



R. C. LEWONTIN

**THE GENETIC BASIS OF
EVOLUTIONARY CHANGE**



NEW YORK AND LONDON

COLUMBIA UNIVERSITY PRESS

1974

R. C. Lewontin is Alexander Agassiz Professor
of Zoology at Harvard University.

Library of Congress Cataloging in Publication Data

Lewontin, Richard C 1929-

The genetic basic of evolutionary change.

(Columbia biological series no. 25)

Bibliography: p.

1. Population genetics. 2. Evolution.
3. Variation (Biology) I. Title. II. Series.
[DNLM: 1. Evolution. 2. Genetics. QH431
L678g 1973]

QH455.L48 575.1 73-19786

ISBN 0-231-03392-3

ISBN 0-231-08318-1 (pbk.)

AMS 1970 Subject Classifications 92-02, 92A10

Copyright © 1974 Columbia University Press

Printed in the United States of America

TO THEODOSIUS DOBZHANSKY

*Nel mezzo del cammin di nostra vita
mi ritrovai per una selva oscura,
che la diritta via era smarrita.
Ahi quanto a dir qual era è cosa dura
questa selva selvaggia ed aspra e forte,
che nel pensier rinnova la paura.*

DANTE

PREFACE

This book has grown, or better, exploded out of the Jesup Lectures that I gave at Columbia in 1969. Previous lecturers, in their presentations and in the books that resulted, had laid the foundations of modern evolutionary and systematic studies and had thereby contributed to a mystique of the Jesup Lectures that was overpowering, especially to a former Columbia student. My own consciousness of being an epigone permeated the lectures themselves and has contributed substantially to the delay in turning those lectures into a book. In the end, the delay has been beneficial, because the intervening three years have seen a great increase in theoretical and practical knowledge of the problems discussed, and because my own understanding has made some advance over the naive and disjointed views I then held.

The subject of the lectures and this book, the nature of genetic diversity among organisms, has always seemed the basic problem of evolutionary genetics. Because of the immense methodological difficulties and ambiguities, a characterization of that genetic variation seemed always to elude us. Then, with the discoveries of molecular biology about the relationship between genes and proteins, the possibility of an unambiguous characterization of genetic variation among individuals was opened. The first experiments revealed an extraordinary wealth of genetic diversity and, quite naturally, those

of us involved in the work felt an immense elation in having finally given a direct answer to the major problem that had been plaguing our field. Some sense of that tension and resolution is conveyed in part II of this book.

As we tried to explain the great variation that had been observed, our original elation gave way slowly to disappointment. For no explanation is really satisfactory, and the kind of ambiguity that originally permeated the observations now pervades the theoretical explanations.

The problem may be even more serious. I have had the growing suspicion that in revealing the great variety of genic forms segregating in populations we have given the right answer to the wrong question. That is, the question was never really, How much genetic variation is there between individuals? but rather, What is the nature of genetic variation for *fitness* in a population? If, as some suspect, the genic diversity we have exposed is irrelevant to natural selection, or if, as the theory expounded in part III of this book suggests, the individual locus is not the appropriate unit of observation, then we have indeed given the right answer to the wrong question.

In fact, the methodological problem that is described in part II, and that seemed to be resolved by new methods and concepts, is really much deeper than I have suggested there. For I now realize that the question was not simply, How much genetic variation is there? nor even, How much genetic variation in fitness is there? but rather, How much genetic variation is there that can be the basis of adaptive evolution? To answer that question it is not sufficient to measure genetic variation, which we can now do, nor to measure the present variation in fitness associated with that genetic variation, which we have not done but which may be possible with a proper reorientation of theory. We require, further, that we be able to assess the *potentiality* for adaptive evolution in genetic variation that may currently be nonadaptive. But such an assessment will depend on an understanding of the relation between gene and organism that far transcends any present knowledge of development, physiology, and behavior. In fact, it demands the answer to every other question that now lies open in biology.

Progress, both observational and theoretical, has been rapid in evolutionary genetics in the last few years. As a result, in the three years that have intervened between the Jesup Lectures and the

finishing of this book, a lot has been discovered. Much of it has been published, but much has not, and I am very grateful to my friends and colleagues who have told me of their work or shown it to me in manuscript form. Among these are Francisco Ayala, Avigdor Beiles, George Carmody, Brian Charlesworth, Ian Franklin, Ove Frydenberg, Moto Kimura, Ken-ichi Kojima, Terumi Mukai, Satya Prakash, Dick Richardson, Rollin Richmond, Tom Schopf, Robert Selander, Monte Slatkin, Tsuneyuki Yamazaki, and Eleutherios Zouros. I have discussed many of the concepts with them and with all my colleagues in Chicago, especially Brian Charlesworth, Ian Franklin, and Dick Levins, who have helped me to understand many things that were obscure to me. The book has been substantially improved by the enlightening comments made on the original manuscript by James Crow and Tim Prout, each of whom read it with his characteristic care and intelligence.

Above all, it has been my association with Jack Hubby that has given rise to the experimental work on which much of this book is based. It would be absurd to express my "gratitude" to him. Although his name does not appear on the title page, he is an "author" of this book as much as I am.

The text has been made much more readable and many opacities have been rendered transparent by the careful editorial work of Maria Caliandro. The tedious and unrewarding job of typing the several versions of the manuscript was carried out with her usual scrupulousness by Frances La Duke. Mary Jane Lewontin took on the maddening job of making the thousands of decisions necessary to compiling the index, and I am immensely grateful to her for it.

As is usually the case, I have undoubtedly forgotten to express my thanks to people who have made really important contributions to the work. I ask their indulgence.

Chicago
September 1972

R. C. Lewontin

CONTENTS

PART I / THE PROBLEM

CHAPTER 1 / The Structure of Evolutionary Genetics	3
--	---

PART II / THE FACTS

CHAPTER 2 / The Struggle to Measure Variation	19
CHAPTER 3 / Genic Variation in Natural Populations	95
CHAPTER 4 / The Genetics of Species Formation	159

PART III / THE THEORY

CHAPTER 5 / The Paradox of Variation	189
CHAPTER 6 / The Genome as the Unit of Selection	273

BIBLIOGRAPHY	319
--------------	-----

INDEX	337
-------	-----

**THE GENETIC BASIS OF
EVOLUTIONARY CHANGE**

PART I / THE PROBLEM

CHAPTER 1 / THE STRUCTURE OF EVOLUTIONARY GENETICS

When different people consider the work of a revolutionary like Darwin, they see different aspects of it as representing the "real" or "fundamental" element that separates it from the preexistent conformity of thought. To many, Darwinism means "evolution" and the commitment to an evolutionary world view, but historical evidence makes clear that Darwin only applied rigorously to the organic world what was already accepted as characteristic of the inorganic universe and of human culture (Lewontin, 1968). To others, especially students of the evolutionary process, Darwin's unique intellectual contribution was the idea of natural selection. For them, Darwinism is the theory that evolution occurs because, in a world of finite resources, some organisms will make more efficient use of those resources in producing their progeny and so will leave more descendants than their less efficient relatives.

Yet it is by no means certain, even now, what proportion of all evolutionary change arises from natural selection. Attitudes toward the importance of random events as opposed to selective ones vary from time to time and place to place. The famous Committee on Common Problems of Genetics, Paleontology and Systematics, whose work led to the publication of *Genetics, Paleontology and Evolution* (Jepsen, Mayr, and Simpson, 1949) embodied within it divergent views on this question. In his article entitled "Speciation

and Systematics," Mayr made clear that, in his view, the divergence between isolated populations is the result of their adaptation to different environments and that "geographical races are invariably to a lesser or greater degree also ecological races" (p. 291). But Muller's essay in the same volume puts emphasis on "cryptic genetic change" (p. 425) that is not reflected in phenotypic differentiation but that may result in sufficient genetic divergence between groups to result in speciation. For Mayr, natural selection is vital in the divergence between isolated populations while for Muller natural selection is always primarily a cleansing agent, rejecting "inharmonious" gene combinations, and not necessarily the causative agent in the initial divergence between incipient species. Nor is this conflict of viewpoints yet resolved. During the last few years there has been a flowering of interest in evolution by purely random processes in which natural selection plays no role at all. Kimura and Ohta suggest, for example (1971a), that *most* of the genetic divergence between species that is observable at the molecular level is nonselective, or, as proponents of this view term it, "non-Darwinian," although they do not deny that the evolution of obviously adaptive characters like the elephant's trunk and the camel's hump are the result of natural selection. If the empirical fact should be that most of the genetic change in species formation is indeed of this non-Darwinian sort, then where is the revolution that Darwin made?

The answer is that the essential nature of the Darwinian revolution was neither the introduction of evolutionism as a world view (since historically that is not the case) nor the emphasis on natural selection as the main motive force in evolution (since empirically that may not be the case), but rather the replacement of a metaphysical view of variation among organisms by a materialistic view (Lewontin, 1973). For Darwin, evolution was the conversion of the variation among individuals within an interbreeding group into variation between groups in space and time. Such a theory of evolution necessarily takes the variation between individuals as of the essence. Ernst Mayr has many times pointed out, especially in *Animal Species and Evolution* (1963), that this emphasis on individual variation as the central reality of the living world is the mark of modern evolutionary thought and distinguishes it from the typological doctrine of previous times.

In the thought of the pre-Darwinians, the Platonic and Aristotelian notion of the "ideal" or "type" to which actual objects were imperfect approximations was a central feature. Nature, and not just living nature, was understood by the pre-Darwinians only in terms of the ideal; and the failure of individual cases to match the ideal was a measure of the imperfection of nature. Such a metaphysical construct is not without importance in science, as Newton's mechanics prove so well. The first law in the *De Motu Corporum* is that

Every body perseveres in its state of rest, or of uniform motion in a right line, unless it is compelled to change that state by forces impressed thereon.

Yet Newton points out immediately that even "the great bodies of the planets and comets" have such perturbing forces impressed upon them and that no body perseveres indefinitely in its motion. The metaphysical introduction of ideal bodies moving in ideal paths, so essential to the proper development of physics and so consonant with the habits of thought of the seventeenth century, was precisely what had to be destroyed in the creation of evolutionary biology. Darwin rejected the metaphysical object and replaced it with the material one. He called attention to the *actual* variation among *actual* organisms as the most essential and illuminating fact of nature. Rather than regarding the variation among members of the same species as an annoying distraction, as a shimmering of the air that distorts our view of the essential object, he made that variation the cornerstone of his theory. Let us remember that the *Origin of Species* begins with a discussion of variation under domestication.

The conflict between the real and the ideal was also important in a second realm that is relevant to evolution. What we know as the science of genetics is meant to explain two apparently antithetical observations—that organisms resemble their parents and differ from their parents. That is, genetics deals with both the problem of heredity and the problem of variation. It is in fact the triumph of genetics that a single theory, down to the molecular level, explains in one synthesis both the constancy of inheritance and its variation. It is the Hegelian's dream. But this synthesis was not possible until sufficient importance was attached to variation. Francis Galton attempted to construct a theory of inheritance based upon the degree

of resemblance of offspring to their parents. Galton's Law of Filial Regression placed the emphasis on the fact that the offspring of extreme parents tended to "regress" back to the mean of the parental generation. The law was derived from observations of the mean height of all offspring whose parents belonged to a specific height class, but it placed no weight at all on the variation between parental pairs whose offspring were the same height, nor between sibs, nor between sibships whose parents belonged to the same height class. Galton's scheme depended entirely upon the regression of *means* on *means*.

In striking contrast, Mendel placed his emphasis on the *variations* among the offspring, rather than on any average description of them, *and derived his laws from the nature of the variations*. Thus, for Mendelism, as for Darwinism, the fact of variation and its nature are central and essential. Of course, at a second level, Mendel idealized his laws, much as Newton did, and every student knows that Mendel's F_2 ratios were suspiciously close to those 3 to 1 ideals. But this in no way vitiates the centrality of variation in Mendel's thought. Modern evolutionary genetics is then a union of two systems of knowledge, both of which took variation to be the essential fact of nature. It is not surprising, therefore, that the study of genetically determined variation within and between species should be the starting point of evolutionary investigation.

A DIGRESSION INTO FORMALISM

Dynamic Sufficiency When we say that we have an evolutionary perspective on a system or that we are interested in the evolutionary dynamics of some phenomenon, we mean that we are interested in the change of state of some universe in time. Whether we look at the evolution of societies, languages, species, geological features, or stars, there is a formal representation that is in common to all. At some time t the system is in some state E , and we are interested in the state of the system, E' , at a future time, or past time, τ time units away. We must then construct laws of transformation T that will enable us to predict E' given E . Formally, we may represent this as

$$E(t) \xrightarrow{T} E'(t + \tau)$$

The laws of transformation T cannot be of an arbitrary form. Usually they contain some parameters Π , values that are not themselves a function of time or the state of the system. Second, they will contain the elapsed time τ , except in the description of equilibrium systems in which no change is taking place. They may or may not refer specifically to the absolute time t , depending on whether the system carries in its present state some history of its past. For example, if I wish to know what proportion of a population will be alive a year from now, I need to know how long ago the individuals were born, since survival probabilities change with age. But if I wish to know what proportion of my teacups will last through the next year, I do not have to know how old they are since, to a first order of approximation, their breakage probability per year is independent of their age. Finally, and essentially, the laws of transformation must contain the present state of the system E and obviously must produce as part of their output the new state E' . The laws of transformation are a machinery that must be built to process information about the current state E and to produce, as an output, the new state E' . But that means that the description of the system, E , must be chosen in such a way that laws of transformation can indeed be constructed using it.

For example, one cannot predict the future position of a space capsule from its present position alone. No set of laws can be constructed that will transform $E(t)$ into $E'(t + \tau)$ if E is the position of the capsule in three-dimensional space. It is necessary, in addition, to specify the present velocity of the capsule in three orthogonal directions, and its present acceleration in three orthogonal directions. If the state description is a function of those nine variables, then laws of transformation are possible and, as a result, capsules get to the moon and back. We will say that the state description with all nine variables is a *dynamically sufficient description* because, given that description, it is possible to find laws $T(E, \Pi, \tau, t)$:

$$E(t) \xrightarrow{T(E, \Pi, \tau, t)} E'(t + \tau)$$

The transformation of state in time has a geometrical interpretation. Let us take each variable used in specifying the state of the system as an axis in a Cartesian space. Then the state of the system at any time is represented as a point in that space, located by the projection onto the various axes. Evolution of the system is move-

ment of the point through the space, tracing out a trajectory, and the laws of transformation are the equation whose solution is that trajectory. The axes of the space are the *state variables*, and the space they span is the *state space* of our system.

Looked at in this way, the problem of constructing an evolutionary theory is the problem of constructing a state space that will be dynamically sufficient, and a set of laws of transformation in that state space that will transform all the state variables. It is not always appreciated that the problem of theory building is a constant interaction between constructing laws and finding an appropriate set of descriptive state variables such that laws can be constructed. We cannot go out and describe the world in any old way we please and then sit back and demand that an explanatory and predictive theory be built on that description. The description may be dynamically insufficient. Such is the agony of community ecology. We do not really know what a sufficient description of a community is because we do not know what the laws of transformation are like, nor can we construct those laws until we have chosen a set of state variables. That is not to say that there is an insoluble contradiction. Rather, there is a process of trial and synthesis going on in community ecology, in which both state descriptions and laws are being fitted together.

Tolerance Limits In the development of a real science about a real and practical world, it is impossible and undesirable to search for an exactly sufficient description. The nature of the physical universe is such that the change of state of every part of it affects the change of state of every other part, no matter how remote. While a space capsule evolves in a nine-dimensional space for all practical purposes, an absolutely exact treatment of its motion would have to take into account the fact that it affects the motion of the earth and moon and of every other celestial body in some tiny degree. Yet no serious person would suggest that we really need to take into account the impetus given to the earth at the moment of launching. In each domain of practice we have a notion of the appropriate accuracy of prediction, and we are satisfied if our theory gives results that are somehow close enough. More exactly, corresponding to each state of a system E we establish a *tolerance set* ϵ of states that are similar enough to be regarded as indistinguishable. That does not mean that

they *are* indistinguishable, but only that we do not care about the differences among states within a tolerance set. In practice, then, a sufficient dimensionality is one that allows us to describe the evolution of tolerance sets in time rather than the evolution of exact state descriptions.

In population ecology and evolutionary genetics, the tolerance limits remain matters of debate and choice. Ought we to be satisfied with theories that predict only that one community will have more species than another or that one population will be more polymorphic than another? If so, a very low dimensionality may be sufficient. Or do we really want to predict the number of breeding individuals of each species each year, or the gene frequencies at various loci, and if so, how accurately? Exactly the same domain of science may require quite different degrees of accuracy in different applications and thus use models of very different dimensionality. For example, population ecologists are generally satisfied to explain to one order of magnitude the increases and decreases in population size of the organisms studied, and for this purpose net fecundity and mortality are usually sufficient. Game and fish management, however, may require prediction of population changes to an accuracy of 10 to 20 percent, and for this purpose complete age-specific mortality and fecundity schedules are required. Finally, the human demographer needs to project human population sizes to better than 1 percent accuracy, and to do so needs fecundity and mortality figures by age, sex, socioeconomic class, education, geographical location, and so on. The building of a dynamically sufficient theory of evolutionary processes will really entail the simultaneous development of theories of different dimensionalities, each appropriate to the tolerance limits acceptable in its domain of explanation.

Empirical Sufficiency There is a second problem of theory construction in evolution, which we may term the problem of *empirical sufficiency*. The laws of transformation contain two elements that require measurement: the state variables that make up E and the parameters that make up Π . Even when a dynamically sufficient state space and a set of transformation laws have been arrived at, some of the state variables or the parameters may turn out to be, in practice, unmeasurable. Such unmeasurability is often not absolute; instead, the accuracy of measurement is low compared to the

sensitivity of predictions to small perturbations in the values of the variables. To return to our space capsule example, when the capsule leaves its "parking orbit" around the earth, the smallest error in exit angle, smaller than can be controlled, will cause it to miss the moon by many miles. That is why mid-course corrections are necessary.

But empirical sufficiency is not always a matter of accuracy. It may lie much deeper. An example to which I shall return is the measurement of fitness of genotypes. One component of fitness is the probability of survival from conception to the age of reproduction. But by definition the probability of survival is an ensemble property, not the property of a single individual, who either will or will not survive. To measure this probability we then need to produce an ensemble of individuals, all of the same genotype. But if we are concerned with the alternative genotypes at a single locus, we need to randomize the rest of the genome. In sexually reproducing organisms, there is no way known to produce an ensemble of individuals that are all identical with respect to a single locus but randomized over other loci. Thus a theory of evolution that depends on the characterization of fitness of genotypes with respect to single loci is in serious trouble, trouble that cannot be cleared up by a quantitative improvement in the accuracy of measurement. The theory suffers from an epistemological paradox.

It is a remarkable feature of the sociology of science that evolutionary biologists have persistently ignored the problem of empirical sufficiency. The literature of population genetics is littered with estimates lacking standard errors and with methods for deciding between alternatives that have no sensitivity analyses or tests of hypotheses. No one has been exempt from this methodological naïveté, including myself, so that any specific discussion of the problem becomes immediately offensive to almost everyone. There are, however, a few positive landmarks in the assessment of these methodological difficulties that may be mentioned to the credit of their discoverers.

Since the invention by Muller of the C/B technique in 1928, many investigations have been made of the distribution of viabilities and fecundities of chromosomal homozygotes in various species of *Drosophila*. Yet it was not until 25 years later that Wallace and Madden (1953) and Dobzhansky and Spassky (1953) showed what

proportion of the observed variance among chromosomal homozygotes and heterozygotes was, in fact, genetic, as opposed to experimental error. Since the error variance turned out to be between 59 and 99 percent of the total variance in different samples of heterozygotes and between 24 and 68 percent in homozygotes (Dobzhansky and Spassky, 1953, table 6), it is difficult to know what to make of studies without estimates of error.

An important parameter to be estimated for an understanding of the differentiation between populations is the effective breeding size, N . An elaborate theory exists for the estimation of this quantity from the allelism of lethal genes. The estimation procedure involves the reciprocal of the difference between two small numbers, a fact that in itself makes the use of the technique dubious. In an empirical test of procedure, Prout (1954) showed that in practice one cannot detect the difference between a population of 5000 and an infinite population.

Since the first experiments of L'Heritier and Teissier (1933) and of Wright and Dobzhansky (1946), adaptive values of *Drosophila* genotypes in population cages have been estimated from changes in genotype frequencies, but despite the use of a number of statistically sophisticated estimation techniques, standard errors of fitness estimates from population cages were not commonly calculated until Anderson, Oshima, Watanabe, Dobzhansky, and Pavlovsky did so in 1968, with rather disturbing results. Fitness estimates as disparate as 0.72 and 0.19 were not significantly different and estimates of 0.54, 0.47, and 0.59 had standard errors of 0.78, 1.15, and 1.23, respectively. Admittedly these experiments involved the estimation of nine fitness values, but this simply points up the problem of estimation for even a small number of genotypes under rigorously controlled laboratory conditions. The possibility of fitness estimation with smaller standard errors in natural populations seems remote, under the circumstances.

While dynamic sufficiency is an absolute and basic requirement for the building of an evolutionary theory, empirical sufficiency adds yet another stricture that may render a formally perfect theory useless. If one simply cannot measure the state variables or the parameters with which the theory is constructed, or if their measurement is so laden with error that no discrimination between alternative hypotheses is possible, the theory becomes a vacuous

exercise in formal logic that has no points of contact with the contingent world. The theory explains nothing because it explains everything. It is my contention that a good deal of the structure of evolutionary genetics comes perilously close to being of this sort.

POPULATION GENETICS

Population genetics sets a much more modest goal than general evolutionary theory. If we take the Darwinian view that evolution is the conversion of variation between individuals into variation between populations and species in time and space, then an essential ingredient in the study of evolution is a study of the origin and dynamics of genetic variation within populations. This study, population genetics, is *an* essential ingredient, but it is not the entire soup. While population genetics has a great deal to say about changes or stability of the frequencies of genes in populations and about the rate of divergence of gene frequencies in populations partly or wholly isolated from each other, it has contributed little to our understanding of speciation and nothing to our understanding of extinction. Yet speciation and extinction are as much aspects of evolution as is the phyletic evolution that is the subject of evolutionary genetics, strictly speaking. That is not to say that speciation and extinction are not the natural extensions of changes within populations, but only that our present theories do not deal with these processes except on the most general and nonrigorous plane.

Even the partial task set for population genetics is a tremendously ambitious program. If we could succeed in providing a description of the genetic state of populations and laws of transformation of state that were both dynamically and empirically sufficient, we would create a complete theory concerning a vastly more complex domain than any yet dealt with by physics or molecular biology.

The present structure of population genetics theory may be represented as

$$G_1 \xrightarrow{T_1} P_1 \xrightarrow{T_2} P_2 \xrightarrow{T_3} G_2 \xrightarrow{T_4} G'_1 \xrightarrow{T_1}$$

where G_1 and G_2 represent a genetic description of population at times t and $t + \Delta t$, and P_1 , P_2 and G_2 represent phenotypic and genotypic descriptions of states during the transformation

and the laws of transformation are

- T_1 : a set of epigenetic laws that give the distribution of phenotypes that result from the development of various genotypes in various environments
- T_2 : the laws of mating, of migration, and of natural selection that transform the phenotypic array in a population *within* the span of a generation
- T_3 : an immense set of epigenetic relations that allow inferences about the distribution of genotypes corresponding to the distribution of phenotypes, P'
- T_4 : the genetic rules of Mendel and Morgan that allow us to predict the array of genotypes in the next generation produced from gametogenesis and fertilization, given an array of parental genotypes

It would appear that both genotypes and phenotypes are state variables and that what population genetic theory does is to map a set of genotypes into a set of phenotypes, provide a transformation in the phenotype space, then map these new phenotypes back into genotypes, where a final transformation occurs to produce the genotypic array in the next generation. Figure 1 shows these transformations schematically. From this schema one would imagine that both phenotypic and genotypic state variables would enter into a sufficient dimensionality for the description of population evolution, and that the laws of population genetics would be framed in terms of both genetic and phenotypic variables. Yet an examination of population genetic theory shows a paradoxical situation in this respect. One body of theory, what we might call the "Mendelian" corpus, used almost exclusively by those interested in the genetics of natural populations, seems to be framed entirely in genetic terms. The other theoretical system, the "biometric," used almost exclusively in plant and animal breeding, appears to be framed in completely phenotypic terms. In Mendelian population genetics, for example, the expression

$$\Delta q = \frac{q(1-q)}{2} \frac{d \ln \bar{w}}{dq} \quad (1)$$

expresses the change in relative *allele frequency* Δq of an allele at a locus after one generation, in terms of the present allele frequency q

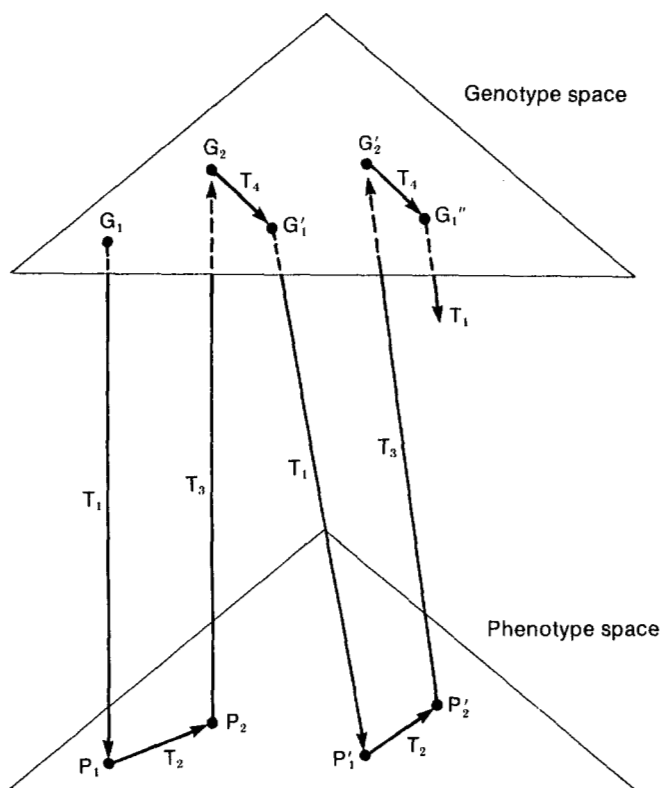


FIGURE 1

Schematic representation of the paths of transformation of population genotype from one generation to the next. G and P are the spaces of genotypic and phenotypic description. G_1 , G'_1 , G_2 , and G'_2 are genotypic descriptions at various points in time within successive generations. P_1 , P'_1 , P_2 , and P'_2 are phenotypic descriptions. T_1 , T_2 , T_3 , and T_4 are laws of transformation. Details are given in the text.

and the mean fitness \bar{w} of the genotypes in the population.

In biometric genetics, the prediction equation

$$\Delta P = ih^2 = i \frac{\sigma_g^2}{\sigma_p^2} \quad (2)$$

predicts the change in mean phenotype, ΔP , in one generation in terms of i , the difference in phenotype between the population as a whole and the selected parents, the phenotypic variance of the character in the population, σ_p^2 , the additive genetic variance, σ_g^2 , and the heritability of the trait, h^2 .

Apparently, then, we have two parallel systems of evolutionary dynamics, one operating in the space of genotypes and bypassing the phenotypic space, and another operating entirely in the phenotypic domain. But this impression is illusory and arises from a bit of sleight-of-hand in which variables are made to appear as merely parameters that need to be experimentally determined, constants that are not themselves transformed by the evolutionary process. In equation (1) these pseudoparameters are the fitnesses associated with the individual genotypes in computing the function \bar{w} . Fitness, however, is a function of the phenotype, not the genotype, although in special circumstances it might turn out that a one-to-one constant correspondence existed between genotype and fitness. More usually, however, relative fitnesses of phenotypes will be a function of the phenotype composition of the population as a whole, so that the fitnesses assigned to genotypes in each generation will themselves follow a law of transformation that depends upon the genotype-phenotype relations. Although, for convenience, geneticists usually use a "constant genotypic fitness" model, this has led to a number of paradoxes that can be resolved properly only when phenotypic relations are taken fully into account. An example is the paradox of *genetic load*, which I will discuss more fully in chapter 5.

The biometric model presents even greater difficulty. The heritability h^2 and the genetic and phenotypic variances are themselves determined by the genetic variation in the population and undergo constant change in the course of the population's evolution. The laws of change of these variables cannot be framed without reference to the genetic determination of phenotype, including the degree of dominance of genes, the amount of interaction between them, and the relative frequencies of the alleles at the loci determining the character under selection. Thus, while equation (2) masquerades as a phenotypic law, genetic state variables must be added to provide a sufficient dimensionality. Because the transition between generations depends upon genetic laws, no sufficient description in terms of phenotypes alone is ever possible, and attempts like those of Slatkin (1970) can only succeed under extremely simplified conditions with very limited applicability. It is only fair to point out that for some purposes of plant and animal breeding, equation (2) is a sufficient predictor because the value of h^2 may evolve very slowly as compared with the mean phenotype, especially if a very large number of

genes, each of small effect, are influencing the trait under selection. For a long-term prediction of progress under selection, or for an estimate of the eventual limit to the selection process, however, equation (2) is insufficient. *The sufficient set of state variables for describing an evolutionary process within a population must include some information about the statistical distribution of genotypic frequencies. It is for this reason that the empirical study of population genetics has always begun with and centered around the characterization of the genetic variation in populations.*