

EVOLUTION

Rapid change explained by a larger population

In eukaryotes, observations of rapid adaptation often seem at odds with estimates of mutation rate and effective population size (N_e). A new analysis of a classic example of rapid adaptation — the evolution of insecticide resistance in *Drosophila melanogaster* — explains how complex alleles can evolve quickly and suggests that assumptions about adaptation in eukaryotes need to be reconsidered.

Within a few years of the introduction in the 1950s of insecticides that target acetylcholine esterase, resistance mutations in the acetylcholine esterase (*Ace*) gene had emerged and alleles carrying combinations of four *Ace* point mutations are now found at high frequencies in natural populations of *D. melanogaster* worldwide. Karasov and colleagues examined the evolution of these alleles by analysing a 1.5 kb region spanning *Ace* in ancestral African fly populations and in pre-1950 and recent populations from other continents. They found no evidence that the resistance alleles pre-dated the environmental change, which has been one suggested explanation for rapid adaptation. Instead, the resistance alleles, including a complex allele that involves three mutations, must have evolved and spread within the subsequent 1,500 generations.

Intriguingly, the authors also found many identical resistance mutations on haplotypes that differ at sites close to the adaptive mutations. This could be explained by recombination and mutation events during the increase in frequency of the adaptive mutation (this is known as a ‘hard’ selective sweep) or by several independent, identical adaptive mutations that occur on different haplotypes and increase in frequency simultaneously (a ‘soft’ selective sweep). Karasov *et al.* demonstrated that, even with strong selection, the observed mutation pattern is highly unexpected under the model of hard sweeps. Furthermore, they showed by simulation and analysis that only if the population is much larger, such that the parameter Θ — a product of mutation rate and N_e — is far greater than standard estimates, could the empirical data be explained. This is because many more mutations would enter the population at each generation and soft selective sweeps would be very common.

The authors suggest that N_e for *D. melanogaster* over the past 1,000–1,500 generations must have been at least 100-fold larger than commonly believed. Estimates of N_e are usually based on standing variation, but the authors explain that such estimates are very sensitive to even rare periods of small population size, and that the N_e over short periods of time during which adaptation takes place could generally be much larger — on the order of the census size. They suggest that adaptation in eukaryotes that have extremely large census sizes can exploit existing genetic variation and is not limited by ‘waiting’ for a mutation to occur.

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ORIGINAL RESEARCH PAPER Karasov, T., Messer, P.W. & Petrov D. A. Evidence that adaptation in *Drosophila* is not limited by mutation at single sites. *PLoS Genet.* **6** e1000924 (2010)
FURTHER READING Charlesworth, B. Fundamental concepts in genetics: effective population size and patterns of molecular evolution and variation. *Nature Rev. Genet.* **10**, 195–205 (2009)

