THE THEORY OF EVOLUTION, BEFORE AND AFTER BATESON

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William Bateson, as his widow emphasized, was a naturalist. He was therefore interested in the grandest of all natural processes which a biologist can contemplate, namely evolution. His work on *Balanoglossus* was an important contribution to its study. But he was then led to the study of variation, and interested himself particularly in what he called meristic variation, that is to say variation in the numbers of similar parts in like organisms. It became clear to him that much variation occurs in definite steps without intermediates, or with very rare intermediates. And he saw that this kind of variation must have been very important in evolution. In fact it was even more important than he knew. Two very similar species, all of whose taxonomic differences are, in his phrase, substantive rather than meristic, may yet differ sharply in their chromosome number, and this latter difference may account for the sterility of their hybrids.

Now many of the differences between domestic races of plant and animal species do not blend in the hybrids or in their progeny. A study of differences of this kind led inevitably to the discovery of Mendelian inheritance. But Bateson was far too honest a man not to see at a fairly early stage that his discoveries did not solve the problem of evolution. The differences between different domestic breeds are often far more striking than those between related species; but they usually only affect a limited number of organs or functions, and they do not hinder hybridization. Thus a white silkie fowl differs far more from the wild *Gallus gallus* as regards its feathers than do *Gallus sonnerati* or *Gallus varius*. But it does not differ in many other important respects, particularly in crossability. Thus Mendelism appeared to have no immediate bearing on the problem of evolution, except to show that the explanations given sixty years ago of how evolution had occurred were almost certainly false.

Bateson was almost unique among great men of science in being able to formulate his major contribution to scientific method in the lapidary phrase "Treasure your exceptions". It was this which led him to be more interested in one polydactylous cat than in ninety and nine with rather large feet. It was this which led him, though a staunch Mendelian, to investigate the exceptions to Mendel's laws which provided their explanation. The first of these exceptions was linkage, or a failure of the independent assortment of factors which Mendel had discovered. But Bateson was particularly interested in the exceptions which he classed under the heading of anisogamy. It is generally found that reciprocal crosses between two hermaphrodites give indistinguishable results. When they do not, after transient effects due to differences in the nutrition of seeds after

fertilization have passed off, the female and male gametes of one or both must differ in some way as regards their genotype. In fact anisogamy can be due to at least five different causes.

1. Plastids or plasmagenes may be transmitted wholly or mainly on the female side.

2. A virus may be wholly or mainly so transmitted. No sharp line can be drawn between these first two causes. It may or may not be possible to do so in future.

3. The chromosome number may be different on the two sides, as in the *caninae* group of roses.

4. Selection may act in a different way on male and female gametes or haploid cells of different genotype. This covers such cases as pollen lethals and the Renner phenomenon in *Oenothera*. Extra chromosomes are often transmitted by nearly half the ovules and by few or no functional pollen tubes.

5. Linkage intensity between a pair of loci may differ in female and male gametogenesis.

In fact Miss Saunders hit on the genetics of double stocks (*Matthiola incana*) which involves both anisogamy due to a pollen lethal, and linkage, at a very early stage; and this was not fully elucidated during Bateson's lifetime. I want to emphasize how broad is the field opened up, once one starts systematically studying what was at first sight a single type of exception.

Besides treasuring his exceptions, Bateson was very sceptical of explanations of many facts which he accepted without question. And in particular he never accepted the word "gene" with its rather wide connotations. Mendel had used the phrase "differendierendes Merkmal", or differentiating character, for his genetical units. Here he was probably influenced by his Thomism. It is much easier for a Thomist than for adherents of most other philosophies to think of a quality being transmitted. Had Mendelism been discovered and accepted in mediaeval Europe an atomistic theory of substantial forms might have been developed. Bateson used the neutral word "factor". This word has been dropped, partly because it was used in a number of different ways. I think it could and should be revived, with a more precise definition. Later I shall try to show why it is needed for an adequate account of evolution.

Genetics is the study of a class of differences between related organisms, namely those differences which turn out to be determined genetically, that is to say not by the environments of the individuals showing them. It is however a postulate of physiological genetics that any difference which is usually determined genetically can also be determined by non-genetical causes. If that were not the case, genetics would be an inscrutable mystery. We could never know the causal path between a gene and the scorable character.

I suggest that the word factor be used for the cause of an observable difference which shows Mendelian segregation. This is often, but not always, a difference between two allelomorphic genes. Thus, a round pea differs from a wrinkled one in the following way. Both contain much the same amount of carbohydrate at corresponding stages. In their early stages both contain stachyose, a sugar composed of two glucose and two galactose residues. In a round pea this is converted into starch in the final stage, in a

wrinkled pea it is not; so the pea contains a lot of soluble sugar, and collapses on drying. Very likely the wrinkled pea, like a galactosuric baby, lacks an enzyme concerned in transforming galactose into glucose. The synthesis of this enzyme in round peas is controlled by a gene at a locus in a certain chromosome, though there may be several steps between the gene and the enzyme. The wrinkled pea at the same locus contains a gene which does not make this enzyme, though it may make a similar but inactive protein. The wrinkled character is therefore recessive. It may be found, as has been found in similar cases in animals, that the homozygous round pea contains twice as much of this enzyme as the heterozygous. If so the factor would be detectable at various different levels, though it is a difference between two allelomorphic genes.

Now a gene is a material structure, and is roughly localized; but it is not exactly definable. If what seem to be the most active parts of it are transferred to a different part of a chromosome, it may alter its functions. Even if we had a precise knowledge of the chemical structure of a nucleus we could not say that changes in some parts would affect one gene and one only, and thus draw sharp boundaries between genes. The situation is quite comparable to that regarding cerebral localization. On the other hand we could define a factor exactly. We could say that because in a particular chromosome an adenine residue has been substituted for a guanine, in, say, the 25473—rd nucleotide counting from the free end of the longest chromosome, the plant makes a polyphenoloxidase with rather different properties. A factor, I suggest, can be anything from a difference of a few atoms in a single nucleotide, to an inversion or the presence of an extra chromosome; for these too are inherited in a Mendelian manner. If this is so, and a similar analysis of extranuclear factors is possible, all evolution is the accumulation or loss of factors. I think the early Mendelians perhaps went astray in taking too materialistic a view of the nature of a factor. Suppose that, as in Suskind, Yanovsky, and Bonner's (1955) work, a mutation causes the replacement of an enzyme by another protein no longer enzymatically active, but like enough to the enzyme to unite with the same antibodies. The new protein may be larger or smaller than the enzyme. The factor, which is the difference between the genes producing them, must be given a conventional sign, but is probably rarely a mere addition or substraction. It could be example be the substitution of N for C, O and H, which converts thymine into cytosine.

While, then, factors are units, though not necessarily or even usually material units, genes are not necessarily units. I do not go as far as Goldschmidt, and say that a gene can only be detected because it has mutated, and that therefore an unmutated gene is in principle unobservable, and so an hypothesis which should be eliminated from biology. On the contrary, I think that if we could isolate a normal human *X* chromosome and keep it in a suitable medium, we could observe the synthesis by it or under its influence of the globulin which is lacking in haemophilics. If we could do the same with a rabbit *X* chromosome we should be entitled to say that this chromosome, like those of men and dogs, carried a locus which, if it mutated, might be responsible for haemophilia.

The pre-Batesonian theories of evolution were, as we now see, excessively vague.

Darwin's theory was substantially correct, so far as it went. But he did not distinguish between phenotype and genotype; and we now know that within a pure line, or within what Bateson called an eversporting variety and we now call a balanced lethal system, such as double-throwing stocks, selection can continue indefinitely without evolutionary effect. What was worse, Darwin (1878, p. 10) stated that "if strange and rare deviations of structure are really inherited, less strange and commoner deviations may be freely admitted to be inheritable". The opposite is the case. If I find a *Drosophila* in an inbred line with many bristles lacking, it probably carries a mutant gene. If I find one with a rather smaller number than the average, it is probably due to an environmental effect which is not inherited. Bateson's principle of treasuring the exceptions is fully justified. Darwin also realised that heritable variations must have a cause; but he sought for this in the direct effects of use and disuse, which are rarely, if ever, so operative in the case of nuclear factors, though disuse can certainly produce extranuclear factors, such as absence of chloroplasts in algae, and adaptations due to use can be transmitted by bacteria at least for hundreds of generations.

Galton and Weismann helped to make the distinction between genotype and phenotype, but they did not achieve it, as they were unaware of the facts of dominance and epistasy. And Galton, with his emphasis on measurable characters, actually deflected genetics from its most immediately fruitful subject-matter. Karl Pearson exaggerated this emphasis, but fortunately forged mathematical tools which have been of immense value to geneticists. Bateson never used them, and it was left to Fisher and Wright to incorporate them into genetical methodology.

Let us now see how the theory of natural or artificial selection looks in its new guise. If we consider one of the simplest possible cases, the change which may take place in a single generation of sexually propagated annual higher plants or animals, we shall find that we have to consider five distinct populations. Where generations overlap matters are more complicated. I shall further assume hermaphroditism or equality in the numbers of the sexes, and that the populations studied are large. And I shall consider a closed area, into which there is no immigration. In three of these five populations we shall distinguish phenotypes and genotypes. The first of them, S, consists of all the organisms of the species in the area considered. Ideally we should like to score them at the moment of fertilization. I assume that they are actually described as early in the life cycle as is possible with the characters under consideration. They are classified by their phenotypes, and, ideally, by their genotypes. The last of our five populations, $\acute{S}$, consists of the progeny of S, counted and classified at the same stage in their life cycle as was S.

The second population, which I call the parental population P, is fictitious. It consists only of those members of S which are parents of one or more members of $\acute{S}$. But each is represented as many times as it has offspring in $\acute{S}$. So its total number is twice the number in $\acute{S}$. Thus a hermaphrodite plant which had two offspring in $\acute{S}$ as a seed parent and three as a pollen parent would be represented five times in P. Where generations overlap, Fisher's (1930) notion of reproductive value can be used.

Now P may differ from S in the frequency of phenotypes, genotypes, or both. These

differences may be so small as to be explicable by random sampling, that is to say chance. If not they are attributable to selection. If a particular genotype or phenotype is significantly commoner in P than in S this can be due to three different kinds of selection. This type may have survived better than the average in the interval between the time when S was scored and the time when P produced progeny. It may have been better represented in P because each individual in it was, on the average, more fertile than other types. Or it may have been so because its progeny, on the whole, survived better between the moment when they were formed as zygotes and that when they were scored as members of $\acute{S}$. If we could score S and $\acute{S}$ at once after fertilization we could eliminate this last kind of selection. We can sometimes, as with the characters round and wrinkled, yellow and green cotyledons, in the pea, get rather close to doing so.

The parents P produce a population G of gametes. We cannot score them except occasionally on the basis of their carbohydrates, but we can often estimate the frequencies of various genotypes among them with considerable precision. There is probably little selection among gametes in higher animals, but there is a great deal in higher plants, especially among pollen tubes, and in them we should consider a selected gametic population H. G will contain a few gametes of types not expected from the parental genotypes, due to mutation in the widest sense of that word, including such accidents as primary non-disjunction. Mutation can occur at any stage of the life cycle, but it is most convenient to consider it as concentrated in gametogenesis. The genotypic composition of G is so much simpler than that of S or P that it is desirable, where possible, to use it as a measure of evolutionary change. The genotypic composition of the next generation $\acute{S}$ depends not only on H but on the mating system. A large change in this, for example mating between two previously separate populations, or the introduction of inbreeding in a previously outbred population, can produce great changes in S. I assume that the mating system is not, in fact, changed.

Now if S and $\acute{S}$ could be classified at once after fertilization, then any differences in gene frequencies between them could only be due to selection, that is to say to differences between S and P, or G and H, apart from the very small differences due to mutation and random sampling, provided Mendelian inheritance occurs. Genotype frequencies can change through some generations towards whatever equilibria are given by the mating system. For example genes which were originally in coupling may gradually separate. Such secondary effects are rarely important. The effects of selection are hardly ever reversed except by counter-selection. Now this is not obviously true. It is a deduction from Mendelism, as I think Fisher (1930) first clearly pointed out. Karl Pearson showed that if, as he believed, Galton's law of ancestral heredity were correct, there would be a very considerable swing back after selection ceased. And in the rare cases where Mendelian segregation does not occur, for example in rye plants carrying a chromosome fragment whose descendants get into more than half the gametes, it is not true.

Unfortunately in practice there has always been some natural zygotic selection before S and $\acute{S}$ are scorable. However, all artificial selection is concerned in creating differences between P and S. It is also clear that only indirect methods based on

genetics can reveal the nature of the selection of H from C, or that acting between fertilization and the scoring of $\acute{S}$.

It is hard enough to compare phenotype and genotype frequencies in S and P, except in animals and plants whose breeding is artificially controlled. Even if we could find how many eggs each female moth in a natural population laid, we could not estimate the relative success of different phenotypes as fathers. Only in men can we get data, still very rough, on this important question.

Darwin inevitably considered selection on the basis of phenotypes. It is, I think, important to distinguish between selection and evolution based on phenotypes and on genotypes, and my wife has suggested that, so far as possible, a different terminology should be used in the four fields. I shall therefore use Simpson's (1953) terminology for phenotype selection. Selection which alters the mean of any character between S and P he called *linear*. (I should prefer a word which expressed his meaning more clearly). If it reduces the variance of a character, weeding out extremes, he called *centripetal*. If it increases the variance he called it *centrifugal*. Centripetal selection is very common. (*cf.* Haldane, 1953). It is often to some extent also linear. Karn and Penrose (1951) found that the mean human birth weight was about 1% higher in children who survived the hazards of birth and of the first month of life than in the population originally at risk, while the variance was reduced by about 10%. Centrifugal selection is much rarer. It occurs, however, when any polymorphism is being established. If, for example, black moths are rare in a population, and owing to selection there are more blacks in P than in S, the variance of any index of colour or brightness is increased, so selection is centrifugal as well as linear.

Genotypic selection requires little special terminology. We must, however, distinguish between selection which alters gene frequencies and that which does not. I call the former *effective*, and the latter *ineffective*, even though is often strong. Selection based on heterosis, that is to say favouring heterozygotes for a pair of allelomorphic genes or chromosomal arrangements, may be effective for a while, but leads to a stable equilibrium where it is ineffective, even if, as in structurally heterozygous *Drosophila* species, it is very intense. Selection based on negative heterosis is always effective, since one allel or the other is eliminated. It is perhaps legitimate to describe selection against mutants as ineffective when it just balances mutation.

For the phenotypic evolutionary effects of selection we may use the terminology of Mather (1953) and Waddington (1953). If the mean of $\acute{S}$ differs from that of S and we think this is not due to environmental change, we may speak of *directional* evolution. If the variance of $\acute{S}$ is reduced, because there are fewer members of genotypes whose mean differs widely from the population mean, we speak of *normalizing* evolution. If it is reduced because genotypes which vary greatly in different environments are eliminated, we speak of *stabilizing* evolution. If it is increased, for whatever reason, we speak of *disruptive* evolution. I am not quite happy about this word, for the establishment of a stable polymorphism is not, in my opinion, a disruption, though it may sometimes precede one. It must also be remembered that, as Thoday (1953) has pointed out, evolution which stabilizes one character necessarily destabilizes another.

To attain uniformity in different environments organisms must react differently. If some human genotypes have a stabler temperature in a variety of environments than do others, it may be because their sweating is more increased by high temperatures and therefore more variable in a range of climates.

Finally, we have to consider genotypic evolution. And here the essential is very simple. Either gene frequencies change, or they do not. Changes in relative frequencies of genotypes without change of gene frequency are of little importance. The unit process of evolution is the substitution of a Batesonian factor.

I have used the word evolution for the difference between S and $\acute{S}$. Of course a major evolutionary change is the resultant of millions of such differences. But it is the resultant of nothing else. I think that what Waddington calls normalizing selection is better called normalizing evolution. The weeding out of phenotypically extreme genotypes, for example homozygotes at a locus, can be wholly ineffective. If so it does not normalize.

I do not wish my terminology to be adopted without full discussion. I can only hope to contribute to the terminology which will be adopted ten years hence, and perhaps be useful for another thirty years, after which it may become a menace to original thinking.

Without a knowledge of genetics we can never say that selection will be effective. Thus in all plant species the number of seeds produced is very variable, as Salisbury (1943) has shown. There must always be linear selection in favour of the plants producing most seeds. But the main cause of high seed production is a favourable environment. And evolution is probably as often directional towards the production of fewer seeds as towards the production of more. Further, selection is usually centripetal. Extremes for most characters are generally eliminated. But it may be ineffective for three reasons. Most of the variation may be due to the environment, as in a pure line or a clonal population. Or selection may favour heterozygotes or merely eliminate mutants. If so an equilibrium is reached, and evolution is neither stabilizing nor normalizing. We can, however, say with confidence that in all species selection against most mutants is occurring. If there were no selection against them the mutations would produce disruptive evolution. The selection against them is always centripetal and may be linear.

Natural selection, then, may or may not change gene frequencies. But nothing else can do so anything like as fast. Chance effects may be important in small populations, but will rarely matter to a whole species, though they may be important when one or two individuals cross a geographical barrier such as the sea between a continent and an island, and may found a new species. And they may allow for the simultaneous establishment of several factors which are harmful singly, but adaptive in combination. Mutation is at best slow, and could not usually overcome a selective disadvantage of one in ten thousand.

We are left, I think, with no alternative but to believe that natural selection has been the main evolutionary agency, and also with surprisingly little evidence for effective selection. Fortunately we have such evidence, particularly as to effective selection of

insects for resistance to insecticides, and for cryptic coloration where human industrialism has changed the colour of a landscape. But in man, the best observed species, the observed selection is usually if not always at least largely ineffective, preserving an existing equilibrium either by the elimination of mutants or by favouring mediocrity, whether in intelligence, stature, or blood pressure.

If natural selection is effective, one can calculate the rate of change of gene frequencies. If an autosomal gene **A** is being favoured by selection, and the relative fitnesses and frequencies of the three genotypes are :—

	AA		**Aa**		**aa**
Fitness	$1+K$	:	1	:	$1-k$
Frequency	u^2	:	$2u$	:	1 ,

then if K and k are positive, the number of generations n, needed to change the ratio u from u_0 to u_n is

$$n = K^{-1} ln \left(\frac{k+Ku_n}{k+Ku_0} \right) - k^{-1} \, ln \left(\frac{K+ku_n^{-1}}{K+ku_n^{-1}} \right)$$

nearly, provided K and k are small.*

If u_0 is very small and u_n very large, say 10^{-4} and 10^4, which are frequencies such as would be kept in being by mutation, this becomes

$$n = K^{-1} \, ln \, u_n - k^{-1} \, ln \, u_0 + (K^{-1} - k^{-1}) \, ln(Kk^{-1})$$

nearly, which if $u_n = u_0^{-1} = 10^4$, is about $9.2 \, (K^{-1} + k^{-1})$, or about 5000 generations if K and k are each .001. If, however, K or k is zero, that is say **a** or **A** is fully recessive, the time needed is very much longer, even if there is some inbreeding. 5000 generations is a short time on a geological scale.

However, another consideration limits the rate at which natural selection can act (Haldane, 1957). Consider Kettlewell's (1956) data on the spread by natural selection of the dominant gene for melanism in *Biston betularia*. On releasing equal numbers of dark and light moths in a smoke-polluted wood in the morning, and trapping on the following night, he found about two dark moths to each light one. This was due to predation of the conspicuous light form by birds. The reproductive capacity of the light moths was reduced to about a half of what it would have been in an unpolluted wood. This must have happened about 1800 A.D., in a few areas where the melanics were then very rare. So effectively the reproductive capacity of the species was halved. The species did not become extinct. But if selection of the same intensity had been going on for nine other genes it would certainly have done so, for only one moth in a thousand would have survived for a day.

If selection is by death (or relative sterility which comes to the same thing) we can calculate the total number of deaths needed to replace one gene by another, or to change the species by one Batesonian factor, or, to use his earlier phrase, one discontinuity (Haldane, 1957). This is independent of the intensity of selection when this is small, and is about equal to the population number multiplied by $ln \, p$ and by a

* *ln* means natural logarithm, or decimal logarithm multiplied by 2.3.

further factor varying from about 1 to 10 or so with the amount of dominance and inbreeding, where p is the factor by which the frequency of the originally rare gene is increased. If this is 10^4 as in the example given, the number of deaths is about 10 to 100 times the population number. I suggest 30 as a fair average. I repeat that about as many deaths are needed to establish, by Darwinian selection, a factor with very slight selective value or phenotypic effect, such as the difference between the A_1 and A_2 agglutinogens in man, as a factor with a striking effect and high selective value, such as the difference between winged and apterous forms in an insect. The deaths are spread over more generations, but their number is, in fact, slightly larger. The factor is the unit of evolution by natural selection.

If selection were such as to reduce the mean reproductive value of the population 10% below that of the fittest genotypes, this would mean that an evolving species could incorporate, on the average, about one new factor in every 300 generations. This figure is, of course, a guess at the rate of evolution. But such a rate as one factor in thirty generations would only be likely when conditions were changing very rapidly (as of course, they are at present through human interference with nature) or when an organism had recently colonised a new environment. In both these cases the original type would be in fairly serious danger of extinction.

The next step in an account of natural selection would perhaps be a guess at the number of factors by which two fairly closely related species differ. This number is probably not very different from the number by which each of them differs from their latest common ancestor, perhaps in the Pliocene. I have guessed that this number may be of the order of a thousand for two closely related mammalian species. This would accord well with the time, of the order of half a million years, which seems to be needed to form such a species. I suspect the number may be less in higher plants. Even so, Blake (1793) was nearly correct in his statement that "To create a little flower is the labour of ages", though he should perhaps have added "except by allopolyploidy".

I think that by the year 2050 or so we may be able to estimate these numbers, and I wish to suggest how it may be done. There is a strong suggestion that some proteins in living cells are very closely causally related to genes, that is to say that a change in the gene will cause a change in the protein without changes in more than a few intermediate molecules at the most, even if ribonucleic acid always acts as such an intermediate. Whether other large molecules such as antigenic polysaccharides are equally close to genes, or whether the genes control their synthesis by making special enzymes we do not yet know. The latter hypothesis seems to me a little more likely.

We know that some factors, or gene substitutions, produce quite small changes in protein molecules, even when they alter their properties a great deal. Thus, Ingram finds that normal haemoglobin and the insoluble haemoglobin of sickle cell anaemia only differ in one of the thirty peptides into which he can break both up with trypsin. The difference may be of a single amino-acid*. The work of Harris, Sanger, and Naught (1956) gives us an idea of what we may expect. Insulin is a fairly simple

* Since the lecture was delivered, Ingram (1957) has confirmed this guess.

protein consisting of 48 amino-acid residues. The homologous insulins from five mammalian species have been completely characterised. Those of the pig and whale (species not stated) are identical. The others differ from them in respect of one or more of three adjacent amino-acid residues. In one threonine is an alternative to alanine, in the second serine to glycine, in the third isoleucine to valine. At this level the factor, or difference between two residues, is a carbon atom either with two hydrogens, or with two hydrogens and an oxygen. If, as is at least possible, they are formed by different but very similar genes, the chemical differences between these genes may also consist of a few atoms.

I suggest that about the year 2000 biochemistry and genetics may have progressed so far as to make the following programme possible. Two species will be chosen sufficiently close to give fertile hybrids, but yet undoubtedly differing according to the usual criteria. All the proteins, and perhaps other large molecules, of each will be isolated and examined in detail. Some will be found to be identical while others differ. The genetics of these differences will be determined by similar examinations of the F_1, F_2, and back-crosses. We shall then know at least most of the factors by which these species differ, and at least roughly what effects they have on the chemical makeup of the species. I suggest that a hundred or so workers could carry out such a programme in thirty years. Whether such a programme will be carried out depends on the interests of future generations. I can at least imagine a society, perhaps in Africa, sufficiently interested in biology as such to carry it through. It would be as interesting to bet on the results of such an investigation as on those of the investigation of the relative speeds attained by the members of a group of perissodactyls.

Bateson would, I am sure, have endorsed Blake's (1820) statement "For Art and Science cannot exist but in minutely organized Particulars, And not in generalizing Demonstrations of the Rational Power". Some of Bateson's adversaries, such as Karl Pearson, held the opposite view, and Bateson was a little too sceptical about generalizing demonstrations for my own taste. His references to Blake in letters, by the way, are enough to show that he would not have objected to a citation of his opinions on scientific method. Bateson's (1894, p. 17) own formulation concerning the processes of evolution was as follows:—"We know much of what these processes *may* be; the deductive method has been tried, with what success we know. It is time now to try if these things cannot be seen as they are, and this is what variation may show us".

I doubt whether, even a hundred years hence, we shall be in a position to describe all the factors by which two species differ in exact biochemical terms as differences between gigantic molecules of desoxyribonucleic acid. But some of them, at least, should be so describable. And the mere discovery of how many factors there are, and how they are related to the factors which differentiate the members of a species from one another, will tell us a very great deal about the detail of evolution.

I believe, then, that a precise and complete answer to the main problem with which Bateson was concerned can be given, and I hope will be given at least in some cases. It can be precise and complete because a gamete contains a finite number of atoms, of which only a fraction are arranged in self-replicating patterns. Such an answer would

not necessarily imply that an account of life had been given in chemical terms. If I can state the precise differences between two texts of the same poem I have not described the poem completely, much less elucidated its full meaning. But I may have elucidated the history of its transmission.

But supposing this problem had been solved, we should be a very long way from having solved the problem of evolution. One cannot see all the questions which posterity will ask. But already we can ask two kinds of question. What advantage, if any, did this factor confer ? And why did this factor arise; or if you prefer a different phrasing, why did this gene change in this particular way ? I shall try to show that these questions are not quite separate.

In Bateson's day Darwinism, as generally taught, showed signs of degenerating into Paleyism or Panglossism. Darwin (1878, p. 428) himself was not quite guiltless. "And as natural selection works solely by and for the good of each being, all corporeal and mental endowments will tend to progress towards perfection", he wrote in the penultimate paragraph of the Origin. Bateson was by no means convinced that all was for the best in the best of all possible worlds.

I will mention one piece of recent work which supports Bateson's scepticism as to the efficiency of natural selection. Sakai (1957) studied the competition between two varieties of rice, Red and Upland. The former is a weed, the latter an agricultural variety. A pure crop of Upland gives a much higher yield, by several different criteria, than one of Red. But Red is highly competitive. A Red plant lowers the yield of its neighbours, whether they are Upland or Red, but if surrounded by Upland, gives a higher yield than Upland in pure stand. It follows from Sakai's data that if we had a mixed crop and selected the highest yielding plants, we would usually select Red, and the end result of the selection would be a crop with a lower yield than that of the original mixed crop, or of pure Upland. The same result would occur if natural selection were based on the yields. I do not think that results of this kind are likely to be so common in competition within a species as in competition between species, but they can and do occur. The ecology of competition should be an important subject of genetical research in the future.

The second question is, I think, more fundamental. Darwin (1878, p. 125) quoted, though without reference, Walsh's (1863) "Law of equable variability". Vavilov and others have shown in more detail that comparable variations occur in related species. It was thought that, at least when their genetical determination was similar, they were usually due to mutations at homologous loci. Harland played the main part in disproving this unduly simple hypothesis, which is nevertheless, I think, fairly often true. Homologous organs may however depend on genes at different loci in closely related species. Spurway (1949) discussed this question in some detail. She pointed out that though mutations with similar phenotypic effects may, and often do, occur in related species, they may be rare or absent in one such species, and common in another. The simplest explanation of this fact is that the disturbance of a particular developmental process is more or less harmless in one species, but lethal or sublethal in another closely related one. Thus in *Drosophila subobscura* three recessives on different chromosomes

give white bristles between the ommatidia, usually with some slowing down of larval development. In the very similar species *Drosophila pseudoobscura* no such mutation has been reported. Perhaps the interruption of this particular developmental process slows down development in *Drosophila pseudoobscura* so much as to be effectively lethal. If so one species but not the other has the possibility of evolving a form with bristles of this type. Again although millions of mice have been observed, no recessive yellows have been found (if we discount an ancient account by Hagedoorn) like those which are well known in guineapigs, rabbits, dogs, and so on. The dominant yellow is lethal when homozygous and gravely upsets metabolism even in heterozygotes. It seems possible that the locus which gives yellow mutants in the guineapig and *Rattus rattus* also mutates in mice but gives lethal recessives.

If an organism were completely integrated developmentally in one sense of that very vague word, any mutation would be grossly harmful or even lethal. It is not in the least obvious why, for example, two genes at different loci which block the development of yellow pigment in mouse hairs also block the reabsorption of bone by osteoclasts. If development were more integrated, such cases would be commoner. In tetrapod vertebrates polydactyly is a common variation. But only once, in the ichthyosaurs, has it been used in evolution, though one might expect to find it in other swimming groups. It is presumably harmful, perhaps because, for the reason given later, it is very hard to stabilize phenotypically. Digits and even entire limbs, can, on the other hand, be lost. Similarly the number of limbs in insect imagines is extremely constant, though *Drosophila* mutants with extra legs are known, and in my laboratory Mrs. Trent has recently found one which occasionally has only four, though such animals have not yet lived to breed.

It seems that in the course of evolution capacities for further evolution are constantly being lost. But they may be gained. For example the birds have a remarkable capacity for the evolution of combs, ceres, wattles, and such-like structures, the Orchidaceae for fantastic changes in floral morphology. I need not here repeat other examples which Spurway gave, nor her suggestions for research on this problem.

The vast majority of mammalian species have seven cervical vertebrae. Some sloth species have more or less than seven, and what is more, as Bateson (1894) pointed out, the number can vary within such a species. Here it would seem likely that the capacity for variation has been gained in evolution. It is unfortunate that the giraffe and camel, for example, did not possess this capacity.

The capacity for genetic variation of which I have spoken is very similar to what Thoday (1953) meant by genetic flexibility. I have not previously used this phrase because I am not sure that he and I are discussing quite the same fact. And a species may be very flexible as regards one group of variations, and very inflexible as regards another, so one must be careful of stating that one species is more genetically flexible than another.

Until comparative genetics have been studied from this point of view, genetics will be able to make very little contribution to the understanding of the broad outlines of

evolution. The fossil record, like the human historical record, appears at first sight as a story of missed opportunities. I think this appearance is probably deceptive in both cases. We can probably see why the ancient Greeks could not develop a pan-Hellenic federal government, or the ancient Romans a democratic system for their empire, if it is less obvious why the Chinese did not develop science from their magnificent technology. We cannot yet see why the bipedal Dinosaurs failed to develop brains which would have made their hands as useful as our own or even those of a monkey, while the Synapsids did so after a hundred million years of eclipse and another hundred million of progressive evolution. We cannot guess why a number of groups in at least three different animal phyla, and a very few dioecious plants, have independently evolved morphologically differentiated sex chromosomes, while other groups have not. One can point to the advantages of this system of sex determination, and one can guess with some plausibility as to how it was evolved. But if the advantages are as great as has been suggested, and the evolutionary steps as simple, why is it absent, for example, in fish and in most Nematocera ?

My own guess is that in a few thousand years our successors may know enough genetics to be able to say that many of the major features of evolution were due to the fact that some groups kept possibilities open which others did not. This is fairly obvious at the morphological level. Tortoises and snakes have obviously fewer evolutionary possibilities than the less specialized reptilian groups, horses and whales than the less specialized mammalian groups. Sexuality seems to be an advantage because it allows for greater possibility of variation, and perhaps for no other reason. But even so I have no idea why in the vertebrates and arthropods self-sterile hermaphrodites are wholly exceptional, whereas they are the rule in the higher plants and some molluscan groups.

We have got to ask, at a higher level, the questions which Bateson asked in "Materials for the study of variation". We cannot even frame our questions correctly as yet. The suggestion which I have made here that the possibilities of genetically determined variation, and of evolution based on it, are much wider in some groups than in others, may turn out to be false. It is conceivable, say, that a single mutation perhaps with little effect by itself, could unlock the developmental processes in a lily flower, and make it as plastic under further mutations as an orchid. It is quite characteristic of genetics that the study of a single individual and its progeny may open up entirely new prospects. I think particularly of Bridges' X X Y *Drosophila* females which he used to prove the chromosome theory of heredity.

One at least, of the questions which Bateson (1894, p. 27) put in the introduction to "Materials for the study of variation" has been definitely answered. "The question" he wrote "which the Study of Variation may be expected to answer, relates to the origin of that Discontinuity of which species is the objective expression. Such Discontinuity is not in the environment; may it not, then, be in the living thing itself". Thanks to the work of Bateson and others, we can now answer this question, at least in part. There are two reasons (and perhaps more than two) for this discontinuity between species and varieties. Living things are made up of small and large molecules. Many of the small ones are common to all living things, others to most of them. But the large

ones, such as proteins and polysaccharides, are characteristic of species or of genotypes within a species, though some may be found in several, or even many, different species. And their formation is controlled by large molecules or sections of large molecules, which we call genes. These are built up from the ubiquitous types of small molecule, and can only vary discontinuously. Many of the discontinuities observed by naturalists depend on discontinuities in the possible patterns of genes. We do not yet know why the number of these possible patterns is restricted, as it is; why, for example, nucleic acids do not appear to include xanthine residues. But even if they did, the atomic structure of matter forbids continuous variation at the genic level. Bateson's question has therefore been answered in principle.

There is, however, a second answer, which often applies to meristic variation. When the number of like parts, for example, teeth, vertebrae or petals, can vary, it is usual to find a whole number of such parts and unusual to find a miniature or incomplete member of the meristic series. Bateson (1894, pp. 270-272) discussed the problem of "The least size of particular teeth", but came to no very firm conclusion, though he foreshadowed the conclusion of Grüneberg. Grüneberg (1952) has studied this phenomenon in the third upper molars of a particular pure line of mice. These teeth are sometimes missing. But when they are present they are variable in size and can be decidedly smaller than the normal, though in no way rudimentary or incomplete. He concluded that the mean size of the tooth rudiment in this line was small and somewhat variable. When, at a certain critical stage, the rudiment fell below a threshold, it regressed or did not develop further. Similarly we may suppose that when a rudiment is too large at a critical stage of development it may divide into two or even more parts, giving an extra limb, for example.

The physical principle at work may in some cases be surface tension, though this theory has been heavily criticized. The mechanism may often be that propounded by Turing (1952). However that may be, the formal physical principles, and therefore the mathematical analysis, of the formation of vertebrae in a tail may be not unlike that of drops in a liquid filament, even if the forces concerned are of quite a different nature. There may be yet other physical causes of discontinuity, but they are to be looked for, I think, in the minute particulars of the chemistry and physics of living matter. This was, I think, Bateson's view. He took the comparison of a zebra's markings with ripple marks quite seriously.

From a broad philosophical point of view these two causes of discontinuity are not different. Matter consists of atoms not because electrons and atomic nuclei are the only possible forms into which it can aggregate, but because the other forms, such as mesons, are unstable and short-lived. The forces which hold an atomic nucleus together or disrupt it are like enough to those operative in a drop of water to allow argument from the latter to the former. So, I suggest, are those operative in a tooth or petal rudiment.

It is interesting that these two causes of discontinuity are independent. Genes producing meristic variation are not usually constant in penetrance and expression. This is so for example for most genes causing polydactyly and ectrodactyly. And it is to be expected. Mandeville's (1950) gene for absence of upper lateral incisors in

man may reduce their size or cause their disappearance. Presumably the normal genotype produces a rudiment which hardly ever disappears or splits, and gives a tooth of a fairly uniform size. Mandeville's gene, in heterozygotes, gives a rudiment near the critical size, which may either disappear or give a small though not always obviously abnormal tooth. If, to take a possible cause, as the result of the formation of an abnormal protein, the average time between cell divisions in the rudiment is increased by five per cent, it is not to be expected that this will just be enough to bring down the size of the rudiment in question below its critical level in all cases, without any effect on the neighbouring teeth. The evolution of a human species, all of whom lacked this particular tooth and nothing else, would presumably require a particular combination of factors, Meristic variation is seldom strictly Mendelian just because these two different causes of discontinuity are operating. Bateson's (1894) generalizations about symmetry in meristic variation are a contribution to biology which is independent of his genetical work, and deserves further study and development.

To sum up, a few of Bateson's questions about evolution have been answered in some detail. The general question of the efficacy of natural selection has, I believe, been answered, though my answer involves more mathematics than Bateson would have liked, if less than Karl Pearson would have liked. But we can now begin to formulate further questions. Some of these questions can be answered on the biochemical level. For example to the question "Why are most desert beetles black, instead of being cryptically coloured ?" Kalmus (1941) after a study of *Drosophila* mutants, answered that the blackening process is a tanning of the cuticular proteins which prevents the beetles from losing water through their cuticles. It may be that our successors will be able to give equally satisfactory answers at this level to questions which still elude us, such as "Why was there a trend to reduce the formation of cartilage bones in the evolution of the Stegocephalia ?", or "Why are the morphological characters of the Solanaceae correlated with low resistance to virus infections ?"

However, as I have said, the explanation of the major features of evolution will be much more complicated, even if, as I think it will, it involves a great deal of biochemistry. It will also involve palaeogeography and palaeoclimatology. It is difficult to think that the emergence of our ancestors from the water in the Devonian was unrelated to the frequency of lagoons in that period, if in fact they were as frequent as is commonly stated. On the other hand it is not yet possible to correlate the extinction of the dinosaurs in the upper Cretaceous with any geological events. As we begin to learn about the genetics and evolution of behaviour we shall begin to ask meaningful questions on the psychological level as well as on the morphological and physiological levels. And these questions will be as important to botanists as to zoologists. The flowering plants are, on the whole, symbiotic with insects, especially Hymenoptera and Lepidoptera, and with mammals and birds. The insects mainly assist them in pollination, the mammals and birds in seed dispersal. It is, therefore, advantageous to plants to produce brightly coloured and characteristically smelling flowers and fruits, parts of which can be eaten or drunk. The origin of these structures however depended on the possibility of simultaneous morphological and biochemical evolution in plants, and

psychological evolution in animals. Were the Carboniferous insects incapable of developing an instinct to visit the same kind of flower, and the Jurassic dinosaurs incapable of developing an instinct to pluck sweet fruits? Or did the limited variability of plants limit the possibility of such evolution? We may have to ask questions on still higher levels. But there is little chance of asking them correctly, let alone of answering them, before we have answered some of the simpler ones.

No doubt in a few thousand years, when all the questions which have yet been put have either been answered or shown to be meaningless, the theory of evolution will be as unlike Darwin's formulation of it as relativistic quantum mechanics are unlike the mechanics of Galileo and Newton. Bateson's discontinuities in evolution may be capable of description in other terms, as Newtonian particles can be described as wave packets. But I think that Bateson's fundamental notion of discontinuity in the evolutionary process, which he enunciated seven years before the rediscovery of Mendel's work, will remain, though doubtless with some modifications, a component of any theory of evolution.

I wish that time had been given me to describe Bateson as I knew him from 1919 till his death. He could be described as an angry and obstinate old man. But his anger was largely reserved for inaccuracy and loose thinking, and for certain types of injustice. His obstinacy made it difficult to convince him of the truth of theories which had previously been asserted without adequate evidence and were now being substantiated. Correns (1902) in a brilliant guess embodied in a diagram without adequate explanation, had put forward the theory of the linear arrangement of genes on chromosomes. Bateson, quite rightly, had not accepted the hypothesis. When Bridges and Sturtevant proved it, he was hard to convince, though he was finally convinced of the fact that genes were associated with chromosomes. On the other hand he instantly accepted new generalisations provided they were statements of fact not involving theoretical superstructures. Thus, he was, I think, the first person to believe my own generalisation about sex ratio and unisexual sterility in hybrid animals, though not, of course, the rather incoherent explanation of it which I gave. He then displayed a characteristic combination of anger at my ignorance with great generosity in helping me with his immense knowledge of the by-ways of entomological literature. To me, at least, he showed no signs whatever of a senile failure of original thought. On the contrary his last posthumously published paper on the genetics of bolting in root crops initiated a line of research which was later developed by Waddington in his studies on genetic assimilation.

It would be stupid to suggest that all geneticists should model themselves on Bateson. Edward Lear's autobiographical line "His mind is concrete and fastidious" applies very well to him. This made him, I think, unduly suspicious of generalizations. But it gave him an eye for detail such as perhaps only Calvin B. Bridges among his contemporary geneticists possessed. Genetics need workers of very different temperaments. But we could all benefit from imitating Bateson's good points, and above all his respect for facts, although they told, and even because they told, against the theories which he had adopted.

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