thesis

Change is good

Think of evolution: adaptation through time as a consequence of variation, selection and iteration. If you're a physicist, or an applied mathematician, you might think of an abstract dynamical process — some kind of stochastic flow over a fitness landscape, with populations generally evolving from areas of lower fitness toward those of higher. They may ultimately come to reside, perhaps, on peaks in that landscape, these positions representing local optima — a particular set of characteristics from which further adaptation and improvement is difficult.

This idea of adaptation as a climb through a fitness landscape was originally suggested by biologist Sewall Wright (*Proc. 6th Int. Congr. Genet.* 355–366; 1932). Today it takes a central place in mathematical thinking about the processes behind evolutionary adaptation. But does it really make sense? Surprisingly, the answer is only now becoming clear.

Wright proposed this now-familiar idea in the 1930s, nearly 60 years after Charles Darwin's death. Before that — going back to Darwin himself — theorists saw evolution from a 'micromutationalist' point of view, emphasizing the extremely gradual and incremental nature of the process. A population, in this view, becomes more adapted to its environment gradually, through countless tiny changes, never taking any evolutionary leaps. It was further supposed that the infinitesimal character of each adaptation enabled organisms to fit their environments precisely by virtue of many fine-tuned adjustments.

In principle, one might think of such evolution as occurring on a gentle landscape with a single peak, but why bother? Mathematically, these ideas took form in a theory developed by Ronald Fisher, who built a statistical approach that followed the effects of individual genes on an organism's phenotype, in essence assuming infinitesimal contributions from an infinite number of genes that have no interactions with one another. Naturally, this made the mathematics easier — like a theory of gases of non-interacting particles.

Only in the 1980s did experiments finally test this perspective, revealing that the genetic changes driving evolution often cause quite large effects on an organism's character. Sometimes radical adaptive changes in a species' phenotype took place on the basis of only a small number of genetic changes. Studies with bacteria placed into new environments also found that adaptation early on generally took place through genetic changes having larger fitness effects than those occurring in later adaptation (for a review, see H. Allen Orr, *Nature Rev. Genet.* **6,** 119–127; 2005).

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Over the past three decades, and spurred by these inconvenient results, biologists have come to respect the complexity of the genetic interactions that lie behind adaptation. Genetic changes do not generally contribute independently to fitness, but interact with one another (so-called epistatic interactions). Hence the natural rise of the notion of a fitness landscape, and the idea that evolution reflects adaptive walks over complex landscapes where the resulting dynamics may be very surprising and counter-intuitive.

A host of theoretical developments — associated with researchers such as Motoo Kimura, John Maynard Smith, Stuart Kauffman and Wright — have emphasized the richness of this view, where the nature of evolution should reflect the character of the fitness landscapes we see in reality. In particular, as Kauffman has argued, there seems to be something in nature that makes these fitness landscapes effectively searchable; organisms may have evolved so as to interact in a way that makes further evolution possible (see Kauffman's 2003 book, *Investigations*).

This view makes it possible to explore questions that the older, gradualist view suppressed. Do most natural adaptations result from new genetic mutations or instead from newly realized benefits from existing genetic variation? Does most adaptation occur through infinitesimal benefits from a large number of mutations, or rather from a few mutations that have large phenotypic effects? Does a population evolve in fitness gradually towards an optimum, or does the speed change — improvement happening at first quickly, perhaps, and then later more slowly? Does the complexity of an organism tend to make further adaptation slower and more difficult?

Biologists have embraced these questions, yet one niggling issue has remained. However fruitful the metaphor of fitness landscape has been, fundamental justification for it has been lacking. Is there any way to derive the existence of fitness landscapes from known principles of biology? Finally, at least one researcher has suggested that the answer is yes.

But not obviously yes. As physicist Ping Ao points out, the evolutionary process can be represented dynamically as a Langevin equation — essentially a high-dimension dynamical system with an additive stochastic driving component. The trouble with the landscape idea stems from the fact that, in this context, the force driving evolution cannot easily be represented as the gradient of some potential function (which would then play the role of the landscape). This follows from a mathematical symmetry condition — the requirement that the force field be curl free — which, on evolutionary principles, is generally just not true.

But it turns out that the landscape picture can be meaningful anyway, if interpreted correctly; the key is that landscape doesn't quite take the meaning of fitness. In a series of papers, Ao has argued that a relatively simple reformulation of the dynamical system used to describe evolution — essentially a change of variables — is sufficient. The result is a consistent mathematical description of evolution as a flow, where the force looks like the gradient of what Ao calls 'Wright's potential function' (which is not directly biological fitness, although it is related to it).

This is a satisfying outcome, providing a justification for much of the intuitive insight into evolution that comes from the landscape paradigm. Flushed with this success, Ao suggests that it may be possible to go further — that in understanding evolutionary dynamics more clearly, we may also find clues to resolving many other puzzles of non-equilibrium physics, including a clarification of how it is that systems following time-independent microphysics can still be said to 'approach equilibrium'.

However things turn out, Ao's refreshing work appears to have settled some worrying issues in the mathematics of evolution. Might we also learn that physics is ultimately less general than biology? We'll have to wait and see. ❐

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