**SELECTION AND DRIFT**

– If mutation is absent, genetic drift leads to fixation—with or without selection.

– *Q* How does selection affect the probability that an allele that occurs in a population of size *N* will become fixed or lost?

*A*: Consider the Wright-Fisher model with selection:

• Life Cycle:

\[ \text{Adults (N)} \xrightarrow{\text{meiosis}} \text{Gametes (\infty)} \xrightarrow{\text{R.U.G}} \text{Zygotes (\infty)} \]

\[ \xrightarrow{\text{viability selection}} \text{Teens} \xrightarrow{\text{density regulation}} \text{Adults (N)} \]

• Must resort to Markov Chain methods. Note that, for 2 alleles (and, hence, 3 diploid genotypes), \( P(j \mid i) \) is derived from trinomial sampling of genotypes of the selection survivors.
– Except for very small populations, Markov Chains are difficult to handle.
– Population geneticists have resorted to “diffusion approximations” to estimate fixation probabilities and times, and more.

– Let \( U(p) \) = probability of fixation of an allele with initial frequency \( p \).

• Some results for multiplicative fitnesses: \( w_{AA} = (1 + s)^2 \), \( w_{Aa} = 1 + s \), \( w_{aa} = 1 \).

(1) \( U(p) \approx \frac{1 - e^{-4Ns}}{1 - e^{-4Ns}} \).

(2) Fixation probability for a newly arisen mutant.

– Newly arisen mutant has initial frequency \( p = 1/2N \)

– Probability of fixation = \( U(\frac{1}{2N}) \approx \frac{1 - e^{-2s}}{1 - e^{-4Ns}} \)

– If \( s \leq 0 \) and \( |s| \ll 1 \) (i.e., A slightly deleterious or neutral), \( U(\frac{1}{2N}) \approx \frac{1}{2N} \)

– If \( 0 < s \ll 1 \) (i.e. A slightly advantageous, \( U(\frac{1}{2N}) \approx 2s \)

• Note: This leads to an expression for a “non-neutral” rate of substitution:

\[ \approx \ (\text{new mutations with advantage } s) \times \text{(probability of fixation)} \]

\[ \approx \ (2Nu) \times (2s) = 4Nus \]

– Conclude: Even if population size is very large (or \( \infty \! \)), a new mutant stands a good chance of being lost due to drift, whether it is selectively favored or not.
SELECTION, MUTATION, AND DRIFT

- Assume two-way mutation (so fixation is not terminal).

- Q: What is the distribution of allele frequencies at equilibrium under selection-mutation-drift balance?

A: Define \( \hat{\phi}(p) dp = \) fraction of populations with allele frequencies between \( p \) and \( p + dp \) at equilibrium.

- Note, \( \hat{\phi}(p) \) is a continuous distribution.

- Turns out that \( \hat{\phi}(p) = Kp^{4Nv-1}(1-p)^{4Nu-1}\left[\overline{w}(p)\right]^{2N} \)

  where, \( u, v = \) forward and backward mutation rates
  \( K = \) constant
  \( \overline{w}(p) = \) mean fitness in a population with allele frequency \( p \).

- Note that \( \left[\overline{w}(p)\right]^{2N} \) term accentuates peaks and valleys if \( \overline{w}(p) \neq 1 \).
  - selection dominates as \( N \) gets larger.

- Conclusions

  (1) \( \hat{\phi}(p) \) concentrated at equilibria predicted by deterministic models when selection is very strong relative to mutation, drift (i.e., \( s >> 4u, s >> 2N \))

    - i.e., \( \hat{\phi}(p) \) will track peaks in \( \overline{w} \).

  (2) As the strength of mutation increases relative to selection, \( \hat{\phi}(p) \) concentrates increasingly around equilibrium frequency of a deterministic mutation model.

  (3) As drift gets stronger, (\( N \) smaller) relative to selection, mutation, \( \hat{\phi}(p) \) "spreads out" around deterministic predictions.

    - greater tendency for populations to become fixed.

  (4) As \( N \) decreases with \( s = u = v \), mutation becomes more important than selection since mutational effects are relatively stronger than selection when there is little variance.