

## RECOMBINATION AND THE RATE OF EVOLUTION

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THE process of genetic recombination has evolved because it confers a selective advantage on its possessors. Two fundamentally different suggestions have been made as to the nature of this selective advantage. The first, originating with WEISMANN (1904) and formulated more precisely by FISHER (1930) and MULLER (1932), is that populations with genetic recombination evolve more rapidly than those without, and hence survive environmental changes which cause the extinction of asexual populations. Although widely accepted, this explanation has a drawback (which was clearly recognized by FISHER); it relies on selection acting between groups or species and not between individuals. It is the species which evolves or goes extinct, not the individual. To the extent that species go extinct much less frequently than individuals die, group selection is less effective than individual selection. This has led some evolutionists to doubt whether an adaptation as complex as sexual reproduction and genetic recombination could have evolved by a process as inefficient as group selection.

The alternative explanation, strongly argued by WILLIAMS (1968, 1973), is that recombination is an immediate advantage because an individual which produces a more variable progeny is more likely to produce at least some offspring of very high fitness. If inter-individual selection is very intense, so that only those individuals with the optimal genotype for the local environment are able to survive, it is possible that sexual reproduction might be an immediate advantage. Perhaps the strongest evidence in favor of this explanation is the fact that in those species in which sexual and asexual generations alternate, the sexual generation always precedes dispersal into new and hence unpredictable environments. There are difficulties with this explanation (see MAYNARD SMITH 1971), but it certainly deserves further investigation.

To make matters still more confusing, it seems likely that to understand the evolution of parasexual processes in prokaryotes we shall have to consider selection acting not only at the level of the cell and the population, but also at the level of the sex-determining factors themselves, since these are self-replicating entities capable of multiplication which is to some degree independent of the cell in which they find themselves.

In addition to the possible advantages conferred by sex, there is an immediate and large disadvantage associated with it, at least in organisms with anisogamy. Thus consider two allelic genes  $A$  and  $A^1$ , and suppose if  $A$  is present in an oocyte it causes that oocyte to undergo meiosis, to discard half the genes in the oocyte to the polar bodies and to accept in their place genes from another individual, whereas allele  $A^1$  causes the oocyte to develop parthenogenetically without

TABLE 1

*The ratio R of the rate of evolution of a sexual as compared to an asexual population*

	$\frac{R}{L}$
FISHER (1930)	$L$
CROW and KIMURA (1965)	$\frac{NuL}{s} \log N$
MAYNARD SMITH (1968)	1
ESHEL and FELDMAN (1970)	can be $< 1$
MAYNARD SMITH (1971)	$L$
KARLIN (1973)	depends on $D_0$

## Notation:

- $N$  = population size  
 $L$  = number of simultaneously evolving loci  
 $u$  = rate of favorable mutation per locus  
 $s$  = selective advantage per locus  
 $D_0$  = initial value of linkage disequilibrium

meiosis. Clearly allele  $A$  has only half the chance of being transmitted to the next generation that allele  $A^1$  has. No such immediate two-fold disadvantage is associated with sexual reproduction in organisms with isogametes, as is apparent if one considers the biomass associated with each genome rather than the number of cells. Since sex and meiosis almost certainly preceded anisogamy, this disadvantage of sex need not be taken into account when considering the origin of sex, although it is highly relevant when considering its maintenance in higher organisms.

## SEX AND THE RATE OF EVOLUTION

If sexual populations evolve more rapidly than asexual ones, this fact has important consequences for evolution, whether or not it is also the reason why sex itself has evolved. It would therefore be pleasing if population genetics could give an agreed estimate of how different the rates actually are. Unfortunately they cannot, as is shown in Table 1, which lists some of the answers which have been given. The discrepancies exist because different authors have considered different models or sets of assumptions—for example, finite or infinite populations, a suddenly or a continuously changing environment, two or many loci. What the table does show is how dependent the answer is on the model. By comparing some of these models, we can get some insight into the problem.

The simplest model (MAYNARD SMITH 1968) considers an infinite haploid population. It is supposed that the environment has just changed, so that the common alleles  $a$  and  $b$  at two loci have become unfavorable and initially uncommon alleles  $A$  and  $B$  have become favorable. The genotypes, with their fitnesses and frequencies, are as follows:

genotype	<i>ab</i>	<i>Ab</i>	<i>aB</i>	<i>AB</i>
frequency	$P_{ab}$	$P_{Ab}$	$P_{aB}$	$P_{AB}$
fitness	1	$1+s$	$1+t$	$(1+s)(1+t)$

Considering first an asexual population, it is easy to show two things:

(i) The initial frequencies are in linkage equilibrium—that is,  $D = P_{ab} P_{AB} - P_{Ab} P_{aB} = 0$ —if prior to the environmental change the alleles *A* and *B* were maintained by recurrent mutation.

(ii) If in any generation  $D = 0$ , then  $D = 0$  after one generation of selection.

It follows that  $D = 0$  throughout the replacement of *a* and *b* by *A* and *B*. Now the only difference that sexual reproduction can make is to bring  $D$  closer to zero. Since  $D = 0$  anyway, sex can make no difference to the rate of evolution.

Note that it was assumed that fitnesses are multiplicative. ESHEL and FELDMAN (1970) have since shown that with non-multiplicative fitnesses sex can even slow the rate of evolution.

The main conclusion from the model is that sex is only an advantage if the initial population is in linkage disequilibrium, with  $D < 0$ . I suggested that the obvious situation in which sex would be advantageous is as follows. Suppose there are two habitats, in which genotype *Ab* and *aB* respectively are optimal, and that a new habitat becomes available for colonization in which *AB* is optimal. The initial colonists may be a mixture of *Ab* and *aB* genotypes. If so, sex would greatly accelerate the increase of *AB* genotypes.

This still seems to me an important situation in which sex is advantageous. Another reason why there may be initial linkage disequilibrium is that actual populations are finite, not infinite. KARLIN (1973) has shown that for finite populations the effect of sex depends critically on initial conditions. Thus if the expected initial frequency of the favoured genotype *AB* is very small, the genotype will be completely absent from most finite populations. In such populations,  $D < 0$ , and sexual reproduction will accelerate evolution.

What if evolution occurs simultaneously not at 2 but at  $L$  loci? MAYNARD SMITH (1971) obtained an approximate solution to this problem. Suppose there is a finite haploid population of size  $N$  which is initially genetically homogeneous for the alleles  $abc \dots l$ . The environment then changes so that alleles  $ABC \dots L$  are favourable. With the notation of Table 1, it turns out that if (very approximately)  $N < 1/10u$  sex makes little difference to the rate of evolution. For large  $N$ ,  $R \approx L$ , the number of simultaneously evolving loci. This conclusion was stated by FISHER (1930), without proof and without qualification about population size.

STEADY-STATE MODELS OF EVOLUTION

It is clear that if there is a sudden environmental change, an initially homogeneous sexual population can adapt substantially more rapidly than an asexual one. However this conclusion is of doubtful relevance to the real world. The response of a sexual population to a sudden environmental change usually depends on genetic variance already present, as is clear from artificial selection

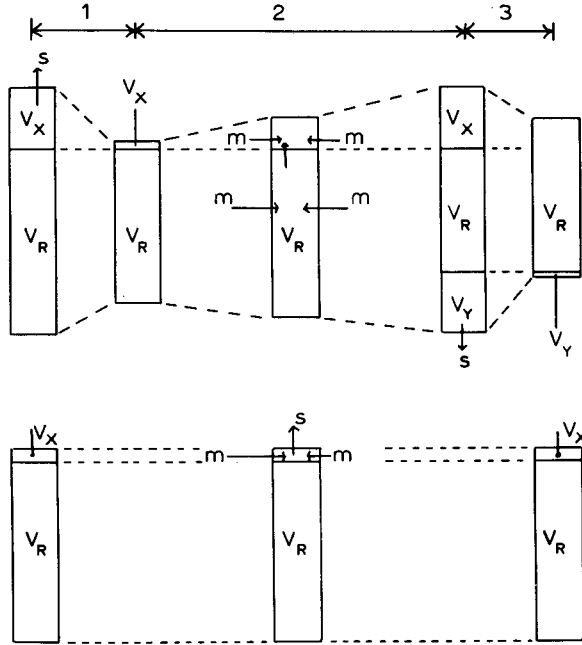


FIGURE 1.—Models of evolution in a sexual population: above: intermittent selection; below: long-continued selection.  $V_X$ ,  $V_Y$ : genetic variance for characters  $X$  and  $Y$ ;  $V_R$ : residual genetic variance;  $m$ : mutation;  $s$ : selective fixation.

experiments. What we would like to do is compare the rates of evolution which can be sustained indefinitely in a continuously changing environment.

This distinction between responses to intermittent and to long-continued directional selection is crucial. It is illustrated in Figure 1, which compares two extreme models of evolutionary change in a sexual population. In Figure 1A, it is supposed that selection for any phenotypic character or group of characters is intermittent in magnitude or direction. There are three periods illustrated:

Period 1. Intense directional selection for a group of characters "X" reduces the genetic variance  $V_x$  of these characters; because of linkage and pleiotropism there will be a small reduction in the variance  $V_R$  of characters not under directional selection.

Period 2. Directional selection relaxed. The variance  $V_x$  is restored; the restoration is ultimately caused by new mutation, but there may be changes in the secondary effects of genes so that new genes come to affect character  $X$ .

Period 3. Intense directional selection for character  $Y$ .

According to this model the response of sexual populations to changes in the environment resembles the response of a captive population to artificial selection in that it depends on pre-existing genetic variance. A model of this kind is appropriate only if periods of directional selection are separated by much longer periods of relaxed or normalizing selection.

An alternative model is shown in Figure 1B. It is supposed that there is long-

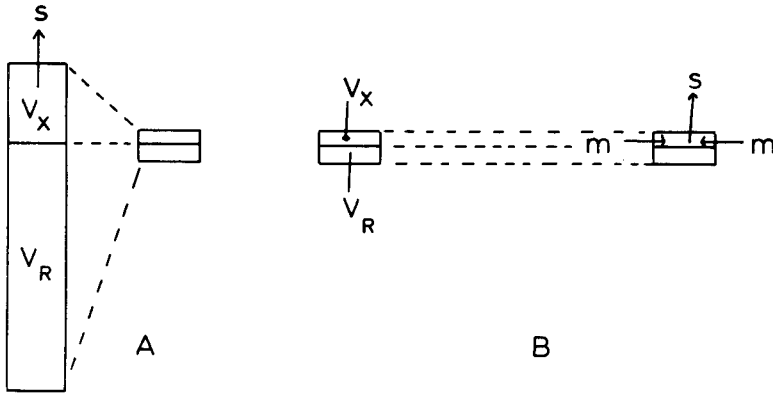


FIGURE 2.—Models of evolution in an asexual population: A: intermittent selection; B: long-continued selection; notation as in Figure 1.

continued directional selection for a single group of characters. The additive genetic variance of the selected characters will be small, and there will be a short-term balance between new mutation and fixation by selection. I shall refer to this as a steady state model.

In contrast, Figure 2 pictures evolution in an asexual population. Such a population is composed of a number of clones. Figure 2A shows the response of an asexual population to intense directional selection for character X. Such selection is equivalent to selecting only that clone with the optimal genotype; it eliminates not only the genetic variance for X, but all genetic variance. It will be clear that evolution in an asexual population normally consists of changes within individual clones. If the environment changes, a clone can only adapt to that change by incorporating newly occurring mutations. The appropriate model is Figure 2B.

The first serious attempt to compare quantitatively the expected rates of evolution of sexual and asexual populations in a "steady-state" model (Figures 1B and 2B) was made by CROW and KIMURA (1965). Unfortunately I cannot accept their conclusions (MAYNARD SMITH 1968; CROW and KIMURA 1969) because they seem to me to rest on the (unstated) assumption that every favorable mutant that occurs is different from every other one. It may seem that this assumption does not matter, because the rate of specific favorable mutations may be of the order of  $10^{-8}$  per generation, and hence reoccurrences are not frequent. However it turns out that sex only becomes important as  $N$  approaches  $1/u$ , so the difficulty is a serious one.

I have recently obtained an approximate solution to the steady-state model considered by CROW and KIMURA, but without the offending assumption that mutations are unique events. With the notation of Figure 1, if  $N < s/10u$ , then sex makes little difference. As  $N$  increases to order  $1/u$ , the ratio  $R$  reaches a maximum of (very approximately)

$$R \simeq \frac{1}{4s} \log (W_{MAX}/\bar{W}),$$

where  $W_{MAX}/\bar{W}$  measures the intensity of selection. Thus  $\bar{W}$  is the mean fitness

of the population, and  $W_{MAX}$  the fitness the population would attain if environmental conditions were held constant and the population were given time to complete its adaptation to it.  $W_{MAX}/\bar{W}$  measures the extent to which the population lags behind the environment. If  $W_{MAX}/\bar{W}$  exceeds some critical value (which will depend on the type of organism concerned) the population will go extinct. Therefore by assuming  $W_{MAX}/\bar{W}$  constant, I assume that environmental conditions are changing as rapidly as possible consistent with the continued survival of the species.

To get some idea of the meaning of this result, suppose that  $u = 10^{-8}$  and  $s = 0.01$ . Then for  $N < 10^5$  sex confers no advantage. The maximum advantage for sex occurs for  $N$  of the order  $10^8$ , and will be greatest if the intensity of selection is high and the advantage per locus small; for  $s = 0.01$ , the maximum value of  $R$  would perhaps lie in the range 25–75.

It is clear that sexual reproduction can accelerate evolution very substantially, particularly in large populations evolving simultaneously at many loci. But many problems remain. First, to what extent has the origin and maintenance of sexual reproduction been brought about by its long-term effects on the rate of evolution, and to what extent by its short-term effects on the fitness of offspring? Second, to what extent is the rate of evolution of populations limited by the supply of new genetic variability (and hence by the mutation rate) as is assumed in steady state models, and to what extent is it limited by the intensity of selection acting on pre-existing genetic variability?

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