

In this short review, Pouyet and Gilbert tackle a huge topic that has been a major focus of the field for decades, putting their own spin on the question of the relative importance of drift and selection in molecular evolution. This is an ambitious topic to approach, and the authors highlight some important factors to consider in thinking about this topic, especially focusing on linked selection, demography, and biased gene conversion. Overall, however, I think this review suffers from some flaws that substantially limit its value at the present.

First, there are many places throughout the review where it seems like a desire for brevity has led to some imprecise or potentially confusing statements. For example:

- On page 2, I'm not sure it is correct to say that "whether a majority of polymorphisms in the genome are neutral or selected" is a major point of debate. While there are big arguments about whether the majority of polymorphisms are affected by linked selection, I'm not sure even an ardent selectionist would argue the majority of polymorphisms in the genome themselves have selection coefficients different from 0.
- On page 3, the definition of balancing selection does not encompass negative frequency dependent selection, or other alternate mechanisms that maintain variation such as spatially varying selection.
- Also on page 3, the definition of sexual selection does not really encompass variation in reproductive success; I'm not sure a mutation would be considered subject to sexual selection if it increased survival in males but was neutral in females, yet that is completely consistent with the listed definition.
- On page 7, I think most definitions of demography would encompass more processes than just changes in population size (e.g., population splits and migration).
- On page 8, I'm not sure it is precise to say that biased gene conversion has no impact fitness. In the extreme case of a e.g. a recessive lethal mutation, no amount of segregation distortion can force it to increase in frequency too much in the population. The fitness effects of the mutations are still expressed in the next generation. I think the important point is that the transmission advantage can cause 'faster-than-neutral' increase in frequency (and shorter time to fixation with a higher prob of fixation), but only if the phenotypic effect of the mutation is small enough to be overcome by the transmission advantage.

Second, the way the authors discuss linked selection is not always very clear to me. This is most relevant to some statements in the conclusion, in particular the statement: "to infer selection, one must not only disprove genetic drift [...] but also disprove the additional prevalent non-adaptive processes [such as linked selection]." The major thrust of this statement seems to be getting at estimates of selection coefficients of particular mutations, e.g. in the context of determining the causal locus under selection. But if the goal is more general, such as to detect regions of the genome subject to a selective sweep, most methods rely on the existence of linked selection for their power. E.g., a reduction in diversity around a hard sweep can only be observed if recombination rate is low enough that some nearby region of the genome evolves by linked selection; most methods to detect selection in resequencing data are generally detecting the perturbations to the neutral coalescent induced by selection. Throughout the review, the authors seem to move between focusing on the challenge of identifying the precise

sites under selection (where linkage poses a real issue as they discuss on the bottom of page 6), and the more general question of the prevalence of selection in genomes, where linkage can be a major help, in the sense that the impact of selection on linked neutral variants is one of the main ways we can detect it.

Finally, related to the above point, it is not really clear to me what the major message of this review is intended to be. As discussed above, the focus of the conclusion seems to be on the challenge of identifying causal variants in selection scans. This is a valuable point and one that is worth discussion, especially as in some cases the more robust the signature of selection, the harder it can be to pinpoint the causal mutation (e.g. in regions of low recombination, the region of the genome impacted by a sweep can make selection easier to detect, but harder to disentangle). However, the introduction seems to set up a different question, on the relative importance of drift and selection; this is a greater focus in the sections on demography and biased gene conversion. Overall, jumping back and forth makes the entire piece a little hard to follow and it makes the overall message somewhat muddled.

I think many of these issues could be resolved by a longer manuscript. A piece like this – that is tackling a big topic with a goal of avoiding polemics and trying to bring clarity to the debate – really needs space to breath, to expand on definitions, to pull apart the different messages with enough text to explore them. At just under 2500 words, this review is trying to tackle too many things in too few words, in my opinion.