

ON THE FALSIFIABILITY OF NEO-DARWINISM

Søren Løvtrup
 Department of Zoophysiology
 University of Umeå
 S-901 87 Umeå, Sweden

Received June 7, 1976, and November 22, 1976

ABSTRACT: The Mendelian theory of population genetics, the synthetic theory, or neo-Darwinism, embodies those features which were most criticized in Darwin's original theory. Although voices of dissent have been few, it has never been unanimously acclaimed by the biological community. One reason why this issue has never been settled is that the adversaries of the theory have been unable to muster empirical data which by its adherents were accepted as falsifying evidence. In the present article it is suggested that this state of affairs does not imply that neo-Darwinism cannot be falsified, but rather that it is protected from falsification by a number of ad hoc hypotheses. Largely unnoticed, another theory of evolution exists, almost as old as Darwinism. It is shown that this theory, here called the 'comprehensive theory,' can account for known empirical observations without recourse to any of these ad hoc hypotheses.

*

*

*

"False facts are highly injurious to the progress of science, for they often endure long, but false views, if supported by some evidence, do little harm, for everyone takes a salutary pleasure in proving their falseness; and when this is done, one path towards error is closed and the road to truth is often at the same time opened" (Darwin, 1906, p. 926).

Neo-Darwinism, the Mendelian theory of population genetics, is today the generally acclaimed theory of evolution. When this theory was introduced half a century ago the fortune of Darwinism was at an ebb: most people were convinced that evolution was a fact, but were also convinced that Darwin's theory did not offer an acceptable explanation of the causes of evolution.

It is remarkable that neo-Darwinism was so readily received, for the main objections raised against Darwinism were not resolved by the new theory. I shall not try to account for the immediate appeal of the new theory; I propose to show here that the reason why it has survived for so long is that the adherents of the theory have saved it by means of an array of ad hoc hypotheses¹. If neo-Darwinians had allowed their theory to be falsified, it would have been done long ago.

The present discussion is subdivided into three main sections, one dealing with two theories of evolution, one with their most important premises and one with the testing of the theories.

*

*

*

¹An ad hoc hypothesis may be used to save a theory. If, for instance, the theory has been falsified by empirical evidence, then it is always possible to introduce some auxiliary assumption ad hoc such that the theory escapes refutation. But if, as is usually the case, the ad hoc hypothesis is not independently testable, then the falsifiability, and hence the scientific status, of the theory has been reduced. If this process is repeated often enough one may reach the stage that the theory is no longer an empirical theory but a metaphysical one (cf. Popper, 1972).

Evol. Theory 1:267-283 (December, 1976)

The editors thank T.H. Frazzetta and another referee for help in evaluating this paper.

Two theories of evolution

What exactly are the premises of neo-Darwinism, and what the predictions? I shall try to answer this question and do the same for an alternative, the comprehensive theory, which differs from neo-Darwinism with respect to two basic premises.

Neo-Darwinism

On the basis of present knowledge we are entitled to the premise that evolutionary changes in all organisms are the outcome of genomic changes, primarily changes in gene frequencies. The Mendelian theory of population genetics can account for changes in gene frequencies in succeeding generations of bisexual organisms. On this account it has been claimed that this theory is the theory of evolution, being able to explain the workings of the phylogenetic evolution through which the organic world of today arose.

If this claim is correct then it must hold that the premises implied by the population-genetic theory have been fulfilled at all stages of evolution. The fundamental assumption in this theory is that at least two alleles of the same gene occur in the members of an interbreeding population, and that these genes differ with respect to the fitness they convey on the phenotype, i.e. the organism. Under these conditions differential elimination of the phenotypes, a process called natural selection, will alter the frequency of the two alleles until equilibrium is reached or one of the alleles is eliminated.

The presence of the allele to be selected for is thus presumed, and it may be concluded that if neo-Darwinism is to account for all stages of phylogenetic evolution then all the necessary mutations must always have been available at the proper moment. To prove that I am not misinterpreting the theory, I shall quote King (1972, p. 70): "There is always sufficient genetic diversity present in any natural population to respond to any selection pressure."

Since it cannot be assumed that all mutations were present at the outset of phylogenetic evolution, it must be concluded that new mutations always arise ahead of the need. King (p. 70): "There the actual mutation rates always are in excess of the evolutionary needs of the species."

The phenotypic fitness of a mutation must be evaluated with reference to the environment. Under constant conditions natural selection will change the genotype frequencies until no further increase in the fitness of the population's phenotype is possible. The state reached may correspond to a unique and optimal adaptation to the environment. If several adaptive peaks are possible, the situation will only be optimal. King (p. 70): "Therefore, natural populations are at, or very near, either the best of all possible genetic constitutions, or at an adaptive peak of genotype frequencies." Since this is such an important point in my argument I shall quote one more authority: "In a group not already at the selective optimum, selection should, given a sufficient store of appropriate variation, move the group to that optimum" (Simpson, 1953, p. 140). I have italicized Simpson's unorthodox reservation.

If the environment changes, natural selection will enter into action again and drive the population to a new optimum. In doing so, the environment is exerting a selection pressure on the organisms determining both the outcome and the pace of evolution. The environment is thus the true driving force, one might even say creative agent, in evolution, natural selection being merely its henchman. Here I do not agree with King (p. 71): "Evolution is directed entirely by natural selection." I do believe that natural selection exerts a directive influence on evolution, but in a sense different from that implied by King.

Since the predictable response to environmental change is adaptation, extinction is unexplainable by the theory. This conclusion was stated by Mayr (1960, p. 141): "And yet the whole pathway of evolution is strewn left and right with the bodies of extinct types. The frequency of extinction is a great puzzle to me."

These are the main predictions of neo-Darwinism. There is one more point implicit in the theory, based on empirical observations. This is that all mutations, except some deleterious ones, have very slight effects. For convenience these mutations will here be called micromutations. In order to account for phylogenetic evolution it is therefore necessary to assume that all major evolutionary changes have occurred through systematic accumulation of micromutations. This stand was also adopted by Darwin, and the agreement on this point is the foremost justification for the name "neo-Darwinism".

Most of the criticism raised against Darwin's theory in the course of time has concerned this particular premise. The objections have been focused on two points. First, critics have pointed out that many of the transitions known to have occurred, for instance from reptile forelimb to bird's wing or from insectivore forelimb to bat's wing, cannot possibly have occurred in numerous small steps, for the intermediate stages would constitute severe handicaps to their bearers. In conformance with current practice, defenders of the theory have proposed possible intermediates (e.g. Bock, 1969; Ostrom, 1974). Second, some critics have called attention to the fact that evolution has been associated with the origination of entirely new properties of various kinds, for example hairs, feathers, segmentation (metamery), teeth, compound eyes, whalebone, hemoglobin or hemocyanin (cf. Goldschmidt, 1940). Some of these innovations cannot possibly have arisen through accumulation of small mutations related to pre-existing features and it is possible that none did. In their opinion this phenomenon of emergence therefore contradicts the general validity of the Darwinian and neo-Darwinian hypothesis of innovation through accumulation of micromutations.

The comprehensive theory

Population geneticists are usually forced to work with those mutations which happen to appear in their material. And even if in some cases it has been possible to record the rate of appearance and disappearance of mutation, they cannot make any general statements about the rate of mutations. This handicap is overcome in studies of evolution on the molecular level, and one of the discoveries made is that "specific mutations do not recur at reasonably high rates; a species may have to wait millions of years before a specific adaptive mutation occurs and begins to increase towards fixation" (King, 1972, p. 71).

This observation concerns molecular point mutations and, as we shall see in the next section, these are likely to be more frequent than the (point?) micromutations studied by geneticists. The other type of mutations known to occur, chromosome mutations (including frameshifts) and genome mutations, are even less frequent than point mutations. Therefore it is fully justifiable to submit as a hypothesis that sometimes not all necessary micromutations are available when needed.

If we try to infer the consequences of this premise we shall see first that the outcome and pace of evolution is dependent on the occurrence of mutations, i.e. on a mutation pressure. If and when a mutation occurs which under the given conditions is advantageous--the environment is still the reference against which fitness is measured--then the selection will enter into action and the new mutation will undergo fixation.

Under these circumstances the prevailing genetic constitution in some organism A may very well be the "best of all possible" among those realizable on the

basis of the prevailing mutations. This does not preclude, however, that in a completely different environment an organism B arises whose fitness is superior to that of A even in the environment of the latter. Therefore, although it may be justifiable to speak of "adaptation" even in this case--all organisms are after all adjusted to their environment, or otherwise they could not survive--it is obvious that the word has a different, less absolute, implication than when employed in neo-Darwinian contexts.

And if the situation envisaged above is realized, then the survival of A must depend on random isolation. If such isolation is eliminated, populations of B will invade the territory of A and, unless some kind of ecological equilibrium is possible, will cause the extinction of the latter. Thus, extinction is a predictable element of evolution.

What are the consequences of our premise for the applicability of the neo-Darwinian mathematical superstructure? In order to answer this question, it may be profitable to form an opinion about the extent of change which has accompanied phylogenetic evolution. Stebbins (1974, p. 301) has stated that of minor advances in grade, most of which "would be recognized only by taxonomists and comparative morphologists," one would have arisen every 2000 years during the billion years of eucaryote evolution. If we generously allow 400 micromutations for the establishment of such a minor advance, this would mean that a survey of all living eucaryotes would permit the discovery, if perceptible, of an anagenetically successful micromutation every five years.

Stebbins also discusses the frequency of major advances, such as "the origin of multicellular from unicellular organisms, of the digestive tube, coelom, and central nervous system of animals, of vertebrate limbs, lungs, elaborate sense organs, warm blood, the placenta, and elaborate social behaviour." He estimates that about "100 major advances. . . have occurred throughout the evolutionary history of the eucaryotes," thus one every 10 million years.

The estimated rate of origination of the micromutations associated with minor advances is so low that it may be assumed that when they first appear in a particular species they are present in one individual or in the offspring of one individual. Under these conditions fixation of the rare mutations implied in the premise given above is possible only through strict inbreeding. Thus only those few examples of the neo-Darwinian mathematics which deal with inbreeding are relevant to evolutionary innovations; in all other cases the initial allele frequencies assumed are too high to be realistic.

The survival of the inbreeding population appears to depend on either of two factors, competitive dominance or isolation. It is unlikely that a micromutation can confer dominance on an organism (cf. Eldredge and Gould, 1972). However, if the macromutations to be discussed presently are a reality, then it is possible that organisms possessing a new mutation may spread and conquer the territory possessed by their immediate ancestors.

If the fitness increase due to the new mutations is more moderate, survival of the organisms carrying the new mutations presupposes isolation. This may be non-random isolation if the mutations involve a specialization permitting the organisms to leave their original 'niche' and thus avoid competition with their immediate ancestors. Or it may be a random isolation, accomplished by factors beyond the control of the organisms themselves. In either case there is the possibility that taxonomic divergence occurs, for isolation is a necessary but not a sufficient precondition for taxonomic divergence.

I shall now introduce one more premise, namely that certain mutations, macromutations, may in one step entail very large modifications in the organization, structure, etc. of an organism. This premise does not necessarily imply that the mutation is different from others on the molecular level, only

that mechanisms exist through which amplification of mutational effects are possible.

Allowing for large-step modifications as well as emergence, this premise abolishes the two objections to neo-Darwinism discussed above. It is not necessary to assume that birds arose ready for flight in one stroke, but it is necessary that the change was extensive enough that it allowed the incipient birds to become isolated. This isolation should involve some kind of specialization acquired through the possession of the new type of limb, for it is implausible that the origin of birds, even the initial stages, was due to random isolation.

I have here outlined a theory of evolution which differs from neo-Darwinism with respect to two premises, one concerning the rate of useful mutation and one concerning the extent of their effect. Since this theory includes neo-Darwinism, I have suggested calling it the comprehensive theory (Løvtrup, in press). But it is also comprehensive in another sense. Thus, while neo-Darwinism claims that population genetics has a monopoly in explaining the mechanism of evolution, I envisage that all biological branches which can contribute to our understanding of evolution should be incorporated in the comprehensive theory. Among these disciplines embryology, or epigenetics, may be of particular importance, as will be shown in a later section.

We have seen that these two theories differ with respect to their predictions about evolutionary events, and in the following text we shall see which set of predictions corresponds best to actual observations.

The premises

Among the premises of a theory of evolution are some concerned with the agents responsible for the execution of the various evolutionary events. A comprehensive list of this kind must include at least the following five factors: mutations (+ recombination of genes), selection, environment, isolation and random drift. Of these it is only the assumptions about the first two which differ substantially in the two theories outlined above, and only these will therefore be discussed in the present section.

Mutation

Many observations suggest (1) that mutations constitute a continuum with respect to the extent of their effect, (2) that their frequency is inversely related to their effect, and (3) that disadvantageous mutations are more common than advantageous ones (cf. Crow, 1972). If these premises are accepted, the distribution of mutations may be represented by the diagram in Figure 1, in which I have submitted that greatly beneficial mutations are possible, although highly improbable, events. From this figure we may outline the range of mutations that can be observed by researchers in various biological disciplines. Thus, geneticists can work only with mutations which occur at relatively high frequencies, as indicated by a horizontal line. The frequency implied by the latter must be quite high in evolutionary terms. Further, they cannot observe neutral and quasi-neutral mutations, as shown by two vertical lines at some distance from the line of neutrality. What remains are two sections, a tiny one representing beneficial, and large one representing deleterious, mutations. Molecular geneticists can observe these mutations plus the intermediate range of neutral and quasi-neutral mutations.

All other biologists do not work with mutating genes, but study the effects of mutations on living and extinct organisms. Their working range is cut off to the right by the line of viability, it is thus narrower than the one available

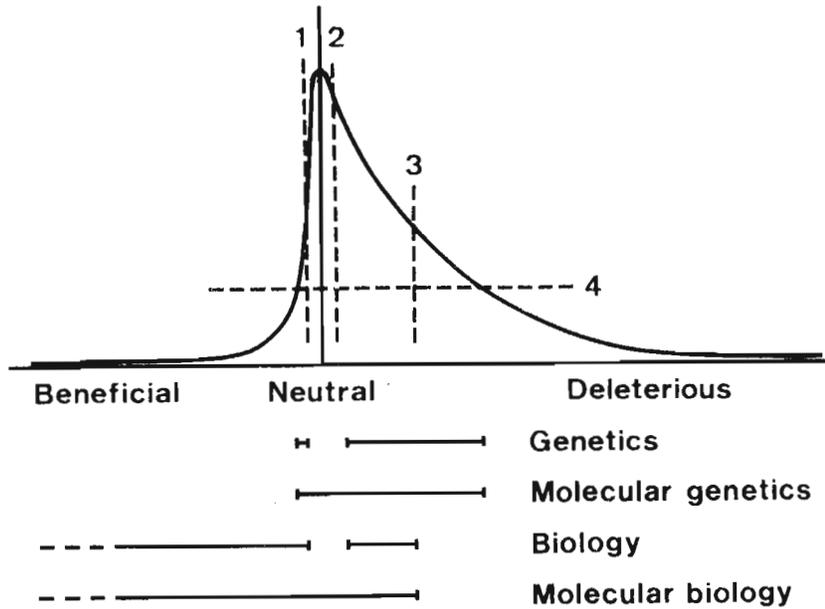


Figure 1. Conjectural relation between the frequency and the effect of new mutations. Lines 1 and 2 delimit the range of neutral and quasi-neutral mutations. To the left of line 3 the mutations are viable; to the right they are lethal. Mutations above line 4 are frequent enough to be observable within a finite period of time; below are the very rare mutations. Since probability is involved, it is evidently impossible to establish a sharp boundary. In this respect the figure therefore is somewhat misleading. Below the drawing is indicated the range of mutations the effects of which can be observed and studied in various biological disciplines. The terms "Molecular biology" and "Biology" are slightly ambiguous, but misunderstandings are not likely to arise. Based in part on Crow (1972).

* * *

to genetic studies, which encompass lethal mutations, but to the left there is no limitation at all. A difference obtains between molecular and all other biologists similar to the one encountered by their genetic colleagues.

It is seen that the interpretation of Figure 1 given here corresponds exactly to at least some geneticists' claim about the nature of mutations, namely, (1) that neutral mutations do not exist, (2) that beneficial mutations are rare and of slight effect and (3) that deleterious mutations are much more frequent and often extensive in their effects. This is clearly an honest empiristic-positivistic stand, i.e. the truth about Nature corresponds exactly to our empirical observations. But is it truly warranted to extrapolate observations made during 50, 500 or even 5000 years to the three billions of years of biological evolution?

The geneticists have two reasons to reject neutral mutations: first, because they cannot be recorded, and second, because they should have no chance of fixation. With the advent of molecular genetics, and our understanding of the nature of point mutations, there is no longer any justification for rejecting neutral mutations. A substitution of one amino acid for a closely related one in a protein molecule may have perceptible effects on the function of a polypeptide in some instances, but there is no reason to believe that this is always the case. In fact, studies on molecular genetics have led to the conclusion that "an evolutionary significant proportion of new mutations are either neutral or very slightly advantageous" (King, 1972, p. 71).

It is still true that neutral mutations cannot be fixed through natural selection: the only way this can occur is through random drift. Under these conditions the rate of mutant fixation should be determined by the rate of mutation, thus by the "mutation pressure". Kimura (1968) published results in support of this view.

Goldschmidt (1940) advanced the view that large-scale evolutionary changes were the result of macromutations involving the whole genome, "systematic mutations". This view has been rejected "by the consensus of geneticists" (Simpson, 1953, p. 85). Yet, recently it was demonstrated that there is a clear correlation between evolution of the karyotype and taxonomic divergence (Wilson *et al.*, 1975). These authors suggest their finding to be a vindication of Goldschmidt's theory, and thus a falsification of the "consensus of geneticists". Waddington (1969) has suggested that systemic mutations are similar to the large genomic changes occurring when cultured mammalian cells become "established lines," or immortal.

If the calculations of Stebbins quoted above are relevant, it follows that the mutations recorded in genetic experiments are trivial in an evolutionary context. No empirical observations made so far contradict this conclusion. And as we have seen, the generalizations about the nature of mutations made on this basis have been falsified in part, and are further questionable because they imply an extrapolation whose validity has never been ascertained. Therefore, even if we have not so far discussed the plausibility of macromutations, we may still infer that the objections raised against them carry little weight.

Selection

It is not unusual to find adherents of neo-Darwinism stating that selection is "creative". To demonstrate this I shall quote two authorities. First Simpson: "Only one point requires further mention. . . , and that is the old and oft-repeated objection that selection is not 'creative,' that it eliminates but does not produce. Even if this were true, selection would be an essential evolutionary factor, but it would have a more limited role and we would be forced to look elsewhere for some orienting factor, involved in the production of new forms and adaptive types" (1953, p. 139). Simpson here seems to confuse orientation, which is the result of selective elimination, and production of innovation, which is the outcome of mutation. If the quoted statement does not imply that selection can accomplish innovation, then the writing is very ambiguous.

I think this notion about the creativity of natural selection can be traced back to Darwin. In spite of the fact that both friends and foes told him that natural selection cannot be the vera causa of evolution (cf. Himmelfarb, 1959), he never came to realize that the role of natural selection, although important, is different from what he had envisaged.

Dobzhansky wrote: "Selection . . . creates order out of randomness" (1970, p. 431) and "selection does not create the materials that it selects" (p. 98). These two statements are both correct, but it is unfortunate to read in the same book that selection is both creative and not creative. It would be better to characterize the role of natural selection as either "ordering" or "directive".

Mutations are creative events, but they are random, and more likely to be deleterious than beneficial. Therefore, mutations alone can, at best, create but chaos, and at worst, regress. In order to account for the fact that progressive phylogenetic evolution has occurred, it is necessary to introduce one further agent which can impose order and direction on the mutational processes. It is possible to force any stochastic process in one direction by eliminating

all incidents going the opposite way. This, I submit, is the function of Darwin's and Wallace's Natural Selection. By differential elimination it serves to make room for the bearers of the most favourable properties, the possessors of the best prevailing genotypes.

It will be seen that my view of the contribution of selection coincides with that of Bateson (1909, p. 96): "So again, as the course of descent branches in the successive generations, Selection determines along which branch Evolution shall proceed, but it does not decide what novelties that branch shall bring forth. 'La Nature contient le fond de toutes ces variétés, mais le hazard ou l'art les mettent en oeuvre', as Maupertuis most truly said."

The evidence

I have above outlined two theories of evolution and also sketched their most important predictions. In the present section we are going to compare their predictions to see which of the theories stand up to testing. The following subjects will be dealt with: Macromutations, adaptation, rate and extinction.

Macromutations

It is obvious that I am not going to refer to direct observations of macromutations. If this were possible, the present issue would have been settled long ago. The only way this can be done is through indirect evidence. Evolutionary innovations which seem to be due to macromutations occur at all levels of organization, but I shall here confine myself to the morphological level. We shall begin with a discussion of Darwinian objections to macromutations. Next we shall see how a quantitative morphological feature, the body size of some amniotes, appears to change during evolution, and lastly we shall deal with the phenomenon of epigenetic amplification, which, it is submitted, may explain how large-scale morphological changes come about.

Darwinian objections

Since the notion of evolution through accumulation of minute changes is an inheritance from Darwin, I shall begin with a brief outline of Darwin's rejection of the idea that evolution might occur in large steps. On this point Darwin was, in fact, in an awkward situation, having admitted himself that in cultivated plants and animals large-scale modifications occur from time to time. This difficulty he circumvented with the following postulate: "But as species are more variable when domesticated or cultivated than under their natural conditions, it is not probable that such great and abrupt variations have often occurred under nature, as are known occasionally to arise under domestication" (Darwin, 1885, p. 201).

This is hardly a counterargument, for given sufficient time even highly improbable events may take place. Darwin therefore continued his pleading in the following way: "My reasons for doubting whether natural species have changed as abruptly as have occasionally domestic races. . . are [that] according to our experience, abrupt and strongly marked variations occur in our domesticated productions, singly and at rather long intervals of time. If such occurred under nature, they would be liable. . . to be lost by accidental causes of destruction and by subsequent inter-crossing; and so it is known to be under domestication, unless abrupt variations of this kind are specially preserved and separated by the care of men" (pp. 201-202).

Thus, Darwin does not exclude that large-scale mutations may occur in Nature, but he considers it impossible that inbreeding takes place. But how can we be sure of that? It would seem that one single instance of inbreeding occurring in Nature would suffice to falsify this hypothesis, unless it is required that the inbreeding should concern organisms possessing macromutations. In that case it might be difficult to falsify the hypothesis, because macromutations are so rare: on the other hand, Darwin's postulate then approaches an ad hoc hypothesis. Still worse, facing the difficulty that even his individual differences might be lost, Darwin made allowance for inbreeding in this case (p. 72).

The advocates of the neo-Darwinian theory have a similar attitude towards large-scale mutations. This was formulated by Fisher (1958, p. 44) in what may be called 'Fisher's axiom': "A considerable number of such [large-scale] mutations have now been observed, and these are, I believe, without exception, either definitely pathological (most often lethal) in their effects, or with high probability to be regarded as deleterious in the wild state."

It was shown above that to some extent this statement is corroborated by genetic observations, but that this is irrelevant in an evolutionary perspective. In any case, it would be very difficult, maybe impossible, to test this hypothesis, and I believe that the main purpose of the axiom is to be an ad hoc hypothesis, aimed at saving the synthetic theory which, as we have seen, fails if beneficial mutations are extremely rare.

Body size

An evolutionary theory should be falsifiable through reference to the fossil record. In point of fact, if this is done, all observed evidence rather suggests that evolution has involved large-step modifications. To save his stand on this point, Darwin introduced a further hypothesis: "I have attempted to show that the geological record is extremely imperfect" (1885, p. 312), and in spite of the many finds made since then this view is still upheld by most adherents of neo-Darwinism. The bad point about Darwin's argument is that if macromutation theory is correct, then the fossil record will forever be "extremely imperfect" from a Darwinian point of view. Thus the micromutation theory cannot be falsified through paleontological evidence, and I therefore submit that Darwin's statement is an ad hoc hypothesis.

Schindewolf (1950) and many others, both before and after him, have claimed that the fossil record is perfect enough to show that evolution has proceeded in large steps. Since these objections have been based on qualitative data, which may be relatively easy to ignore, I have, together with some colleagues (Løvtrup *et al.*, 1974), investigated a quantitative character, the body size of animals. We submitted the hypothesis that this parameter does not change in small installments in the course of evolution, but rather in steps of powers of two. This thesis was tested by recording the mean body size for several species in various groups of living mammals and birds, and subjecting these values to cluster analysis. In view of the rather inaccurate data which are available, and in particular of the fact that the body size is influenced by environmental factors, the outcome was a fair corroboration of the hypothesis. This finding does not, of course, falsify the Darwinian standpoint for, presuming that the animals in question no longer undergo evolution, the observed distribution may simply represent the optimal "adaptive" values. This position was in fact taken by Hutchinson (1959) who found a mean length ratio of 1.28 in various related sympatric species. On the basis of his premises Hutchinson concluded that the corresponding body volume ratio of about 2 is an ecological requirement for coexistence.

Yet, if Darwinism be correct, we might anticipate to find in the fossil record series with those many intermediate steps supposedly linking the living forms. This point was tested on data bearing on fossil horses and camels, and once more it was found that the size distribution was as predicted by our hypothesis.

The outcome of these studies suggests two distinctly different explanations. First, if evolution has involved countless transitional links then, evidently, the fossil record is very incomplete. However, it seems that anyone who advocates this view must also account for the fact that, against all odds, the recorded finds happen to fit closely a geometrical scale of two. If the overwhelming improbability of this happening is accepted, then only the second interpretation seems warranted, namely, that the postulated course of size variation is corroborated by paleozoological observations and that, consequently, the Darwinian notion of small-step evolution is falsified with respect to body size.

A corollary of this conclusion is that the fossil record, without being incomplete, of course, is far less incomplete than asserted by Darwin and his followers. Should this be granted, then the view of Schindewolf mentioned above is strengthened, implying that even on the qualitative level evolution may have taken place in large steps.

Epigenetic amplification

Darwin objected to the evolutionary importance of large-step mutations in part because he doubted that inbreeding occurs in Nature. But he had some further objections: "But against the belief in such abrupt changes, embryology enters a strong protest. It is notorious that the wings of birds and bats, and the legs of horses or other quadrupeds, are undistinguishable at an early embryonic period, and that they become differentiated by insensibly fine steps. He who believes that some ancient form was transformed suddenly. . . will further be compelled to believe that many structures beautifully adapted to all the other parts of the same creature and to the surrounding conditions, have been suddenly produced; and of such complex and wonderful coadaptation, he will not be able to assign a shadow of an explanation" (1885, pp. 203-204).

Thus, (1) ontogenesis proceeds in "insensibly fine steps" and (2) major changes cannot ensure harmony. It appears to me that in his example Darwin proves what he wants to disprove. The very fact that the cartilaginous primordia of essentially all quadruped limbs are indistinguishable shows that from the same starting point exceedingly different limbs may arise. That the processes through which this is accomplished occur by "insensibly fine steps" is evidently irrelevant from a phylogenetic point of view, and in an evolutionary perspective the changes may well be "abrupt". The crucial lesson to be learnt from Darwin's example is that several different forms can result from the same primordium under the influence of growth regulators. In many instances the latter undoubtedly are acting simply by modifying the relative rates of various growth processes, as suggested by Goldschmidt (1940).

And so far as harmony is concerned, it may suffice to dwell at the quantitative aspect and point out that most organisms increase substantially in size without upsetting the harmony of the body. And an excellent corroboration of the postulate that hormones are involved in controlling the growth processes may be found in the fact that in many animals there is a sexual dimorphism with respect to size. Of special interest is that among the seals the males may be two or four times larger than the females.

The implication of the Darwinian notion that evolution occurs in small installments is that the formation of the body is the outcome of a summation of

infinitesimal steps, which are specified as a blueprint in the genome. This conception is in clear contrast to the epigenetic element of the comprehensive theory. The principal aspects of the contribution of epigenesis may be visualized by means of an analogy, a computer. The working of the latter requires, besides the hardware, a set of operation instructions and a set of data. When these are available, pressing a button will start off an unprogrammed but predictable process which is creative insofar as it yields a hitherto unknown answer on a particular problem. If alterations are made in either the instructions or the data, the outcome will change. If the modifications are made at random, and the computing process is sufficiently complex, then I think it is possible to predict that the ensuing changes will form a continuum with respect to their effect, that the disadvantageous ones will prevail over the advantageous ones, and that their frequency will be inversely related to their effect. In short, it should be possible to illustrate the outcome of random modifications by a diagram similar to that in Figure 1.

The process of fertilization initiates an unprogrammed creative process which, in principle at least, is predictable. The information stored in the genome corresponds mainly to the data, but may comprise operation instructions. The rest of the fertilized egg embodies largely operation instructions--and the energy supply--but may contain some data. On one point the analogy is wanting: in the egg the operation instructions and the data together constitute the hardware.

Hormones and other agents which can control the rate of growth processes can be of great morphogenetic consequence. Thus, once the quadruped limb primordium is formed, gradients in the rates of ossification suffice to explain the formation of every type of vertebrate limb from the horse leg to the bat wing. But, of course, this mechanism implies the formation of the primordium in the first place, and thus the occurrence of the early morphogenetic processes bringing into existence the vertebrate body plan. There are many observations supporting the view that these early ontogenetic stages constitute an epigenetic, creative process, in which partake a number of morphogenetic elements, notably cells, but also some extracellular substances. The notable fact is that in most embryos the "body plan" is fully formed by means of these agents before any extensive transcription of the genome takes place. As I have tried to show elsewhere, it is possible to specify some, probably most, of the cell types and the extracellular elements which are involved in the shaping of various embryos, and they are remarkably few (cf. Løvtrup, 1974).

It was suggested that both in computer processes and in epigenesis random alterations in operation instructions and data may produce extensive changes in the result. It is important to stress that the changes in the input may be trivial in many cases, the outcome depending primarily on the way the subsequent processes are affected. In general the effect will be greater, for good or worse, the sooner the alteration becomes engaged. This phenomenon, that a slight change may have a large effect, is what I have called "epigenetic amplification". It is the central subject of classical developmental genetics (Hadorn, 1955).

Darwin quoted von Baer's demonstration of phylogenetic recapitulation during vertebrate ontogenesis, but failed to see the important clue to evolutionary modification which is hidden here. We may note with respect to von Baer's observations that each and every instance of embryogenesis is a construction of the body de novo. By a series of gradual modifications the bodies of the various vertebrate forms are created, and if we endeavour to understand the mechanisms of phylogenetic variation, what we have to do is to establish those responsible for ontogenetic modification, for the latter are at one level the cause of the former, as postulated by Garstang (1922) many years ago.

In the comprehensive theory the evolution of form is therefore to be accounted for primarily through the origination, at a very limited number of occasions during the course of evolution, of new epigenetic mechanisms involved in morphogenesis. On this view many of the phenomena which Darwin felt as stumbling-blocks to his theory, for instance the vertebrate eye, may be painlessly resolved. After all, eyes are created each and every time most vertebrates develop.

Adaptation

The basic implication of "adaptation" is usefulness for a more basic end. Indeed, Darwin's book is a sermon on teleology, of the trivial, not the divine, kind. But this is a very dangerous field to tread, for if the usefulness is not obvious, then one only has to give free rein to the imagination; any "explanation" will do, since none of them make any testable predictions. In this respect, much of what Darwin wrote is an endless series of ad hoc hypotheses.

As we have seen, neo-Darwinism predicts that all organisms are adapted, often optimally and uniquely, to their environment. That many organisms are adapted to their environment in the sense of being specialized cannot be questioned. But that this adaptation is unique in any case must remain an ad hoc hypothesis, for we have no means of measuring the absolute degree of adaptation. However, if the idea of adaptation to a specific environment has any sense, then it must follow that every kind of organism should be able to preserve their particular environment unchallenged by other beings. The extinction of the majority of the marsupials in South America, following the invasion of the eutherians, should not have been possible if the former were optimally adapted to their specific environment.

Elimination arising through adverse organic or inorganic factors in the environment is predicted by the comprehensive theory, but it is not accepted as part of evolution in the neo-Darwinian theory. To explain this kind of event, Fisher (1958, p. 45) introduced the concept "deterioration of the environment". This expedient is, I submit, an ad hoc hypothesis, aimed at saving the theory. The true nature of this proposition is clearly revealed by the fact that "environmental deterioration" can be demonstrated only through the decline of a given population; no other predictions are implied.

Rate

According to neo-Darwinism changes in the environment constitute the driving force in evolution; whenever such occur, evolutionary changes will be initiated. Since the various elements in the inorganic and organic environment interact in multifarious ways one would, a priori, expect that evolution had proceeded with comparable rates in the several phylogenetic lines. In actual fact, highly different rates of evolution have been recorded: some taxa have evolved very fast, for instance Mammalia, while others have remained almost unchanged for hundreds of millions of years, e.g. Lingula, Latimeria and Sphenodon.

Simpson (1953) has tried to account for these differences, but since these "explanations" cannot be independently tested, they seem to be ad hoc hypotheses. Many evolutionists interpret the observations as the result of different "selection pressures," the rate of evolution being proportional to the latter. Thus, for instance, it is implied that Latimeria has been exposed to little or no directional selection pressure and that consequently its environment has remained essentially constant for millions of years, while that of its close neighbours has changed over and over during the same time. This appears to be an unlikely idea; furthermore, the notion of "selection pressure is an

ad hoc hypothesis. It serves to explain differences in rate of evolution, but it can be recorded only by differences in rate of evolution.

The comprehensive theory makes a number of predictions, all of which are corroborated by empirical observations. First, the evolutionarily important mutations are so rare that they cannot be expected to occur in all phylogenetic lines. Hence, evolutionary rates may differ greatly from one phylogenetic line to another. The peculiar feature about the various animals mentioned above is that they did not evolve, but that they survived. In the normal course of events they should have become extinct.

Second, it has been observed repeatedly in the fossil record that the early history of a new taxon is distinguished by a high rate of taxonomic divergence (cf. Schindewolf, 1950). Simpson (1953, p. 223) suggests that in this phenomenon of adaptive radiation "the more direct factor [is]. . . the number of prospective adaptive zones opened. . . to the groups involved". And indeed, from a neo-Darwinian point of view this is the necessary and sufficient condition for a new "explosive" phase of evolution. In the comprehensive theory, the presence of "adaptive zones" is a necessary but not a sufficient precondition for this happening, for no amount of ecological territory can give rise to taxonomic divergence if the proper mutations happen to be lacking.

The comprehensive theory may supply an epigenetic explanation of the fact that, apparently, the occurrence of such mutations is more frequent during the early history of a new taxon. If a new body plan arises, distinguishing some higher taxon, then this new plan permits a number of potentially viable modifications. The chances of their realization must be higher, the fewer have already come into existence; hence it will be high initially and decrease with time.

Finally, if, as suggested here, much of evolutionary innovations occurs through regulatory mechanisms, involving primarily hormones, then it may be predicted that the rate of evolution will increase as the endocrinological machinery is developed. That the rate of evolution increases with the advance on the "scale of beings" is a fact observed already by Darwin. Therefore, some of the recorded differences in rate of evolution may primarily be indices of morphological or physiological complexity. This contention may to some extent make superfluous the use of selection pressure as a explanatory expedient.

Extinction

If an organism is optimally adapted to its environment, and if the environment is the agent which drives the selection, then, indeed, we might only expect to observe continuous changes in the preserved fossils. In fact, the latter demonstrate that innumerable phylogenetic lines have ended more or less abruptly.

As we have seen, Fisher (1958) introduced an ad hoc hypothesis, "deterioration of the environment," to explain this phenomenon. But it is absolutely impossible to demonstrate this phenomenon in any other way than that a taxon is on the way to undergo, or has undergone, extinction. According to the comprehensive theory the phenomenon of extinction is predictable. Thus, if the major evolutionary innovations are extremely rare events, then they will occur only in a few phylogenetic lines. And if these innovations concern tolerance towards the inorganic parameters of the environment, and if these change beyond the range acceptable in those organisms which did not acquire the innovation, then the latter will become extinguished. The extinction of the dinosaurs seems to be explainable in this way; apparently these warmblooded animals died out because they could not keep up their body temperature in the cold climate prevailing at the end of the Mesozoic.

Likewise, if organisms acquire features which ensure their dominance over other organisms with which they can compete because they can occupy the same

ecological territory, then the latter organisms will become extinguished through a process of selection, no matter how closely or distantly the organisms are related taxonomically. As mentioned above, the extinction of the indigenous marsupials in South America illustrates this phenomenon.

The crucial difference between the synthetic and comprehensive theories concerns the question: Are the proper mutations always ready for selection at the right moment? If yes, then there is a constant adjustment to the environment, and therefore adaptation (at least locally optimal because the right mutations are available) and no extinction except by catastrophes. With unlimited variation available selection can cope with any more gradual calamity. But variability is sometimes demonstrably not available, as for adaptation to soils with toxic metals (Antonovics *et al.*, 1971). If the answer to the question of the availability of mutations is no, then the frequency of a suitable allele is often zero, and hence there is no progressive Darwinian evolution. The proper mutation may come tomorrow or never; that is all a matter of chance. It is almost certain that sooner or later organisms will encounter inorganic or organic environmental conditions with which they cannot cope, and therefore extinction is predictable.

Conclusion

Darwin's theory, as well as the synthetic theory, asserts that the material of evolutionary innovation resides in the micromutations observable in the members of any species, and that these through accumulation can give rise to large-scale modifications. The comprehensive theory presented here contests this, and postulates that the latter generally are the result of extremely rare macromutations which at various occasions have accomplished more or less extensive one-step modifications. It is further contended that in such events epigenetic amplification is generally of great importance.

It has often been claimed that neo-Darwinism is close to a tautology, making few testable predictions. What I have tried to show is that both theories of evolution outlined here make predictions which can be tested with reference to empirical observations relating to life in the past and the present. When confronted with this evidence, neo-Darwinism must take recourse to a number of ad hoc hypotheses, whereas the comprehensive theory manages well without these. In fact, it appears that the survival of neo-Darwinism is contingent upon this ad hoc scaffolding, which permits the adherents to reject any kind of refuting evidence.

The comprehensive theory deprives Natural Selection of its role of Creator in cooperation with the environment, but it appears to me that the role which we can ascribe to it is not less grandiose. In fact, in the mess of variation created by mutation and recombination, resulting in disorder more often than order, natural selection has in many phylogenetic lines imposed a direction leading to progressive perfection, by eliminating everything but the best available at every station. If Darwin had been content to ascribe this function to his Natural Selection, his theory would have survived indefinitely, I believe. But the failure of the theory does not detract from the greatness of Darwin and Wallace in invoking selection as an evolutionary agent.

The comprehensive theory advocated here is an eclectic theory. I cannot give a complete list of its founders and supporters. I shall, however, try to mention the most important names. First, among those who have postulated that evolution proceeds in large steps may be mentioned the following biologists: von Baer, Bateson, Cope, D'Arcy Thompson, Grassé, T.H. Huxley, Hyatt, Kùlliker, Mivart, Parsons, de Vries and Willis (cf. Rádl, 1909; Thompson, 1942; Himmelfarb, 1959; Eiseley, 1961; Russell, 1916, 1962; Vorzimmer, 1970; Hull, 1973; Boesinger,

1974, Pfeifer, 1974). Some have further stressed the importance of epigenetics for evolutionary progress, notably Garstang (1922), Woodger (1929), Goldschmidt (1940), Schindewolf (1950), Russell (1962), Vandel (1968) and Waddington (1969). Among recent works critical of Darwinism I may mention Barzun (1958), Polanyi (1958), Whyte (1965), von Bertalanffy (1969), Macbeth (1971) and Grassé (1973).

It is difficult to find a feature common to all these people, but I believe there is one, namely that none of them has been an established population geneticist. (Goldschmidt was a geneticist, but with a much wider field of interest.) And this may be one reason why the criticism has been neglected so far by those towards which it was primarily directed, the neo-Darwinian population geneticists. With the book recently published by Lewontin (1974) this situation has changed. Having gained reputation as an experimental population geneticist, Lewontin reached the point of thinking about the epistemological basis of his trade. I shall illustrate his conclusion by two quotations: "If one simply cannot measure the state variables or the parameters with which the theory is constructed, or if their measurement is so laden with error that no discrimination between alternative hypotheses is possible, the theory becomes a vacuous exercise in formal logic that has no points of contact with the contingent world. The theory explains nothing because it explains everything. It is my contention that a good deal of the structure of evolutionary genetics comes perilously close to being of this sort" (pp. 11-12) and "To concentrate only on genetic change, without attempting to relate it to the kinds of physiological, morphogenetic, and behavioral evolution that are manifest in the fossil record, is to forget entirely what it is we are trying to explain in the first place" (p. 20).

Clearly, a new and more general theory is needed. Can we hope that biologists, at least the next generation, will take a fresh view on the question of the mechanism of phylogenetic evolution? If they do so, the best place to start is the comprehensive theory which, so far as the essential aspects are concerned, is almost as old as Darwinism.

References

- Antonovics, J., Bradshaw, A.D., and Turner, R.G. 1971. Heavy metal tolerance in plants. Adv. Ecol. Res. 7:1-85.
- Barzun, J. 1958. Darwin, Marx, Wagner: Critique of a Heritage (rev. 2nd ed.). Doubleday, Garden City, N.Y.
- Bateson, W. 1909. Heredity and variation in modern lights, in Darwin and Modern Science (ed. A.C. Seward), pp. 85-101. Cambridge University Press, Cambridge.
- Bertalanffy, L. von. 1969. Chance or law, in Beyond Reductionism: New Perspectives in the Life Sciences (ed. A. Koestler and J.R. Smythies). Hutchinson, London.
- Bock, W. 1969. The origin and radiation of birds. Annals New York Acad. Sci. 167:147-155.
- Boesiger, E. 1974. Evolutionary theories after Lamarck and Darwin, in Studies in the Philosophy of Biology: Reduction and Related Problems (ed. F.J. Ayala and T. Dobzhansky), pp. 21-44. Macmillan, London.
- Crow, J.F. 1972. Darwinian and non-Darwinian evolution. Proc. 6th Berkeley Symp. Math. Statist. Probab. 5:1-22.
- Darwin, C. 1885. The Origin of Species by Means of Natural Selection (6th ed., with add. and corr.). John Murray, London.
- _____. 1906. The Descent of Man and Selection in Relation to Sex (2nd ed.). John Murray, London.
- Dobzhansky, T. 1970. Genetics of the Evolutionary Process. Columbia University Press, New York.

- Eiseley, L. 1961. Darwin's Century: Evolution and the Men Who Discovered It. Doubleday, Garden City, New York.
- Eldredge, N., and S.J. Gould. 1972. Punctuated equilibria; an alternative to phyletic gradualism, in Models in Paleobiology (T.J.M. Schopf, ed.), pp. 82-115. Freeman, San Francisco.
- Fisher, R.A. 1958. The Genetical Theory of Natural Selection (2nd rev. ed.). Dover, New York.
- Garstang, W. 1922. The theory of recapitulation: A critical re-statement of the biogenetic law. J. Linn. Soc. London 35:81-101.
- Goldschmidt, R. 1940. The Material Basis of Evolution. Yale University Press, New Haven.
- Grassé, P.P. 1973. L'évolution du Vivant. Albin Michel, Paris.
- Hadorn, E. 1955. Letalfaktoren. G. Thieme Verlag, Stuttgart.
- Himmelfarb, G. 1959. Darwin and the Darwinian Revolution. Chatto & Windus, London.
- Hull, D.L. 1973. Darwin and his Critics. Harvard University Press, Cambridge, Mass.
- Hutchinson, G.E. 1959. Homage to Santa Rosalia or Why are there so many kinds of animals? Am Nat. 93:145-149.
- Kimura, M. 1968. Evolutionary rate at the molecular level. Nature 217:624-626.
- King, J.L. 1972. The role of mutation in evolution. Proc. 6th Berkeley Symp. Math. Statist. Probab. 5:69-100.
- Lewontin, R.C. 1974. The Genetic Basis of Evolutionary Change. Columbia University Press, New York.
- Løvtrup, S. 1974. Epigenetics a Treatise on Theoretical Biology. Wiley, London.
- _____. (In press). The Phylogeny of Vertebrata. Wiley, London.
- Løvtrup, S., Rahemtulla, F., and Höglund, N.-G. 1974. Fisher's axiom and the body size of animals. Zool. Scripta 3:53-58.
- Macbeth, N. 1971. Darwin Retried: An Appeal to Reason. Gambit, Boston.
- Mayr, E. 1960. In Evolution after Darwin (ed. S. Tax and C. Callender), Vol. 3, p. 141. University of Chicago Press, Chicago.
- Ostrom, J. 1974. Archaeopteryx and the origin of flight. Quart. Rev. Biol. 49:27-47.
- Pfeifer, E.J. 1974. United States, in The Comparative Reception of Darwinism (ed. T.F. Glick), pp. 164-206. University of Texas Press, Austin.
- Polanyi, M. 1958. Personal Knowledge: Towards a Post-Critical Philosophy. Routledge & Kegan Paul, London.
- Popper, K.R. 1972. Conjectures and Refutations: The Growth of Scientific Knowledge (4th rev. ed.). Routledge and Kegan Paul, London.
- Rádl, E. 1909. Geschichte der biologischen Theorien. II Teil. Geschichte der Entwicklungstheorien in der Biologie des XIX. Jahrhunderts. Engelmann, Leipzig.
- Russell, E.S. 1916. Form and Function. A Contribution to the History of Animal Morphology. John Murray, London.
- _____. 1962. The Diversity of Animals: An Evolutionary Study. Brill, Leiden.
- Schindewolf, O.H. 1950. Grundfragen der Paläontologie. Schweitzerbart, Stuttgart.
- Simpson, G.G. 1953. The Major Features of Evolution. Columbia University Press, New York.
- Stebbins, C.L. 1974. Adaptive shifts and evolutionary novelty: a compositionist approach, in Studies in the Philosophy of Biology Reduction and Related Problems (ed. F.J. Ayala and T. Dobzhansky), pp. 285-306. Macmillan, London.
- Thompson, D.A.W. 1942. On Growth and Form (2nd ed.). Cambridge University Press, Cambridge.

- Vandel, A. 1968. La Génèse du Vivant. Masson, Paris.
- Vorzimmer, P.J. 1970. Charles Darwin: The Years of Controversy; The Origin of Species and its Critics 1859-1882. Temple University Press, Philadelphia.
- Waddington, C.H. 1969. Paradigm for an evolutionary process, in Towards a Theoretical Biology. 2. Sketches (ed. C.H. Waddington), pp. 106-128. Edinburgh University Press, Edinburgh.
- Whyte, L.L. 1965. Internal Factors in Evolution. George Braziller, New York.
- Wilson, A.C., Bush, G.L., Case, S.M., and King, M.-C. 1975. Social structuring of mammalian populations and rate of chromosomal evolution. Proc. Nat. Acad. Sci. USA 72:5061-5065.
- Woodger, J.H. 1929. Biological Principles. Routledge & Kegan Paul, London.