

## The cost of evolution and the imprecision of adaptation

(Haldane's dilemma/multi-level feedback/human evolution/maximization)

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**ABSTRACT** Comparisons of six hypothetical cases suggest that Haldane overestimated the cost of natural selection by allele substitution. The cost is reduced if recessive alleles are advantageous, if substitutions are large and few, if selection is strong and substitutions are rapid, if substitutions are serial, and if substitutions in small demes are followed by deme-group substitutions. But costs are still so heavy that the adaptations of complex organisms in complex and changing environments are never completed. The rule probably is that most species most of the time are not fully adapted to their environments, but are just a little better than their competitors for the time being.

During the "evolution" of a man-made machine, the maker of it can take it apart and eliminate inferior and substitute improved parts without throwing away whole machines. But in organic evolution, each slightest separate improvement made by natural selection in the great number of parts, processes, and behaviors in an evolving organism is made at the cost of eliminating—throwing away—all the whole individuals that lack the improvement. This is "the cost of natural selection," or of adaptive evolution. Calculation of this cost and of its consequences is one of the most important pieces of unfinished business in modern evolution theory.

### THEORY: THE COST OF SELECTION

Haldane (1), in 1957, calculated that gene (allele) substitutions by selection cost so much that populations must (in effect) choose between evolving at low cost per generation but unadaptively slowly, or more rapidly but at a cost so high as to risk extinction. These alternatives constitute what is sometimes called "Haldane's dilemma." His conclusions have been much criticized, especially by means of complex mathematics; for partial reviews of the criticisms, see ref. 2, pp. 72-74 and ref. 3, pp. 98-102. Here, I shall re-examine the cost of selection in another way, by means of six hypothetical cases and simple arithmetic; the cases cannot prove generalizations but can suggest them or (sometimes) falsify them. And I shall then consider how costs limit actual, complex evolutionary processes and the precision of adaptations, including our own.

#### Two-class, 1-episode cases

**Case A.** Suppose that, in a population of four billion individuals, only one male and one female are homozygous for a recessive allele which allows them alone to survive an atomic holocaust which eliminates all the other individuals. (If all individuals survive, but only the two can reproduce, the others being sterilized by radiation, the effect is the same.) Then one complete allele substitution will have been made by selection (selective elimination) in one generation, at a cost of

$$N_0(4 \text{ billion}) - N_1(2) = 3,999,999,998$$

individuals, and no additional selective substitutions can be made and paid for at the same time, although other, nonselective, random changes comparable to those expected of the "founder effect" may occur in the population's gene pool.

**Case B.** Now suppose that the two survivors escape other hazards and produce ten offspring of which two ( $\delta$  ♀) are homozygous for another recessive allele which allows them to survive (say) a protein shortage which results in the deaths (or failure to reproduce) of the other eight individuals. Then another complete allele substitution will have been made in one generation at a cost of

$$N_0(10) - N_1(2) = 8$$

individuals, and again no additional selective substitutions can be made and paid for at the same time.

These cases suggest the following generalizations which, with modifications, carry over to more complex cases.

[1] In simple, 2-class, 1-episode cases the cost of an allele substitution is  $N_0 - N_1$  individuals,  $N_0$  being the number of individuals in the initial population, and  $N_1$  the number that survive selective elimination and produce the next generation. These cases contradict Haldane's generalization (ref. 1, p. 520) that the cost of one allele substitution "always" exceeds the number of individuals in one generation of a population.

[2] The cost of substitution is the same whether paid in selective deaths (individuals that die prematurely) or in reduced reproduction (individuals not born).

[3] The relation of cost to ability to pay is independent of population size. The cost of a substitution, in numbers of individuals eliminated, is enormously greater in very large than in very small populations, but the larger populations can pay the enormously greater costs. I have never seen this simple but important generalization clearly stated. (But population size has other effects on rates and costs of substitutions; see ¶ 10, 13, 15, 16, 19, and 21.)

[4] The cost of a substitution ( $N_0 - N_1$ ) is independent of the magnitude of genetic or phenotypic difference, if the difference results in complete substitution in one episode. The cost is the same for substitution of one allele, a set of linked alleles, a whole chromosome, a whole genotype, or a whole deme gene pool in deme-group selection.

[5] The theoretical cost of a segment of evolution is therefore in proportion to the number of separate substitutions. An evolutionary advance made by 10 separate small substitutions costs 10 times as much as the same advance made by one large substitution. (And the cost-advantage of the larger substitution is increased if the larger phenotypic difference results in stronger selection and more rapid substitution; see ¶ 14.)

[6] A consequence of ¶ 5 is that multi-level (feedback) selection should favor genetic systems in which genes (alleles) are linked or combined into sets which are selected as wholes. "Regulator genes" (4), which regulate the actions of sets of other genes, may have this effect, although I am not sure about this. However, the initial formation of a linked set of favorable alleles presumably requires that each allele be substituted separately, at the same cost (in elimination of whole individuals) as other allele substitutions. Only after a linked or regulated set of genes has been formed at this cost can it reduce the cost of further

substitutions. So, I doubt if linkages and gene-regulators reduce the costs of evolution of new genetic-structural-functional-behavioral systems, although they may reduce the costs of secondary diversifications.

[7] "Truncation selection" is sometimes suggested as an alternative or supplement to linkage. It supposes an array of genotypes (individuals) distributed along a "scale of fitness," with all those above a dividing line surviving, and all those below selectively eliminated (e.g., ref. 3, p. 100, Fig. 17, with further references). But fitness ( $W$ ) expresses statistical chances of survival, not certainties. The truncation hypothesis first postulates a series of individuals graded in fitness, and then gives the same individuals new fitnesses, of either 1 (sure to survive in this case, although  $W = 1$  is not by definition a guarantee of survival; in fact no genotype can be sure to survive) or 0 (no chance of surviving). This change of fitnesses in mid-hypothesis is not logically permissible. I do not see how "truncation" can reduce the costs of allele substitution in real cases.

[8] In simple, 2-class, 1-episode cases, the minimum cost of one substitution is also the maximum cost that a population can pay in one generation, if  $N_1$  is the minimum viable size of the population. The equation is then

$$\text{Maximum payable cost} = N_0 - N_1 \text{ minimum.}$$

If this maximum is paid for one substitution in one generation, no additional costs of other selective substitutions can be paid in the same generation, although other, random genetic changes may occur. The total cost paid in one generation may be, and probably usually is, divided into fractions paid against several or many separate concurrent substitutions, but since the maximum cost paid per generation cannot exceed  $N_0 - N_1 \text{ minimum}$  (if it does, the population becomes extinct), payments made to one fractional substitution reduce the payments that can be made to others. A corollary is that, in these cases, the number of individuals substituted in one generation cannot exceed  $N_1$ ; a population after selection cannot contain more new-allele bearers than the number of individuals in the population. Additional "surplus" individuals cannot increase the amounts of substitutions that can be made (see ¶ 10). (These limits are modified in serial substitutions, e.g., Case F.)

[9] A consequence of ¶ 8 is that genetically solvent populations, that are well adapted to their environments and carry relatively small unpaid substitutional debts, can make and pay for new adaptations better than can populations still heavily in debt. This is another way of saying that costs of selection limit amounts and rates of evolution.

[10] Most populations produce surplus individuals, more than the number ( $K$ ) the environment can carry, and their "use" in allele substitutions is sometimes thought to "cost the populations nothing." But surplus individuals do cost something, in reproductive effort and consumption of resources, and if they are used in substitutions, the use is not cost-free.

To clarify the effect of surpluses on costs, consider a population held to  $N = K$  adults, with each generation producing  $10K$  progeny which are selectively reduced to  $K$  adults. The surplus is  $9K$  per generation. But only  $K$  individuals (the number in the reduced population) can be substituted (see ¶ 8), and this requires a surplus and a cost only equal to  $K$ . The additional  $8K$  individuals cannot increase the amount of substitution, but must be (selectively) eliminated. So, they add to, or inflate, the costs of substitutions in the same way that increase of money without increase of goods inflates prices (cf. ¶ 3). (But if presence of surplus individuals increases the probability that advantageous alleles will be available for substitution, their production and elimination can be thought of as the cost of

Table 1. Costs of substitution in Case C

Generation	No. of		Cost
	As	as	
$n_0$	$(N - 2)$	2	$\frac{N}{2} - 1$
	$\frac{N - 2}{2}$	2	
$n_1$	$(N - 4)$	4	$\frac{N}{2} - 2$
	$\frac{N - 4}{2}$	4	
$n_2$	$(N - 8)$	8	$\frac{N}{2} - 4$
	$\frac{N - 8}{2}$	8	
$n_3$	$(N - 16)$	16	$\frac{N}{2} - 8$
	$\frac{N - 16}{2}$	16	
Cost to this point, about $2N - 15$			

For each generation the numbers of As and as before and after selection are given under "No. of," and the cost of the selective episode is given on the right.

increasing the quality rather than the quantity of substitutions.)

[11] Another consequence of ¶ 8 is that, if a population pays the maximum cost of one allele (or other) substitution ( $N_0 - N_1 \text{ minimum}$ ) in each generation, a maximum of  $x$  substitutions can be made in  $x$  generations. This maximum is probably reduced in many ways in real cases, but there presumably is a direct relation: the more generations, the more substitutions that can be made. This would seem to give an advantage in rate of evolution to small plants and animals with many generations in a given time. However, maximum and comparative rates may not be important. Multilevel feedback selection may adjust the rate of evolution of each organism to the rate most effective for it, regardless of evolution rates of other organisms.

#### Two-class, $n$ -episode cases

The following cases C, D, and E each supposes a "haploid population." This is somewhat unrealistic but simpler than the diploid case, which is "mathematically tedious and does not add much to a general understanding of the concept's mechanics" (ref. 3, p. 117). *Note: the calculations in these cases are not intended to be precise, but only approximations.* Also, survival coefficients of 1 are unrealistic; no genotypes can be sure to survive. And the fractional individuals in Cases D and E are unrealistic; when individuals are few, outcomes will vary by chance; but when " $As < \frac{1}{2}$ ," an elimination may be assumed to be completed. All these unrealities simplify the cases without, I think, impairing the generalizations they introduce.

Case C. Given: a large haploid population of  $N$  individuals, of which  $N - 2$  carry an inferior allele  $A$  with survival coefficient  $\frac{1}{2}$ , and 2 carry a superior mutant allele  $a$  with survival coefficient 1; 1 episode of selection per generation; and each generation after selection breeding back to  $N$  individuals, the As and as reproducing at the same rate. Then, costs are as calculated in Table 1. *This result is an approximation which is close only for large values of  $N$ .* (For a small value of  $N$ , see Case D.) When  $N$  is large, however, the costs of the substitution in the first four generations add up to almost twice the number of individuals in one generation. In later generations, as the

Table 2. Costs of substitution in Case D

Gener- ation	No. of		Cost
	As	as	
$n_0$	8.0	2.0	Reduced to
	4.0	2.0	give ( $\times 10/6.0$ )
$n_1$	6.7	3.3	Reduced to
	3.3	3.3	give ( $\times 10/6.6$ )
$n_2$	5.0	5.0	Reduced to
	2.5	5.0	give ( $\times 10/7.5$ )
$n_3$	3.3	6.7	Reduced to
	1.7	6.7	give ( $\times 10/8.4$ )
$n_4$	2.0	8.0	Reduced to
	1.0	8.0	give ( $\times 10/9.0$ )
$n_5$	1.1	8.9	Reduced to
	0.6	8.9	give ( $\times 10/9.5$ )
$n_6$	0.6	9.4	Reduced to
	0.3	9.4	
			<u>0.3</u>
Cost to As < 1/2, about 13.3			

This table should be read as a continuous sentence: "Generation  $n_0$  consists of 8 As and 2 as, which are reduced by selective elimination to 4 As and 2 as, which (multiplied by a factor of 10/6.0 to bring the population back to 10) give an  $n_1$  of 6.7 As and 3.3 as, which are reduced. . .". The cost of each episode of selection is given on the right.

number of As decreases, the loss per generation decreases too, but the final, total cost of the substitution will be several or many times  $N$ .

**Case D.** Given: the same situation as in Case C, but with  $N = 10$ , beginning with 8 As and 2 as. Then costs are as calculated in Table 2. (This calculation is carried to only one decimal place.)

**Case E.** Given: the same situation as in Case D, except As with survival coefficient of only  $1/4$ . Then, costs are as calculated in Table 3.

Comparisons of the 2-class,  $n$ -episode cases (C, D, and E) add the following generalizations to those derived from the 2-class, 1-episode cases.

[12] Although an allele substitution completed in one generation costs less than  $N$  individuals, when a substitution is spread over several generations, the cost increases to more than  $N$ , in some cases many times more.

[13] Large populations pay costs in relation not only to their larger size ( $N$ ) but also to the larger number of generations ( $n$ ) required to complete a substitution (compare Cases C and D). The cost of substitutions is therefore relatively as well as absolutely much greater in large than in small populations.

Table 3. Costs of substitution in Case E

Gener- ation	No. of		Cost
	As	as	
$n_0$	8.00	2.00	Reduced to
	2.00	2.00	give ( $\times 10/4.00$ )
$n_1$	5.00	5.00	Reduced to
	1.25	5.00	give ( $\times 10/6.25$ )
$n_2$	2.00	8.00	Reduced to
	0.50	8.00	give ( $10/8.50$ )
$n_3$	0.59	9.41	Reduced to
	0.15	9.41	
			<u>0.44</u>
Cost to As < 1/4, about 11.69			

To be read in the same way as Table 2.

Table 4. Cost of substitution in relation to the force of selection

Case	Survival coefficient of As	Cost
D	1/2	about 13.3
E	1/4	about 11.7
B	0	8

[14] Costs vary inversely with the force of selection and the consequent rate of substitution. Comparison of Cases C and A shows that, in large populations, when selection becomes so strong that all individuals carrying a disfavored allele are eliminated in one episode, the cost of substitution is reduced from several or many times  $N$  to less than  $N$ ; the populations may be reduced to a few individuals, but may recover. And Table 4 shows a relation between force of selection (the reverse of the survival coefficient) and cost of substitution in smaller populations. This relationship has been denied by some evolutionists. Lewontin (ref. 5, p. 219) presents an equation which supposedly shows that intensity of selection does not affect cost of replacements, ". . . since the greater the selection, the greater the load per generation, but the fewer the generations required to complete the gene replacement." But this sums disfavored individuals as if they were a fixed quantity (in which case simple addition rather than an equation would make the point), whereas in real cases the quantity is increased in each generation by reproduction of individuals not yet eliminated. That the cost is in fact (inversely) related to the force of selection and the rate of substitution seems to me clear and important.

**Serial cases**

**Case F.** Now consider a more complex case, of serial substitution, which modifies (but does not invalidate) some of the preceding generalizations. Suppose that, in a given population, 1000 offspring are conceived; that 100 of them are homozygous for recessive alleles that kill them before or during birth, their loss going to the costs of eliminations of the lethal alleles; that of the remaining 900, 500 die nonselective deaths, by accidents including random predation; that of the remaining 400, 390 are selectively eliminated before maturity, their loss going to the costs of substitutions of alleles that affect immatures; and suppose finally that, of the 10 individuals that reach maturity, 2 ( $\delta$ ,  $\varrho$ ) are homozygous for a recessive allele that allows them alone to survive a protein shortage and to reproduce, beginning the next generation with 1000 conceptions. Then, in addition to one complete allele substitution made and paid for in the final episode of selection, several additional substitutions have been partly made by selective eliminations in preceding episodes in the same generation, so that the sum of substitutions made and paid for far exceeds the maximum of one complete substitution in one generation in simpler, 1-episode cases ( $\P 8$ ).

This case suggests two additional generalizations.

[15] Substitutions made in series need not interfere with each other, and there is no obvious limit to the number of serial substitutions that may go on concurrently in an organism with a complex ontogeny. However, large populations can perhaps contain more serial substitutions and divide the costs more finely than small populations can.

[16] Selective eliminations of lethal alleles, and nonselective eliminations, reduce the numbers of individuals in a population but do not affect the ratio of cost/ability to pay, which is primarily independent of population size ( $\P 3$ ), and need not interfere with other selective substitutions. In fact, reduction of

the size of a population by lethals may accelerate substitutions later in ontogeny, and reduce their cost.

Case F is unrealistic in detail—so many lethal alleles are unlikely to appear in a population at one time—but is intended only to introduce the concept of serial substitutions. This is not new. Frazzetta (3), for example, expounds it. But he suggests that, as successive (serial) eliminations reduce the size of a population, the possibility of effective evolution of later stages is reduced, and that (ref. 3, p. 107) “. . . in species that produce myriads of offspring which, by the reproductive age, are reduced to a mere handful . . . selection at older age levels will be no more than a veto on what is left from selection acting at an earlier age.” However, among insects with complete metamorphosis, many of which do produce myriads of offspring which are reduced to relative handfuls of adults, and among which adult characters cannot be acted on at earlier ages, adults often do evolve rapidly and effectively. An example is speciation in *Drosophila*, and especially the apparently recent, explosive diversification of adult *Drosophila* in the Hawaiian Islands (ref. 6, with additional references). In this as in other cases, multi-level feedback selection presumably results in evolution of genetic and population systems that allow effective evolution of all stages of an organism.

[17] All the preceding hypothetical cases have been kept simple by omitting Mendelian complexities: by considering only advantageous recessive alleles in Cases A and B, and only haploid populations in Cases C, D, and E, and by disregarding actual Mendelian probabilities in Case F. Selective eliminations of deleterious recessive alleles in diploid populations are more complex and more costly, as Haldane (1) and many others have emphasized. Space cannot be taken to analyze these complexities here. They modify but do not falsify the following conclusions.

[18] The mathematical concepts of “fitness” ( $W$ ) (which is not the same as Darwinian fitness) and “genetic load” are avoided here, except that fitness ( $W$ ) is mentioned in ¶ 7. They are confusing and in some ways unrealistic concepts, which seem to me to add nothing to understanding of the cost of natural selection. They are defined and discussed in appropriate books (e.g., refs. 7 and 8).

### CONCLUSION: COSTS OF SELECTION

[19] Haldane (1) considered chiefly eliminations of deleterious recessive alleles, and for this and other reasons overestimated the cost of selection. The cost is reduced and/or payment is accelerated if recessive alleles are advantageous; if substitutions are large and few; if populations are small; if selection is strong and substitutions rapid; and if substitutions are serial.

[20] The most cost-effective process may be one in which substitutions of favorable recessive, large or linked, serial alleles occur rapidly and at low cost in small demes in a larger population, and are followed by deme-group substitutions. (This pattern of evolution, emphasized by Sewall Wright, is now generally accepted.) If the individuals in each deme are “linked” by mating preferences or reciprocal altruistic behaviors (9), and if the demes are not too numerous, deme substitutions may be rapid and low-cost too. But costs will still be heavy, and will probably severely limit rates of evolution in actual cases.

[21] However, maximum rates of substitutions and of resultant evolution are not necessarily advantageous. Small populations may complete allele substitutions more rapidly and (for this and other reasons) may evolve more rapidly than large populations, but the large populations may evolve more effectively (10). Multi-level feedback selection presumably de-

termines the mode and rate of evolution most effective in each case.

### THEORY: THE COMPLEXITY AND COST OF ADAPTATION

**Man As an Example.** Preceding calculations allow something to be said about numbers of allele and other substitutions in actual cases. For example, if *Homo* separated from *Australopithecus* four million years ago and if generations have averaged 20 years, 200,000 separate, minimum-cost, 2-class, 1-episode allele substitutions may have been made during the evolution of *Homo* (compare ¶ 11).

Of course this is not a serious estimate but only a first step toward one. Most substitutions probably cost much more than the theoretical minimum. On the other hand, many may have been not of single alleles but of sets of alleles, whole genotypes, and whole demes, and many may have been serial, occurring at different stages of ontogeny. Moreover, different substitutions probably affected each other complexly, so that their costs cannot simply be added together. In view of these conflicting and confusing factors, we can hardly hope to count numbers of substitutions but can only estimate their sums as amounts which are not quantifiable but which do, or do not, seem consistent with amounts of evolution that have occurred. During the evolution of *Homo*, although substitutions possibly equivalent to several hundred thousand separate allele replacements may have occurred, they are better considered as forming an unquantifiable amount which at first thought is not obviously inconsistent with the change from ape to man.

However, second thoughts raise doubts about this. The parts, processes, and interactions that may be acted on by selection in man are numerous and complex beyond calculation. For example, hormones directly or indirectly affect calcification of bone in man in 150 ways that are reasonably well established, and probably in additional ways that are still unknown (ref. 11, pp. 289–296). Each of these hormonal effects on bone is presumably under some degree of selection, and the hormones have a multiplicity of other effects on other organs and processes, each also presumably under selection. And the hormone system is only one among many other complex, complexly interacting systems in man. A human individual is indeed an inconceivably complex, complexly organized set of interacting parts and processes, on which selection acts in inconceivably complex ways, and the environment which determines the directions and forces of selection is inconceivably complex too, and continually changing. How, in this context of inconceivable complexity and endless environmental change, can slow and costly natural selection result in precise or perfect adaptation? I think it cannot and does not.

**Other Evidence.** I have four reasons for thinking that adaptations are usually not precise or perfect.

First: man's own adaptations are imperfect. Our backs, hearts, feet, etc. are not yet fully adapted to the two-legged posture that our ancestors assumed more than five million years ago, and we are still imperfectly adapted psychologically to our new social environment.

Second: among the carabid beetles I work on, closely related species that seem to be living in the same way in similar environments usually differ in many small, apparently nonadaptive details. I used to take on faith that these details are precise adaptations to present or past environmental differences that I cannot see. Now, I think they may be manifestations of adaptive imprecision.

Third: as a species evolves complex adaptations to its environment by a costly, slow process of selection, its environment

evolves too, partly by evolution of associated species. A species' "target" of adaptation is therefore continually moving and never reached, and the species must continue its evolution endlessly if it is to keep its place in its community. This has recently been called "The Red Queen's Hypothesis" (ref. 12, p. 17, with note 32), after Alice's Red Queen, who had to keep running just to stay where she was, but it has been at least hinted at before, for example by Fisher (ref. 13, pp. 46-47) and Kimura and Ohta (ref. 2, p. 79).

And fourth: if adaptations were perfect, adaptive evolution would stop, but it has not.

### CONCLUSION: THE IMPRECISION OF ADAPTATION

That adaptations are expected to be in theory and are in reality imprecise or imperfect has been suggested by Darwin (cited by de Beer) and emphasized by de Beer (ref. 14, pp. 9-11), who calls it "a principle of great importance." Considerations summarized in the present paper suggest that most species most of the time are in fact far from perfectly adapted to their environments, but are just a little better than their competitors, for the time being. If so, the current fashion among evolutionists of assuming that selection must have "maximized" particular reproductive strategies or feeding behaviors, and of basing mathematical models on the assumption, is dangerously unrealistic. Selection evidently can produce striking adaptations (e.g., man's erect posture) rapidly, by focusing on them, but the primary adaptations may not be as precise as they seem to us to be, and secondary modifications (e.g., those secondary to man's erectness) may evolve much more slowly and much less precisely.

**NOTE.** This paper is intended only as a new introduction to an important but confusing subject, and has deliberately been kept simple, with few references. Grant and Flake (15-17) treat the cost of selection more mathematically (stressing Wright's subdivided-population model, but differing from my conclusions in several ways) and give additional references.

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