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A DEFENSE OF BEANBAG GENETICS

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My friend Professor Ernst Mayr, of Harvard University, in his recent book *Animal Species and Evolution* [1], which I find admirable, though I disagree with quite a lot of it, has the following sentences on page 263.

> The Mendelian was apt to compare the genetic contents of a population to a bag full of colored beans. Mutation was the exchange of one kind of bean for another. This conceptualization has been referred to as "beanbag genetics." Work in population and developmental genetics has shown, however, that the thinking of beanbag genetics is in many ways quite misleading. To consider genes as independent units is meaningless from the physiological as well as the evolutionary viewpoint.

Any kind of thinking whatever is misleading out of its context. Thus ethical thinking involves the concept of duty, or some equivalent, such as righteousness or *dharma*. Without such a concept one is lost in the present world, and, according to the religions, in the next also. Joule, in his classical papers on the mechanical equivalent of heat, wrote of the duty of a steam engine. We now write of its horsepower. It is of course possible that ethical conceptions will in future be applied to electronic calculators, which may be given built-in consciences!

In another place [2] Mayr made a more specific challenge. He stated that Fisher, Wright, and I "have worked out an impressive mathematical theory of genetical variation and evolutionary change. But what, precisely, has been the contribution of this mathematical school to evolutionary theory, if I may be permitted to ask such a provocative question?" "However," he continued in the next paragraph, "I should perhaps leave it to Fisher, Wright, and Haldane to point out what they consider their major contributions." While Mayr may certainly ask this question, I may not answer it at Cold Spring Harbor, as I have been officially informed that

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I am ineligible for a visa for entering the United States.[1] Fisher is dead, but when alive preferred attack to defense. Wright is one of the gentlest men I have ever met, and if he defends himself, will not counterattack. This leaves me to hold the fort, and that by writing rather than speech.

Now, in the first place I deny that the mathematical theory of population genetics is at all impressive, at least to a mathematician. On the contrary, Wright, Fisher, and I all made simplifying assumptions which allowed us to pose problems soluble by the elementary mathematics at our disposal, and even then did not always fully solve the simple problems we set ourselves. Our mathematics may impress zoologists but do not greatly impress mathematicians. Let me give a simple example. We want to know how the frequency of a gene in a population changes under natural selection. I made the following simplifying assumptions [3]:

1) The population is infinite, so the frequency in each generation is exactly that calculated, not just somewhere near it.

2) Generations are separate. This is true for a minority only of animal and plant species. Thus even in so-called annual plants a few seeds can survive for several years.

3) Mating is at random. In fact, it was not hard to allow for inbreeding once Wright had given a quantitative measure of it.

4) The gene is completely recessive as regards fitness. Again it is not hard to allow for incomplete dominance. Only two alleles at one locus are considered.

5) Mendelian segregation is perfect. There is no mutation, non-disjunction, gametic selection, or similar complications.

6) Selection acts so that the fraction of recessives breeding per dominant is constant from one generation to another. This fraction is the same in the two sexes.

With all these assumptions, we get a fairly simple equation. If q_n is the frequency of the recessive gene, and a fraction k of recessives is killed off when the corresponding dominants survive, then

$$q_{n+1} = \frac{q_n - k q_n^2}{1 - k q_n^2}.$$

[1] In spite of this ineligibility I have, since writing this article, been granted an American visa, for which I must thank the federal government. However, I am not permitted to lecture in North Carolina, and perhaps in other states, without answering a question which I refuse to answer. Legislation to this effect does not, in my opinion, help American science.

Norton gave an equation equivalent to this in 1910, and in 1924 I gave a rough solution when selection is slow, that is to say k small. But one might hope that such a simple-looking equation would yield a simple relation between q_n and n; if not as simple as $s = \frac{1}{2} gt^2$ for fall in a uniform gravitational field, then as simple as Kepler's laws of planetary motion. Haldane and Jayakar [4] have solved this equation in terms of what are called automorphic functions of a kind which were fashionable in Paris around 1920, but have never been studied in detail, like sines, logarithms, Gamma and Polygamma functions, and so on. Until the requisite functions have been tabulated, geneticists will be faced with as much work as if a surveyor, after measuring an angle, had to calculate its cosine or whatever trigonometrical function he needed. The mathematics are not much worse when we allow for inbreeding and incomplete dominance. But they are very much stiffer when selection is of variable intensity from year to year and from place to place (as it always is) or when its intensity changes gradually with time. If we had solved such problems, our work would be impressive.

Let me add that the few professional mathematicians who have interested themselves in such matters have been singularly unhelpful. They are apt to devote themselves to what are called existence theorems, showing that problems have solutions. If they hadn't, we shouldn't be here, for evolution would not have occurred.

Now let me try to show that what little we have done is of some use, even if we have done a good deal less serious mathematics than Mayr believes. It may be well to cite the first formulation of beanbag genetics. This was by the great Roman poet Titus Lucretius Carus just over two thousand years ago (*De rerum natura*, IV, l. 1220):

> Propterea quia multa modis primordia multis
> Mixta suo celant in corpore saepe parentes
> Quae patribus patres tradunt ab stirpe profecta,
> Inde Venus varia producit sorte figuras
> Maiorumque refert vultus vocesque comasque.

A free rendering is: "Since parents often hide in their bodies many genes mixed in many ways, which fathers hand down to fathers from their ancestry; from them Venus produces patterns by varying chance, and brings back the faces, voices, and hair of ancestors." Very probably the great materialistic (but not atheistic) philosopher Epicurus had expressed the

theory more exactly, if less poetically, in one of his lost books. Lucretius elsewhere described genes as "genitalia corpora" and claimed that they were immutable. What is important is that whether he called them primordia or even seeds, he always thought of them as a set of separable material bodies. When Mendel discovered most of the laws according to which Venus picks out the hidden genes from the mixture, and Bateson and Punnett further discovered linkage, we could get going; and it was Punnett [5] who first calculated the long-term effect of a very simple program of selection.

Now let me begin boasting. So competent a biologist as Professor L. T. Hogben [6] has recently written, "The mutation of chromosomes or of single genes is admittedly the pace-maker of evolution." A strong verbal argument could be made out for this statement. In racing, a "pacemaker" runs particularly fast, but I suppose Hogben means that mutation determines the rate of evolution, which would be faster if mutation were more frequent. The verbal argument might run as follows: "Evolution is the resultant of a number of processes, including adaptation of individuals during their development, migration, segregation, natural selection, and mutation. Now in this list the slowest process is mutation. The probability that a gene will mutate in one generation rarely exceeds one hundred thousandth, and may be much less than a millionth. Whereas selective advantages of one in ten are quite common, a species may spread over a continent in a few centuries, and so on. Since mutation is the slowest process, it must set the pace, or be the 'rate-determining process,' for the remainder." This is quite as good an argument as those on which most human ethical and political decisions are based. When Muller had determined a few mutation rates, Wright and I, around 1930, began to calculate the evolutionary effects of mutation. We showed that in a species with several hundred thousand members mutations could not be a pacemaker. Almost all mutations occurred several times in a generation in one member or another of a species. But this again is a verbal argument. Only algebraical argument can be decisive in such a case. No doubt Wright's original "model" or hypothesis was too simple, but it was, I believe, near enough to the truth. I put in some rather ugly algebra to show that it made no appreciable difference whether selection occurred before or after mutation in a life cycle. I do not regret this effort. It is necessary to test all sorts of possibilities in such a case. I was trying to build a mathematical theory of

atural selection. In doing so I calculated the equilibria between mutation of arious types of genes and selection against them. As soon as this was done became possible to estimate human mutation rates, and I did so [7]. ater on I improved this estimate, and since then many others have done better. The estimation of human mutation rates, which is a by-product f my mathematical work, has since assumed some political importance. lad I devoted my life to research and propaganda in this field, rather than) expanding the bounds of human knowledge, I should doubtless be a /orld-famous "expert." I believe that the estimation of the rate at which -rays, gamma rays, neutrons, and so on, produce mutations in animals ould be vastly improved. But what I believe to be the most accurate ıethod [8, 9] has not been given a serious trial, probably because it in-olves a good deal of mathematics. However, the work of Carter [10] nd of Muramutsu, Sugahara, and Okazawa [11] shows that it is practi-able, but expensive.

Now, Professor Mayr might say, "We must thank Haldane for the first stimate of a human mutation rate, but his argument is very simple in-eed; in his own words, 'the rates of production by mutation and elimina-ion by natural selection [of a harmful gene] must about balance.' So if ve can find out how many people die of hemophilia or sex-linked muscu-ır dystrophy per year, we can find out how many genes for these condi-.ons arise by mutation." Anyone can understand this argument, and it as been used to estimate many human mutation rates, even though one stimate, based on years of careful work, is out by a factor of 2 through n elementary mathematical error. But as it stands it is no better than most olitical arguments. Selection and mutation must balance in the long run, ut how long is that? In two rather complicated mathematical papers 12, 13] I showed that while harmful dominants and sex-linked recessives each equilibrium fairly quickly, the time needed for the frequency of an utosomal recessive to get halfway to equilibrium after a change in the nutation rate, the selective disadvantage, or the mating system, may be everal thousand generations. In fact, the verbal argument is liable to be allacious. As few people have read my papers on the spread or diminution f autosomal recessives, and still fewer understood them, the "balance" nethod, which I invented, is applied to situations where I claim that it ads to false conclusions.

I am in substantial agreement with David Hume when he wrote (*A trea-*

347

tise of human nature, Book 1, Part 3, Section 1): "There remain therefore algebra and arithmetic as the only sciences, in which we can carry on a chain of reasoning to any degree of intricacy, and yet preserve a perfect exactness and certainty." Not only is algebraic reasoning exact; it imposes an exactness on the verbal postulates made before algebra can start which is usually lacking in the first verbal formulations of scientific principles.

Let me take another example from my own work. From the records of the spread of the autosomal gene for melanism in the moth *Biston betularia* in English industrial districts, I calculated [3] that it conferred a selective advantage of about 50 per cent on its carriers. Few or no biologists accepted this conclusion. They were accustomed to think, if they thought quantitatively at all, of advantages of the order of 1 per cent or less. Kettlewell [14] has now made it probable that, in one particular wood, the melanics have at least double the fitness of the original type. As Kettlewell very properly chose a highly smoke-blackened wood where selection was likely to be intense, I do not think his result contradicts mine. The mathematics on which my conclusion was based are not difficult, but they are clearly beyond the grasp of some biologists. In a recent book [15] it was stated that this melanism must originally have been recessive, in which case even the large advantage found by Kettlewell would have taken some thousands of years to produce the changes observed in fifty years. I suspect this curious mistake is due to the fact that in an elementary exposition one may produce an argument which ignores dominance and gives a result of the right order of magnitude. But such an exposition may not stress that the argument breaks down when applied to rare recessives. I think that in this particular instance Professor Mayr may have unwittingly been a little less than fair to us beanbaggers. On his page 191 [1] he says that my "classical" calculations in a book published in 1932 were deliberately based on very small selective intensities and implies that I only reached the same conclusion for industrial melanism in 1957. In fact, it was not till 1957 that biologists took my calculation of 1924 seriously. I did not stress it in 1932 because I thought such intense selection was so unusual as to be unimportant for evolution. If biologists had had a little more respect for algebra and arithmetic, they would have accepted the existence of such intense selection thirty years before they actually did so.

When Landsteiner and Wiener discovered the genetical basis of human fetal erythroblastosis, I pointed out [16] that the death of Rh-positive

babies born to Rh-negative mothers could not yield a stable equilibrium and suggested that the modern populations of Europe were the result of crossing between peoples who, like all peoples then known, possessed a majority of Rh-positive genes and peoples who had a majority of Rh-negative genes. A distinguished colleague had calculated an equilibrium but had not dipped far enough into the bag to notice that it was unstable. Since then two relict populations have been discovered, in northern Spain and in one canton of Switzerland, with a majority of Rh-negative genes. If the mortality of the babies were higher, such differences would constitute a barrier to crossing, and I do not doubt that differences of this sort play a part in preventing hybridization between mammalian species. They can, for example, kill baby mules. I therefore regard the above paper as a contribution both to anthropology and to general evolution theory.

Once one has developed a set of mathematical tools, one looks for quantitative data on which to try them out. There are perhaps three main lines of such machine tool design, which may be called the Tectonic (from Greek τέκτων, a Wright), the Halieutic (from Greek ἁλιεύτης, a Fisher), and my own. Morton and C. A. B. Smith are developing a fourth, for use in human genetics. P. A. P. Moran [17] may be starting a fifth, or he may merely have made a hard road into an impassable swamp. A worker looks for numerical data on which his own favorite tools will bite. Thus Wright has collected data on small more or less isolated populations to which his theory of genetic drift is applicable. Fisher was probably at his best with samples from somewhat larger populations, for example his brilliant demonstration [18] of natural selection in Nabours' samples of wild *Paratettix texanus*, which is still perhaps the best evidence for heterosis in wild populations. Perhaps I am at my best with still larger populations. Thus I was, I think, the first to estimate quantitatively the rate of morphological change in evolving species [19]. My estimates are of the right order of magnitude, but based on estimates of geological time less reliable than those of Simpson [20]. I therefore fully accept Simpson's emendations (his pp. 10–17) of my figures. The question was the rate at which the mean of a morphological character changes. For one tooth measurement on fossil Equidae, paracone height, the rate of increase of the mean per million years ranged from 2.4 per cent to 7.9 per cent; for another, ectoloph length, from 0.6 per cent to 3.4 per cent. The rate of increase of the ratio of these lengths, which is of greater evolutionary importance, ranged from 0.9

per cent to 5.5 per cent. The total time covered was about 50 million years. On the other hand, I suggested that human skull height had increased by over 50 per cent per million years during the Pleistocene. The fossil data could have been so analyzed earlier. If I was the first to do so it was because, as the result of my mathematical work, such numbers had come to have more meaning for me than for others.

We can now come back to the justification of mathematical genetics. I leave out the body of mathematics which has grown up around human genetics. Here we cannot experiment and must squeeze all the information out of available figures, whereas where experiment is possible, not only is experiment often easier than calculation, but its results are more certain. In the consideration of evolution, a mathematical theory may be regarded as a kind of scaffolding within which a reasonably secure theory expressible in words may be built up. I have given examples to show that without such a scaffolding verbal arguments are insecure. Let me take an example from astronomy. I do not doubt that when Newton enunciated his gravitational theory of planetary movement many people said that if the sun attracted the planets they would fall into it. This is not so naïve as might be supposed. Cotes, of whose early death Newton wrote, "If Mr. Cotes had lived, we might have known something," showed that if the system "of planets, struggling fierce towards heaven's free wilderness," as Shelley put it, were attracted by the sun with a force varying as the inverse cube of the distance, they would move in spirals, and either fall into the sun or freeze in the free wilderness. Newton felt that he had to show not only that the inverse-square law led to stable elliptic motion, but that spheres, whose density at any point was a function of distance from their center, attracted one another as if they were particles. If he had not done so, he was aware that someone might readily disprove his highly ambitious theory. This does not mean that in explaining Newtonian gravitational theory to students one need go into these or many other details.

It is, in my opinion, worth while devoting some energy to proving the obvious. Thus, suppose a population consists of two genotypes A and B, of which B is fitter than A so long as it is rare. For example, B could be a mimic only advantageous when rare compared with its model, or a self-sterile but interfertile genotype of a plant species. It is intuitively obvious that B will spread through a population till its mean fitness falls to equal that of A, and a stable equilibrium will result. But is it sure that this equi-

librium will be stable? Every physicist and cybernetician knows that if regulation is too intense, a system may overshoot its equilibrium and go into oscillations of increasing amplitude. Haldane and Jayakar [21] found that in several cases investigated by them there was no danger of such instability. In a microfilm on population genetics circulated in A.D. 2000 we may either find the statement, "Haldane and Jayakar showed that such equilibria are almost always stable," or, "Haldane and Jayakar believed that they had demonstrated the stability of such equilibria. They overlooked the investigations of X on termites, where, as Y later showed, the equilibrium is unstable." But even if we have given the wrong answer, we deserve a modicum of credit for asking the right question.

I could give many more examples. Thus, posterity may or may not think that my concept of the cost of natural selection—that is to say, the number of genetic deaths required to bring about an evolutionary change [22]—is important. I think it defines one of the factors, perhaps the main one, determining the speed of evolution. It has been accepted by some and criticized by others. If it is shown to be false, the demonstration of its falsity will probably reveal the truth, or at least a closer approximation to the truth. And so I could continue on a large scale. If I were on trial for wasting my life, my defense would at least be prolonged, even if unsuccessful; for I have published over 90 papers on beanbag genetics, of which over 50 contained some original statements, whether or not they were important or true, besides 200 papers on other scientific topics.

The existing theories of population genetics will no doubt be simplified and systematized. Many of them will have no more final importance than a good deal of nineteenth-century dynamical theory. This does not mean that they have been a useless exercise of algebraical ingenuity. One must try many possibilities before one reaches even partial truth. There is, however, a danger that when a mathematical investigation shows a possible cause of a phenomenon, it is assumed to be the only possible cause. Thus Fisher [23] showed that if heterozygotes for a pair of autosomal alleles are fitter than either homozygote, there will be stable polymorphism, and later work has extended this theorem to multiple alleles. Numerous cases have been discovered where such heterosis, both at single loci and for chromosomal segments, has been observed in nature. It has therefore been assumed that, except where rarity confers an obvious advantage, the Halieutic mechanism is at work. Now Haldane and Jayakar [24] have

shown that, without any superiority of heterozygotes, selection of fluctuating direction will sometimes preserve polymorphism. There is no reason to think that this often happens, but it may sometimes do so. However, if I had made this calculation in 1920, as I might have done, while Fisher had published his work somewhat later, my explanation, which I do not doubt is more rarely true than Fisher's, might have been accepted as the usual explanation of stable polymorphism. It seems likely that this has happened in other cases, though naturally I do not know what these are. The best way to avoid such contingencies is to investigate mathematically the consequences following from a number of hypotheses which may seem rather farfetched and, if they would lead to observed results, looking in nature or the laboratory for evidence of their truth or falsehood.

One such possibility is the origin of "new" genes in higher animals or plants by viral transduction from species with which hybridization is impossible, conceivably even from members of a different phylum. While no doubt exaggerated claims have been made by the Michurinist school, some of its claims, such as the facilitation of hybridization by grafting, have been verified outside the Soviet Union. Transduction could account for some grafting effects which could not be regularly repeated. In terms of orthodox American genetics, such transduction would be described as a mutation leading to a neomorph. It is obvious that transduction could help to explain some cases of parallel evolution.

Let me be clear that I think the above hypothesis is improbable. But it serves to underline a fundamental point. Let us suppose that it had been proved that all evolutionary events observed in the fossil record and deduced from comparative morphology, embryology, and biochemistry could be explained on the basis of the generally accepted "synthetic theory"; this would not demonstrate that other causes were not operating. I think we have come near to showing that the synthetic theory will account for observed evolution and that a number of other superficially plausible theories, such as those of Lamarck, Osborn, and de Vries, will not do so. This does not exclude the possibility that other agencies are at work too. To take an example from astronomy, it was believed until recently that celestial mechanics were almost wholly dominated by gravitational forces. It is now believed that cosmic magnetic fields are also important.

Of course, Mayr is correct in stating that beanbag genetics do not explain the physiological interaction of genes and the interaction of genotype

and environment. If they did so they would not be a branch of biology. They would be biology. The beanbag geneticist need not know how a particular gene determines resistance of wheat to a particular type of rust, or hydrocephalus in mice, or how it blocks the growth of certain pollen tubes in tobacco, still less why various genotypes are fitter, in a particular environment, than others. If he is a good geneticist he may try to find out, but in so doing he will become a physiological geneticist. If the beanbag geneticist knows that, in a given environment, genotype *P* produces 10 per cent more seeds than Q, though their capacity for germination is only 95 per cent of those of Q, he can deduce the evolutionary consequence of these facts, given further numbers as to the mating system, seed dispersal, and so on. Similarly, the paleontologist can describe evolution even if he does not know why the skulls of labyrinthodonts got progressively flatter. He is perhaps likely to describe the flattening more objectively if he has no theory as to why it happened.

The next probable development of beanbag genetics is of interest. Sakai [25] described competition between rice plants. A plant of genotype *P* planted in the neighborhood of plants of genotype Q may produce more seeds than when planted in pure stand, while its neighbors of genotype Q produce less. Roy [26] has described cases of this kind but also cases where, when *P* and Q are grown in mixture, both *P* and Q produce more seed. In such a case, if the mixed seed is harvested and sown, *P* may supplant Q, or a balanced polymorphism may result. Of course if *P* and Q interbreed, the results will be very complicated. But I have no doubt that such cases occur in nature, and are of evolutionary importance. Given quantitative data on yields of mixed crops, a beanbag geneticist can work out the consequences of such interaction, even if he does not know its causes.

Another probable development is this. It is likely [27] that as the result of duplications one locus in an ancestor can be represented by several in descendants. If so, this is one of the important evolutionary processes, and its precise "beanbag" genetics will require investigation, even though the relative fitnesses of the various types, and the reasons for them, besides the causes of duplication, are matters of physiological genetics.

I would like to make one more claim for beanbag genetics. It has been of some value to philosophy. I consider that the theory of path coefficients invented by Sewall Wright may replace our old notions of causation. A path coefficient answers the question, "To what extent is a set of events

B determined by another set A?" Path coefficients were invented to deal with problems such as the determination of piebaldness and otocephaly in guinea pigs, which are beyond the present scope of beanbag genetics. But Wright showed how to calculate them exactly in the case of inbreeding, which he treated on "beanbag" principles. Again Haldane [28] discussed how to argue back from a handful of beans to the composition of the bag. Jeffreys [29] made this paper the basis of his theory of inverse probability. Jeffreys is generally regarded as a heresiarch and takes my theory more seriously than I do myself. Nevertheless, there is presumably some measure of truth in it, and even if Birnbaum [30] has shown how to do without it, I may take some credit for stimulating him to lay a stronger foundation than my own for the theory of inverse probability.

The dichotomy between physiological and beanbag genetics is one of the clearest examples of the contrast between what my wife, Spurway [31], calls Vaiṣnava and Śaiva* biology. Modern Hindus can, on the whole, be divided into Vaiṣnavas—that is to say, worshippers of Viṣnu, usually in one or other of his most important incarnations, Rama and Kriṣna—and Śaivas, or worshippers of Śiva. Viṣnu has, on the whole, been concerned with preservation and Śiva with change by destruction and generation. This is a very superficial account. Spurway may be consulted for further details. Devotees of Viṣnu do not deny the existence of Śiva, nor conversely are they necessarily exclusive in their worship, and many state that both deities are aspects of the same Being. Neither sect has actively persecuted the other. Roughly speaking, Darwin was a Śaiva when he wrote on natural selection and a Vaiṣnava when he wrote on the adaptations of plants for cross-pollination, climbing, and so on. A biologist who is always a Śaiva, and does not worry about how living organisms achieve internal harmony and adaptation to their environment, is as narrow as a Vaiṣnava who takes an organism as given and does not interest himself in its evolutionary past or its success in competition with other members of its species. It is very difficult to combine the two approaches in one's thought at the same moment. It may be easier a century hence. Thus, we know that human sugar metabolism depends on the antagonistic action of pancreatic insulin and one or more diabetogenic hormones from the anterior pituitary. Insulin production and anterior pituitary function are both under genetic control, but we do not know enough about this even to speculate

* *Ś* and *ṣ* are both near to the English *sh*.

fruitfully on the level of beanbag genetics, except to say that several different genotypes may achieve good homeostasis, while other combinations of the genes concerned are less well adapted for homeostasis, though they may have other advantages. Even this is a mere speculation. There may be only one adaptive peak in Wright's sense.

As I happen to be responsible for some of the mathematical groundwork of enzyme chemistry [32], I can say that the mathematical basis of physiological genetics is about fifty years behind that of beanbag genetics. If a metabolic process depends on four enzymes acting on the same substrate in succession, one can calculate what will happen if the amount of one of them is halved, provided that one is working with enzymes in solution in a bottle. We know far too little of the structural organization of living cells at the molecular level to predict what will happen if the amount is halved in a cell, as it is in some heterozygotes. If the enzyme molecules are arranged in organelles containing just one of each kind, the rate of the metabolic process will probably be halved. But if they are in a random or a more complicated arrangement, it may be diminished to a slight extent, or even increased; for the activities of some enzymes are inhibited by an excess of their substrate. This is a conceivable cause of heterosis, though I do not think it is likely to be common.

Now let me pass over to a counterattack. One of the central theses of Mayr's book is that speciation is rarely if ever sympatric. One species can only split into two as the result of isolation by a geographic barrier, save perhaps in very rare cases. Let me say at once that Mayr's arguments have convinced me that sympatric speciation is much rarer than some authors have believed, and a few still believe. But when, in his chapter 15, he discusses other authors' hypotheses as to how sympatric speciation might occur, his arguments are always verbal rather than algebraic. And sometimes I find his verbal arguments very hard to follow. Thus, on page 473 he makes seven assumptions, of which (1) is "Let *A* live only on plant species 1," and (4) is "Let *A* be ill adapted to plant species 2." These two assumptions seem to me to be almost contradictory. If *A* lives only on species 1, the fact that it is ill adapted to species 2 is irrelevant. If emus only live in Australia, the fact that they are ill adapted to the Antarctic has no influence on their evolution. If the assumptions had been "(1) Let *A* females only lay eggs on species 1," and "(4) Let *A* larvae (not all produced by *A* mothers) be ill adapted to species 2," I could have applied mathematical

analysis to the resulting model. I propose to do so in the next few years. But I hope I have given enough examples to justify my complete mistrust of verbal arguments where algebraic arguments are possible, and my skepticism when not enough facts are known to permit of algebraic arguments.

In earlier chapters Mayr seems to show a considerable ignorance of the earlier literature of beanbag genetics. Thus, on page 215 he writes that "the classical theory of genetics took it for granted that superior mutations would be incorporated into the genotype of the species while the inferior ones would be eliminated." The earliest post-Mendelian geneticists, such as Bateson and Correns, wrote very little about this matter. Fisher [23] pointed out that if a heterozygote for two alleles was fitter than either homozygote, neither allele would be eliminated. He may well have been anticipated by Wright or some other geneticists, but at least since 1922 this has been a well established conclusion of beanbag genetics. In my first paper on the mathematical theory of natural selection [3], I ignored Fisher's result as I was dealing with complete dominance; in my second [33] I referred to it and, as I think, extended it slightly. As Mayr cites neither of these papers of mine, he can hardly mean that the first was classical and the second post-classical! I agree with him that when I first read Fisher's 1922 paper I probably did not think this conclusion as important as I now do, and that many writers on beanbag genetics ignored it for some years. But were they classical?

Mayr devotes a good deal of space to such notions as "genetic cohesion," "the coadapted harmony of the gene pool," and so on. These apparently became explicable "once the genetics of integrated gene complexes had replaced the old beanbag genetics." So far as I can see, Mayr attempts to describe this replacement in his chapter 10, on the unity of the genotype. This does not mention Fisher's fundamental paper [34] on "The correlation between relatives on the supposition of Mendelian inheritance," in which, for example, epistatic interaction between different loci concerned in determining a continuously variable character was discussed. This chapter contains a large number of enthusiastic statements about the biological advantages of large populations which, in my opinion, are unproved and not very probable. The plain fact is that small human isolates, whether derived from one "race," like the Hutterites, or two, like the Pitcairn Islanders, can be quite successful. I have no doubt that some of the statements in Mayr's chapter 10 are true. If so, they can be proved by the methods of

beanbag genetics, though the needed mathematics will be exceedingly stiff. Fisher and Wright have both gone further than Mayr believes toward proving some of them. The genetic structure of a species depends largely on local selective intensities, on the one hand, and migration between different areas, on the other. If there is much dispersal, local races cannot develop; if there is less, there may be clines; if still less, local races. The "success" of a species can be judged both from its present geographical distribution and numerical frequency and from its assumed capacity for surviving environmental changes and for further evolution. I do not think that in any species we have enough knowledge to say whether it would be benefited by more or less "cohesion" or gene flow from one area to another. We certainly have not such knowledge for our own species. If inter-caste marriages in India become common, various undesirable recessive characters will become rarer; but so may some desirable ones, and the frequency of the undesirable recessive genes, though not of the homozygous genotypes, will increase. Since there is little doubt that extinction is the usual fate of every species, even if it has evolved into one or more new species, the optimism of chapter 10 does not seem justified. Sewall Wright has been the main mathematical worker in this field, and I do not think Mayr has followed his arguments. Here Wright is perhaps to blame. So far as I know, he has never given an exposition of his views which did not require some mathematical knowledge to follow. His defense could be that any such exposition would be *misleading*. I have given examples above to illustrate this possibility.

I am reviewing Mayr's book in the *Journal of Genetics*, and my review will, on the whole, be favorable. But if challenged, I am liable to defend myself, and have done so in this article. If I have not defended Sewall Wright, this is largely because I should like to read his defense. In my opinion, beanbag genetics, so far from being obsolete, has hardly begun its triumphant career. It has at least proved certain far from obvious facts. But it needs an arsenal of mathematical tools like the numerous functions discovered or invented to supply the needs of mathematical physics. Of course, it also needs accurate numerical data, and these do not yet exist, except in a very few cases. The reason is simple enough. Suppose we expect equal numbers of two genotypes, say, normal males and colorblind males, from a set of matings and find 51 per cent and 49 per cent; then if we are sure that this difference is meaningful, it will have evolu-

357

tionary effects which are very rapid on a geological time scale. But to make sure that the difference exceeded twice its standard error (which it would do by chance once in twenty-two trials), we should have to examine 10,000 males. To achieve reasonable certainty, we should have to examine 25,000. We often base our notions of the selective advantage of a gene on mortality from some special cause. Thus babies differing from their mothers in respect of certain antigens are liable to die around the time of their birth. But this may well be balanced wholly or in part by greater fitness in some other part of their life cycle. If it were found that color-blind males had a 10 per cent higher mortality than normals from traffic accidents, this could be balanced by a very slightly greater fertility or frequency of implantation as blastocysts. One of the important functions of beanbag genetics is to show what kind of numerical data are needed. Their collection will be expensive. Insofar as Professor Mayr succeeds in convincing the politicians and business executives who control research grants that beanbag genetics are misleading, we shall not get the data. Perhaps a future historian may write, "If Fisher, Wright, Kimura, and Haldane had devoted more energy to exposition and less to algebraical acrobatics, American, British, and Japanese genetics would not have been eclipsed by those of Cambodia and Nigeria about A.D. 2000." I have tried in this essay to ward off such a verdict.

Meanwhile, I have retired to a one-storied "ivory tower" provided for me by the Government of Orissa in this earthly paradise of Bhubaneswar and hope to devote my remaining years largely to beanbag genetics.

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