Title
Understanding soft sweeps: a signature of rapid adaptation

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Understanding soft sweeps: a signature of rapid adaptation

Adaptation has been traditionally thought of as a slow, gradual process in which de novo adaptive mutations enter a population one at a time. In such a mutation-limited scenario, the rate of adaptation strongly depends on the waiting time until a new adaptive mutation enters the population. However, this paradigm of gradual adaptation contrasts with the many examples of repeatable and rapid adaptation observed in natural populations, in which the same adaptive mutation arises almost simultaneously on independent haplotypes. Such rapid adaptation can have important societal consequences. For example, rapid adaptation has been observed to result in resistance to antibiotics in bacterial populations, anti-malaria drugs in *Plasmodium falciparum* populations, insecticides in *Drosophila* populations and, most recently, vaccines in SARS-CoV-2 populations.

> "this paradigm of gradual adaptation contrasts with the many examples of repeatable and rapid adaptation observed in natural populations"

In two seminal papers, Hermisson and Pennings provide a framework for understanding when adaptation should be gradual versus rapid. They consider two scenarios of adaptation, proceeding either via shifts in frequencies of standing genetic variation (SGV) already present in a population at the time of a change in selection pressure, or via de novo adaptive mutations entering the population.

In the case of SGV, rapid adaptation is expected to be common when SGV has survived purifying selection and drift when selection pressures change to favour the allele. Hermisson and Pennings consider a parameter R_α, which is the ratio of selective pressures when a mutation is beneficial after an environmental change versus when a mutation confers deleterious effects prior to an environmental change. If $R_\alpha > 1$, such that mutations are only weakly deleterious compared to the beneficial strength of selection, then SGV will likely still remain at the onset of positive selection, thereby increasing the probability of rapid adaptation.

In the case of recurrent de novo mutaions, rapid adaptation is expected to be common when the mutation rate (μ), population size (N_e), or their combination (θ, which is equal to $4*N_e*\mu$) is high. Hermisson and Pennings found that when θ is greater than 0.01, and in particular >1, such that a new beneficial mutation is almost guaranteed in a single generation, adaptation is expected to proceed via multiple de novo mutations rising to high frequency almost simultaneously.

A surprising finding is that the probability of multiple copies of the adaptive allele 'sweeping' to high frequency is independent of the selection coefficient. It was commonly thought that when selection is very strong, the sojourn time of a selective sweep is very short; thus, the probability of a second or third mutation increasing in frequency simultaneously is small. However, strong selection also increases the probability that new beneficial mutations enter the population faster. Therefore, with less time but more successful alleles per unit time, the effect of the selection coefficient cancels out.

Hermisson and Pennings consider the signatures that rapid versus gradual adaptation may leave in the data. They coin these signatures as 'soft sweeps' and 'hard sweeps', respectively. In a soft sweep, multiple haplotypes bearing the adaptive allele rise to high frequency in the population, whereas in a 'hard sweep' only a single haplotype with the adaptive mutation rises to high frequency. An insight Hermisson and Pennings made is that soft sweeps should leave more subtle signatures in the data than hard sweeps. This is because the presence of independent haplotypes bearing the adaptive alleles preserves ancestral diversity in the vicinity of a sweep, and classic signatures associated with hard sweeps, such as sharp dips in diversity surrounding the adaptive allele, are not present.

> "The distinction between hard and soft sweep signatures is important"

The distinction between hard and soft sweep signatures is important for methods that detect sweeps in genomic data. Prior to the work by Hermisson and Pennings, methods to detect sweeps only looked for hard sweeps and thus missed many signatures of adaptation. While Hermisson and Pennings point to several plausible biological examples of soft sweeps, it was not until later that soft sweeps were quantified more systematically via novel selection scans leveraging whole-genome, phased haplotype data from large population samples. The insights from Hermisson and Pennings motivated much subsequent work on the development of statistics capable of detecting and quantifying the prevalence of hard versus soft sweeps from data in numerous systems.

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Competing interests
The author declares no competing interests.

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