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) $U(p) \approx \dfrac{1-e^{-4Nsp}}{1-e^{-4Ns}}$.

(2) Fixation probability for a newly arisen mutant.

– Newly arisen mutant has initial frequency $p = 1/2N$

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

– If $s \le 0$ and $|s| << 1$ (i.e., A slightly deleterious or neutral), $\boxed{U\left(\dfrac{1}{2N}\right) \approx \dfrac{1}{2N}}$

– If $0 < s << 1$ (i.e. A slightly advantageous, $\boxed{U\left(\dfrac{1}{2N}\right) \approx 2s}$

- Note: This leads to an expression for a “non-neutral” rate of substitution:
  = (new mutations with advantage s) × (probability of fixation)
  ≈ $(2Nu) \times (2s) = 4Nus$

- Conclude: Even if population size is very large (or ∞!), 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.