looking briefly at some of the related biochemistry. Without going into detail, different alleles of the same gene produce related proteins, which in turn produce the variations in expressed characteristics associated with that gene. Typically these proteins (or combinations of them) are powerful biological catalysts called *enzymes*, capable of modifying reaction rates by factors of 10,000 and more. For this reason, genes exercise extensive control over the ongoing reactions in a cell—the enzymes they produce modulate ongoing reactions so strongly that they are the major determinants of the cell's form. Moreover, the products of any given enzyme-controlled reaction may, and generally do, enter into several subsequent reactions. Thus the effects of changes in a single enzyme are often widespread, causing gross changes in cell form and function. The human hereditary disorder called phenylketonuria results from an (undesirable) allele of a single gene; the presence of this allele has pronounced effects upon a whole battery of characteristics ranging from hair color and head size through intelligence. It is equally true that several genes may jointly determine a given characteristic, e.g., eye color in humans.

All of this adds considerably to the complexity of the system, but the greatest complexities come about because the effects of different enzymes are not additive—a phenomenon known as *epistasis*. For example, if a sequence of reactions depends upon several enzymes, for practical purposes the sequence does not proceed at all until all of the enzymes are present; subtraction of one enzyme stops the reaction completely. More complicated reactions involving positive and negative feedback are common, particularly those in which the output of a reaction sequence is a catalyst or inhibitor for some intermediate step of the reaction. The main point is that the effect of each allele depends strongly upon what other alleles are present and small changes can often produce large effects. The amalgam of observed characteristics—the *phenotype*—depends strongly upon these epistatic effects.

Because of epistasis there is no simple way to apportion credit to individual alleles for the performance of the resulting phenotype. What may be a good allele when coordinated with an appropriate set of alleles for other genes, can be disastrous in a different genetic context. Thus adaptation cannot be accomplished by selecting among the alleles for one gene independently of what alleles appear for other genes. The problem is like the problem of adjusting the "height," "vertical linearity," and "vertical hold" controls on a television set. A "best setting" for "height," ignoring the settings of the other two controls, will be destroyed as soon as one attempts to better the setting of either of the other two controls. The problem is vexing enough when there are three interdependent controls, as anyone who

has attempted these adjustments can testify, but it pales in comparison to the genetic case where dozens or hundreds of interdependent alleles can be involved. Roughly, the difficulty of the problem increases by an order of magnitude for each additional gene when the interdependencies are intricate (but see the discussions in chapter 4 and pp. 160-61).

Given the pervasiveness of epistasis, adaptation via changes in genetic makeup becomes primarily a search for *coadapted* sets of alleles—alleles of different genes which together significantly augment the performance of the corresponding phenotype. (In chapter 4 the concept of a coadapted set of alleles will be generalized, under the term *schema*, to the point where it applies to the full range of adaptive systems.) It should be clear that coadaptation depends strongly upon the environment of the phenotype. The large coadapted set of alleles which produces gills in fish augments performance only in aquatic environments. This dependence of coadaptation upon characteristics of the environment gives rise to the notion of an *environmental niche*, taken here to mean a set of features of the environment which can be exploited by an appropriate organization of the phenotype. (This is a broader interpretation than the usual one which limits niche to those environmental features particularly exploited by a given species.) Examples of environmental niches fitting this interpretation are: (*i*) an oxygen-poor, sulfur-rich environment such as is found at the bottom of ponds with large amounts of decaying matter—a class of anaerobic bacteria, the thiobacilli, exploits this niche by means of a complex of enzymes enabling them to use sulfur in place of oxygen to carry out oxidation; (ii) the "bee-rich" environment exploited by the orchid *Ophrys apifera* which has a flower mimicking the bee closely enough to induce pollination via attempted copulation by the male bees; (iii) the environment rich in atmospheric vibrations in the frequency range of 50 to 50,000 cycles per second—the bones of the mammalian ear are a particular adaptation of parts of the reptilian jaw which aids in the detection of these vibrations, an adaptation which clearly must be coordinated with many other adaptations, including a sophisticated information-processing network, before it can improve an organism's chances of survival. It is important to note that quite distinct coadapted sets of alleles can exploit the same environmental niche. Thus, the eye of aquatic mammals and the (functionally similar) eye of the octopus exploit the same environmental niche, but are due to coadapted sets of alleles of entirely unrelated sets of genes.

The various environmental niches $E \in \mathcal{E}$ define different opportunities for adaptation open to the genetic system. To exploit these opportunities the genetic system must select and use the sets of coadapted alleles which produce the appropriate phenotypic characteristics. The central question for genetic systems is: How

are initially unsuited structures transformed to (an observed range of) structures suited to a variety of environmental niches ? To attempt a general answer to this question we need a well-developed formal framework. The framework available at this point is insufficient, even for a careful description of a candidate adaptive plan for genetic systems, unlike the case of the simpler artificial system. A fortiori, questions about such adaptive plans, and critical questions about efficiency, must wait upon further development of the framework. We *can* explore here some of the requirements an adaptive plan must meet if it is to be relevant to data about genetics and evolution.

In beginning this exploration we can make good use of a concept from mathematical genetics. The action of the environment $A \in \mathfrak{A}$) is typically summarized in mathematical studies of genetics by a single performance measure $\mu_E$ called *fitness*. Roughly, the fitness of a phenotype is the number of its offspring which survive to reproduce (precise definitions will be given later in connection with the appropriate formal models, see section 3.1). This measure rests upon a universal, and familiar, feature of biological systems: Every individual (phenotype) exists as a member of a population of similar individuals, a population constantly in flux because of the reproduction and death of the individuals comprising it. The fitness of an individual is clearly related to its influence upon the future development of the population. When many offspring of a given individual survive to reproduce, then many members of the resulting population, the "next generation," will carry the alleles of that individual. Genotypes and phenotypes of the next generation will be influenced accordingly.

Fitness, viewed as a measure of the genotype's influence upon the future, introduces a concept useful through the whole spectrum of adaptation. A good way to see this concept in wider context is to view the testing of genotypes as a sampling procedure. The sample space in this case is the set of all genotypes $A \in \mathfrak{A}$ influence or alter the sampling plan (the kinds of samples to be taken in the future)? Looking backward instead of forward, we encounter a closely related question: How does the history of the outcomes of previous samples influence the current sampling plan? The answers to these questions go far toward determining the basic character of any adaptive process.

We have already seen that the answer to the first question, for genetic systems, is that the future influence of each individual $A \in \mathfrak{A}$ is directly proportional to the sampled performance $\mu_E(A)$. This relation need not be so in general—

there are many well-established procedures for optimization, inference, mathematical learning, etc., where the relation between sampled performance and future sampling is quite different. Nevertheless reproduction in proportion to measured performance is an important concept which can be generalized to yield sampling plans—*reproductive plans*—applicable to any adaptive problem (including the broad class of problems where there is no natural notion of reproduction). Moreover, once reproductive plans have been defined in the formal framework, it can be proved that they are efficient (in a reasonable sense) over a very broad range of conditions.

A part of the answer to the second question, for genetic systems, comes from the observation that future populations can only develop via reproduction of individuals in the current population. Whatever history is retained must be represented in the current population. In particular, the population must serve as a summary of observed sample values (performances). The population thereby has the same relation to an adaptive process that the notion of (complete) state has to the laws of physics or the transition functions of automata theory. Knowing the population structure or state enables one to determine the future without any additional information about the past of the system. (That is, different sampling sequences which arrive at the same population will have exactly the same influence on the future.) The state concept has been used as a foundation stone for formal models in a wide variety of fields; in the formal development to follow generalizations of population structure will have this role.

An understanding of the two questions just posed leads to a deeper understanding of the requirements on a genetic adaptive plan. It also leads to an apparent dilemma. On the one hand, if offspring are simple duplicates of fit members of the population, fitness is preserved but there is no provision for improvement. On the other hand, letting offspring be produced by simple random variation (a process practically identical to enumeration) yields a maximum of new variants but makes no provision for retention of advances already made. The dilemma is sharpened by two biological facts: (1) In biological populations consisting of advanced organisms (say vertebrates) no two individuals possess identical chromosomes (barring identical twins and the like). This is so even if we look over many (all) successive generations. (2) In realistic cases, the overwhelming proportion of *possible* variants (all possible allele combinations, not just those observed) are incapable of surviving to produce offspring in the environments encountered. Thus, by observation (1), advances in fitness are not retained by simple duplication. At the same time, by observation (2), the observed lack of identity cannot result from simple random variation because extinction would almost certainly

follow in a single generation—variants chosen completely at random are almost certain to be sterile.

In attempting to see how this "dilemma" is resolved, we begin to encounter some of the deeper questions about adaptation. We can only hint at the dilemma's resolution in this preliminary survey. Even a clear statement of the resolution requires a considerable formal structure, and proof that it is in fact a resolution requires still more effort. Much of the understanding hinges on posing and answering two questions closely related to the questions generated by the concept of fitness. How can an adaptive plan (specifically, here a plan for genetic systems) retain useful portions of its (rapidly growing) history along with advances already made? How is the adaptive plan to access and use its history (the portion stored) to increase the likelihood of fit variants ($A \in \mathcal{A}$ such that $\mu_E(A)$ is above average)? Once again these are questions relevant to the whole spectrum of fields mentioned at the outset.

The resolution of the dilemma lies in the action of the genetic operators within the reproductive plan . The best-known genetic operators exhibit two properties strongly affecting this action: (1) The operators do not directly affect the size of the population—their main effect is to alter and redistribute alleles within the population. (The alleles in an individual typically come from more than one source in the previous generation, the result, for example, of the mating of parents in the case of vertebrates, or of transduction in the case of bacteria.) (2) The operators infrequently separate alleles which are close together on a chromosome. That is, alleles close together typically remain close together after the operators have acted.

Useful clues to the dilemma's resolution emerge when we look at the effect of these operators in a simple reproductive plan, $_1$. This plan can be thought of as unfolding through repeated application of a two-phase procedure: During phase one, additional copies of (some) individuals exhibiting above-average performance are added to the population while (some) individuals of subaverage performance are deleted. More carefully, each individual has an expected number of offspring, or rate of reproduction, proportional to its performance. (If the population is to be constant in size, the rates of reproduction must be "normalized" so that their average over the population at any time is 1.) During phase two, the genetic operators in are applied, interchanging and modifying sets of alleles in the chromosomes of different individuals, so that the offspring are no longer identical to their progenitors. The result is a new, modified population. The process is iterated to produce successive generations of variants.

More formally, in an environment which assigns an observable performance

to each individual, $_1$ acts as follows: At the beginning of each time period $t$, the plan's accumulated information about the environment resides in a finite population $\mathfrak{A}(t+1)$

One key to understanding $_1$'s resolution of the dilemma lies in observing what happens to small sets of adjacent alleles under its action. In particular, what happens if an adjacent set of alleles appears in several different chromosomes of above-average fitness and not elsewhere? Because each of the chromosomes will be duplicated an above-average number of times, the given alleles will occupy an increased proportion of the population after the duplication phase. This increased proportion will of course result whether or not the alleles had anything to do with the above-average fitness. The appearance of the alleles in the extra-fit chromosomes might be happenstance, but it is equally true that any correlation between the given selection of alleles and above-average fitness will be exploited by this action. Moreover, the more varied the chromosomes containing the alleles, the less likely it is that the alleles and above-average fitness are uncorrelated.

What happens now when the genetic operators are applied to form the next generation? As indicated earlier, the closer alleles are to one another in the chromosome the less likely they are to be separated during the operator phase. Thus the operator phase usually transfers adjacent sets of genes as unit, placing them in new chromosomal contexts without disturbing them otherwise. These new contexts further test the sets of alleles for correlation with above-average fitness. If the selected set of alleles does indeed augment fitness, the chromosomes containing the set will again (on the average) be extra fit. On the other hand, if the prior associations were simply happenstance, sustained association with extra-fit chromosomes becomes increasingly less likely as the number of trials (new contexts) increases. The net effect of the genetic plan over several generations will be an increasing predominance of alleles and sets of alleles augmenting fitness in the given environment.