Comments on S. Løvtrup's paper "On the falsifiability of neo-Darwinism"

O. Mayo* and J.A. Bishop†

*Biometry Section,
Waite Agricultural Research Institute,
University of Adelaide,
ADELAIDE, South Australia 5064.

†Department of Genetics,
University of Liverpool,
LIVERPOOL, England,
UNITED KINGDOM.

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ABSTRACT: There are many important problems in the synthetic theory of evolution. These include its weak falsifiability, arising from its limited precise predictive power, the relationship between selection and variability, the lack of a population-genetical theory of gene interaction, and the question whether extinction should be predictable. It is argued that Løvtrup's "comprehensive" theory only addresses these problems differently from the synthetic theory by the use of the subsidiary hypothesis of pre-adaptation, long shown to be false in almost all cases where it has been examined closely.

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1. Introduction

Løvtrup (1976) has claimed that neo-Darwinism is defective in a number of important respects, and has claimed that a "comprehensive theory" incorporating neo-Darwinism but with a number of substantial differences and improvements can yield better predictions than neo-Darwinism, as well as avoiding the errors of that theory. He makes four main points in developing his theory:

(i) "sometimes not all necessary micromutations are available when needed"; this, Løvtrup considers, allows the following two points to be deduced:
(ii) "the outcome and pace of evolution is [sic] dependent upon the occurrence of mutations, i.e. on a mutation pressure";
(iii) "extinction is a predictable element of evolution";
(iv) "macromutations may in one step entail very large modifications in the organisation, structure, etc. of an organism."

In order to see to what extent these points are valid or original, we must briefly examine some aspects of Darwinism in a correct historical context, after which we may examine Løvtrup's specific contribution, and then determine how it relates to neo-Darwinism, both as an alternative and as it bears on the real problems of neo-Darwinism.

2. Neo-Darwinism in Perspective

> "The mutationist has no explanation to give of adaptation as an observable fact; the furthest he can go towards recognising it is in the lukewarm theory of pre-adaptation, in which a new form is supposed to arise spontaneously, and, if it has the good fortune to discover an unoccupied environment to which its new characters happen specially to fit in, to establish itself there as a successful species."
> "(The selectionist) is quite indifferent as to the cause of mutations, so long as they are produced somehow, with the rather minute frequency necessary to maintain a stock, or pool, of heritable variability. Given that heritable variability, it can be seen, or rather, I should say it can be rigorously demonstrated, that differences in the rates

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> of death and reproduction will produce a constant modification of the species, in whatever directions lead to a more perfect adaptation to the circumstances in which it exists."

The quotations above, from Fisher (1934), provide a context within which to examine Løvtrup's criticisms of neo-Darwinian theory. It is our contention that Løvtrup's description of this theory serves to obfuscate the real problems in that theory, and so it is first necessary to show where his account of this theory is inadequate. He quotes King (1972) to the effect that "there is always sufficient genetic diversity present in any natural population to respond to any selection pressure," and Mayr (1960) to the effect that "the frequency of extinction is a great puzzle." The former quotation is a gross overstatement of the middle range of neo-Darwinian opinions (there are more than one, which one would hardly infer from Løvtrup's account). Extinction of species must on occasion imply inability to adapt, so that either sufficient variability cannot have existed or change was simply too rapid. Since it is *not* a basic assumption of neo-Darwinism that "new mutations must always arise ahead of the need" (to quote Løvtrup), extinction is explicable as a failure to adapt. (This is not the only explanation, of course.)

It is a noteworthy aspect of attempts to make macroevolution quantitative that they generally contribute nothing to our understanding of either speciation or extinction. This may be stated of the information flow approach of Theodoridis and Stark (1969, 1971), as noted by Mayo (1972), and also the related energy flow approach of Felsenstein (1978). The latter, however, which yields a relatively fresh model of the evolution of hierarchical relationships, appears less unpromising.

The apparent frequency of extinction is by no means puzzling to many biologists. Darwin himself discussed extinction in Chapter 4 of "The Origin of Species" and with particular reference to extinction caused by natural selection wrote:

> "We can see that any form which is represented by few individuals will run a good chance of utter extinction, during great fluctuations in the nature of the seasons, or from a temporary increase in the number of its enemies. But we may go further than this; for, as new forms are produced, unless we admit that specific forms can go on indefinitely increasing in number, many old forms must become extinct."

Extinction was not a problem for Darwin, nor is it a problem for many holding neo-Darwinian views. Many examples are available and have been widely discussed. One moth for instance became extinct in the industrial city of Sheffield, U.K., apparently because the mutation controlling the cryptic melanic form did not occur there. The species reappeared in the city some years later because the mutation arose elsewhere and enabled the species to recolonise the area from which it had been eliminated (Kettlewell, 1976, p.63). Similar events occur whenever successful application of pesticidal poisons temporarily renders a habitat unsuitable. Extinction occurs unless a rare mutation that confers resistance is available for selection. Local extinction may persist only briefly even in the absence of a mutant because recolonisation occurs when the toxicity is lost. Extinction and recolonisation are important events in the theory of number in biological populations (Andrewartha and Birch, 1954). They are clearly also important in neo-Darwinian theory. The absence of a species from a locality is frequently due to the physical or biotic characteristics of that place being unsuitable; the species has not been able to adapt. Where permanent, active existence is not possible, there are a variety of genetically-mediated means such as diapause, hibernation, aestivation and

dormancy that permit species to flourish in a temporarily favourable habitat.

The different polymorphisms which have arisen as a result of the environmental factor malaria form a good example of the different outcomes which are possible in populations continuously exposed to a selective agent. Mutations which lead to similar levels of adaptation have become polymorphic; haemoglobin S in parts of Africa and thalassaemia in the Mediterranean are two imperfect "solutions" found through natural selection to the "problem" of malarial death or debility. There is no reason to suppose that the population of Iceland, transported to a malarial region, would evolve any one of these polymorphisms quickly enough (except by intermarriage) or indeed any other. It might die out. It is well known that all the genes raised to high frequency by malarial selection are disadvantageous in the absence of malaria; a change in the environment may in general change Darwinian fitness.

The criticisms of Goldschmidt (1940) and others have been adequately answered. Løvtrup takes no account of the work of Fisher (1930, 1954) or Duncan and Sheppard (1963, 1965). His criticisms of the idea that change could come about through the accumulation of minor variations amount to no more than the assertion that what he finds hard to accept must be wrong. Batesian mimicry, to take a specific example, used to be an area where Goldschmidt's pre-adaptationist ideas were strongly put forward. (For similar reasons it was a bone of contention between Mendelians and Darwinians earlier this century (Provine, 1971).) It has been conclusively shown that, far from representing pre-adaptation, mimetic patterns have a complex genetic origin. Superficial examination suggests that such patterns are determined by allelomorphic genes; detailed analysis shows, in fact, they are determined by several loci (at least 6 in the butterfly *Papilio memnon* L.) usually tightly linked as a supergene (Clarke and Sheppard, 1963, 1971, 1973, 1977 and Clarke, Sheppard and Thornton, 1968). The mimetic pattern is perfected by the modulation of other loci in the gene complex that are not associated with supergenes (Sheppard, 1969). Evidence is also available that indicates that other adaptations discussed by Goldschmidt have also been achieved by the accumulation of a series of large and small mutations (e.g. haemoglobin (Weatherall and Clegg, 1976) and myoglobin (Romero-Herrera *et al.*, 1978)).

In this context, it is of great interest that both gain of an atavistic extra digit in guinea pigs (Wright, 1977) and evolutionary loss of limbs in tetrapods (Lande, 1978), both of which may appear to involve macromutations, can arise through the joint contributions of many small effects of a large number of genes. Canalisation of development makes threshold effects appear like macromutations (cf. e.g. Rendel, 1967).

Darwin (Origin, Ch. 4) wrote, "It may metaphorically be said that natural selection is daily and hourly scrutinising, throughout the world, the slightest variations, rejecting those that are bad, preserving and adding up all that are good...".

In the neo-Darwinian theory mutations are as likely to occur before as after the environmental event that makes them advantageous. The fact that mutations occur spontaneously whatever the environment into which they are being introduced cannot justifiably support the hypothesis of pre-adaptation or of purpose in evolution. There is, for example, a rare mutant specimen of the peppered moth that is phenotypically similar to the modern melanic and which was collected in eighteenth-century London some 150 years before melanism became commonplace in the species there. A gene determining a deleterious haemorrhagic trait in *Rattus norvegicus* was detected in the nineteen thirties (Dunning and Curtis, 1939). It was subsequently found to be similar or identical to the allele found that determines resistance to the

drug Warfarin in Welsh populations of rats. Warfarin was introduced as a poison in 1953 and resistance became apparent in 1960 (Greaves and Ayres, 1969; Bishop *et al.*, 1977). There is an homologous allele in the mouse (Wallace and MacSwinney, 1976) and (very rarely) in man (O'Reilly *et al.*, 1964; Denson, 1978). Resistance to Warfarin thus evolved independently in several species and in several European populations of *R. norvegicus*. These observations cover the period before and after the introduction of the drug, and in man Warfarin is used in a restricted way for therpeutic purposes only.

Resistance to organophosphorus poisons in cattle ticks has arisen independently a number of times at different localities as a result of separate mutations of the same cistron (Stone *et al.*, 1976). These forms of resistance and that to other poisons emerged at rates that depend on the time of mutation, the strength of the selection, the degree of resistance conferred and other properties of the character (Stone, 1972). Dieldrin is one toxic substance that is anomalous. Populations of arthropods as diverse as mosquitoes and cattle ticks rapidly become resistant to it. One can assume that populations are pre-adapted (in the "comprehensive" sense), that they are already polymorphic (both hypotheses) or that the locus associated with resistance has a high mutation rate (synthetic). Pre-existing polymorphism through previous exposure to natural analogues of the artificial toxin is the most attractive possibility, though clear evidence of this is not available in the case of dieldrin. A particularly clear example of the process, however, comes from the resistance of several Australian marsupial species to the fluoroacetate poison "Compound 1080" widely used to poison rabbits and rodents (Oliver, King and Mead, 1977). Since plants containing substantial concentrations of fluoroacetates form part of the diet of these marsupials, it may be hypothesised that the resistance to "1080" evolved by natural selection rather than pre-adaptation.

There are sometimes genetical solutions to the problems imposed by a particular environment. One species of plant seems to have adapted to the presence of copper in its soil in different ways (McNair, 1976). *Drosophila melanogaster* in some cases has unifactorially, in others, polygenically determined resistance to D.D.T. (Crow, 1954, 1957); it may adapt to high ethanol concentrations in its larval environment by detoxifying with the product of the ADH *fast* allele or by a polygenically determined process (Briscoe *et al.*, 1975; McKenzie and McKechnie, 1978).

Morphologically similar adaptations may have quite distinct functions. Bishop *et al.* (1978) discuss the function of melanism in two species of moth and in a ladybird beetle. In one moth, *Biston betularia*, there is unequivocal evidence that melanism assists camouflage; in the second moth *Gonodontis bidentata* the function is not known but it is not primarily involved in camouflage while in the beetle melanism may be some sort of direct response to air pollution or an adaptation to living in a clouded environment with little sunshine. The production of melanin is due to lack of functional enzymes in a biochemical pathway (MacIntyre and O'Brien, 1976) and its apparent imperfection has been exploited in two, possibly three, different ways in these species.

3. Løvtrup's Comprehensive Theory

In Section 2, we have shown that the hypothesis which Løvtrup submits as a key point of his "comprehensive" theory, "sometimes not all necessary micromutations are available when needed", is in fact a customary part of neo-Darwinism, and provides one of the many possible explanations of extinction.

His second key point is that the outcome and rate of evolution are dependent on the occurrence of particular mutations. This has been advanced also by Ohta (1972b, 1974), and it is widely recognised that evolutionary rates depend on variability, which is affected by population size and breeding system, by mutation and by selection (cf. Boucot, 1975 and Johnson and Michevich, 1977).

The statement that advantageous mutations arise so rarely that when one occurs in a single individual, "fixation...is possible only through strict inbreeding" not only is based on no evidence whatsoever but also ignores the demonstrations from Fisher (1930) onward that the probability of survival of new mutations is directly dependent upon their selective advantage. The statements which follow about the irrelevance of population genetical theory dealing with outbreeding populations are similarly not based on evidence or argument. The polymorphisms associated with malaria would appear to be a counter-example to Løvtrup's views on the role of inbreeding.

Løvtrup's third premise, that macromutations may allow quantum jumps in structure or foundation, is only non-Darwinian to the extent that it implies pre-adaptation. Otherwise, apart from the fact that mutations having all manner of different effects on the phenotype are known, it presumably simply refers to the growing body of evidence (cf. e.g. Ohta, 1972a,b and Sparrow and Nauman, 1976) that major evolutionary departures may be related to major changes in genome size or organisation. Løvtrup's prime example of a prediction of his theory, that body size differences do not form a continuum, may (should it be correct) also be satisfactorily accounted for by his defective and incomplete subset of the neo-Darwinian theory. However, Roff (1977) has shown that Løvtrup's analysis of body size differences is invalid so that his conclusions cannot be justified at the present, and in any case even if there are phenotypic clusters in size among existing or extinct species, this need not have any implications for the mechanism of evolutionary change. It is, therefore, not clear where precisely his theory may be expected to be useful.

Løvtrup's theory implicitly postulates the existence of optimal fitness, which is not required by the synthetic theory and which is in any case not a meaningful concept (Fisher, 1941; Fraser and Mayo, 1974).

4. Problems in neo-Darwinism

There are important problems in the synthetic theory of evolution. First, there is the problem of falsifiability, as Løvtrup notes. Maynard-Smith (1972) and King (1975) have constructively suggested a number of experiments, bearing on the general theory and on the problem of neutral alleles respectively, which may falsify parts of the theory. Williams (1973) has presented a very cogent account of the general question of falsifiability of evolutionary hypotheses. Van Valen (1976) following these ideas has shown that the importance of competitive natural selection for evolution can be deduced from simple premises about limitations of resources, variability of existing forms, inheritance of these variations, etc. Thus, approaches to the formalisation of parts of evolutionary theory are meeting with more success than previously. (These problems were of course not unfamiliar to Darwin himself; cf. e.g. the quotation in Section 2 above.)

Secondly, there is the problem of variation. It is not surprising that some workers (mistakenly, in our opinion) have concluded, in recent years, that there should always be sufficient variants available for improved adaptation in the face of environmental change, given the realisation that outbreeding organisms are probably heterozygous at 10% or more of all structural

gene loci. This prodigious degree of variation, which implies to some that "mutational pressure (is) the main cause of molecular evolution and polymorphism" (Ohta, 1974), carries with it the implication that many deleterious genes are being fixed, as well as neutral ones, if random fixation is important (Mayo, 1970; Kimura and Ohta, 1974). The basic facts of gene fixation are thus unclear. In this context, we should also perhaps mention the problem of species which appear to have been invariant over very large geological times, despite the fact of substantial environmental change. Such constancy at the gross phenotypic level, possibly not matched at the molecular level, requires investigation.

Thirdly, there is the problem of gene interaction. Selective forces acting on genotypes at a single locus are becoming adequately understood, but multi-locus theory is inadequate (cf. Lewontin, 1974; Ewens and Thomson, 1977). To take two specific examples, Fisher's (1930) fundamental theorem of natural selection has proved extraordinarily difficult to generalise to non-additive variation in fitness (cf. e.g. Samuelson, 1978). Secondly, while much progress is beginning to be made on the problem of the maintenance of variability by mutation at many linked loci, this is still only for the case of additive gene action (Lande, 1976). Thus, another large gap exists in our understanding of the process of natural selection.

Fourthly, the process of speciation is not well-understood at the genetical level. It is this fact which allows ideas like pre-adaptation to persist, in disguised form on occasion, and by providing descriptions which are not explanations to impede investigation of the real problems. Ideas such as those of Sparrow and Nauman (1976) about genome evolution or Løvtrup on body size (cf. also Riedl, 1977) need to be investigated more closely. The population genetics of mutations affecting gene regulation may provide another area where large changes may occur without immediate genetically lethal effect, though as we have seen the basic idea of the importance of macromutations has been shown in one case (mimicry) to be a result of inadequate knowledge.

Finally, there is the problem of extinction. Løvtrup claims that "(i)t 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." This is an adaptation to the species level of Keynes's dictum that "in the long run we are all dead." Current cosmological theory suggests that the universe is running down; on this basis the extinction of all known species is certain. Løvtrup's prediction has no timetable and is not therefore usable.

Neo-Darwinism, of course, cannot predict in general any more precisely. However, Van Valen (1973) has shown that all taxonomic groups for which data exist tend to become extinct at a rate that is approximately constant for a given group. From this, he has deduced that "the effective environment of any homogeneous group of organisms deteriorates at a stochastically constant rate." The idea that the environment is continually deteriorating for any given species was first made quantitative by Fisher (1941), but Van Valen's extensions and new concepts may make it possible to assess extinction in a far more precise manner than heretofore. At the moment, however, it is not possible to specify precisely when a species will become extinct. Thus, both theories, correctly described, simply imply that environmental conditions outside the range of adaptability of a species will lead to the extinction of that species. Since only a limited range of environmental factors is controllable by an organism, and since the state of the environment may not be precisely predictable, this is all one would expect.

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