EVOLUTION

Different by design

The predictions of the model apply to any clonal population — including metastatic cancer cells, which develop diverse metabolic efficiencies when subjected to chemotherapy

Look at bacteria in a simple, homogeneous environment and you will see a variety of different metabolic phenotypes. It has been supposed that this rich phenotypic diversity must be transitory, but a new model concludes that stable diversity can be maintained in a population. Metabolic trade-offs that exist naturally in populations favour the coexistence of subpopulations sitting on different parts of the same fitness landscape and thus lead to diverse phenotypes.

It had previously been reported that clonal populations of bacteria grown in a chemostat maintain considerable diversity. Stimulated by this experimental finding, the authors developed a mutation-selection model to describe how the fitness landscape varies as key

parameters are altered. The simplest model incorporated the effect of a single metabolic trade-off, between resource-uptake rate and cell yield; some genotypes take up nutrients quickly but use it inefficiently, whereas others have a slower uptake but use resources efficiently.

Owing to these trade-offs, the fitness landscape has a high but narrow peak and a lower fitness but flatter component. As expected, at low mutation rates, the theory predicts low diversity in the population, which is dominated by individuals at the high fitness peak. By contrast, under high mutation rates, the theoretical population is dominated by individuals from the lower and flatter landscape that consists of a larger number of mutationally robust but inefficient genotypes.

What was not previously recognized was that, at intermediate mutation rates, both 'fit' and 'flat' subpopulations can be maintained. When only one trade-off is considered, the fit and flat subpopulations coexist only in a narrow range of intermediate mutation rates. However, as more trade-offs are added, the population has a wider range of intermediate mutation rates in which the lineages occupying both the fit and the flat parts of the landscape coexist. It is this coexistence that supports the rich

and stable diversity of phenotypes seen even in a homogeneous environment.

The population dynamics highlighted in this work cannot be accounted for by previously invoked principles, such as weak selection (if a heterogeneous population is allowed to evolve, one fit genotype will predominate) or by a simple balance between mutation and selection. Furthermore, the trade-offs that are incorporated in the model are also seen in real physiological settings — even in eukaryotes — so the model is true to real-life situations.

The predictions of the model apply to any clonal population — including metastatic cancer cells, which develop diverse metabolic efficiencies when subjected to chemotherapy — and to different taxonomic levels, from cells within individuals to species within ecosystems. The findings also warn against using antimicrobial drug treatments that kill cells by increasing the mutation rate. Such treatments would, in fact, be predicted to shift the population towards a flatter and therefore more robust fitness peak.

Tanita Casci

ORIGINAL RESEARCH PAPER Beardmore, R. E. et al. Metabolic trade-offs and the maintenance of the fittest and the flattest. *Nature* 27 Mar 2011 (doi:10.1038/nature09905)