Subject: Genetics and plant breeding **CBCS Pattern Practical Examination**

M.Sc (Ag.) III Semester **Course: Population and Biometrical Genetics**

Unit -1 Genes in Population

Unit-2 Forces changing gene frequencies

Introduction

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.

These two parts of the subject are often distinguished by different names, the first being referred to as "Population Genetics" and the second as "Biometrical Genetics" or "Quantitative Genetics." Some writers, however, use "Population Genetics" to refer to the whole. The terminology of this distinction is therefore ambiguous. The use of "Quantitative Genetics" to refer to the whole subject may be justified on the grounds that the genetics of populations is not just a preliminary to the genetics of quantitative differences, but an integral part of it.

The theoretical basis of quantitative genetics was established round about 1920 by the work of Fisher (1918), Haldane (I924-32, summarised 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. As in any healthily growing science, there are differences of opinion, but these are chiefly matters of emphasis, about the relative importance of this or that aspect.

GENETIC CONSTITUTION OF A POPULATION

FREQUENCIES OF GENES AND GENOTYPES

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.

EXAMPLE 1 The M-N blood groups in 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 .bulation of Mourant (1954), show the blood group frequencies among Eskimoes 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.

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 anyone locus must add up to unity, or 100 per cent.

Hypothetical example, suppose there are two alleles, A_1 and A_2, and we classify 100 individuals and count the numbers in each genotype 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 1/2(2P+H), and the relationship between gene frequency and genotype frequency among the individuals counted is as follows:

p=P+ ½ H

q=Q+ ½ H

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 above, 0·835 + ½ (0.I56) = 0.913, and the frequency of the N gene is 0.009 + ½ (0. I 56) = 0.087, the sum of the frequencies being I .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.

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. 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. 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, Meanwhile we shall suppose they are not operating. It is difficult to find examples of genes not subject to selection. For the purpose of illustration, however, we may take the human blood-group genes since the selective forces acting on these are probably not very 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. 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.

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 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.

HARDY-WEINBERG EQUILIBRIUM

In a large random-mating population both gene frequencies and genotype frequencies are constant from generation to generation, in the absence of migration, mutation and selection; and the genotype frequencies are determined by the gene frequencies. These properties of a population were first demonstrated by Hardy and by Weinberg independently in 1908, and are generally known as the Hardy-Weinberg Law.

Such a population is said to be in Hardy-Weinberg equilibrium. Deduction of the HardyWeinberg Law involves three steps: (I) from the parents to the gametes they produce; (2) from the union of the gametes to the genotypes in the zygotes produced; and (3) from the genotypes of the zygotes to the gene frequency in the progeny generation. These steps, in detail, are as follows:

1. Let the parent generation have gene and genotype frequencies as follows:

A_1	A_2	A_1A_1	A_1A_2	A_2A_2
p	*q*	*P*	*H*	*Q*

Two sorts of gametes are produced, those bearing A_1 and those bearing A_2. The frequencies of these gametic types are the same as the gene frequencies, *p* and *q*, in the generation producing them, for this reason: A_1A_1 individuals produce only A_1 gametes, and A_1A_2 individuals produce equal numbers of A_1 and Aa gametes (provided, of course, there is no anomaly of segregation). So the frequency of A_1 gametes produced by the whole population is P + ½ H, which is the gene frequency of A_1.

2. Random mating between individuals is equivalent to random union among their gametes. We can think of a pool of gametes to which all the individuals contribute equally; zygotes are formed by random union between pairs of gametes from the pool. The genotype frequencies among the zygotes 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 as shown in the following table, where the gene frequencies are assumed to be the same among male as among female gametes:

			Female gametes and their frequencies	
			A_l	A
			P	q
Male gametes and their frequencies	A_1	p	A_1A_1	A_1A_2
			p2	pq
	A_2	q	A_1A_2	A_2A_2
			pq	q2

So the genotype frequencies of the zygotes are

A_1A_1	A_1A_2	A_2A_2
p2	*2pq*	*q2*

Note: these genotype frequencies depend only on the gene frequency in the parents, and not on the parental genotype frequencies, provided the parents mate at random.

3. Finally we use these genotype frequencies to determine the gene frequency in the offspring generation. The gene frequency of A_1 is p2 + ½ (2pq) = p(p +q) =P, which is the same as in the parent generation.

The properties of a population with respect to a single locus, expressed in the Hardy-Weinberg law and demonstrated above, are:

(1) A large random-mating population, in the absence of migration, mutation, and selection, is stable with respect to both gene and genotype frequencies: there is no inherent tendency for its genetic properties to change from generation to generation.

(2) The genotype frequencies in the progeny produced by random. mating among the parents are determined solely by the gene frequencies among the parents. Consequently:

(a) The population in Hardy-Weinberg equilibrium has the relationship between the gene and genotype frequencies in anyone generation. And,

(b) These Hardy-Weinberg genotype frequencies are established by one generation of random mating, irrespective of the genotype frequencies among the parents.

Mating frequencies and another proof of the Hardy-Weinberg law:

Let us now look more closely into the breeding structure of a random-mating population, distinguishing the types of mating according to the genotypes of the pairs. This provides a general method for relating genotype frequencies in successive generations. It also provides another proof of the Hardy-Weinberg law; a proof more cumbersome than that already given but showing more clearly how the Hardy-Weinberg frequencies arise from the Mendelian laws of segregation.

The procedure is to obtain first the frequencies of all possible mating types according to the frequencies of the genotypes among the parents, and then to obtain the frequencies of genotypes among the progeny of each type of mating according to the Mendelian ratios.

Consider a locus with two alleles, and let the frequencies of genes and genotypes in the parents be, as before,

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

There are altogether nine types of mating, and their frequencies when mating is random are found thus:

			Genotype and frequency of male parent		
			A_1A_1	A_1A_2	A_2A_2
			P	H	Q
Genotype and frequency of female parent	A_1A_1	P	P^2	PH	PQ
	A_1A_2	H	PH	H^2	HQ
	A_2A_2	Q	PQ	HQ	Q^2

Now we have to consider the genotypes of offspring produced by each type of mating, and find the frequency of each genotype in the total progeny, assuming, of course, that all types of mating are equally fertile and all genotypes equally viable. Thus, for example, matings of the type AlAI x AlAI produce only AlAI offspring. So, of the total progeny, a proportion p2 are AlAI genotypes derived from this type of mating. Similarly a quarter of the offspring of AIA2 x AIA2 matings are AlAI' So this type of mating, which has a frequency of H2, contributes a proportion iH2 of the total AlAI progeny.

Mating		Genotype and frequency of progeny		
Type	Frequency	A_1A_1	A_1A_2	A_2A_2
$A_1A_1\times A_1A_1$	P^2	P^2		
$A_1A_1\times A_1A_2$	2PH	PH	PH	
$A_1A_1\times A_2A_2$	2PQ		2PQ	
$A_1A_2\times A_1A_2$	H^2	¼ H^2	½ H^2	¼ H^2
$A_1A_2\times A_2A_2$	2HQ		HQ	HQ
$A_2A_2\times A_2A_2$	Q^2			Q^2
SUMS		$(P + ½H)^2$	2(P+½H) (Q+½H)	$(Q+ ½H)^2$
	=	p^2	2pq	q^2

To find the frequency of each genotype in the total progeny we add the frequencies contributed by each type of mating. The sums, after simplification, they are seen to be equal to p2, 2pq, and q2. These are the Hardy-Weinberg equilibrium frequencies, and we have shown that they are attained by one generation of random mating, irrespective of the genotype frequencies among the parents.

CHANGES OF GENE FREQUENCY

a study of the agencies through which changes of gene frequency, and consequently of genotype frequencies, are brought about. There are two sorts of process:

systematic processes, which tend to change the gene frequency in a manner predictable both in amount and in direction; and

the dispersive process, which arise in small populations from the effects of sampling, and is predictable in amount but not in direction.

only with the systematic processes, and we shall consider only large random mating populations in order to exclude the dispersive process from the picture. There are three systematic processes: **migration, mutation, and selection.**

MIGRATION

Let us suppose that a large population consists of a proportion, m, of new immigrants in each generation, the remainder, 1 - m, being natives. Let the frequency of a certain gene be qm among the immigrants and qo among the natives. Then the frequency of the gene in the mixed population, q_1 will be

$$\boxed{\begin{aligned} q_1 &= mq_m + (1 - m)q_0 \\ &= m(q_m - q_0) + q_0 \end{aligned}}$$

The change of gene frequency, Δq, brought about by one generation of immigration is the difference between the frequency before immigration and the frequency after immigration. Therefore

$$\boxed{\begin{aligned} \Delta q &= q_1 - q_0 \\ &= m(q_m - q_0) \end{aligned}}$$

Thus the rate of change of gene frequency in a population subject to immigration depends, as must be obvious, on the immigration rate and on the difference of gene frequency between immigrants and natives.

MUTATION

The effect of mutation on the genetic properties of the population differs according to whether we are concerned with a mutational event so rare as to be virtually unique, or with a mutational step that recurs repeatedly. The first produces no permanent change, whereas the second does.

Non-recurrent mutation: Consider first a mutational event that gives rise to just one representative of the mutated gene or chromosome in the whole population. This sort of mutation is of little importance as a cause of change of gene frequency, because the product of a unique mutation has an infinitely small chance of surviving in a large population, unless it has a selective advantage. For Example: As a result of the single mutation there will be one A_1A_2 individual in a population all the rest of which is A_1A_1 The frequency of the mutated gene, A_2, is therefore extremely low.

Now according to the Hardy-Weinberg equilibrium the gene frequency should not change in subsequent generations. But with this situation we can no longer ignore the variation of gene frequency due to sampling. With a gene at very low frequency the sampling variation, even though very small, may take the frequency to zero, and the gene will then be lost from the population. The conclusion, therefore, is that a unique mutation without selective advantage cannot produce a permanent change in the population.

Recurrent mutation: It is with the second type of mutation recurrent mutation-that we are concerned as an agent for causing change of gene frequency. Each mutational event recurs regularly with characteristic frequency, and in a large population the frequency of a mutant gene is never so low that complete loss can occur from sampling. We have, then, to find out what is the effect of this "pressure" of mutation on the gene frequency in the population.

Suppose gene A_1 mutates to A_2 with a frequency u per generation. (u is the proportion of all A_1 genes that mutate to A_2 between one generation and the next.) If the frequency of A_1 in one generation is p_0 the frequency of newly mutated A_2 genes in the next generation is up_0. So the new gene frequency of A_1 is $p_0 - up_0$, and the change of gene frequency is $- up_0$. Now consider what happens when the genes mutate in both directions. Suppose for simplicity that there are only two alleles, A_1 and A_2, with initial frequencies p_0 and q_0. A_1 mutates to A_2 at a rate u per generation, and A_2 mutates to A_1 at a rate v. Then after one generation there is a gain of A_2 genes equal to up_0 due to mutation in one direction, and a loss equal to vq_0 due to mutation in the other direction. Stated in symbols, we have the situation:

Mutation rate $A_1 \underset{v}{\overset{u}{\rightleftharpoons}} A_2$

Initial gene frequencies p_0 q_0

Then the change of gene frequency in one generation is

$$\Delta q = up_0 - vq_0$$

The point of equilibrium can be found by equating the change of frequency, LJq, to zero. Thus at equilibrium

$$pu = qv$$

or

$$\frac{p}{q} = \frac{v}{u}$$

and

$$q = \frac{u}{u + v}$$

Three conclusions can be drawn from the effect of mutation on gene frequency.

Measurements of mutation rates indicate values ranging between about 10-4 and 10-8 per generation (one in ten thousand and one in a hundred million gametes). With normal mutation rates, therefore, mutation alone can produce only very slow changes of gene frequency; on an evolutionary time-scale they might be important, but they could scarcely be detected by experiment unless with micro-organisms.

The second conclusion concerns the equilibrium between mutation in the two directions. Studies of reverse mutation (from mutant to wild type) indicate that it is usually less frequent than forward mutation (from wild type to mutant), on the whole about one tenth as frequent The equilibrium gene frequencies for such loci, resulting from mutation alone, would therefore be about o· 1 of the wild-type allele and 0'9 of the mutant; in other words the "mutant" would be the common form and the "wild type" the rare form. Since this is not the situation we find in natural populations it is clear that the frequencies of such genes are not the product of mutation alone. We shall see in the next section that the rarity of mutant alleles hs attributable to selection.

The third conclusion concerns the effects of an increase of mutation rates such as might be caused by an increase of the level of ionizing radiation to which the population is subjected. Any loci at which the gene frequencies are in equilibrium from the effects of mutation alone will not be affected by a change of mutation rate, provided the change affects forward and reverse mutation proportionately. This can be seen from consideration of the equilibrium gene frequencies

SELECTION

The proportionate contribution of offspring to the next generation is called the fitness of the individual, or sometimes the adaptive value, or selective value. If the differences of fitness are in any way associated with the presence or absence of a particular gene in the individual's genotype, then selection operates on that gene. When a gene is subject to selection its frequency in the offspring is not the same as in the parents, since parents of different genotypes pass on their genes unequally to the next generation. In this way selection causes a change of gene frequency,

and consequently also of genotype frequency. The change of gene frequency resulting from selection is more complicated to describe than that resulting from mutation, because the differences of fitness that give rise to the selection are an aspect of the phenotype.

We therefore have to take account of the degree of dominance shown by the genes in question. Dominance, in this connexion, means dominance with respect to fitness, and this is not necessarily the same as the dominance with respect to the main visible effects of the gene. Most mutant genes, for example, are completely recessive to the wild type in their visible effects, but this does not necessarily mean that the heterozygote has fitness equal to that of the wild-type homozygote.

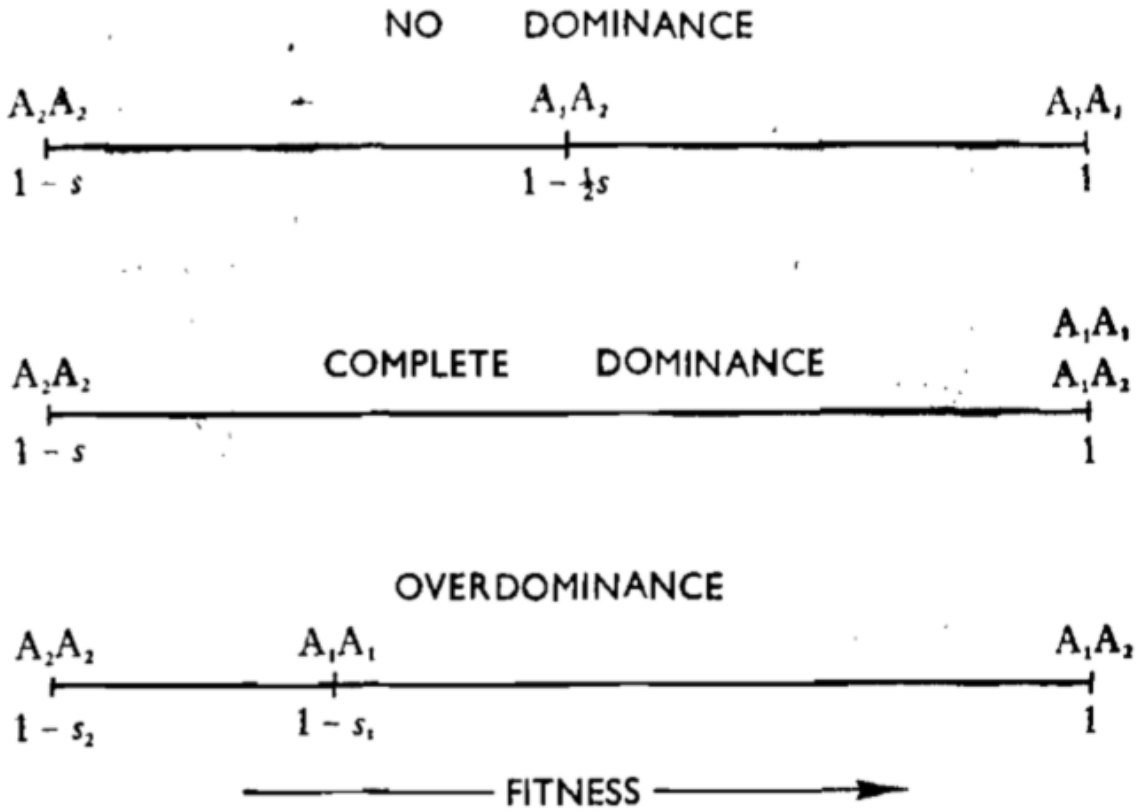

FIG. Degrees of dominance with respect to fitness.

We may therefore treat the change of gene frequency as taking place between the counting of genotypes among the zygotes of the parent generation and the formation of zygotes in the offspring generation. The strength of the selection is expressed as the coefficient of selection, s, which is the proportionate reduction in the gametic contribution of a particular genotype compared with a standard genotype, usually the most favored. The contribution of the favored genotype is taken to be 1, and the contribution of the genotype selected against is then 1 - s. This expresses the fitness of one genotype compared with the other. Suppose,

for example, that the coefficient of selection is s = 0·1; this means that for every 100 zygotes produced by the favored genotype, only 90 are produced by the genotype selected against.

Change of gene frequency under selection:

We have first to derive the basic formulae for the change of gene frequency brought about by one generation of selection. The different conditions of dominance have to be taken account of, but the method is the same for all, and we shall illustrate it by reference to the case of complete dominance with selection acting against the recessive homozygote. Let the genes A_1 and A_2 have initial frequencies *p* and *q*, A_1 being completely dominant to A_2, and let the coefficient of selection against A_2A_2 individuals be s. Multiplying the initial frequency by the fitness of each genotype we obtain the proportionate contribution of each genotype to the gametes that will form the next generation, thus:

Genotypes	A_1A_1	A_1A_2	A_2A_2	Total
Initial frequencies	p^2	$2pq$	q^2	1
Fitness	1	1	1 - s	
Gametic contribution	p^2	$2pq$	q^2 (1 – s)	1- s q^2

The total gametic contribution is no longer unity, because there has been a proportionate loss of sq^2 due to the selection. To find the frequency of Az gametes produced-and so the frequency of A_2 genes in the progeny-we take the gametic contribution of A_2A_2 individuals plus half that of A_1A_2 individuals and divide by the new total, Thus the new gene frequency is

$$q_1 = \frac{q^2(1-s)+pq}{1-sq^2}$$

The change of gene frequency, Δq, resulting from one generation of selection is

$$\Delta q = q_1 - q$$
$$= \frac{q^2(1-s)+pq}{1-sq^2} - q$$

Which on simplification reduces to:

$$\Delta q = -\frac{sq^2(1-q)}{1-sq^2}$$

From this we see that the effect of selection on gene frequency depends not only on the intensity of selection, s, but also on the initial gene frequency.

Selection may act against the dominant phenotype and favour the recessive: we then put 1 - s for the fitness of A_1A_1 and of A_1A_2 genotypes. The expression for Δq is given in Table below. The difference may best be appreciated by considering the effects of total elimination (S = 1). The expression for selection against the dominant allele then reduces to $\Delta q = 1 - q$, which expresses the fact that if only the recessive genotype survives to breed the frequency of the recessive allele will become 1 after a single generation of selection. But, on the other hand, if there is complete elimination of the recessive genotype the frequency of the dominant allele does not reach 1 after a single generation. The difference between the effects of selection in opposite directions becomes less marked as the value of s decreases.

If there is incomplete dominance the expression for Δq is again different. The case of exact intermediate dominance is given in Table. Here we put 1 – ½ s for the fitness of A_1A_2 and 1 - s for the fitness of A_2A_2 genotype. For selection in the opposite direction in this case we need only inter change the initial frequencies of the two alleles, writing *p* in the place of *q*.

Change of gene frequency, Δq, after one generation of selection under different conditions of dominance specified

Conditions of dominance and selection	*Initial frequencies and fitness of the genotypes*			*Change of frequency, Δq, of gene A_2*	
	A_1A_1 p^2	A_1A_2 $2pq$	A_2A_2 q^2		
No dominance selection against A_2	1	$1-\frac{1}{2}s$	$1-s$	$-\frac{\frac{1}{2}sq(1-q)}{1-sq}$	(1)
Complete dominance selection against A_2A_2	1	1	$1-s$	$-\frac{sq^2(1-q)}{1-sq^2}$	(2)
Complete dominance selection against A_1 –	$1-s$	$1-s$	1	$+\frac{sq^2(1-q)}{1-s(1-q^2)}$	(3)
Overdominance selection against A_1A_1 and A_2A_2	$1-s_1$	1	$1-s_2$	$+\frac{pq(s_1p-s_2q)}{1-s_1p^2-s_2q^2}$	(4)

When s is small the denominators differ little from 1, and the numerators alone can be taken to represent Δq sufficiently accurately for most purposes. Finally, selection may favour the heterozygote, a condition known as over-dominance. In this case we put $1 - S_1$ and $1 - S_2$ for the fitness of the two homozygotes. The expression for Δq is given in above Table. This special case will be given more detailed attention later.

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