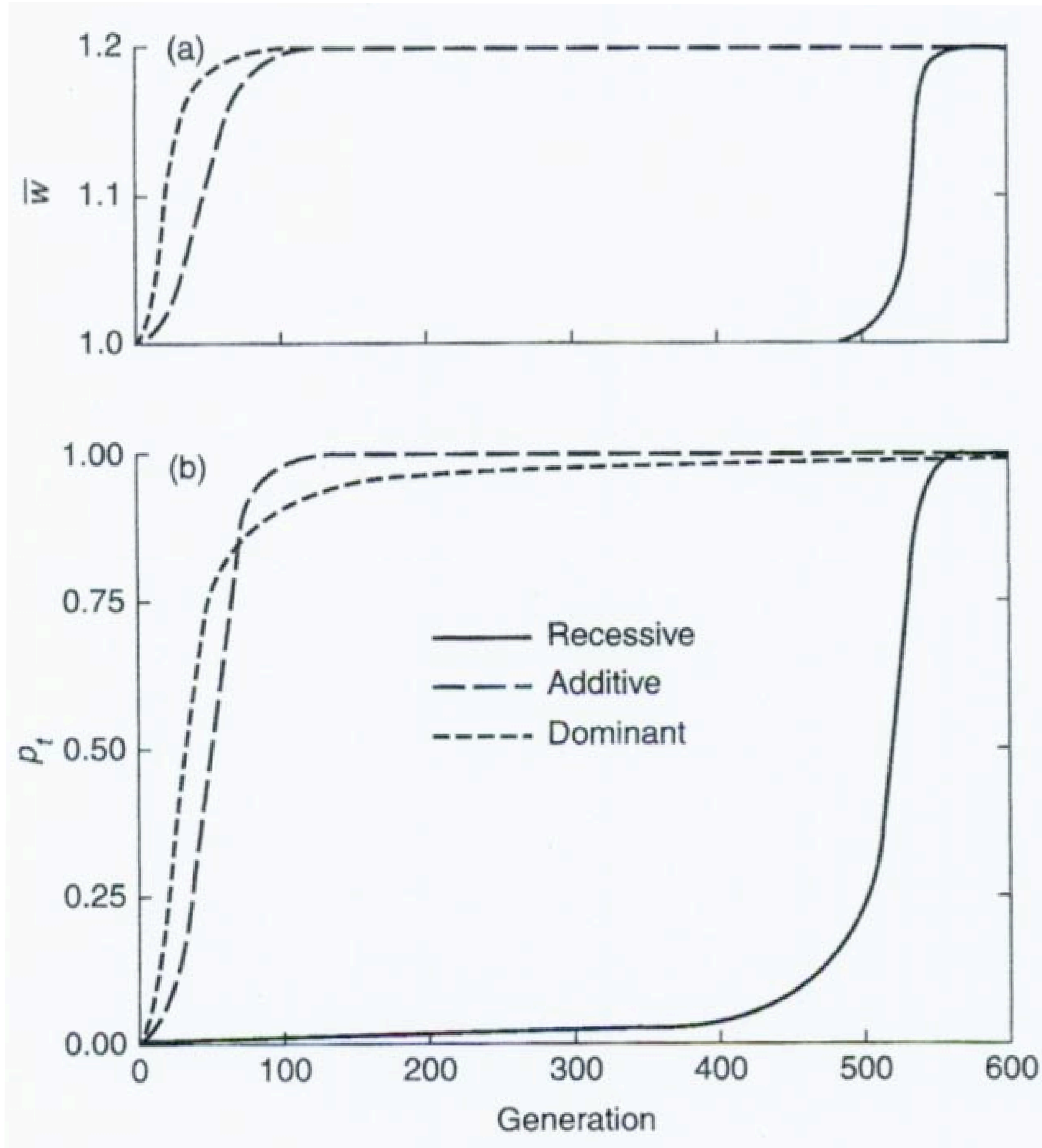
Hedrick example 3.2: selection against a homozygote **lethal** (a phenotype that results in “early death”), *Glued* in *Drosophila melanogaster*.



At high frequencies, lethals decline quickly, but persist at low frequencies (except in this case heterozygotes for *Glued* are also disadvantaged.)

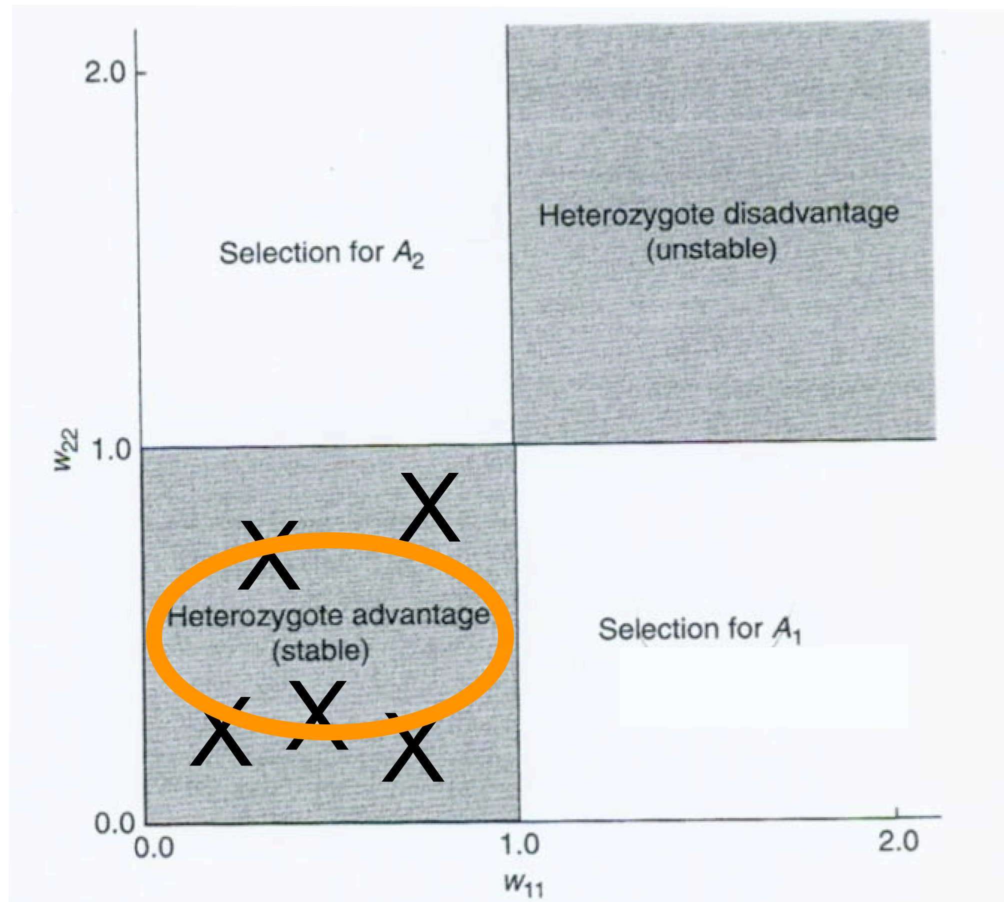


Where selection favors an allele, frequencies of the favored allele will rise more quickly for favored dominant (and additive) alleles than for favored recessive alleles Fig 3.5, p(init) = 0.01 s = 0.1



Heterozygote advantage, a.k.a. **overdominance**: both homozygotes, A_1A_1 and A_2A_2 have a selective disadvantage over the heterozygous genotype A_1A_2.

This can be a stable condition across the generations.



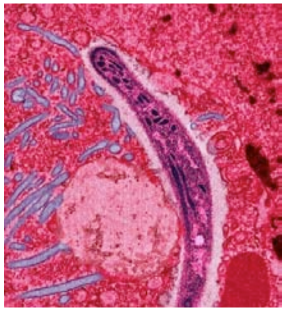
Heterozygote advantage, a.k.a. overdominance, examples:

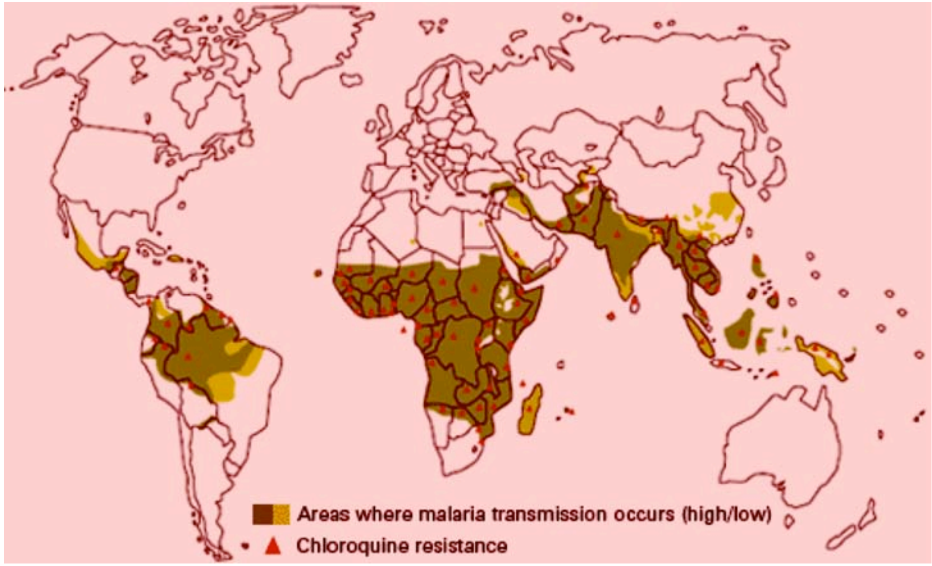
-Rodent warfarin resistance, unlike wild type homozygotes, heterozygotes resist poisoning. In the absence of warfarin, heterozygotes are overall healthier than homozygotes.

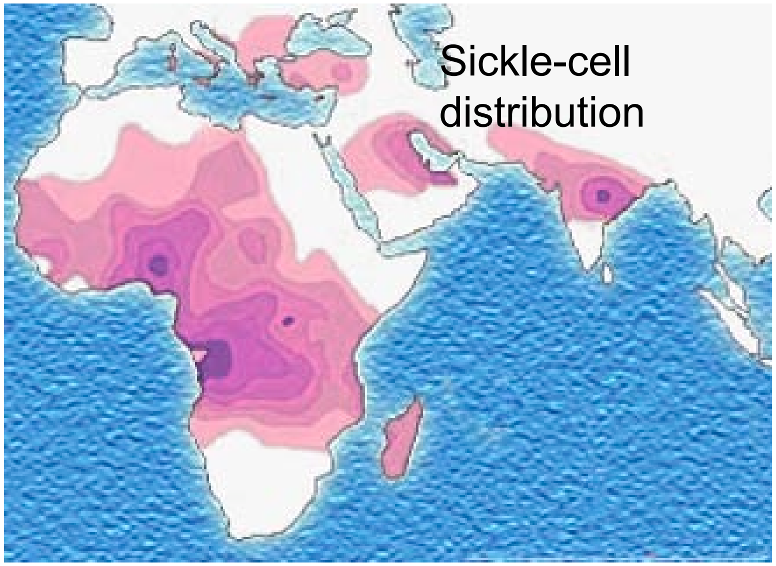
-Sickle cell anemia (heterozygotes are more resistant to malaria)

Sickle-cell disease: red blood cells have an abnormal, rigid, sickle shape, with their movement restricted through blood vessels, depriving downstream tissues of oxygen. Chronic, lifelong and sometimes painful.

Incompletely recessive; carriers are resistant to malaria (their blood cells rupture before the apicomplexan protozoan can reproduce).







Heterozygote advantage, a.k.a. overdominance, examples:

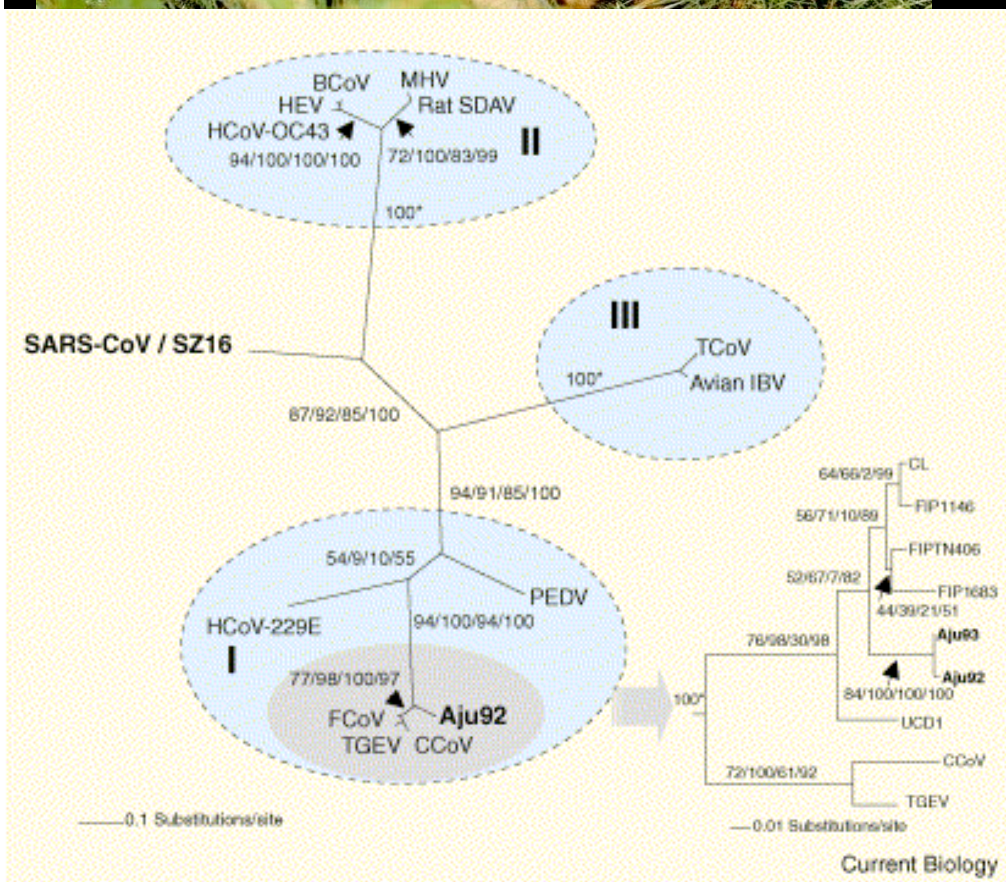
-Cystic fibrosis: autosomal recessive, gene mutation: affects function of a chloride channel. Leads to frequent infections, male infertility.

- heterozygote advantage has been proposed against various diseases, eg cholera, diarrhea, TB, lactose intolerance

Heterozygote advantage, a.k.a. overdominance, examples:

-Immune system genes, such as the **major histocompatibility complex (MHC)**; called leukocyte antigen system (HLA) in humans

Lack of diversity in the MHC is of major conservation concern in the case of species with reduced genetic diversity



Example: SARS-like coronavirus outbreak in cheetah in the 1980s.

In domestic cats virulent FIPV mediates fatal disease in about 5-10% of infected cats. Within six months of the arrival of cheetah coronavirus, 100% of the cheetahs had seroconverted, 90% percent of the 60 cheetahs in the park developed disease symptoms, with a mortality of 60% within 2-3 years.

This was the most extreme outbreak of coronavirus in any species yet recorded.

S. J. O'Brien and colleagues

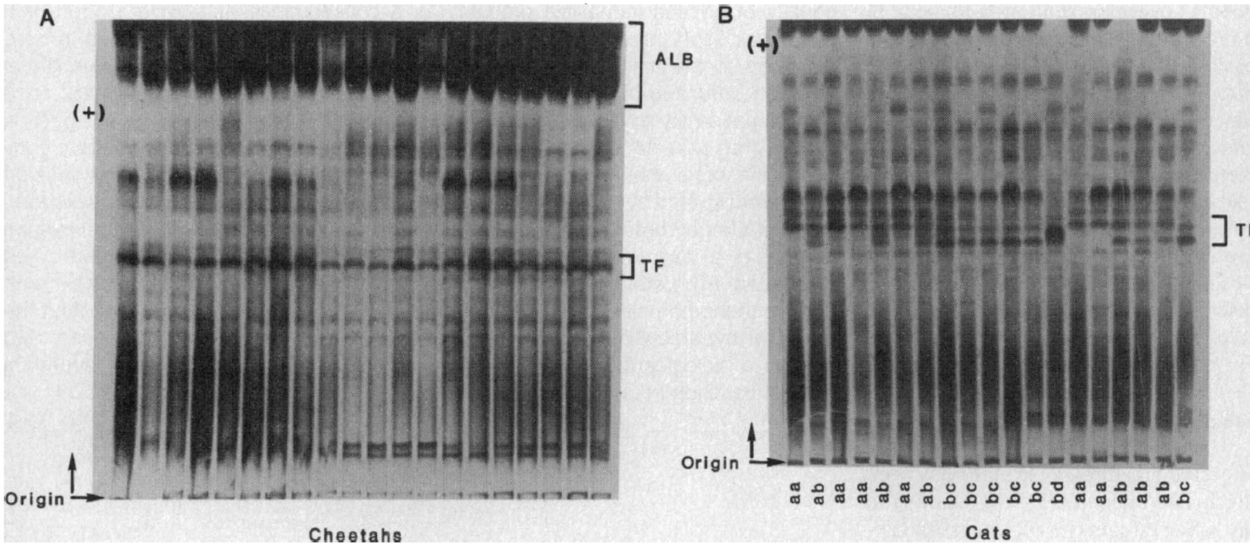


Fig. 2. (A) Polyacrylamide gel loaded with 20 cheetah plasma samples and stained for proteins with Coomassie brilliant blue. Invariant transferrin (TF) and albumin (ALB) bands are indicated. Transferrin was identified in duplicate gels stained with iron-specific Nitroso-R stain (*19*). (B) Polyacrylamide gel loaded with 20 domestic cat samples and stained as in (A). Three domestic cat alleles of TF were observed in the cat survey (*22*, *42*).

S. J. O'Brien and colleagues, 1985

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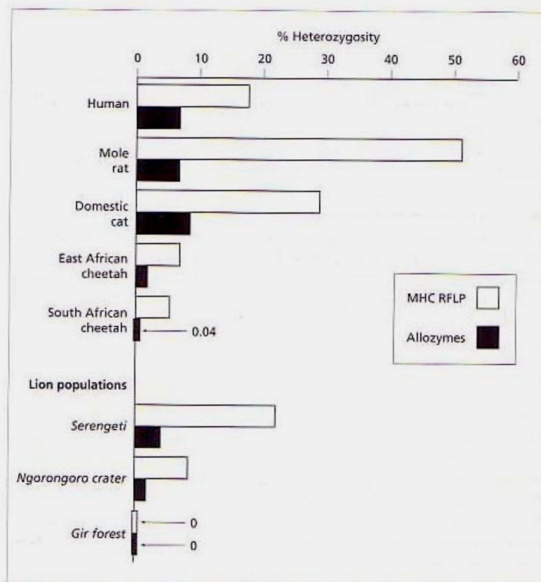
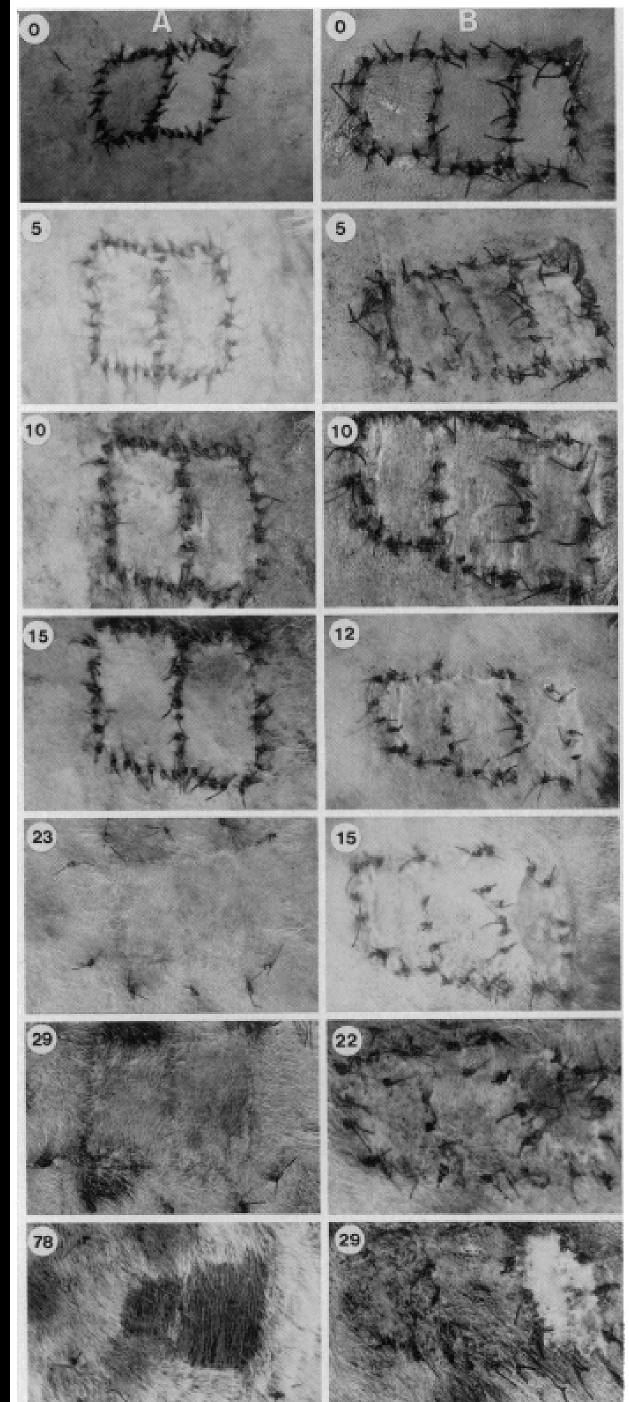
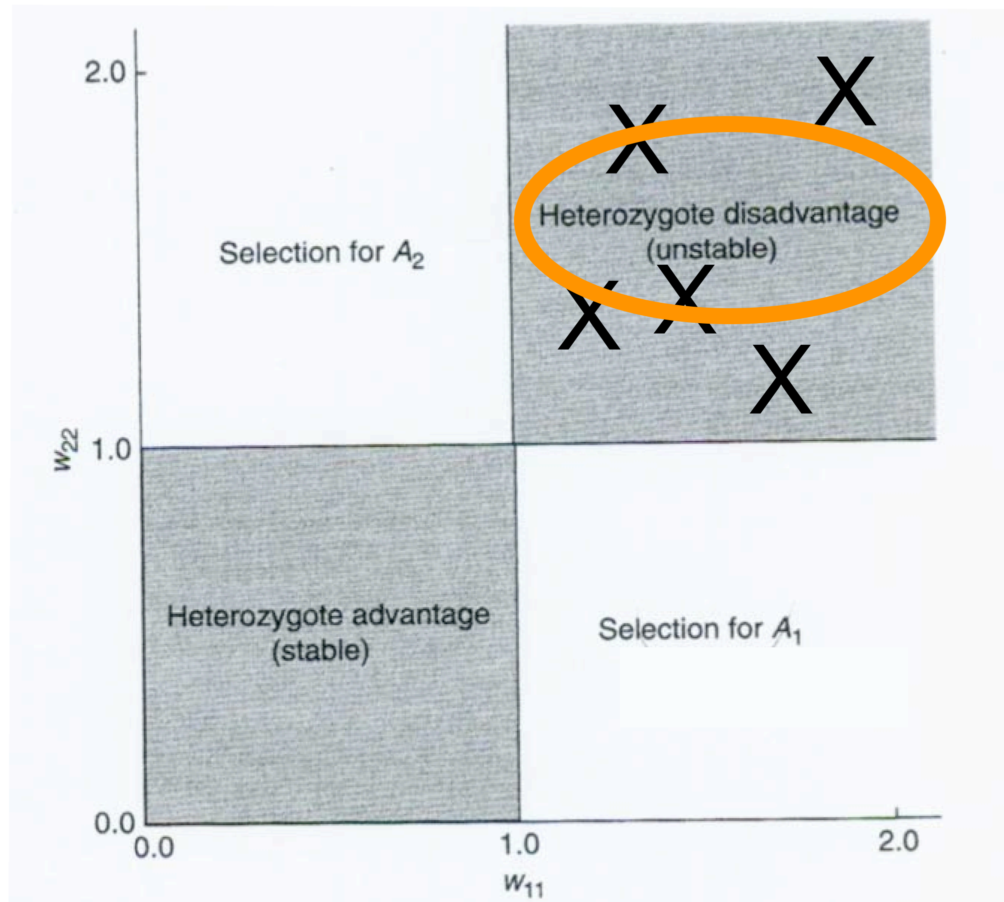


Fig. 4.9 Heterozygosity in different animal populations showing the limited genetic variation in cheetahs and lions. The Serengeti lion population numbers about 300, while just 100 live in the Ngorongoro crater (also in Tanzania) following a dramatic bottleneck in 1962. The Gir Forest (India) population today numbers about 250, although it also suffered a severe bottleneck at the turn of the century. Data from Yuhki and O'Brien (1990).



Heterozygote disadvantage, a.k.a. **underdominance**: both homozygotes, A_1A_1 and A_2A_2 have a selective **advantage** over the heterozygous genotype A_1A_2.

This is **not** a stable condition across the generations.



Heterozygote disadvantage, example, page 145 in Hedrick

Not stable

Not stable

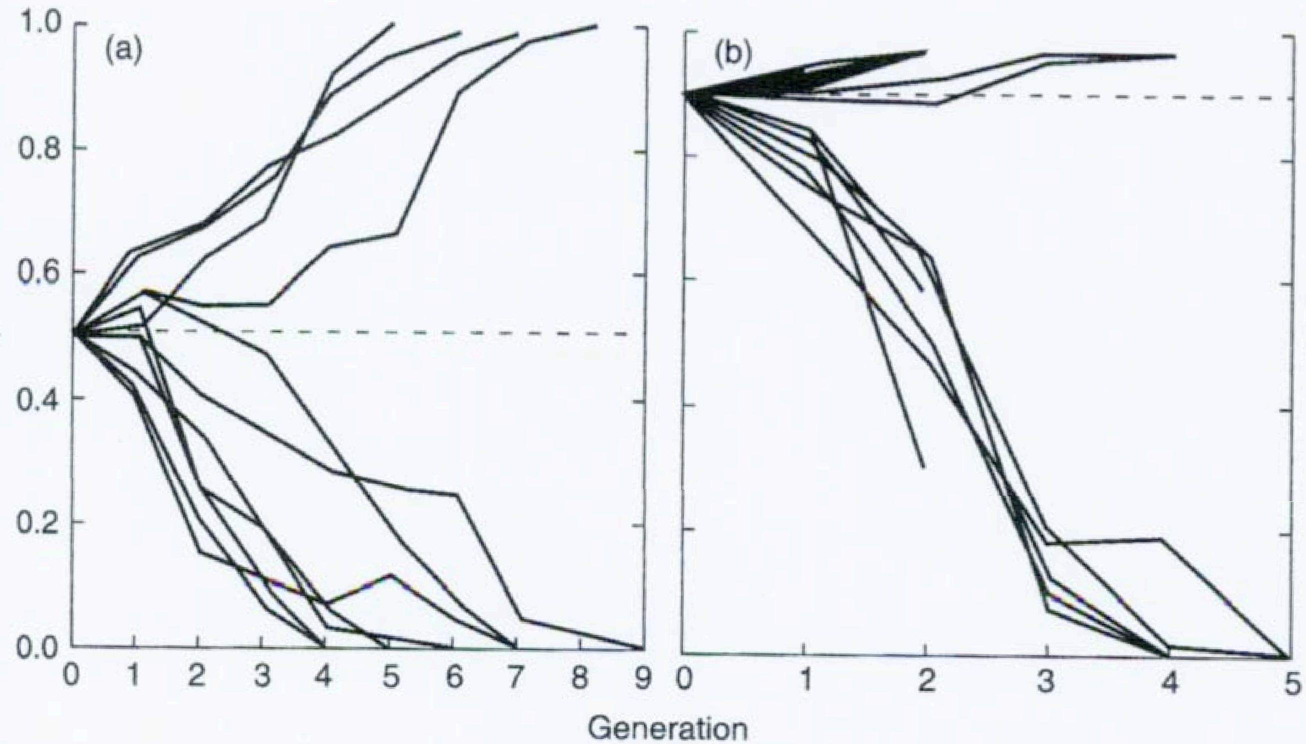
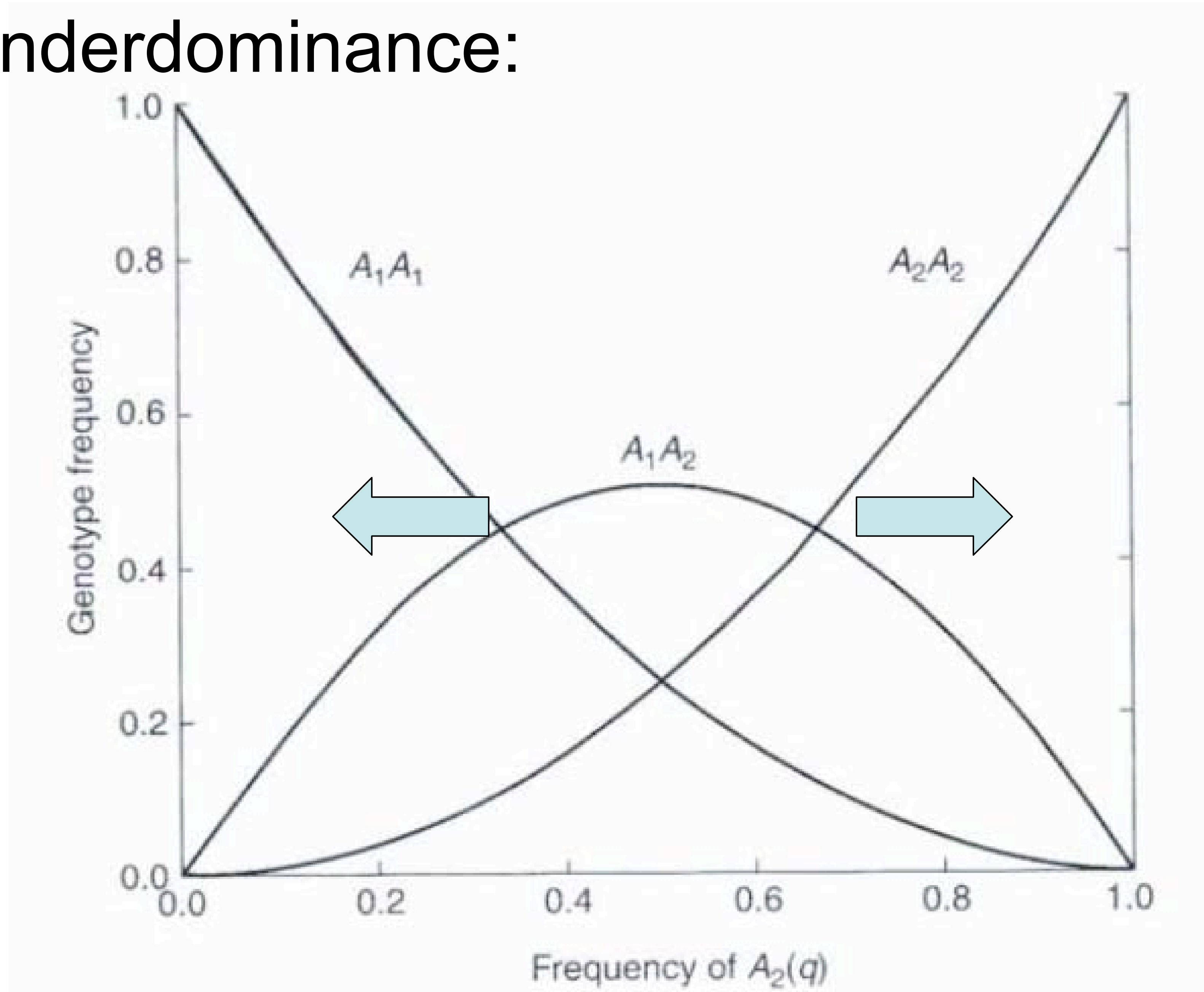


Figure 3.9. The change in chromosomal frequency over time when the heterozygote has a disadvantage and the unstable equilibrium (indicated by the broken lines) is at 0.5 (a) or 0.9 (b) for translocations in *D. melanogaster* (from Foster *et al.*, 1972). The solid lines indicate different experimental replicates.

Effect of heterozygote disadvantage, or underdominance:



Effect of heterozygote advantage, or overdominance: