

EVOLUTION

Something new

The steps that lead to evolutionary novelty are seemingly simple ones — heritable genetic variation causes phenotypic changes, which become the material for selection. However, genetic systems are famously robust — how does selection even hope to see a mutation amidst so much genetic buffering? And how does a novel feature actually arise? Two studies explore these two questions, respectively, in an experimental and computational setting.

Although organisms resist genetic or environmental change, this robustness can be broken by the inactivation of phenotypic capacitors: these genes hide a large amount of genetic variation, which is unleashed when they are functionally compromised. How many ways are there to break a robust network? To answer this question, Siegal and Levy turned to viable knockouts of individual genes in budding yeast to identify those that, when absent, lead to high variation in multiple non-redundant phenotypes.

More than 4,000 single-knockout haploid strains were screened for 220 cellular phenotypes using automated image analysis. Over 300 genes (5% of the yeast genome) qualified as capacitors: these are involved in crucial cellular processes (such as maintaining chromosome stability) and are highly connected — that is, they are network hubs — and the higher their

network connectivity, the greater their potential for phenotypic change. Loss of phenotypic robustness might therefore be a common cause of evolutionary change, caused by disrupting one of the many non-essential components of cellular networks.

Alon and colleagues have investigated a different question: how do organisms generate novelty? That is, how are random mutations converted into potentially useful properties? The answer lies in the design of biological systems.

The authors used a computational simulation in which 'organisms' (logic circuits or RNA secondary structures) were asked to evolve over many generations in different types of environment. When the organisms evolved towards a fixed goal, the 'solutions' were non-modular, that is, they cannot be separated into independently performing units. If, conversely, the goal varied between different but related goals (that is, containing a different combination of subgoals) then the solution was always modular. In addition, organisms that were trained on switching goals adapted to a new subgoal with fewer mutational steps — and therefore much more quickly — than organisms that have previously evolved to a fixed goal, and the more complex the goal the greater the advantage of being trained by the goal-switching strategy.

The conclusion is that organisms exposed to related goals store a memory of their past environment that, importantly, also makes them more adaptable to future environments. Therefore, organisms are designed for translating random changes into useful phenotypes.

The papers propose new ways of viewing the dynamic relationship between genotype and phenotype, and reinforce the importance of genetic architecture in mediating between mutational processes, phenotypic evolution and, increasingly, the environment.

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FURTHER READING Pigliucci, M. Is evolvability evolvable? *Nature Rev. Genet.* **9**, 75–82 (2008) | Wagner, G. P. et al. The road to modularity. *Nature Rev. Genet.* **8**, 921–931 (2007) | Ohya Y. et al. High-dimensional and large-scale phenotyping of yeast mutants. *Proc. Natl Acad. Sci. USA* **102**, 19015–19020 (2005)

