Chapter 8 – Selection in a Finite Population

Fixation Probabilities of New Mutations
Rates of Substitution of Selected Alleles
Genetic Hitchhiking

Simulating Drift and Selection

- see Box 8.1
- Step 1: calculate new allele frequency due to viability selection

\[ f'_A = \frac{v_{AA}f_A^2 + v_{Aa}f_A(1 - f_A)}{\bar{V}} \]

- Step 2: randomly draw 2N gametes for next generation
with $s = 0$

- probability of fixation = initial frequency
- $1/2N$ for a new mutation
- the “gambler’s ruin” paradox

with $s \neq 0$

- $w_{AA} = 1+2s$; $w_{Aa} = 1+s$ (additive fitness)
- $Pr$(fixation) for a new mutation = $u$

$$u(s,N) = \frac{1-e^{-2s}}{1-e^{-4Ns}}$$

- fixation probability for “strongly selected” alleles
  $$u \approx 2s$$

- “strongly selected” if $2Ns > 1$
- “nearly neutral” if $-1 < 2Ns < 1$
Nearly Neutral Theory

- what happens in small populations when selection is weak?
- changes in allele frequency due to drift and selection are approximately equal \[ |2Ns| \approx 1 \]
What qualifies as nearly neutral?

- Hamilton: \(2s = 1/2N_e\) or \(4N_e s = 1\)
  - value at which “the processes of genetic drift and selection are equal”
- Hartl & Clark: \(12Ns_1 \approx 1\)
- Hedrick: \(s < 1/(2N)\) or \(2Ns < 1\)
- Ohta & Gillespie (1996): \(s \approx 1/N\) or \(Ns \approx 1\)
- Nielsen & Slatkin (2013): \(-1 < 2Ns < 1\)
**Nearly Neutral Theory - Summary**

- The rate of neutral evolution is independent of population size
  \[ 2N\mu \times \frac{1}{2N} = \mu \]
- Substitution rate equals mutation rate
- In contrast, the fate of nearly neutral mutations depends on population size
- When \( N \) is small, the effect of genetic drift can be comparable to that of selection, making slightly deleterious mutations “effectively neutral”
- Thus, lineages experiencing small population size should accumulate both neutral and nearly neutral mutations, leading to a faster rate of sequence evolution

---

**Woolfit & Bromham 2003** Increased rates of sequence evolution in endosymbiotic bacteria and fungi with small effective population sizes. *MBE* 20:1545-1555.

- Higher rate in endosymbiotic bacteria interpreted as a consequence of nearly neutral evolution
Substitution Rate for Selected Alleles

- substitution rate for neutral allele = $\mu$
- for selected alleles:
  
  $$ r(s, N) = 2N\mu u(s, N) $$

  $$ = 2N\mu \frac{1 - e^{-2s}}{1 - e^{-4Ns}} $$

- substitution rate from data:
  - where $d/L$ is proportion of sites that differ between two sequences

$$ r = \frac{d}{2LT} $$

Neutral Rate from Synonymous Sites?

<table>
<thead>
<tr>
<th>TABLE 8.1 Universal genetic code</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
</tr>
<tr>
<td>Ala</td>
</tr>
<tr>
<td>Arg</td>
</tr>
<tr>
<td>Asn</td>
</tr>
<tr>
<td>Asp</td>
</tr>
<tr>
<td>Cys</td>
</tr>
<tr>
<td>Gln</td>
</tr>
<tr>
<td>Glu</td>
</tr>
<tr>
<td>Gly</td>
</tr>
<tr>
<td>His</td>
</tr>
<tr>
<td>Ile</td>
</tr>
<tr>
<td>START</td>
</tr>
</tbody>
</table>
Neutral Rate from Synonymous Sites?

- E.g., β-globin
  - 78 four-fold degenerate sites
  - 30 differ between mouse and human
  - synonymous mutations
  - divergence time: ~80MY
  - $r = 2.4 \times 10^{-9}$

---

**TABLE 8.2** Synonymous and nonsynonymous substitution rates estimated by comparing genes in humans and mice

<table>
<thead>
<tr>
<th>Gene</th>
<th>Codons</th>
<th>Synonymous rate</th>
<th>Nonsynonymous rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histone H3</td>
<td>101</td>
<td>6.38</td>
<td>0.0</td>
</tr>
<tr>
<td>Histone H4</td>
<td>135</td>
<td>6.13</td>
<td>0.027</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>189</td>
<td>4.37</td>
<td>0.95</td>
</tr>
<tr>
<td>Prolactin</td>
<td>197</td>
<td>5.59</td>
<td>1.29</td>
</tr>
<tr>
<td>α-hemoglobin</td>
<td>141</td>
<td>3.94</td>
<td>0.56</td>
</tr>
<tr>
<td>β-hemoglobin</td>
<td>144</td>
<td>2.96</td>
<td>0.87</td>
</tr>
<tr>
<td>γ-interferon</td>
<td>136</td>
<td>8.59</td>
<td>2.80</td>
</tr>
<tr>
<td>HPRT</td>
<td>217</td>
<td>2.13</td>
<td>0.13</td>
</tr>
<tr>
<td>Fibrogin-γ</td>
<td>411</td>
<td>5.82</td>
<td>0.55</td>
</tr>
<tr>
<td>Albumin</td>
<td>590</td>
<td>6.72</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Source: Li et al. (1985). All rates are in units of $10^{-9}$ per site per year.
Purifying Selection

- proportion of non-synonymous mutations strongly selected against? \( A \)

\[
r_N = (1 - \alpha) \mu
\]

- e.g., prolactin

\[
(1 - \alpha) = \frac{r_N}{\mu} = \frac{1.29}{5.59} = 0.23
\]

\[\alpha = 0.77\]

An extraordinary avian radiation: the *Lonchura* munias of Papua New Guinea
Data Set

- 6,146 autosomal RAD-seq loci with 10+ reads per locus for 36 individuals (19 on New Ireland, 17 on New Hanover)
  - 770,864 base pairs per sample
- 250 Z-chromosome RAD-seq loci (10+ reads per locus for all 36 individuals)
  - 32,172 base pairs per sample
- plus comparable data for 16 samples representing the other munia species