Introduction to

QUANTITATIVE GENETICS

Second Edition

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PREFACE

This book was originally intended to provide an introductory textbook of quantitative genetics, with the emphasis on general principles rather on practical applications. I tried to make the book useful to as wide a range of readers as possible, particularly to biologists who, like myself, have no more than ordinary mathematical ability. In preparing this revised edition, my aims have been: (1) to keep the character of the book, and its length, unchanged; (2) to include some account of all the main developments of the last twenty years; and (3) to be less neglectful of plants. I hope that the compromise made between these conflicting aims will be one that will prove useful. My main regret has been the impossibility of mentioning more than a very few of the experimental studies that have illuminated the subject since the book first appeared.

The inclusion of new material means that rather more than before will be beyond the needs of those for whom the subject forms part of a course of general genetics. The section headings should, however, facilitate the selection of what is relevant. The level of mathematics needed is not more than simple algebra: neither calculus nor matrix methods are used. Some knowledge of statistics, however, is needed, particularly of the analysis of variance and of correlation and regression.

Acknowledgements. Dr W. G. Hill read all the draft and offered many comments and suggestions which have been an immense help. Major improvements to many chapters were made as a result of his advice. I am deeply grateful to him. I owe much also to Dr R. C. Roberts, Professor Alan Robertson and Professor N. W. Simmonds, who read substantial parts of the draft, and to many other colleagues who have advised me on particular points. Without the help that I have received, the book would have had many more blemishes. The errors and misconceptions that remain are, of course, entirely my own. I shall be grateful to have these pointed out to me. I am indebted to the authors and publishers for permission to reproduce material from the sources cited. Finally, I would like to thank Mrs D. J. Bogie for her skilful typing of the manuscript.

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INTRODUCTION

Quantitative genetics is concerned with the inheritance of those differences between individuals that are of degree rather than of kind, quantitative rather than qualitative. These are the individual differences which, as Darwin wrote, 'afford materials for natural selection to act on and accumulate, in the same manner as man accumulates in any given direction individual differences in his domestic productions'. An understanding of the inheritance of these differences is thus of fundamental significance in the study of evolution and in the application of genetics to animal and plant breeding; and it is from these two fields of enquiry that the subject has received the chief impetus to its growth.

Virtually every organ and function of any species shows individual differences of this nature, the differences of size among ourselves or our domestic animals being an example familiar to all. Individuals form a continuously graded series from one extreme to the other and do not fall naturally into sharply demarcated types. Qualitative differences, in contrast, divide individuals into distinct types with little or no connexion by intermediates. Examples are the differences between blue-eyed and brown-eyed individuals, between the blood groups, or between normally coloured and albino individuals. The familiar Mendelian ratios, which display the mechanism of inheritance, can be seen only when a gene difference at a single locus gives rise to a readily detectable difference in some such property of the organism. Quantitative differences, in so far as they are inherited, depend on genes whose effects are small in relation to the variation arising from other causes. Furthermore, quantitative differences are usually, though not necessarily always, influenced by gene differences at many loci. Consequently the individual genes, whether few or many, cannot be identified by their segregation; the Mendelian ratios are not displayed, and the methods of Mendelian analysis cannot be applied.

It is, nevertheless, a basic premiss of quantitative genetics that the inheritance of quantitative differences depends on genes subject to the same laws of transmission and having the same general properties as the genes whose transmission and properties are displayed by qualitative differences. Quantitative genetics is therefore an extension of Mendelian genetics, resting squarely on Mendelian principles as its foundation.

The methods of study in quantitative genetics differ from those employed in Mendelian genetics in two respects. In the first place, since ratios cannot be

observed, single progenies are uninformative, and the unit of study must be extended to 'populations', that is, larger groups of individuals comprising many progenies. And, in the second place, the nature of the quantitative differences to be studied requires the measurement, and not just the classification, of the individuals. The extension of Mendelian genetics into quantitative genetics may thus be made in two stages, the first introducing new concepts connected with the genetic properties of 'populations' and the second introducing concepts connected with the inheritance of measurements. This is how the subject is presented in this book. In the first part, which occupies Chapters 1 to 5, the genetic properties of populations are described by reference to genes causing easily identifiable, and therefore qualitative, differences. Quantitative differences are not discussed until the second part, which starts in Chapter 6. These two parts of the subject are often distinguished by different names, the first being referred to as 'population genetics' and the second as 'quantitative genetics' or 'biometrical genetics'.

The theoretical basis of quantitative genetics was established round about 1920 by the work of Fisher (1918), Haldane (summarized 1932) and Wright (1921). The development of the subject over the succeeding years, by these and many other geneticists and statisticians, has been mainly by elaboration, clarification, and the filling in of details, so that today we have a substantial body of theory accepted by the majority as valid.

The theory consists of the deduction of the consequences of Mendelian inheritance when extended to the properties of populations and to the simultaneous segregation of genes at many loci. The premiss from which the deductions are made is that the inheritance of quantitative differences is by means of genes, and that these genes are subject to the Mendelian laws of transmission and may have any of the properties known from Mendelian genetics. The property of 'variable expression' assumes great importance and might be raised to the status of another premiss: that the expression of the genotype in the phenotype is modifiable by non-genetic causes. Other properties whose consequences are taken into account include dominance, epistasis, pleiotropy, linkage, and mutation. The theory then allows us to deduce what will be the genetic properties of a population if the genes have the properties postulated. It allows us also to predict the consequences of any specified breeding plan, including those of natural selection. It therefore forms the basis for understanding evolutionary change. The main practical use of the theory is in comparing the merits of alternative procedures for animal and plant improvement.

The experimental side of quantitative genetics has three roles, complementary to the theoretical side. First, experimental study of populations allows us to deduce the properties of the genes associated with quantitative variation. Second, experimental breeding allows us to test the validity of the theory. And third, there are some consequences of breeding procedures that cannot be predicted from the theory, and questions about these can be answered only by experiment. There is now a large body of experimental data which substantiates the theory in considerable detail, showing that the genes concerned with quantitative variation do have the properties known from Mendelian genetics, and that the outcome of most breeding procedures can be predicted with some confidence. The aim here is to describe all that is reasonably firmly

established and, for the sake of clarity, to simplify as far as is possible without being misleading. Consequently, the emphasis is on the theoretical side. Though conclusions will often be drawn directly from experimental data, the experimental side of the subject is presented chiefly in the form of examples, chosen with the purpose of illustrating the theoretical conclusions. These examples, however, cannot always be taken as substantiating the postulates that underlie the conclusions they illustrate. Too often the results of experiments are open to more than one interpretation. The experimental work mentioned is only a very small, and far from random, sample of what has been done. In particular, a great deal more experimentation has been done with plants and farm animals than would appear from its representation among the work cited.

No attempts has been made to give exhaustive references to published work in any part of the subject; or to indicate the origins, or trace the history of the ideas. To have done this would have required a much longer book, and a considerable sacrifice of clarity. Most of the material in the book is covered more fully in one or other of the sources listed below. These sources are not regularly cited in the text. References are given in the text when any conclusion is stated without full explanation of its derivation. These references are not always to the original papers, but rather to the more recent papers where the reader will find a convenient point of entry to the topic under discussion.

Chief sources

(For full bibliographical details see list of References)

Becker (1975) *Manual of Quantitative Genetics.*
Crow and Kimura (1970) *An Introduction to Population Genetics Theory.*
Jacquard (1974) *The Genetic Structure of Populations.*
Kempthorne (1957) *An Introduction to Genetic Statistics.*
Lewontin (1974) *The Genetic Basis of Evolutionary Change.*
Li (1976) *First Course in Population Genetics.*
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(1977) *Introduction to Biometrical Genetics.*
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I GENETIC CONSTITUTION OF A POPULATION

Frequencies of genes and genotypes

To describe the genetic constitution of a group of individuals we should have to specify their genotypes and say how many of each genotype there were. This would be a complete description, provided the nature of the phenotypic differences between the genotypes did not concern us. Suppose for simplicity that we were concerned with a certain autosomal locus, A, and that two different alleles at this locus, A_1 and A_2 were present among the individuals. Then there would be three possible genotypes, A_1A_1, A_1A_2, and A_2A_2. (We are concerned here, as throughout the book, exclusively with diploid organisms.) The genetic constitution of the group would be fully described by the proportion, or percentage, of individuals that belonged to each genotype, or in other words by the frequencies of the three genotypes among the individuals. These proportions or frequencies are called *genotype frequencies*, the frequency of a particular genotype being its proportion or percentage among the individuals. If, for example, we found one-quarter of the individuals in the group to be A_1A_1, the frequency of this genotype would be 0.25, or 25 per cent. Naturally, the frequencies of all the genotypes together must add up to unity, or 100 per cent.

Example 1.1 The M-N blood groups is man are determined by two alleles at a locus, and the three genotypes correspond with the three blood groups, M, MN, and N. The following figures, taken from the tabulation of Mourant (1954), show the blood group frequencies among Eskimos of East Greenland and among Icelanders as follows:

		Blood group			*Number of individuals*
		M	MN	N	
Frequency,%	Greenland	83.5	15.6	0.9	569
	Iceland	31.2	51.5	17.3	747

Clearly the two populations differ in these genotype frequencies, the N blood group being rare in Greenland and relatively common in Iceland. Not only is this locus a source of variation within each of the two populations, but it is also a source of genetic difference between the populations.

A population, in the genetic sense, is not just a group of individuals, but a breeding group; and the genetics of a population is concerned not only with the genetic constitution of the individuals but also with the transmission of the genes from one generation to the next. In the transmission the genotypes of the parents are broken down and a new set of genotypes is constituted in the progeny, from the genes transmitted in the gametes. The genes carried by the population thus have continuity from generation to generation, but the genotypes in which they appear do not. The genetic constitution of a population, referring to the genes it carries, is described by the array of *gene frequencies*; that is, by specification of the alleles present at every locus and the numbers or proportions of the different alleles at each locus. If, for example, A_1 is an allele at the A locus, then the frequency of A_1 genes, or the gene frequency of A_1, is the proportion or percentage of all genes at this locus that are the A_1 allele. The frequencies of all the alleles at any one locus must add up to unity, or 100 per cent.

The gene frequencies at a particular locus among a group of individuals can be determined from a knowledge of the genotype frequencies. To take a hypothetical example, suppose there are two alleles, A_1 and A_2, and we classify 100 individuals and count the numbers in each genotypes as follows:

		A_1A_1	A_1A_2	A_2A_2	*Total*	
Number of individuals		30	60	10	100	
Number of genes	A_1	60	60	0	120	200
	A_2	0	60	20	80	

Each individual contains two genes, so we have counted 200 representatives of the genes at this locus. Each A_1A_1 individual contains two A_1 genes and each A_1A_2 contains one A_1 gene. So there are 120 A_1 genes in the sample, and 80 A_2 genes. The frequency of A_1 is therefore 60 per cent or 0.6, and the frequency of A_2 is 40 per cent or 0.4. To express the relationship in a more general form, let the frequencies of genes and of genotypes be as follows:

	Genes		*Genotypes*		
	A_1	A_2	A_1A_1	A_1A_2	A_2A_2
Frequencies	p	q	P	H	Q

so that $p + q = 1$ and $P + H + Q = 1$. Since each individual contains two genes, the frequency of A_1 genes is $\frac{1}{2}(2P + H)$, and the relationship between gene frequency and genotype frequency among the individuals counted is as follows:

$$\left.\begin{aligned} p &= P + \tfrac{1}{2}H \\ q &= Q + \tfrac{1}{2}H \end{aligned}\right\} \ldots [1.1]$$

Example 1.2 To illustrate the calculation of gene frequencies from genotype frequencies we may take the M-N blood group frequencies given in Example 1.1. The M and N blood groups represent the two homozygous genotypes and the MN group the heterozygote. The frequency of the M gene in Greenland is, from equation [1.1]

$0.835 + \frac{1}{2}(0.156) = 0.913$, and the frequency of the N gene is $0.009 + \frac{1}{2}(0.156) = 0.087$, the sum of the frequencies being 1.000 as it should be. Doing the same for the Iceland sample, we find the following gene frequencies in the two populations, expressed now as percentages:

	Gene	
	M	N
Greenland	91.3	8.7
Iceland	57.0	43.0

Thus the two populations differ in gene frequency as well as in genotype frequencies.

Causes of change

The genetic properties of a population are influenced in the process of transmission of genes from one generation to the next by a number of agencies. These form the chief subject-matter of the next four chapters, but we may briefly review them here in order to have some idea of what factors are being left out of consideration in this chapter. The agencies through which the genetic properties of a population may be changed are these:

Population size. The genes passed from one generation to the next are a sample of the genes in the parent generation. Therefore the gene frequencies are subject to sampling variation between successive generations, and the smaller the number of parents the greater is the sampling variation. The effects of sampling variation will be considered in Chapters 3–5, and meantime we shall exclude it from the discussion by supposing always that we are dealing with a 'large population', which means simply one in which sampling variation is so small as to be negligible. For practical purposes a 'large population' is one in which the number of adult individuals is in the hundreds rather than in the tens.

Differences of fertility and viability. Though we are not at present concerned with the phenotypic effects of the genes under discussion, we cannot ignore their effects on fertility and viability, because these influence the genetic constitution of the succeeding generation. The different genotypes among the parents may have different fertilities, and if they do they will contribute unequally to the gametes out of which the next generation is formed. In this way the gene frequency may be changed in the transmission. Further, the genotypes among the newly formed zygotes may have different survival rates, and so the gene frequencies in the new generation may be changed by the time the individuals are adult and themselves become parents. These processes are called selection, and will be described in Chapter 2. Meanwhile we shall suppose they are not operating. Human blood-group genes may be taken for the purpose of illustration since the selective forces acting on them are probably not strong. Genes that produce a mutant phenotype which is abnormal in comparison with the wild-type are, in contrast, usually subject to much more severe selection.

Migration and mutation. The gene frequencies in the population may also be changed by immigration of individuals from another population, and by gene

mutation. These processes will be described in Chapter 2, and at this stage will also be supposed not to operate.

Mating system. The genotypes in the progeny are determined by the union of the gametes in pairs to form zygotes, and the union of gametes is influenced by the mating of the parents. So the genotype frequencies in the offspring generation are influenced by the genotypes of the pairs that mate in the parent generation. We shall at first suppose that mating is at random with respect to the genotypes under discussion. *Random mating*, or *panmixia*, means that any individual has an equal chance of mating with any other individual in the population. The important points are that there should be no special tendency for mated individuals to be alike in genotype, or to be related to each other by ancestry. If a population covers a large geographic area, individuals inhabiting the same locality are more likely to mate than in individuals inhabiting different localities, and so the mated pairs tend to be related by ancestry. A widely spread population is therefore likely to be subdivided into local groups and mating is random only within the groups. The properties of subdivided populations depend on the size of the local groups and will be described under the effects of population size in Chapters 3–5.

Hardy–Weinberg equilibrium

The Hardy–Weinberg law

In a large random-mating population with no selection, mutation, or migration, the gene frequencies and the genotype frequencies are constant from generation to generation; and, furthermore, there is a simple relationship between the gene frequencies and the genotype frequencies. These properties of a population are derived from a theorem, or principle, known as the *Hardy–Weinberg* law after Hardy and Weinberg, who independently demonstrated them in 1908. A population with constant gene and genotype frequencies is said to be in *Hardy–Weinberg equilibrium.* The relationship between gene frequencies and genotype frequencies is of the greatest importance because many of the deductions about population genetics and quantitative genetics rest on it. The relationship is this: if the gene frequencies of two alleles among the parents are p and q, then the genotype frequencies among the progeny are p^2, $2pq$, and q^2, thus:

	Genes in parents		*Genotypes in progeny*			
	A_1	A_2	A_1A_1	A_1A_2	A_2A_2	
Frequencies	p	q	p^2	$2pq$	q^2	... [1.2]

(The relationship above refers to autosomal genes; sex-linked genes are not quite so simple and will be explained later.) The conditions of random mating and no selection, required for the Hardy–Weinberg law to hold, refer only to the genotypes under consideration. There may be preferential mating with respect to other attributes, and genotypes of other loci may be subject to selection, without affecting the issue. Two additional conditions are that the genes segregate normally in gametogenesis and that the gene frequencies are the same in males

and females. The reasons for these requirements will be seen in the proof.

The proof of the Hardy–Weinberg law involves four steps, which are summarized in Table 1.1, with the conditions that must hold for the deduction at each step to be valid. The details of the four steps are as follows.

1. *From gene frequency in parents to gene frequency in gametes.* Let the parent generation have gene and genotype frequencies as follows:

	Genes		*Genotypes*		
	A_1	A_2	A_1A_1	A_1A_2	A_2A_2
Frequencies	p	q	P	H	Q

Two types of gamete are produced, those bearing A_1 and those bearing A_2. A_1A_1 individuals produce only A_1 gametes. A_1A_2 individuals, provided segregation is normal, produce equal numbers of A_1 and A_2 gametes. Then, provided all genotypes are equally fertile, the frequency of A_1 among all the gametes produced by the whole population is $P + \frac{1}{2}H$, which by equation [1.1] is the gene frequency of A_1 in the parents producing the gametes. Thus the gene frequency in the whole gametic output is the same as in the parents. This is step 1*a* in Table 1.1. Only some of the gametes form zygotes that will become individuals in the next generation. The gene frequency in the zygotes is unchanged provided the gametes carrying different alleles do not differ in their fertilizing capacity, and provided the zygotes formed represent a large sample of the parental gametes. This is step 1*b*.

2. *From gene frequency in gametes to genotype frequencies in zygotes.* Random mating between individuals is equivalent to random union among

Table 1.1 Steps of deduction in the proof of the Hardy–Weinberg law, and the conditions that must hold.

Step	*Deduction from: to*	*Conditions*
1*a*	Gene frequency in parents → Gene frequency in all gametes	(1) Normal gene segregation (2) Equal fertility of parents
1*b*	Gene frequency in all gametes → Gene frequency in gametes forming zygotes	(3) Equal fertilizing capacity of gametes (4) Large population
2	Gene frequency in gametes forming zygotes → Genotype frequencies in zygotes	(5) Random mating (6) Equal gene frequencies in male and female parents
3	Genotype frequencies in zygotes → Genotype frequencies in progeny	(7) Equal viability
4	Genotype frequencies in progeny → Gene frequency in progeny	

their gametes. The genotype frequencies among the zygotes (fertilized eggs) are then the products of the frequencies of the gametic types that unite to produce them. The genotype frequencies among the progeny produced by random mating can therefore be determined simply by multiplying the frequencies of the gametic types produced by each sex of parents. Provided the gametic frequencies are the same in each sex, the zygotes produced are as shown in Table 1.2. The union of A_1 eggs with A_2 sperms need not be distinguished from that of A_2 eggs with A_1 sperms; so the genotype frequencies of the zygotes are:

	Genotype		
	A_1A_1	A_1A_2	A_2A_2
Frequency	p^2	$2pq$	q^2

3. *From zygotes to adults.* The genotype frequencies in the zygotes deduced above are the Hardy–Weinberg frequencies, as stated in [1.2]. This is, however, not quite the end of the proof because the frequencies will not be observable unless the zygotes survive equally well, at least until they can be classified for genotype. This step may seem trivial, but it must be recognized if the effects of differential viability are to be understood.

4. *From genotype frequencies to gene frequency in progeny.* This final step proves that the gene frequency has not changed. Provided the different genotypes in the progeny survive equally well to adulthood when they can become parents, their frequencies will be as above. The gene frequency in the adult progeny can then be found by equation [1.1]. The frequency of A_1 is $p^2 + \frac{1}{2}(2pq) = p(p+q) = p$, which is the same as in the parent generation. This proves the constancy of the gene frequency from one generation to the next.

Two further aspects of the Hardy–Weinberg law can now be stated. First, since the gene frequencies are the same in parents and progeny, the relationship between gene frequencies and genotype frequencies in [1.2] applies to a single generation. Second, the genotype frequencies in the progeny depend only on the gene frequencies in the parents and not on the genotype frequencies. This can be

Table 1.2

		Female gametes and their frequencies	
		A_1 p	A_2 q
Male gametes and their frequencies	A_1 p	A_1A_1 p^2	A_1A_2 pq
	A_2 q	A_1A_2 pq	A_2A_2 q^2