TH. DOBZHANSKY
Columbia University

Chapter 13

Nature and Origin of Heterosis

Exploitation of heterosis in cultivated plants and animals is to date by far the most important application of the science of genetics in agricultural practice. It is therefore unfortunate that few of the studies so far made on heterosis go beyond crudely empirical observations and descriptions and that little effort is being made to understand the underlying causes of the phenomena involved. Such an understanding is needed particularly because the advances of general genetics make it evident that several quite distinct, and even scarcely related, phenomena are confused under the common label of *heterosis* or *hybrid vigor*.

In what follows, an attempt is made to indicate briefly what seem, to the writer, promising lines of approach to a classification and study of the various kinds of heterosis. The tentative nature of the classification here suggested is fully realized. But it is believed that this classification may nevertheless serve a useful function if it directs the attention of the students of heterosis to factors which are only too often overlooked.

MUTATIONAL EUHETEROSIS

Perhaps the simplest kind of true heterosis—*euheterosis*—is that which results from sheltering of deleterious recessive mutants by their adaptively superior dominant alleles in populations of sexually reproducing and cross-fertilizing organisms.

Although only a small fraction of the existing species of organisms have been investigated genetically, it is reasonable to assume that mutational changes arise from time to time in all species, albeit at different rates. Furthermore, a great majority of the mutations that arise are deleterious, and lower the fitness of their carriers to survive or to reproduce in some or in all

environments. This deleterious character of most mutations seems surprising, especially because in modern biology the process of mutation is regarded as the source of the raw materials from which evolutionary changes are constructed.

A little consideration shows, however, that the adaptively negative character of most mutations is by no means unexpected. Indeed, since every mutation has a finite probability to occur in any generation, the mutants which we observe in our fields and laboratories must have arisen many times in the history of the species. The rare mutants which confer adaptive advantages on their possessors in the environments in which the species normally lives have had the chance to become established in the species populations as components of the *normal* species genotype. In a more or less static environment, the genotypes of most species are close to the upper attainable level of adaptedness.

The above argument may seem to prove too much. In the absence of useful mutants, evolution would come to a standstill. The paradox is resolved if we recall that the environment is rarely static for any considerable periods of time. Furthermore, most living species occur not in a single but in several related environments. Genotypes which are adaptively valuable in a certain environment may be ill adapted in other environments, and vice versa. It should be possible then to observe the occurrence of useful mutations if we place the experimental organisms in environments in which their ancestors did not live.

Progressive improvement of domesticated animals and plants in the hands of breeders constitutes evidence that useful mutations do occur. The genetic variants which are being made use of by breeders have arisen ultimately through mutation. These mutations have been arising from time to time, before as well as after the domestication. But while they were deleterious in the wild state, some of them happened to be suitable from the standpoint of the breeders. They were useful in the man-made environment or they were useful to man. Favorable mutations can be observed also in wild species, provided that the latter are placed in unusual external or genetic environments. This has been demonstrated in experiments of Spassky and the writer on *Drosophila pseudoobscura*. Several laboratory strains of this fly were subjected to intense selection for fifty consecutive generations, and improvements of the viability have been observed in most of them.

Many, perhaps most, deleterious mutants are nearly or completely recessive. Others are more or less dominant to the "normal," or ancestral, state. The fate of the dominant deleterious mutants in populations of sexually reproducing and cross-fertilizing species is different from that of the recessives. By definition, deleterious mutants in wild species lower the fitness of their carriers to survive or to reproduce, and in cultivated species impair the qualities considered desirable by the breeders. Natural and artificial selec-

tion will consequently tend to lower the frequency, or to eliminate deleterious mutants.

Selection against a dominant deleterious mutant is, however, a far more efficient process than that against a recessive mutant. This is because deleterious recessive mutant genes are sheltered from selection by normal dominant alleles in heterozygotes. Deleterious dominants are eliminated by selection within relatively few generations after their origin. Deleterious recessives accumulate in heterozygotes until their frequencies become so high that recessive homozygotes are produced. Dominant alleles are not intrinsically beneficial, and recessives are not necessarily deleterious. But at any one time, we find in cross-fertilizing populations more deleterious recessives than deleterious dominants, because the former are not eliminated by selection as promptly as the latter.

Analysis of wild populations of several species of Drosophila has revealed extensive infestation of the germ plasm by deleterious recessive mutant genes. According to the unpublished data of Pavan and collaborators, 41 per cent of the second chromosomes in Brazilian populations of *Drosophila willistoni* are lethal or semilethal when homozygous. Among the remainder, 57 per cent are sublethal when homozygous. Furthermore, 31 per cent of the second chromosomes make the homozygotes completely sterile in at least one sex, 32 per cent retard the development, and 16 per cent cause various visible abnormalities. Comparable figures for the third chromosomes are 32 per cent of lethals and semilethals, 49 per cent subvitals, 28 per cent steriles, 36 per cent retarded, and 16 per cent containing visible mutants. Since every fly has two second and two third chromosomes, it is easily seen that a great majority of individuals in Brazilian populations carry several deleterious variants in heterozygous condition.

The mass of deleterious recessives carried in normally breeding natural populations has no disastrous effects on the average fitness of members of such populations. This is because the frequency of recessive homozygotes found in a population at equilibrium is equal to the number of the corresponding recessive mutants that arise in every generation. The loss of fitness caused in a normally breeding population by dominant and by recessive mutants is thus proportional to the frequency of the origin of these mutants by mutation.

The situation changes completely if a normally crossbred population is subjected to inbreeding. For inbreeding renders homozygous many recessives that would remain sheltered in heterozygotes under normal crossbreeding. These recessives become suddenly exposed to natural, or to artificial, selection. The loss of fitness in inbred lines of normally cross-fertilized species is the consequence. Conversely, the heterosis observed in the progeny of intercrossed inbred lines is the outcome of restoring the normal reproductive biology and the normal population structure of the species.

BALANCED EUHETEROSIS

Balanced heterosis is due to the occurrence of a rather special class of mutations and gene combinations, which confer on heterozygotes a higher adaptive value, or a higher agricultural usefulness than is found in the corresponding homozygotes.

The conditions most frequently found in heterozygotes are either dominance and recessiveness, when the heterozygote is more or less similar to one of the homozygotes, or phenotypical intermediacy between the homozygotes. A heterozygote may, however, be in some respects phenotypically more extreme than either homozygote. Thus, a heterozygote may be more viable, more productive, or otherwise exceed both homozygotes in some positive or negative quality. This condition is sometimes spoken of as overdominance (Hull).

Although overdominance is, by and large, an exceptional situation, it is of particular interest to a student of population genetics, and especially to a student of heterosis. Suppose that a certain gene is represented in a population by a series of alleles, A^1, A^2, A^3 . . . which are deleterious in homozygous condition, A^1A^1, A^2A^2, A^3A^3 . . . , but which show a relatively higher fitness in heterozygotes A^1A^2, A^1A^3, A^2A^3 . . . , etc. Natural or artificial selection would preserve in the population all the variants A^1, A^2, A^3 . . . , regardless of how poorly adapted the homozygotes may be. In fact, one or all homozygotes may be semilethal or even lethal, and yet selection will establish an equilibrium at which every one of the variants will be present with a definite frequency. This equilibrium can easily be calculated if the selective disadvantages of the homozygotes, compared to the heterozygotes, are known. The resulting situation is referred to as balanced polymorphism.

Balanced polymorphism may be produced by mutations in single genes, provided that the heterozygotes exhibit overdominance in fitness in some environments. This has been demonstrated, among others, by Gustafsson and Nybom. They observed several mutations in barley that were deleterious in homozygotes, but produced heterozygotes superior to the ancestral "normal" homozygotes. Ford and others showed that certain color variants in butterflies, which are inherited as though caused by a single genetic change, are maintained in natural populations by the same mechanism.

Detailed data are available on balanced polymorphism in several species of Drosophila, in which natural populations are very often polymorphic for gene arrangements in some chromosomes. These gene arrangements differ in inversions of blocks of genes. Thus, in certain populations of *Drosophila pseudoobscura* from Southern California, at least 70 per cent of the wild individuals are inversion heterozygotes. In populations of *Drosophila willistoni* from central Brazil (Goyaz), an average individual is heterozygous for as many as nine inversions, and very few individuals are homozygous.

Now, it has been shown by observation both on natural and on experimental populations of some Drosophila species, that the heterozygotes for the naturally occurring inversions possess considerable adaptive advantages over the homozygotes. For example, taking the adaptive value of the heterozygotes for ST and CH inversions in *Drosophila pseudoobscura* to be unity, the adaptive values of the ST/ST and CH/CH homozygotes are about 0.8 and 0.4 respectively. Further, it has been shown that the heterosis in the ST/CH heterozygotes occurs only if the constituent chromosomes are derived from the same population, or from populations of nearby localities. Chromosomes with the same gene arrangements, ST and CH, derived from remote localities (such as Central and Southern California, or Southern California and Mexico) exhibit little or no heterosis.

This finding is most compatible with the assumption that the overdominance in fitness observed in the heterozygotes is the property not of a single gene locus, or of a chromosome structure, but rather of integrated systems of polygenes. Such polygenic systems are coadapted by natural selection to other polygene complexes present in the same populations. The role of the chromosomal inversions in the formation of the heterotic state of balanced polymorphism is due to the suppression of crossing over caused by most inversions, at least in Drosophila. Elimination of crossing over prevents the breakup of the adaptively integrated polygene complexes which are carried in the chromosomes involved.

It should be noted that adaptively integrated polygene complexes can be maintained in crossbreeding populations with the aid of genetic mechanisms other than chromosomal inversions. Any factor which restricts or prevents crossing over in chromosomes, or parts of chromosomes, can accomplish the same biological function. Localization of chiasmata may be such a factor. If, for example, chiasmata are found chiefly or exclusively at some definite points in a chromosome, the genes carried in the sections which intervene between these points are inherited in blocks. Such gene blocks may act exactly as gene complexes bound together by inversions.

Balanced heterosis differs profoundly from mutational heterosis. The latter is due simply to the sheltering of deleterious recessive mutants by their dominant alleles. Balanced heterosis is a result of overdominance. Mutational heterosis is a protective device of a sexual species with a certain population structure against the mutation pressure. Balanced heterosis is an evolutionary contrivance that permits maintenance in a population of a multiplicity of genotypes that may be adaptive in different ecological niches which the population occupies.

LUXURIANCE

Mutational and balanced heterosis resemble each other in one important respect—both are normal adaptive states attained in outbred sexual species

as a result of an evolutionary history controlled by natural or by artificial selection. The normal heterotic state can be disrupted by sudden inbreeding, which is evidently a disturbance of the reproductive biology to which the species is adjusted. The heterotic state can also be restored by intercrossing the inbred lines. This is true heterosis, or euheterosis. Euheterosis is a form of evolutionary adaptation characteristic of sexually reproducing and cross-fertilizing species.

Numerous instances are known, however, when hybrids between species, neither of which can be regarded as inbred, are larger, faster growing, or otherwise exceeding the parental forms in some quality. Similar *luxuriance* is observed in some hybrids between normally self-fertilizing species, races, or strains. This kind of luxuriance of hybrids cannot be ascribed to sheltering of deleterious recessive mutants, because the latter are sheltered in the parental populations. It is also unlikely to arise from overdominance since, at least in wild species, natural selection would be expected to have induced such balanced heterosis in the parental species or strains.

Luxuriance is, from the evolutionary standpoint, an accidental condition brought about by complementary action of genes found in the parental form crossed. Two sets of facts are important in this connection. First, in cases of luxuriance there is usually no indication whatever that the luxuriant hybrids would prove adaptively superior in competition with the parental forms in the natural habitats of the latter. Second, luxuriance appears to be more frequently encountered in domesticated than in wild species.

It stands to reason that increase in body size, or in growth rate, is by no means always an adaptively superior change. To equate size with vigor, fitness, or adaptive value would be a height of anthropomorphic naïveté. The rate of growth and the size attained by an organism in its normal environments are evidently controlled by natural selection. Excessive as well as deficient sizes are adaptively about equally disadvantageous. The checks upon excessively rapid growth and excessive size are, however, very often relaxed under domestication. In man-controlled environments those qualities often become desirable from the standpoint of the breeder if not from that of the organism. Luxuriance is, really, pseudoheterosis.