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Theories of adaptation: what they do and don't say

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Abstract

Theoretical work on adaptation has lagged behind experimental. But two classes of adaptation model have been partly explored. One is phenotypic and the other DNA sequence based. I briefly consider an example of each – Fisher's geometric model and Gillespie's mutational landscape model, respectively – reviewing recent results. Despite their fundamental differences, these models give rise to several strikingly similar results. I consider possible reasons for this congruence. I also emphasize what predictions do and, as important, do not follow from these models.

Introduction

After a delay of many decades – a delay due largely to the reign of the neutral theory – adaptation has begun to receive serious attention. As usual, the reason has more to do with experimental than theoretical progress. At least three kinds of empirical study have renewed interest in adaptation and, in particular, in the genetics of adaptation.

The first is quantitative trait locus (QTL) analyses. In most of these studies, the character difference analyzed is of obvious adaptive significance (e.g., floral differences affecting pollinator attraction in the monkeyflower *Mimulus* [Bradshaw et al., 1998]) and the results plainly provide information on the genetics of adaptation. In other cases, the character difference may be of less obvious adaptive significance but the QTL results themselves suggest that the character diverged under natural selection, i.e., a disproportionate share of 'plus' factors reside in the high line suggesting a history of directional natural selection (Orr, 1998b; Zeng et al., 2000). The second kind of experimental study is molecular population genetic. The discovery of codon bias made it clear that, despite much talk of neutrality, natural selection acts with astonishing subtlety and ubiquity. This conclusion has been supported by more recent work estimating the proportion of amino acid substitutions driven by adaptive evolution. Smith and Eyre-Walker (2002), for instance, recently concluded that about 45% of all amino acid substitutions between *Drosophila simulans* and D. *yakuba* are adaptive. The third kind of experimental study involves microbial experimental evolution. While QTL and molecular population genetic work often involve natural differences between taxa, experimental evolution involves a degree of human intervention. Microbes are typically placed in novel laboratory conditions (e.g., high temperature) and the increase in fitness that occurs during adaptation is tracked through time. Despite this artificiality, these experiments provide extremely high resolution information on the genetics of adaptation, especially when combined with whole genome sequencing. Work in DNA bacteriophage, for example, suggests that 80–90% of nucleotide changes seen during such experiments are adaptive (Wichman et al., 1999), with a

surprising number of changes occurring in parallel, i.e., across independently evolving lines (Wichman et al., 1999; Bull et al., 1997).

This empirical work collectively leaves little doubt that adaptive evolution is common – far more common than many would have been guessed two decades ago. Unfortunately, though, theoretical work on adaptation has continued to lag behind its experimental counterpart and population genetic theory remains largely concerned with neutral or deleterious alleles. Though the reasons for this are partly clear – the neutral theory provides an important null hypothesis and it is easier mathematically to study neutral or deleterious alleles – one begins to get the feeling that population geneticists have been laboring over the wrong thing. This neglect of adaptation likely contributes to the common feeling among working evolutionists that population genetic theory has little to say about their day-to-day research: a theory that slights adaptation is unlikely to be of much use to most evolutionists. Fortunately, a few potential starts to a mature theory of adaptation have now been made (Gillespie, 1984, 2002; Gerrish & Lenski, 1998; Orr, 1998a, 2000; Gerrish, 2001).

Here I briefly review these efforts. These theories can be broken into two classes, those that are phenotype based and those that are DNA sequence based. I consider an example of each: Fisher's geometric model, in which adaptation occurs in a continuous phenotypic space, and Gillespie's mutational landscape model, in which adaptation occurs in a discrete DNA sequence space. I discuss recent results from each model. I also emphasize places where these fundamentally different models yield surprisingly similar results. Finally, I briefly consider possible connections between the models. Throughout, my approach will be non-mathematical and unrigorous. Hopefully, such an informal tour will be of some use to experimentalists who, though interested in adaptation, have neither the time nor background needed to wade through a technical literature.

My goal in the present paper is also partly negative. I emphasize not only what these models allow us to say about adaptation but what they do *not* allow us to say. I take this opportunity, in other words, to clear up several misconceptions about predictions that do and do not follow from these models.

Fisher's geometric model

Population genetic models take such a familiar form that it is easy to overlook a respect in which they are odd. These models begin with selection coefficients but say nothing whatever about where these coefficients come from. It is vaguely assumed of course that selection coefficients emerge from the phenotypic effects of mutations on one or more characters but the mapping from phenotype onto fitness is never made explicit. Although this shortcut suffices for many evolutionary questions, it leaves us in an awkward position when thinking about adaptation. If we want to know, for instance, if mutations of large phenotypic effect are less likely to be favorable than those of small effect, we obviously need a model that allows mutations to have different *phenotypic* sizes, not just different selection coefficients. We need, in other words, a model that systematically maps phenotypic effects onto fitness effects. The simplest such model was introduced by Fisher (1930) in his book *The Genetical Theory of Natural Selection*.

Fisher's so-called geometric model captures the fact that organisms must fit their environment in many ways. They must hunt the right prey, avoid the right predators, resist the right diseases, detoxify the right compounds, and so on. Fisher argued that this problem of conforming to many constraints could be captured by a simple geometric model. In particular, we can imagine that each character in an organism is represented by one axis in a coordinate system. If there are n characters, we have n axes and thus an n-dimensional phenotypic space. Some combination of trait values at these n characters represents the best combination of values in the present environment. For convenience, we can place this (local) optimum at the origin of our n-dimensional coordinate system. Figure 1 shows a simple example of Fisher's model for an organism that is comprised of just two characters ($n = 2$). Because of a recent change in the environment, the population has been thrown off the optimum O and now resides at position A. For simplicity, Fisher's model assumes that fitness falls off from the optimum at the same rate in all directions.

The object of adaptation is to return to the optimum. The problem – and this is the key problem confronting Darwinian evolution – is that the population must attempt this return to the optimum by using *random* mutations, i.e., those