

but by differentiating the equation by which v_x is defined, it appears that

$$\frac{1}{v_x} \frac{dv_x}{dx} + \frac{1}{l_x} \frac{dl_x}{dx} - m = \frac{-l_x b_x e^{-mx}}{\frac{v_x}{v_0} l_x e^{-mx}} = -\frac{b_x v_0}{v_x},$$

or that

$$dv_x - \mu_x v_x dx + b_x v_0 dx = m v_x dx.$$

Consequently the rate of increase in the total value of the population is m times its actual total value, irrespective of its constitution in respect of age. A comparison of the total values of the population at two census epochs thus shows, after allowance for migration, the genuine biological increase or decrease of the population, which may be entirely obscured or reversed by the crude comparison of the number of heads. The population of Great Britain, for example, must have commenced to decrease biologically at some date obscured by the war, between 1911 and 1921, but the census of 1921 showed a nominal increase of some millions, and that of 1931 will, doubtless in less degree, certainly indicate a further spurious period of increase, due to the accumulation of persons at ages at which their reproductive value is negligible.

The genetic element in variance

Let us now consider the manner in which any quantitative individual measurement, such as human stature, may depend upon the individual genetic constitution. We may imagine, in respect of any pair of alternative genes, the population divided into two portions, each comprising one homozygous type together with half of the heterozygotes, which must be divided equally between the two portions. The difference in average stature between these two groups may then be termed the average excess¹ (in stature) associated with the gene substitution in question. This difference need not be wholly due to the single gene, by which the groups are distinguished, but possibly also to other genes statistically associated with it, and having similar or opposite effects. This definition will appear the more appropriate if, as is necessary for precision, the population used to determine its value comprises, not merely the whole of a species in any one generation attaining maturity, but is conceived to contain all the genetic combinations possible, with frequencies appropriate to their actual

probabilities of occurrence and survival, whatever these may be, and if the average is based upon the statures attained by all these genotypes in all possible environmental circumstances, with frequencies appropriate to the actual probabilities of encountering these circumstances. The statistical concept of the excess in stature of a given gene substitution will then be an exact one, not dependent upon chance as must be any practical estimate of it, but only upon the genetic nature and environmental circumstances of the species. The excess in a factor will usually be influenced by the actual frequency ratio $p : q$ of the alternative genes, and may also be influenced, by way of departures from random mating, by the varying reactions of the factor in question with other factors; it is for this reason that its value for the purpose of our argument is defined in the precise statistical manner chosen, rather than in terms of the average sizes of pure genotypes, as would be appropriate in specifying such a value in an experimental population, in which mating is under control, and in which the numbers of the different genotypes examined is at the choice of the experimenter.

For the same reasons it is also necessary to give a statistical definition of a second quantity, which may be easily confused with that just defined, and may often have a nearly equal value, yet which must be distinguished from it in an accurate argument; namely the average effect produced in the population as genetically constituted, by the substitution of the one type of gene for the other. By whatever rules mating, and consequently the frequency of different gene combinations, may be governed, the substitution of a small proportion of the genes of one kind by the genes of another will produce a definite proportional effect upon the average stature. The amount of the difference produced, on the average, in the total stature of the population, for each such gene substitution, may be termed the average effect of such substitution, in contra-distinction to the average excess as defined above. In human stature, for example, the correlation found between married persons is sufficient to ensure that each gene tending to increase the stature must be associated with other genes having a like effect, to an extent sufficient to make the average excess associated with each gene substitution exceed its average effect by about a quarter.

If a is the magnitude of the average excess of any factor, and α the magnitude of the average effect on the chosen measurement, we shall

¹In 1958 the terms *average excess* and *average effect* were shown in italics throughout this section following a suggestion by C. G. Darwin that they needed greater emphasis.

now show that the contribution of that factor to the genetic variance is represented by the expression $pqa\alpha$.¹

The variable measurement will be represented by x , and the relation of the quantities α to it may be made more clear by supposing that for any specific gene constitution we build up an 'expected' value, X , by adding together appropriate increments, positive or negative, according to the natures of the genes present. This expected value will not necessarily represent the real stature, though it may be a good approximation to it, but its statistical properties will be more intimately involved in the inheritance of real stature than the properties of that variate itself. Since we are only concerned with variation we may take as a primary ingredient of the value of X , the mean value of x in the population, and adjust our positive and negative increments for each factor so that these balance each other when the whole population is considered. Since the increment for any one gene will appear p times to that for its alternative gene q times in the whole population, the two increments must be of opposite sign and in the ratio $q : (-p)$. Moreover, since their difference must be α , the actual values cannot but be qa and $(-pa)$ respectively.

The value of the average excess a of any gene substitution was obtained by comparing the average values of the measurement x in two moieties into which the population can be divided. It is evident that the values of a will only be properly determined if the same average difference is maintained in these moieties between the values of X , or in other words if in each such moiety the sum of the deviations, $x - X$, is zero. This supplies a criterion mathematically sufficient to determine the values of a , which represent in the population concerned the average effects of the gene substitutions. It follows that the sum for the whole population of the product $X(x - X)$ derived from each individual must be zero, for each entry qa or $(-pa)$ in the first term will in the total be multiplied by a zero, and this will be true of the items contributed by every factor severally. It follows from this that if X and x are now each measured from the mean of the population, the variance of X , which is the mean value of X^2 , is equal to the mean value of Xx . Now the mean value of Xx will involve a for each Mendelian factor; for X will contain the item qa in the p individuals of one moiety and $(-pa)$ in the q individuals of the other, and since the average values of x in these two moieties differ by² a , the mean value of Xx must be the sum for all factors of the

¹ Replace $pqa\alpha$ with $2pqa\alpha$ (1958)

² After a insert and each individual contains two genes at each locus, (1958)

quantities $pqa\alpha$.¹ Thus the variance of X is shown to be $W = \Sigma (pqa\alpha)$ ¹ the summation being taken over all factors, and this quantity we may distinguish as the *genetic* variance in the chosen measurement x . That it is essentially positive, unless the effect of every gene severally is zero, is shown by its equality with the variance of X . An extension of this analysis, involving no difference of principle, leads to a similar expression for cases in which one or more factors have more than two different genes or allelomorphs present.

The appropriateness of the term genetic variance lies in the fact that the quantity X is determined solely by the genes present in the individual, and is built up of the average effects of these genes. It therefore represents the genetic potentiality of the individual concerned, in the aggregate of the mating possibilities actually open to him, in the sense that the progeny averages (of x , as well as of X) of two males mated with an identical series of representative females will differ by exactly half as much as the genetic potentialities of their sires differ. Relative genetic values may therefore be determined experimentally by the diallel method, in which each animal tested is mated to the same series of animals of the opposite sex, provided that a large number of offspring can be obtained from each such mating.² Without obtaining individual values, the genetic variance of the population may be derived from the correlations between relatives, provided these correlations are accurately obtained. For this purpose the square of the parental correlation divided by the grandparental correlation supplies a good estimate of the fraction, of the total observable variance of the measurement, which may be regarded as genetic variance.

It is clear that the actual measurements, x , obtained in individuals may differ from their genetic expectations by reason of fluctuations due to purely environmental circumstances. It should be noted that this is not the only cause of difference, for even if environmental fluctuations were entirely absent, and the actual measurements therefore determined exactly by the genetic composition, these measurements, which may be distinguished as *genotypic*, might still differ from the genetic values, X . A good example of this is afforded by dominance, for if dominance is complete the genotypic value of the heterozygote will be exactly the same as that of the corresponding dominant homozygote, and yet these genotypes differ by a gene substitution which may materially affect the genetic potentiality

¹ Replace $pqa\alpha$ with $2pqa\alpha$ (1958)

² After mating insert and that the mates are representative of the actual population (1958)

represented by X , and be reflected in the average measurement of the offspring. A similar cause of discrepancy occurs when gene substitutions in different factors are not exactly additive in their average effects. The genetic variance as here defined is only a portion of the variance determined genotypically, and this will differ from, and usually be somewhat less than, the total variance to be observed.

It is consequently not a superfluous refinement to define the purely genetic element in the variance as it exists objectively, as a statistical character of the population, different from the variance derived from the direct measurement of individuals.¹

Natural Selection²

The definitions given above may be applied to any characteristic whatever; it is of special interest to apply them to the special characteristic m which measures the relative rate of increase or decrease. The two groups of individuals bearing alternative genes, and consequently the genes themselves, will necessarily either have equal or unequal rates of increase, and the difference between the appropriate values of m will be represented by a , similarly the average effect upon m of the gene substitution will be represented by a . Since m measures fitness to survive by the objective fact of representation in future generations, the quantity pqa will represent the contribution of each factor to the genetic variance in fitness; the total genetic variance in fitness being the sum of these contributions, which is necessarily positive, or, in the limiting case, zero. Moreover, any increase dp in the proportion of one type of gene at the expense of the other will be accompanied by an increase adp in the average fitness of the species, where a may of course be negative; but the definition of a requires that the ratio $p : q$ must be increasing in geometrical progression at a rate measured by a , or in mathematical notation that

$$\frac{d}{dt} \log \left(\frac{p}{q} \right) = a$$

which may be written

$$\left(\frac{1}{p} + \frac{1}{q} \right) dp = a dt,$$

or $dp = pqa dt$

whence it follows that,

$$adp = pqa dt$$

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and, taking all factors into consideration, the total increase in fitness,

$$\Sigma(adp) = \Sigma(pqaa)dt = Wdt.¹$$

If therefore the time element dt is positive, the total change of fitness Wdt is also positive, and indeed the rate of increase in fitness due to all changes in gene ratio is exactly equal to the genetic variance of fitness W which the population exhibits. We may consequently state the fundamental theorem of Natural Selection in the form:

The rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time.

The rigour of the demonstration requires that the terms employed should be used strictly as defined; the ease of its interpretation may be increased by appropriate conventions of measurement. For example, the ratio² $p : q$ should strictly be evaluated at any instant by the enumeration, not necessarily of the census population, but of all individuals having reproductive value, weighted according to the reproductive value of each.

Since the theorem is exact only for idealized populations, in which fortuitous fluctuations in genetic composition have been excluded, it is important to obtain an estimate of the magnitude of the effect of these fluctuations, or in other words to obtain a standard error appropriate to the calculated, or expected, rate of increase in fitness. It will be sufficient for this purpose to consider the special case of a population mating and reproducing at random. It is easy to see that if such chance fluctuations cause a difference δp between the actual value of p obtained in any generation and that expected, the variance of δp will be

$$\frac{pq}{2n},$$

where n represents the number breeding in each generation, and $2n$ therefore is the number of genes in the n individuals which live to replace them. The variance of the increase in fitness, $\alpha \delta p$,³ due to this cause, will therefore be

$$\frac{1}{2n} (pq\alpha^2),$$

and since,⁴ with random mating, the chance fluctuation in the different gene ratios will be independent, and the values of a and α are no longer distinct,⁵ it follows that, on this condition, the rate of increase

¹ See page 274 (1953, F) ² See note 1, page 35

³ See page 277 (1953) ⁴ Replace ratio $p : q$ with frequencies p (1953) ⁵ See page 302
⁴ Replace, and since with . Now (1953) ⁵ After distinct insert semi colon (1953)

of fitness, when measured over one generation, will have a standard error due to random survival equal to

$$\frac{1}{T} \sqrt{\frac{W}{2n}}$$

where T is the time of a generation. It will usually be convenient for each organism to measure time in generations, and if this is done it will be apparent from the large factor $2n$ in the denominator, that the random fluctuations in W , even measured over only a single generation, may be expected to be very small compared to the average rate of progress. The regularity of the latter is in fact guaranteed by the same circumstance which makes a statistical assemblage of particles, such as a bubble of gas obey, without appreciable deviation, the laws of gases. A visible bubble will indeed contain several billions of molecules, and this would be a comparatively large number for an organic population, but the principle ensuring regularity is the same. Interpreted exactly, the formula shows that it is only when the rate of progress, W , when time is measured in generations, is itself so small as to be comparable to $1/n$, that the rate of progress achieved in successive generations is made to be irregular. Even if an equipoise of this order of exactitude, between the rates of death and reproduction of different genotypes, were established, it would be only the rate of progress for spans of a single generation that would be shown to be irregular, and the deviations from regularity over a span of 10,000 generations would be just a hundredfold less.

It will be noticed that the fundamental theorem proved above bears some remarkable resemblances to the second law of thermodynamics. Both are properties of populations, or aggregates, true irrespective of the nature of the units which compose them; both are statistical laws; each requires the constant increase of a measurable quantity, in the one case the entropy of a physical system and in the other the fitness, measured by m , of a biological population. As in the physical world we can conceive of theoretical systems in which dissipative forces are wholly absent, and in which the entropy consequently remains constant, so we can conceive, though we need not expect to find, biological populations in which the genetic variance is absolutely zero, and in which fitness does not increase. Professor Eddington has recently remarked that 'The law that entropy always increases—the second law of thermodynamics—holds, I think, the

supreme position among the laws of nature'. It is not a little instructive that so similar a law should hold the supreme position among the biological sciences. While it is possible that both may ultimately be absorbed by some more general principle, for the present we should note that the laws as they stand present profound differences—(1) The systems considered in thermodynamics are permanent; species on the contrary are liable to extinction, although biological improvement must be expected to occur up to the end of their existence. (2) Fitness, although measured by a uniform method, is qualitatively different for every different organism, whereas entropy, like temperature, is taken to have the same meaning for all physical systems. (3) Fitness may be increased or decreased by changes in the environment, without reacting quantitatively upon that environment. (4) Entropy changes are exceptional in the physical world in being irreversible, while irreversible evolutionary changes form no exception among biological phenomena. Finally, (5) entropy changes lead to a progressive disorganization of the physical world, at least from the human standpoint of the utilization of energy, while evolutionary changes are generally recognized as producing progressively higher organization in the organic world.

The statement of the principle of Natural Selection in the form of a theorem determining the rate of progress of a species in fitness to survive (this term being used for a well-defined statistical attribute of the population), together with the relation between this rate of progress and its standard error, puts us in a position to judge of the validity of the objection which has been made, that the principle of Natural Selection depends on a succession of favourable chances. The objection is more in the nature of an innuendo than of a criticism, for it depends for its force upon the ambiguity of the word chance, in its popular uses. The income derived from a Casino by its proprietor may, in one sense, be said to depend upon a succession of favourable chances, although the phrase contains a suggestion of improbability more appropriate to the hopes of the patrons of his establishment. It is easy without any very profound logical analysis to perceive the difference between a succession of favourable deviations from the laws of chance, and on the other hand, the continuous and cumulative action of these laws. It is on the latter that the principle of Natural Selection relies.¹

¹ See note 3, page 35

¹ See page 278 (1953)