§ 2.3 Mutation and Drift

- Drift removes variation
- Mutation adds variation
- Let u = mutation rate to $\overbrace{\text{neutral}}^{\text{in terms of selection}}$ alleles

  Pr(mutation at a single gamete at a given locus)
- A mutation that occurs is assumed to produce a unique allele.

Gen 1	A_1	A_1	A_1	A_1	A_1
Gen 2	A_1	A_2	A_1	A_1	A_1
Gen 3	A_1	A_2	A_2	A_3	A_1
⋮					

This assumption is called "infinite alleles model"

2.1) Size = 3000, # 1-step away is 3000·3 (change one nucleotide)
2-steps away is 3000 × 2999·9 (change 2 nucleotides)
= 80,973,000

- $$\underbrace{\hat{H}'}_{\text{Next gen}} = \underbrace{(1-u)^2}_{\text{No mutation in either}} \underbrace{\left[\frac{1}{2N} + \left(1-\frac{1}{2N}\right)\underbrace{\hat{H}}_{\text{Current gen}}\right]}_{\text{Same state given no mutation in either}}$$] Pr(same state | different origin)

• Goal: Approximation to change in heterozygosity

Note, $u \approx 10^{-5}$, N is very large

so $(1-u) \approx 1-2u$ and $\frac{u}{N} \approx 0$

Taylor series

$$G' \approx (1-2u)\left[\frac{1}{2N} + \left(1-\frac{1}{2N}\right)G\right]$$

$$= \frac{1}{2N} - \underbrace{\frac{2u}{2N}}_{0} + \left(1 - 2u - \frac{1}{2N} + \underbrace{\frac{2u}{2N}}_{0}\right)G$$

$$= \frac{1}{2N} + \left(1 - 2u - \frac{1}{2N}\right)G$$

$$= \frac{1}{2N} + \left(1-\frac{1}{2N}\right)G - 2uG$$

$$H' = 1 - G' \approx 1 - \frac{1}{2N} - \left(1-\frac{1}{2N}\right)G + 2uG$$

$$= 1 - \frac{1}{2N} - \left(1-\frac{1}{2N}\right)(1-H) + 2u(1-H)$$

$$= \left(1-\frac{1}{2N}\right)H + 2u(1-H)$$

$$\Delta H = H' - H \approx \underbrace{-\frac{1}{2N}H}_{\text{effect of drift}} + \underbrace{2u(1-H)}_{\text{effect of mutation}}$$

When $\Delta H = 0$, mutation and drift offset, and we have

$$\frac{1}{2N}H = 2u(1-H) \Rightarrow \left(\frac{1}{2N} + 2u\right)H = 2u$$

$$\Rightarrow H = \frac{2u}{\frac{1}{2N}+2u} = \frac{4Nu}{1+4Nu}$$

$$\mathcal{H} + \mathcal{H}f = f$$
$$\mathcal{H} = f(1-\mathcal{H})$$
$$f = \frac{\mathcal{H}}{1-\mathcal{H}}$$

- When mutation and drift offset,

$$\mathcal{H} \approx \frac{4Nu}{1+4Nu}$$ (in humans $4Nu \approx 0.05$)

- Back to interplay

$$\Delta\mathcal{H} \approx -\frac{1}{2N}\mathcal{H} + \underbrace{2u(1-\mathcal{H})}_{\text{lets look at this}}$$

Suppose infinite population and we have mutation

$$\mathcal{H}' = \mathcal{H} + (1-\mathcal{H})\left[1-(1-u)^2\right]$$

In infinite pop, every parent is unique, so

$\mathcal{H}' =$ Pr(parents differ by state) +

Pr(parents same by state) $\cdot$ Pr(at least one mutation)

$$\approx \mathcal{H} + (1-\mathcal{H})\left(1-(1-2u)\right)$$

$$\approx \mathcal{H} + 2u(1-\mathcal{H})$$

$$\Rightarrow \Delta\mathcal{H} = 2u(1-\mathcal{H})$$

- $4Nu \uparrow \Rightarrow \mathcal{H} \uparrow$ so u dominating
  $4Nu \searrow \Rightarrow \mathcal{H} \searrow$ so drift dominating