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EVOLUTION

A tinkerer's tales

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The general framework in which evolution acts — mutation followed by selection — is understood and accepted by (almost) everyone, but what concerns practising evolutionary biologists most is what goes on at the nitty-gritty level. How does a trait get from A to B? How many paths can evolution take? And are they all equally probable? Universal answers to these questions do not exist but three papers have each used a different approach to address one of these fundamental problems.

The three articles examine the routes that evolution takes in creating an adaptive function. One study, by Prud'homme, Gompel and colleagues, concentrated on the black spot that exists on the male wing of some *Drosophila* species. The wing spot has evolved independently in two lineages, where it is used to woo females, and in both cases the evolution of the pattern involves the *yellow* pigmentation gene. What is most interesting is that the *cis*-regulatory elements that have been used in the two cases are distinct, indicating that evolution can use different mechanisms to reach a convergent, adaptive endpoint.

The repeated use of the *yellow* gene in different lineages raises another theme in evolution — constraint. That constraint exists was the strong conclusion to emerge from the work of Weinreich and colleagues when they addressed a related issue: how many paths can a protein take towards a fitter state? Their choice was the evolution of bacterial β-lactamase, which can evolve a 100,000-fold increase in antibiotic resistance by acquiring just five point mutations. Of the 120 hypothetical trajectories to drug-resistant alleles, 102 are inaccessible to evolution. This prediction was based on the probability of fixation of mutant combinations; in fact, the situation is more extreme than this, because of the 18 plausible combinations as few as 2 are probable, indicating that the path to adaptive protein evolution is largely predictable.

Gradual changes and stepwise optimization are fine in principle, but how, in practice, do you end up with the level of precision that is seen in complex molecular interactions? Bridgham and colleagues address this question with respect to the distinct specificity of the mineral corticoid hormone receptor for its ligand, aldosterone. This and similar relationships present a conundrum: the receptor and ligand match each other perfectly, so how could the evolution of one partner be explained unless the other is already present? Modern gene sequences say little about how the system evolved so the authors used phylogenetic information to reconstruct ('resurrect') the sequence of the ancestral receptor. Surprisingly, the receptor already had some affinity for aldesterone — not because aldesterone was present but because of the existence of a structurally related molecule. This is a case of an old molecule being exploited to acquire a new function — a switch that, the authors discovered, was only two amino-acid mutations away. Whereas Weinreich's study looked at all the evolutionary paths that could have occurred, this work examined those mutations that actually took place. The theory of evolution is therefore safe for now, and has been tested in precisely the way Darwin had suggested.

These three studies allow us to inch a little closer to discerning the subtler mechanics of evolution by suggesting that evolution does not generate complexity by creating new parts, but by tinkering with existing components (be they *cis*-regulatory sequences or proteins) and increasing the number of ways in which they interact.

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ORIGINAL RESEARCH PAPERS
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Prud'homme, B. & Gompel, N. *et al.* Repeated morphological evolution through *cis*-regulatory changes in a pleiotropic gene. *Nature* **440**, 1050–1053 (2006)
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