EVOLUTION

Clicking into decline?

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TWENTY five years ago, H. J. Muller[1] pointed out that a finite asexual population may decline in fitness through the chance accumulation of deleterious mutations — a process known as Muller's ratchet[2]. The process has been invoked to explain a variety of phenomena, ranging from clonal senescence in ciliates to the genetic deterioration of the Y chromosome. It is difficult, however, to produce a convincing experimental demonstration of the ratchet. In a report on page 454 of this issue[3], Chao now presents evidence for its operation in an RNA virus.

The virus concerned is $\phi 6$, an RNA phage infecting the bacterium *Pseudomonas phaseolica*. Its genome consists of three segments contained within a single phage particle. If a cell is infected by two genetically different phages, recombination does not occur within segments, but segments may reassociate in forming new particles. This reassociation has the effect of recombining parental genes on different segments. A possible functional explanation of the segmented genome structure (which is not uncommon among RNA viruses[4]) is that it serves to retard Muller's ratchet.

Chao maintained 20 lines of the phage for 40 growth cycles, each cycle involving reduction of the population to a single particle, followed by growth to about 8×10^9 particles. After 40 cycles, the fitness (measured as the rate of multiplication in a paired growth experiment) of these clones was compared to that of a genetically marked parental clone. The transferred clones varied widely in fitness, but the mean value was significantly reduced to 78 per cent of that of the parental clone. Chao interprets this decline as arising from Muller's ratchet.

To evaluate this, we must understand how and when the ratchet operates. Suppose a population consists of N individuals, of which n_0 have no deleterious mutations. If n_0 is a small number, then even though individuals with no mutations are the fittest in the population, it may be that, by chance, all n_0 will die without leaving progeny. If there is recombination, the optimal class can be regenerated, because an individual with no mutations can be produced as a recombinant between two individuals carrying deleterious mutations at different sites. But in the absence of recombination, once the optimal class has been lost it cannot be regenerated (except by the unlikely occurrence of back mutation or compensating mutation): the ratchet has clicked round one notch. This process will occur only in a finite population, but it does not mean that the population must be small. Haigh[5] showed that, assuming multiplicative fitnesses, $n_0=N\exp(-U/s)$, where U is the rate of deleterious mutation per genome, and s the selective disadvantage caused by a single mutation. So if the harmful effect of a single mutation is small, the ratchet will operate even in a very large population. However, it will operate more rapidly if the population is small, or, as in Chao's experiment, is periodically reduced to a single individual.

Processes other than Muller's ratchet may have been involved in the deterioration of the transferred lines. Genetic drift (that is, random sampling in a finite population) has two quite distinct effects on the fitness of a finite population. First, it may by chance eliminate the n_0 fittest individuals, which is the process of Muller's ratchet. Second, it disguises fitness differences, so that the effective selective disadvantage, s, caused by a deleterious mutation is smaller than it would be in the absence of drift. If $s < U/\ln N$ in Haigh's model, then the optimal genotype would not even exist at equilibrium in a population with recombination; that is, n_0 would be less than 1. This is the distinct phenomenon of the 'error threshold' in a finite population[6]. Chao's experimental protocol ensures that any mutant which is capable of forming a detectable plaque at all has the same fitness as the original strain, which means that mutations with small deleterious effects will not be selected against. The process of repeatedly passing each lineage through a bottleneck of any one virus capable of forming a plaque means that the lineage simultaneously faces the twin problems of Muller's ratchet and the error threshold, the latter induced by such extreme genetic drift.

The high mutation rate of RNA viruses, the periodic reduction to a single individual and the absence of reassortment of segments between genetically different viruses would all favour the operation of the ratchet. It is therefore plausible that the decline in fitness of the transferred lines was caused by the accumulation of deleterious mutations. It is harder to decide whether, in nature, the segmental genome structure serves to prevent the ratchet operating. If there is no recombination within segments, the ratchet will

A fresh start for Mount St Helens

EXACTLY 5 months after the cataclysmic eruption of 18 May 1980 removed the top 400 metres of Mount St Helens and the whole of its north flank, leaving a crater 1.5 km across, renewed magmatic activity started the slow reconstruction of the volcano. The lava dome glowing in the centre of the picture first appeared on 18 October of that year (two earlier nascent domes were blown away by explosive eruptions). Then it was around 10 metres high and 25 metres across. At the end of its last active phase in October 1986 (when the photograph above was taken) the dome stood 267 metres above its vent. From photographic monitoring, J.H. Fink *et al.*, on page 435 of this issue, show that the dome grew by a gradual swelling from within (endogenous growth), punctuated by fracturing that allowed lava to flow over the stretched carapace. Although the latter, extrusive mechanism was initially the dominant mode of growth that has since weakened while endogenous growth has continued undiminished. The authors relate this change to the thickening of the dome's crust, which makes fracture less likely. (Photograph by Lyn Topinka, USGS.) R.P.