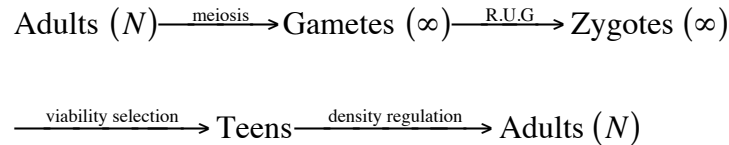


**SELECTION AND DRIFT**

- 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:



- Must resort to Markov Chain methods. Note that, for 2 alleles (and, hence, 3 diploid genotypes),  $P(j | i)$  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:  $w_{AA} = (1 + s)^2$ ,  $w_{Aa} = 1 + s$ ,  $w_{aa} = 1$ .

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

(2) Fixation probability for a newly arisen mutant.

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

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

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

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

- Note: This leads to an expression for a “non-neutral” rate of substitution:
  - = (new mutations with advantage  $s$ )  $\times$  (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  $\hat{\phi}(p) = Kp^{4Nv-1}(1-p)^{4Nu-1}[\bar{w}(p)]^{2N}$ 
  - where,  $u, v$  = forward and backward mutation rates
  - $K$  = constant
  - $\bar{w}(p)$  = mean fitness in a population with allele frequency  $p$ .
  - Note that  $[\bar{w}(p)]^{2N}$  term accentuates peaks and valleys if  $\bar{w}(p) \neq 1$ .
    - 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.,  $s \gg 4u, s \gg 2N$ )
  - i.e.,  $\hat{\phi}(p)$  will track peaks in  $\bar{w}$ .
- (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.