Simulations for the Neutral Zone

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The problem

1. Using Ben's code, Charlie simulated a bunch of populations using Moran, Wright-Fisher or Yule processes. We used several different mutation rates and imposed several different types of frequency dependent selection. The populations were 10-fold replicated.

2. We would like use Ben's time-series models to test whether we can detect selection in them. Unfortunately, mode of frequency dependent selection that was was based on Bentley's model. But the mode of frequency dependent selection used in the TS models was based on McVeigh's. It is unclear to me exactly how they differ, but the upshot is this. When applied to Charlie's simulations, the TS models indeed favour the right selection regime: the neutral simulation gives selection coefficients around zero; the negative-frequency dependent selection simulation give negative selectin coefficients and ditto the positive. But, because the selection function underlying them is different, the TS model does not recover the selection coefficients that went into them. This seems unhappy. It suggests that we should redo the simulations, but this time base them on the McVeigh selection function.

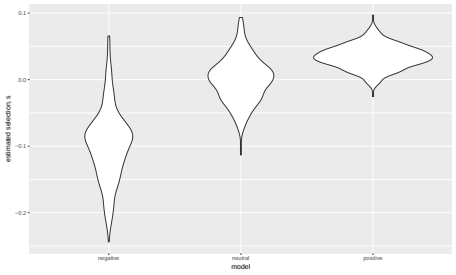

Figure 1: Ben's model (11 July 2018) on charlie's sims

3. There is another reason for redoing them. In Charlie's simulations, the selection function is specified by a number: "+5" (positive FDS), "-5" (negative FDS) and so on. But we don't actually know what that number is. It's not a "selection coefficient" in any real sense — it's just a value that works.

4. Moreover, if we infer the selection coefficient, from the relative fitness of the variants as a function of frequency, it looks funny: there's a cliff-edge at high frequnencies where selection drops to zero.

5. So, all this suggests that we should redo the simulations.

What simulations should we do?

1. In the course of editing the manuscript down, I have come to the conclusion that we should do fewer, and simpler, simulations than originally. This is for several reasons.

2. The original manuscript had an uncomfortable part–review, part–research article. The latter part came from our simulations. In doing a variety of them, we were edging examining the power of the various tests — but we weren't doing it properly. To really examine the power of the various tests, we'd have to do many more simulations and that would lead us into a pure research article. In fact, our simulations are merely *illustrative*; the main argument cannot rest on them, but only on the literature. So we should make it clear that they are only illustrative. And that implies that we should not try lots of different mutation rates and selection regimes.

3. This implies that, for Moran, Wright-Fisher and Yule processes we should do only *one* mutation rate, *one* population size, and *two* selection levels: neutrality and strong negative frequency dependent selection.

4. The reason that we should *only* try *negative* frequency dependent selection is because I have subtly shifted the argument in the paper (or, rather, made it more consistent). The paper begins with the question: "why are there so many things"? There are only two answers to that, really: drift and negative frequency dependent selection. Positive FDS eliminates diversity. Besides, most neutral theorists concede that positive selection occurs (bad mutants occur, and die; rare good mutants sweep to fixation); the real issue is what explains *diversity* and Positive FDS can't.

Details

I suggest the following:

1. Three generative models: Wright-Fisher, Moran and Yule. These are simply based on the original code that Ben made for Charlie.

2. $\mu = 0.001$ and $N = 1000$

3. S = 0 and strong negative FDS.

4. 1 replicate

5. Time steps to ensure equilibrium:

   (a) Wright-Fisher: 5,000.

(b) Moran: 5,000,000

(c) Yule: 500,000

These simulations (as I recall) take quite a long time, and Charlie did them on the HPC. If Ben can code them up, James and I can do that.

I would suggest first doing only the Wright-Fisher simulation. Then I will check that it's all OK. Then, if that's all OK, we do the others.

Although this is all a frightful pain, most of the work is downstream: remaking the figures and doing the tests that I did. But, actually, that's not as hard as it seems. That's because I have, under pressure of space, simplified the whole discussion. For example, I have axed Bentley's turnover test. It's a bad test, used in only a few papers, and will never get used again. It's just not worth spending a 1000 words to knock it down. At best it goes in the supplementary info. Or, since Charlie has had an article accepted in an undergraduate research journal based on his project, we could just reference that.