

PROFESSOR WRIGHT ON THE THEORY OF  
DOMINANCE

IN 1928, as the result of some calculations of the selective intensity, acting on modifying factors, capable of modifying the degree of dominance exhibited by deleterious mutations, I put forward the supposition that the great excess of recessives among observed mutants was the result of many of them having been progressively modified to the recessive condition during a very long period of previous occurrence of the same mutations.

At that date I was unaware of the very large amount of evidence now available to geneticists, as to the modifiability of the degree of dominance, and of the very beautiful examples afforded by polymorphic species, where the variant forms have become dominant to the type, under selection in the opposite direction. The existence of this evidence much diminishes the interest of such rough attempts to estimate the relative intensity as are possible by general reasoning. My only strong reason, however, at that time for proposing that dominance phenomena were subject to evolutionary modification was that a selective intensity could be demonstrated, of a magnitude, which, in the periods available, was sufficiently powerful, unless some unknown cause opposed it, to bring about appreciable modification in the reaction of species to the deleterious mutations which have for long been occurring in them. For an account of the more general evidence on the subject, which was rapidly brought to my notice through the kindness of a number of geneticists, I may refer the reader to a more recent paper, "The Evolution of Dominance."<sup>1</sup>

Following the original paper, however, in May, 1929, Professor Sewall Wright, who had perhaps overlooked or misunderstood the calculations in my paper, put forward some calculations of his own, expressed in a different notation, which, for the general case, gave a result identical with mine. For the special case of a single and completely dominant modifier, which he chose for more detailed consideration, he obtained results apparently unfavorable to my theory, in that the selective intensity calculated was not only small, of the order of the mutation rate of the mutating gene, but decreased progressively to zero with the ad-

<sup>1</sup> *Biol. Reviews*, vi: 345-368.

vance of the process. This result, however, as I pointed out in a short note published the following November, was due to an error in the algebra, the real selective intensity in the case chosen by Wright increasing without limit as the dominant modifier becomes more and more numerous.

In a paper published in January, 1934, Wright accepts my correction to his calculation. He does not refer to its history, or to the fact that, in 1928, I had already shown two facts respecting the selective intensities arrived at. (i) That these depended greatly on the viability of the heterozygote to be modified, and (ii) in cases where this viability is near to the normal, that modification would take place at about one five-thousandth of the rate that at which a population composed wholly of heterozygotes could be modified. For periods of the order of 500,000 generations, therefore, substantial selective modifications of the heterozygote is a necessary consequence of the calculations, upon the accuracy of which we now seem to be agreed.

The importance of the viability of the heterozygotes arises from its influence on their frequency. In putting forward the theory, I postulated only such frequency as could certainly be maintained by mutation against counter-selection. More recent researches into the frequency with which mutant heterozygotes can be found in collections from wild populations suggest that they are in fact much more abundant than the theory suggests. If this is so, the selective process will be proportionately more rapid. The point is to be noted as Wright has asserted that he is discussing a case especially favorable to my views, while in fact restricting himself to the minimal postulates in its favor.

In his recent restatement of his opinion Wright shows that the modifier will not increase in frequency if its increase is opposed by a mutation rate just double that of the primary mutation. This is obvious from the corrected formulae given in my note of 1929, and establishes the unimportant fact that dominance modification will not be affected by modifiers, the increase of which is opposed by a mutation-rate of this magnitude. This does not prevent its being effected by modifiers whose mutations are either favorable, or, if unfavorable, of a lower frequency. It has long been recognized that the mutation-rates of those mutations which make themselves available for study, by occurring in culture, must be among the largest which occur in the species. It is among mutations of this kind that nearly complete

recessiveness is known to be the rule. How far up the scale of rarity this rule holds we do not know, but it is clear that the supposition of adverse mutations only serves to exclude a group of modifiers the mutations of which are not only adverse, but exceptionally frequent. The effect, such as it is, is, of course, counterbalanced if modifiers with equally high mutation rates, but in a favorable direction, are assumed to be equally numerous.

Professor Wright, however, draws a wider but less legitimate inference. He quotes me as saying elsewhere that, "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 seems to infer that by this I imply that magnitudes of the order of mutation rates, say 1 in a million per generation, are to be ignored in every context. Nothing could be further from the truth. In the quotation, I was discussing theories of evolution, such as Lamarckism and Orthogenesis, which purport to give an explanation of evolutionary change, by means of hypothetical causes supposed to produce germinal modifications. These theories are open to the objection that mutation rates of the order of 1 in a million can bring about nothing *if opposed even by very minute counter-selection*. If evolution is to proceed in any direction, to which the selective action of differential death and birth rates is in the slightest degree antagonistic, the supporters of these theories must postulate, I was asserting, much higher mutation rates than those with which geneticists are familiar. In the case of modifiers which improve the viability of a rare heterozygote, it is my theory that these will increase in frequency through the greater viability that they induce, not that they will increase in frequency by mutation in opposition to the selective tendency. In fact, apart from the exceptional case stressed by Wright, it is clear that here also mutation rates have little direct influence on the process.

Professor Wright mentions another argument which should be answered, as it evidently weighs with him, though the fallacy is a simple one. He says, "There should always be other evolutionary pressures of greater magnitude acting in one direction or the other," and appears to think that this implies that a selective intensity of lesser magnitude has therefore no effect.

Let us suppose that all modifiers of dominance are influenced one way or the other by selections other than that caused by their effect as modifiers. Professor Wright does not propose that

the unfavorable selections are more numerous or more intense than, those which are favorable. If the selective intensities due to the other causes which Wright postulates are represented in a frequency diagram, the mean will therefore be at zero. Let us take  $x$  as a typical value of the variate in this distribution, measuring  $x$  as positive when the selective tendency is favorable to dominance modification, and negative when it is unfavorable. The average value of  $x$  is then zero. Suppose that the small selective effect produced by the modification of the heterozygote is represented by a small, but positive, quantity,  $a$ , then in each case the net selective intensity in favor of dominance modification, whether positive or negative, will be  $a + x$ ; and the aggregate effect of all the modifiers will be found by adding together this quantity for each of them. To this sum it is clear that the component  $x$  contributes nothing, since the positive and negative values of  $x$  balance each other. We are left, therefore, with the sum of the positive values  $a$ , each of which is favorable to dominance modification; exactly the same result as if we had ignored the "other evolutionary pressures of greater magnitude" from the start. The fallacy of Professor Wright's reasoning seems to be simply that by concentrating his attention only on the question of whether a gene is finally exterminated or not, he ignores the much more important question of the rate at which it approaches extermination. This rate is affected for all genes capable of modifying the heterozygote, while the balance in favor of fixation or extermination is only turned in the case of that minority for which the value of  $x$  lies between 0 and  $-a$ .

The fallacy may be stated in another form, by stressing the improbability, when  $a$  is small, of a number chosen at random from the population of selective intensities falling between the limits 0 and  $-a$ . But this improbability does not adhere to the conclusion that a selective intensity, however minute, affecting all modifiers consistently in the same direction, will exert an effect proportionate to its magnitude, whether these modifiers are affected by other selective agencies or not, provided that these agencies are not in a conspiracy to oppose dominance modification.

In fact, it would do so even if it happened that there were a gap in the frequency distribution, so that none occurred in the region between 0 and  $-a$ .

Professor Wright's recent allusion to the subject was but a preface to his own interesting speculations on the physiological causation of dominance. It had, perhaps, achieved its purpose when he could write, "If this hypothesis is untenable what alternative is there?" If, however, Professor Wright's views can only be made plausible, by the exclusion of all alternatives, he must find other objections to the selection theory more weighty than those he has revived.

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