THE GENETICAL THEORY OF NATURAL SELECTION

A Review

SEWALL WRIGHT

Department of Zoology, University of Chicago

DURING the latter part of the nineteenth century, increasing difficulty was felt in accepting Darwin's conception of the evolutionary process as one in which variation merely plays the subordinate (though necessary) rôle of providing a field of potentialities, through which the actual direction of advance is determined by natural selection. Theories were developed according to which the "origin of species" was to be sought more directly in the "origin of variation." Most of these were Lamarckian, others, of which de Vries' theory was most important, were not. The rediscovery of Mendelian heredity was a direct consequence of the mutation theory of the origin of species and was naturally seized upon as supporting this view. Only gradually has it become apparent that the real implications of Mendelian heredity are exactly the opposite and that in fact, it supplies the answer to some of the main difficulties felt with Darwin's theory. Dr. Fisher has played a leading part in developing the statistical consequences of Mendelian heredity and here brings together his views in a unified form.* It is a book which is certain to take rank as one of the major contributions to the theory of evolution.

The first chapter is concerned with a comparison of the consequences of blending and particulate heredity. A consequence of blending heredity, which Dr. Fisher shows was well understood by Darwin, and which was felt by him, and others, as a major difficulty with his theory, is the fact that under such heredity, the variability of a population tends to be greatly reduced in each successive generation. The portion of the variance lost per generation is one-half (if there is no assortative mating) and after ten generations only one-tenth of one per cent is left. Thus Darwin felt constrained to believe that an enormous amount of new variation appears in each generation, the differences among brothers being of this sort. This variability must be seized upon at once by natural selection or it will be lost. With even a slight departure from randomness in its occurrence, direction of mutation, rather than natural selection becomes the guiding principle of evolution.

All of this was changed with the demonstration of particulate inheritance and orderly segregation. The frequencies of zygotes of the types *aa*, *Aa* and *AA* tend to remain indefinitely in the proportions of a binomial square $p^2+2pq+q^2$ where p and q are the proportion in which alternative genes are represented in the population. In a population of limited size, to be sure, there is some variability of gene frequency, due to the accidents of sampling from generation to generation, but this brings about only a very low rate of reduction of variance. As to the actual rate of reduction of variance (and of heterozygosis), Fisher here confirms the figure which I had obtained by the method of path coefficients, viz. $\frac{1}{2n}$ per generation, where n is the effective size of the breeding population. The modern geneticist may get an appreciation of the difficulties which confronted

*The Genetical Theory of Natural Selection, by R. A. Fisher Sc. D., F. R. S., Price $6.00. Oxford University Press, New York. 1930.

Darwin, in attempting to account for natural variability and to apply selection as a guiding principle, by considering the case of a self-fertilized line, in which the loss of variance actually is 50% per generation, the same as with a random breeding population under blending heredity. The difference that with any initial variability, the inbred line tends to split up into many diverse lines, while the population under blending heredity becomes fixed as of one type , further emphasizes the difficulty. That pure lines actually show very little genetic variability, Fisher points out, is convincing evidence that substantially all inheritance is Mendelian. A quotation will bring out his conclusions with regard to mutation and selection:

> For mutations to dominate the trend of evolution it is thus necessary to postulate mutation rates immensely greater than those which are known to occur and of an order of magnitude which in general would be incompatible with particulate inheritance. * * * The whole group of theories which ascribe to hypothetical physiological mechanisms, controlling the occurrence of mutations, a power of directing the course of evolution, must be set aside once the blending theory of inheritance is abandoned. The sole surviving theory is that of natural selection and it would appear impossible to avoid the conclusion that if any evolutionary phenomenon appears to be inexplicable on this theory it must be accepted at present merely as one of the facts which in the present state of knowledge seems inexplicable.

I may state at this point that I am in accord with Dr. Fisher on the rôle of mutation, except that I would perhaps allow occasional significance to chromosome aberration, and to hybridization, as direct species forming agencies. It appears to me, however, that in this statement and throughout the book, he overlooks the rôle of inbreeding as a factor leading to nonadaptive differentiation of local strains, through selection of which, adaptive evolution of the species as a whole may be brought about more effectively than through mass selection of individuals.

Distribution of Gene Frequencies

The central problem in the analysis of the statistical consequences of Mendelian heredity is that of determining the distribution of gene frequencies under the pressures of mutation, selection, migration, etc., and not least important, as affected by size of population. Under given conditions, what proportion of the genes will be fixed? How many will have frequencies in the neighborhood of 50%? How many 99%? How rapidly will new mutations attain fixation under favorable selection? Two of the chapters (IV, V), are devoted to a mathematical investigation of such questions. As I have recently presented certain results in this field,* it may be of interest to bring out the points of agreement and disagreement.

My approach to the subject was from a different angle than Dr. Fisher's in being through the problem of inbreeding. I found that the decrease in heterozygosis, to be expected under inbreeding (but ignoring new mutations and selection) could be obtained by an application of the method of path coefficients.[4] The method could be applied to complex pedigrees encountered in livestock, and studies of the history of the Shorthorn breed of cattle have been made by means of it by Dr. McPhee and myself[5] of Clydesdale horses by Calder,[1] and of Jersey cattle by Buchanan Smith.[3] In the case of random mating in a population of N_m males and N_f females, it gave as a close approximation $\frac{1}{8N_m}+\frac{1}{8N_f}$ as the rate of loss of heterozygosis (and hence of variance) per generation. With an equal number of males and females in a total breeding population of n this reduces to the $\frac{1}{2n}$ referred to above. Fisher, studying the problem of evolution of large popula-

*These results were presented at the 1929 meeting of the A. A. A. S. An abstract appeared in the *Anatomical Record* (Vol. 44, p. 287, 1929). The full paper is to appear in *Genetics*.

tions, made the first attempt to find the actual distribution of gene frequencies under various conditions.[2] He reached a solution for the case of unselected genes not replenished by mutation, which indicated loss of variance at the rate of $\frac{1}{2n}$ per generation, just half of the rate indicated by my method. His formula for the distribution of gene frequencies was expressed on a scale of the logarithms of the ratio of alternative gene frequencies $\log \frac{q}{1-q}$, a scale which has the advantage of stretching the important regions close to 0% and 100% and also of making the effect of simple selection uniform at all points. It is interesting to note, however, that on transforming his formula to the simple scale of percentage frequencies it indicates an equal number of genes at all frequencies ($y = 1$). He also obtained a solution for the case in which decrease in heterozygosis is just balanced by mutation.

On noting the discrepancy between his result and mine for decrease in the rate of heterozygosis, I was not able to correct a questionable point in his derivation, but was able to reach a formula for the distribution of gene frequencies in a different way. The result agreed with his solution in form ($y = 1$), but with the rate of decline as $\frac{1}{2n}$ per generation. In the case of loss of variance, balanced by mutation, the distribution differed considerably in form, being $y = \frac{1}{2n[.577 + \log(2n)]q(1-q)}$ instead of his $\pi^{\frac{1}{2}}q^{\frac{1}{2}}(1-q)$. It appeared further from this method that a selective advantage such that genes A and a reproduce in the ratio $1 : 1-S$ introduced an exponential term e^{-4nsq} into the formula. This is valid, however, only for irreversible mutation and then only for extremely small values of the selection coefficient. It now appears that for reversible mutation and in any case for values considerably larger than $\frac{1}{2n}$ it should be e^{-2nsq}. Appreciable rates of recurrence of mutation (u) and reverse mutation (v) were stated* to throw the formula into the form $y = Cq^{4nu-1}(1-q)^{4nv-1}$ a curve which for high mutation rates (relative to $\frac{1}{2n}$) approaches the form of a probability curve and indicates a random drifting of gene frequency about an equilibrium point. The case which has seemed most important to me is that of the effects of migration in a population which is a sub-group of a large one. The formula is similar mathematically to that for mutation. It is given below in a revised form.

These results were communicated to Dr. Fisher, who now finds on reexamination of his method, that the addition of a term which had seemed unimportant gives a confirmation of my formulae in the first two cases. He obtains on the other hand, a somewhat different form for the effect of selection, viz., $y = \frac{2a}{\pi}\left(\frac{1-e^{-4nax}}{1-e^{-4na}}\right)$ where his a is my s, except for a change of sign. The exact case which he deals with, is not one which I had considered, a fact which reflects our differences in viewpoint on the general problem. His formula refers to flux equilibrium with respect to an inexhaustible supply of irreversible mutations. On solving for it by my method I get results substantially identical with his as long as the selection coefficient is less than $\frac{1}{4n}$. Above this there is rapid divergence. His formula is undoubtedly a better approximation, and in fact, I may say that on reexamination, I find that I, in turn, have here neglected terms which should be taken account of. The general formula for a partially isolated population by my method, as now revised, is as follows: $y = C_{4nmq_m}^{4nmq_m-1}q^{4nmq_m-1}(1-q)^{4nm(1-q_m)-1}e^{-2nsq}$ where m is the rate of population exchange with the species as a whole, q_m is the gene frequency in the latter and s measures the differential selection of the group as compared with the species as a whole. If v is actually zero (completely irreversible mutation from an inexhaustible supply of genes), and no im-

*Presented without proof in *American Nat.* 63:556-561 (1929).

migration is assumed, the formula takes a somewhat different form and in fact reduces to Dr. Fisher's result, identically. Summing up, our mathematical results on the distribution of gene frequencies are now in complete agreement as far as comparable, although based on very different methods of attack. He has not yet checked my conclusions as to the effects of recurrent and reversible mutation and of immigration by his method.

Differences in Interpretation

There are, however, important differences in interpretation. Dr. Fisher is interested in the figure $\frac{1}{2n}$, measuring decrease in variance, only because of its extreme smallness, from which he argues that the effects of random sampling are negligible in evolution (except as bearing on the chances of loss of a recently originated gene). I, on the contrary, have attributed to the inbreeding effect, measured by this coefficient, an essential rôle in the theory of evolution, arguing that the effective breeding population, represented by n of the formula may after all be relatively small compared with the actual size of the population. In this view I have been encouraged by the rather high coefficients of inbreeding found even in entire breeds of livestock. Calder, for example, finds a rate of increase of the inbreeding coefficient in Scotch Clydesdale horses of nearly 1% per generation which let it be emphasized again is a direct determination of the value of $\frac{1}{2n}$ for this large breed, assuming as seems to be justified, that there is no important subdivision into local strains.

The core of Dr. Fisher's theory of selection is given in Chapter II. He reaches a formula on which he lays great emphasis as "the fundamental theorem of natural selection." "The rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time." This is given as exact for idealized populations in which fortuitous fluctuations in genetic composition have been excluded *i. e.,* in indefinitely large populations. He calculates the standard error of the rate of advance in fitness, due to such fluctuations, and concludes that this is negligibly small; even over a single generation, in populations of the order of size of natural species. This means that the small random fluctuations in the frequencies of individual genes balance each other in their effect on a selected character to such an extent that irregularities in evolutionary advance are of the second order with respect to the rate of advance. He compares this principle to the regular increase of entropy in a physical system. The only effective offset to undeviating increase in fitness, which he recognizes, is change of environment, living or non-living, which he points out must usually be for the worse. The net effect of natural selection, and change of environment is registered in an increase or decrease in numbers and a somewhat winding course of evolution.

The splitting of species, he attributes to differences in the direction of selection in different parts of the range. The process may be facilitated by geographic (or other) isolation, but he holds that it may also be brought about wholly by selection, the primary selection tending to set up secondary processes (including especially preferential mating *i. e.,* sexual selection), which in the end may lead to complete fission of the species.

It will be seen that Dr. Fisher's conception of evolution is pure Darwinian selection. The extent to which he carries the principle is well illustrated in his theory of dominance (chapter III) in which he attempts to account for the prevalent dominance of type genes, over mutant genes by the natural selection of modifiers of dominance.* I

*This theory was first elaborated by Fisher in papers which appeared in *The American Naturalist* (62:115-126, 571-574, 1928). In a criticism of it (*American Naturalist* 63:274-

have pointed out elsewhere and he has agreed, that the selection pressure on the modifiers is here of the second order, compared with the rate of mutation of the primary gene. It seemed probable to me that such a minute selection pressure would ordinarily be of the second order compared with other selection pressures acting on the same gene, and therefore negligible. Dr. Fisher on the other hand, adheres to the effectiveness of selection in this case.

In order to bring out the point at which we part company with respect to the efficacy of selection, it will be necessary to return to Dr. Fisher's fundamental theorem: "The rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time." One's first impression is that the genetic variance in fitness must in general be large and that hence if the theorem is correct the rate of advance must be rapid. As Dr. Fisher insists, however, the statement must be considered in connection with the precise definition which he gives of the terms. He uses "genetic variance" in a special sense. It does not include all variability due to differences in genetic constitution of individuals. He assumes that each gene is assigned a constant value, measuring its contribution to the character of the individual (here fitness) in such a way that the sums of the contributions of all genes will equal as closely as possible the actual measures of the character in the individuals of the population. Obviously there could be exact agreement in all cases only if dominance and epistatic relationships were completely lacking. Actually, dominance is very common and with respect to such a character as fitness, it may safely be assumed that there are always important epistatic effects. Genes favorable in one combination, are, for example, extremely likely to be unfavorable in another. Thus allelomorphs which are held in equilibrium by a balance of opposing selection tendencies (possibilities of which are discussed in Chapter V) may contribute a great deal to the total genetically determined variance but not at all to the genetic variance in Fisher's special sense, since at equilibrium there is no difference in their contributions. The formula itself seems to need revision in the case of another important class of genes, ones slightly deleterious in effect but maintained at a certain equilibrium in frequency by recurrent mutation (or migration). These contribute to the genetic variance of the species, but not to the increase in fitness. Terms involving mutation (and migration) rates seem to be omitted in the formula as given.

Mutational Flux as a Factor

Consider now the case of a population so large that fortuitous variation of gene frequency is negligible. According to my view, such a population is one in which all mutations which can occur will recur at measurable rates. All genes which are not fixed will be held in equilibrium by opposing selections, or by selection opposed by mutation, the cases just discussed. Thus while there may be a great deal of genetically determined variance, there will be no movement of gene frequencies and hence no evolution as long as external conditions remain constant. This state of equilibrium may be upset by change of external conditions, bringing changes in the direction and intensity of selection. All gene frequencies may then be expected to shift in an orderly fashion until the equilibrium consistent with the new conditions is attained. On return to the old conditions, all gene frequencies should shift back to the old positions. It may be granted that an irregular sequence

297, 1929). I proposed an alternative directly physiological interpretation of the phenomenon. Further discussion may be found in Fisher's reply to this criticism (*American Naturalist* 63:553-556, a counter-reply *ibid* 556-561 and a paper by J. B. S. Haldane, *American Naturalist* 64:87-90 1930).

of environmental condition would result occasionally in irreversible changes (because of epistatic relationships) thus giving a real, if very slow, evolutionary process; but this is not Dr. Fisher's scheme under which evolution should proceed under constant external conditions. He would have the system of equilibria of gene frequencies kept in motion by a steady flux of novel mutations. These to be effective must be advantageous practically from the first, since non-recurrent, unfavorable mutations would be lost (in an indefinitely large population) before they could reach such a frequency as to have any appreciable effect on the situation. Even those advantageous at once would also usually be lost within a few generations of their appearance. They would, however, as Dr. Fisher shows, have a finite chance of reaching high frequencies and ultimately fixation. In their progress, they may be expected to unsettle the equilibria of other genes by creating new favorable (or unfavorable) combinations. Thus the entire system of gene frequencies is thrown into motion and may yield the steady adaptive advance of the theory.

As noted above, this scheme appears to depend on an inexhaustible flow of new favorable mutations. Dr. Fisher does not go into this matter of inexhaustibility but presumably it may be obtained by supposing that each locus is capable of an indefinitely extended series of multiple allelomorphs, each new gene becoming a potential source of genes which could not have appeared previously. The greatest difficulty, seems to be in the posited favorable character of the mutations. Dr. Fisher, elsewhere, presents cogent reasons as to why the great majority of all mutations should be deleterious. He shows that all mutations affecting a metrical character "unless they possess countervailing advantages in other respects will be initially disadvantageous." He shows that in any case the greater the effect, the less the chance of being adaptive. Add to this the point that mutations as a rule probably have multiple effects, and that the sign of the net selection pressure is determined by the greater effects, and it will be seen that the chances of occurrence of new mutations, advantageous from the first are small indeed.

Partial Isolation as a Factor

I would not deny the possibility of very slow evolutionary advance through this mechanism but it has seemed to me that there is another mechanism which would be much more effective in preventing the system of gene frequencies from settling into a state of equilibrium, than the occurrence of new immediately favorable mutations. If the population is not too large, the effects of random sampling of gametes in each generation brings about a random drifting of the gene frequencies about their mean positions of equilibrium. In such a population we can not speak of single equilibrium values but of probability arrays for each gene, even under constant external conditions. If the population is too small, this random drifting about leads inevitably to fixation of one or the other allelomorph, loss of variance, and degeneration. At a certain intermediate size of population, however (relative to prevailing mutation and selection rates), there will be a continuous kaleidescopic shifting of the prevailing gene combinations, not adaptive itself, but providing an opportunity for the occasional appearance of new adaptive combinations of types which would never be reached by a direct selection process. There would follow thorough-going changes in the system of selection coefficients, changes in the probability arrays themselves of the various genes and in the long run an essentially irreversible adaptive advance of the species. It has seemed to me that the conditions for evolution would be more favorable here than in the indefinitely large population of Dr. Fisher's scheme. It would, however, be very slow, even in terms of geologic time, since it can be shown to be

limited by mutation rate. A much more favorable condition would be that of a large population, broken up into imperfectly isolated local strains. The probability array for genes within such a local strain has been given on a previous page. The rate of evolutionary change depends primarily on the balance between the effective size of population in the local strain (n) and the amount of interchange of individuals with the species as a whole (m) and is therefore not limited by mutation rates. The consequence would seem to be a rapid differentiation of local strains, in itself non-adaptive, but permitting selective increase or decrease of the numbers in different strains and thus leading to relatively rapid adaptive advance of the species as a whole. Thus I would hold that a condition of subdivision of the species is important in evolution not merely as an occasional precursor of fission, but also as an essential factor in its evolution as a single group. Between the primary gene mutations, gradually carrying each locus through an endless succession of allelomorphs, and the control of the major trends of evolution by natural selection, I would interpolate a process of largely random differentiation of local strains. As to the existence of such strain differences, the situations described in the herring by Heinke, in Zoarces and Lebistes by J. Schmidt, and in deer mice by Sumner, as well as the situation in man, may be called to mind.

Sexual Selection and Mimicry

To the general biological reader, the later chapters of the book dealing with concrete applications of the selection principle may prove most attractive. A well sustained attempt to rehabilitate Darwin's theory of sexual selection has already been noted. Another chapter deals with mimicry. The validity of both Batesian and Müllerian mimicry is accepted and the possibility of accounting for the origin of each sort by natural selection is developed after careful analysis of opposing arguments which have been widely accepted, especially in the case of Müllerian mimicry. The author naturally applies his theory of direct progress through mass selection. It appears to me, however, that these cases fall at least equally well under the viewpoint which I have developed, which does not require such a minutely continuous path of selective advantage between the original pattern of the species and that ultimately reached.

Evolution In Man

More than one-third of the book is devoted to discussion of the trend of evolution in man. This portion deserves the most careful consideration by all interested in problems of Eugenics. The course of the argument may be summarized briefly as follows: One might expect to find that civilization once started on the earth would give such an advantage that its history would be an uninterrupted succession of triumphs. Instead of this, we find that every civilization, after a period of prosperity, has fallen into decay, and succumbed to the onslaughts of numerically weak, barbarous peoples. The cause of this decay, he finds reason to believe, is genetical rather than social. Evidence indicates that differences in fertility are in part hereditary, whether dependent on physical or mental qualities. The bulk of the evidence from civilized communities, ancient and modern, indicates that fertility is lowest in the upper classes of the population, where qualities which make for individual ability and leadership are most frequent. The reason for this inversion of the normal relation is seen in the tendency (first pointed out by Galton) for infertility as well as ability to rise in the social scale. The result is a tendency to extinction of ability, applying to all classes in society. Examination of conditions in more primitive societies organized on the clan basis, lead to the conclusion that the play of natural selection is here exactly the op-

posite. The evolution of individual qualities he believes reaches its climax just before civilization begins.

The final chapter deals with the conditions necessary for a permanent civilization. The author holds that only a wage system definitely designed to remove the present severe social penalty on fertility and indeed tending to promote fertility would adequately oppose the present tendency toward racial deterioration.

Literature Cited

1. CALDER, A., 1927. *Proc. Roy. Soc. Edinburgh.* 47:118-140.

2. FISHER, R. A., 1922. *Proc Roy. Soc. Edinburgh.* 42:321-341.

3. SMITH, A. D. B., 1926. *Eugenics Review.* 14:189-204. 1928. *Report of Brit. Ass. Adv. Science,* 649-655.

4. WRIGHT, S., 1921. *Genetics.* 6:111-178.

5. WRIGHT, S., 1922. *Amer. Nat.* 61:330-338. 1923, *Jour. Her.* 14:339-348, 405-422. MCPHEE, H. C., and S. WRIGHT. 1925-26. *Jour. Hered.* 16:205-215, 17:397-401.

Books Received

BOOKS are acknowledged in this column as received, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. As far as space permits, books that contain material of special interest to the readers of the JOURNAL *will be reviewed in later numbers.*

THE DRIFT OF CIVILIZATION, A Symposium. *By* the Contributors (26) to the Fiftieth Anniversary Number of the St. Louis Post-Dispatch, including ALBERT EINSTEIN, J. B. S. HALDANE, MAXIM GORKY, SIR PHILIP GIBBS, WM. HOWARD TAFT, RICHARD E. BYRD, etc. Pp. 268. 26 Chapters. Price, $3.00. Simon and Schuster, New York. 1929.

The title of this book is symptomatic. How long are we going to be content to trust the progress of civilization to so casual a process as drifting?

SCIENCE IN SOVIET RUSSIA, *by* J. G. CROWTHER. Pp. 128. 27 Chapters. Price, 7s.6d. Williams & Norgate, Ltd., London. 1930.

THE RETREAT FROM PARENTHOOD, *by* JEAN AYLING. Pp. 293. 33 Chapters. Price, 10s.6d. Kegan Paul, Trench, Trubner & Co., Ltd., London. 1930.

The latest birth statistics indicate the retreat has become a rout. If it continues so, can the drift of civilization continue in any direction but the vertical, and *not up*?

THE ENLARGEMENT OF PERSONALITY, Behavior Patterns and their Formation. *By* J. H. DENISON. Pp. 340. 15 Chapters. Price, $3.00. Charles Scribner's Sons, New York. 1930.

One wonders—has too much enlargement of too many personalities contributed to the drift, and to the rout?

PROBLEMS OF MENTAL DEFICIENCY. Four Pamphlets: (1) Inheritance of Mental Defect, *by* ULRICH A. HAUBER, Ph.D. (2) Social Care of the Mentally Deficient, *by* CHARLES BERNSTEIN, M. D. (3) Moral Aspects of Sterilization, *by* JOHN A. RYAN, D. D. (4) Eugenic Sterilization in the Laws of the States, *by* WM. F. MONTAVON. Price, 10c each, or 25c for the series. National Catholic Welfare Conference, Washington, D. C. 1930.

One group that leaves its problems largely to others, and to whom the drift and the retreat mean little—"See the happy moron. He doesn't give a damn! I wish I were a moron. My God, perhaps I am!"

THE STHENICS, The Chord Invisible, *by* SIR JAMES K. FOWLER. Pp. 81. 11 Chapters. Price, $1.40. The Macmillan Co., New York. 1930.

CHRISTIANITY AND SEX, *by* CHRISTOPHER DAWSON. Pp. 40. Price, one shilling. Faber & Faber, London. 1930.

COMMITTEE FOR LEGALISING EUGENIC STERILIZATION. The Eugenics Society, England. Pp. 32. Price, 6d. The Eugenics Society, London. 1930.

A plea to make the retreat final, if not compulsory in case other means are hopeless.

(*Continued on page* 366)