The Realized Viability of Alleles which Become Fixed

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Introduction

Viability is defined as an expected number of progeny (or descendants) for purposes of modelling selection, yet is measured as an actual number of progeny (or descendants) in natural or artificial populations. If a mutation becomes fixed, the actual average number of progeny will have been greater than one, whether the expected number was greater than one, equal to one, or less than one. It is not possible to determine the expected number of progeny from the actual number. This is one facet of the tautology of natural selection.

The present work studies the dynamics of allele frequencies, conditioned on fixation, for the Wright-Fisher model, the Poisson branching process which approximates it, and the Moran model which is a continuous generation analogue of the discrete generation Wright-Fisher model. (The Moran model has expected time until fixation $N-1$ instead of $2N$ generations for a neutral allele, and probability of fixation s rather than $2s$ for a favored allele; but is still a reasonable continuous analogue for the Wright-Fisher model.) The results are that neutral mutations manifest non-near neutral selection, constant viabilities manifest frequency dependent selection, and deleterious alleles become fixed more rapidly than advantageous alleles.

Neutral alleles are not near-neutral

A classic result for neutral mutations is that the expected time until fixation, conditioned on fixation, is $2N$ generations (Crow & Kimura 1970; Kimura & Ohta 1969). The constant absolute viability which will cause an allele to increase from 1 to N copies in $2N$ generations is $(1+s)$ with $s = (\ln(N))/(2N)$. This viability provides $4Ns = 2\ln(N) >> 1$ if $N > 2$, hence the actual fitness was not near neutral. Essentially the same result is obtained assuming constant relative viability. The Moran model which has $N-1$ generations to fixation also provides a similar result.

Constant viability entails frequency dependent selection

The Wright-Fisher model provides that the expected change in allele frequency in a generation is $\frac{sx(1-x)}{1+sx}$. In particular, an allele will increase most rapidly when its frequency is near 50% and least when it is rare or common (for a favored allele, the increase is slightly smaller when common). To contrast this with fixation of a neutral allele, model neutrality as a Poisson progeny distribution in a branching process with parameter 1 (Karlin & Taylor 1975). This provides that the expected number of progeny is 1, but the expected number of progeny weighted by the number of progeny is 2. This is the appropriate average for looking at the number of progeny one's ancestors had, since all progeny are equally fit, hence are equally likely to ultimately become fixed. Hence under the Poisson progeny distribution with parameter 1, the average viability of one's ancestors is 2 ($s = 1$). However, constant population size provides that the average number of progeny of individuals which are not one's ancestor is $1 - (1/(N-1))$, hence the average viability of a mutation will decrease from 2 to 1 as it increases in frequency from $1/N$ to 1. The average actual increase in frequency each generation will decrease from 1 to 0 during the course of fixation (consistent with the expected time until fixation $2N$ generations). The rate of increase is greater when the mutation is rare and smaller when frequent, contrary to the constant viability model above.

Selection (viability $1+s$ for the mutant and 1 for the wild-type allele) can also be analyzed in the context of the Moran model (Moran 1958; Karlin & McGregor 1962). Time is rescaled by a factor of N so that the frequency of a mutant gene can be considered as a random walk on the integers (or the rational numbers k/N if relative frequencies are employed). The probability that allele frequencies do not change in a "generation" (i.e., $1/N$ of an original generation) is $\frac{x^2+(N-x)^2+sx^2}{N(N+sx)}$ where x is the frequency of the mutant allele, this is also the probability that allele frequencies do not change when conditioning on fixation. The probability that the frequency increases (by 1) given that it changes is $\frac{1+s}{2+s}$, but the probability that it increases, given that it changes and conditioned on fixation is $\frac{\sum_0^x (1+s)^{-i}}{\sum_0^x (1+s)^{-i}+\sum_1^{x-1}(1+s)^{-i}}$. The time until fixation can be calculated with a computer; numerical calculations for a population of 16 individuals with $|s| = 0, .001, .01, .1$ showed that the rate of increase of the mutant allele decreased from approximately 2 individuals per generation (on the original time scale) when rare to one half individual per generation when near fixation.

Deleterious alleles become fixed more rapidly than advantageous alleles

For a population of two individuals, it is readily calculated that the expected time until fixation (conditioned on fixation) under the Moran model is 1 ($=N-1$) generation independent of the value of s. However, numerical calculations show that for larger populations the time until fixation (conditioned on fixation) decreases with the magnitude of selection (for results employing the diffusion approximation see van Herwaarden & van der Wal 2002). For a population of 16 individuals, the expected time until fixation for the specified values of s are 15 ($s = 0$), 15 ($s = .001$), 15 ($s = -.001$), 14.99 ($s = .01$), 14.99 ($s = -.01$), 14.52 ($s = .1$), 14.42 ($s = -.1$). More decimal places confirm that the time until fixation is less for negative than positive values of s.

Discussion

The conclusion of this paper is that the dynamics of an allele provide little information about its intrinsic fitness. If one knows the frequency of mutation and the fraction of mutations which become fixed, one can infer information about the extent to which selection is acting in the genome as a whole, but not which individual mutations were fixed due to chance versus selection. The frequency of substitution of mutations with a given selective value depends on both the mutation rate and the probability of fixation. Conditioning on fixation (or extinction) makes favored and deleterious alleles behave quite similarly.

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