

Fluctuating selection

The second part of my PhD research consists of work on temporal variation in selection coefficients and organism fitness. The potential importance of fluctuating selection on the rate and patterns of molecular evolution has been demonstrated, based on theoretical and simulation arguments (see Gillespie [1991]; Gillespie [1994]). While it is likely that changing environmental conditions affect the fitness and level of genetic variation in natural populations, only a handful of empirical population genetic studies have sought to investigate the issue. Part of the reason this problem remains understudied is the lack of powerful statistical tools for comparing patterns of polymorphism to the predictions under fluctuating selection.

In fact, previous research in this area (Gillespie [1991], Takahata et al. [1975], Karlin and Levikson [1974a]), mostly consists of methods available to detect the influence of fluctuating selection when there are available time series of allele frequencies, measured over many generations (Mueller et al. [1985]). Thus, we wished to develop a methodology to detect effects of fluctuating selection in sequence polymorphism data. We achieved this by using the diffusion approximation to calculate the site frequency spectrum (SFS) which is a summary statistic of the data. The SFS is the number of mutations at frequency i/n where $1 \leq i < n$ and n is the number of individuals sampled.

We considered the model of Karlin and Levikson [1974b]: consider two alleles A and a that have the following fitnesses,

$$\text{Fitness in generation } n: \quad \begin{array}{cc} A & a \\ 1 + \sigma^{(n)} & 1 + \tau^{(n)} \end{array}$$

where σ and τ are identically distributed random variables representing the relative change in fitness due to random environmental changes. We followed their procedure in looking for the diffusion approximation and then calculated the site frequency spectrum. This is done by finding the stationary solution to the diffusion equation and using the formula derived in Kimura [1962] or in Sawyer and Hartl [1992]. We find the density of mutations for a unit overall mutation rate is given by $f(y, \beta)dy$ where

$$f(y, \beta) = \frac{2}{K(\beta)y(1-y)} \log \left(\frac{1 - r_1(\beta)}{y - r_1(\beta)} \cdot \frac{r_2(\beta) - y}{r_2(\beta) - 1} \right) \quad (1)$$

This formula showed that compared to the neutral model (where $f(y) = 1/y$), the occurrence of rare alleles (with y close to 0) is unaffected by the fluctuating environmental effects while the proportion of high-frequency derived alleles (y close to 1) is higher than expected under neutrality. Intermediate frequency alleles, however, are underrepresented with respect to the neutral case. We used this SFS to develop a statistical method to probe DNA polymorphic data for the effect of fluctuating selection. This involved a maximum likelihood ratio test, and we demonstrated that there is good power to detect fluctuating selection compared to neutrality when the number of segregating sites is large, and there is moderate power to differentiate fluctuating selection from directional selection (see Huerta-Sanchez et al. [2007]).

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