§2.5: The Neutral Theory

- <u>Neutral Theory</u>: Most variation in proteins and DNA are neutral (not under selection)

- <u>Molecular Clock</u>: Theory that says substitutions/year are about the same everywhere
  ↑ allows you to convert b/t generations and years

  In this section k_s = substitution rate at a site

- Looking at substitutions b/t closely/related species, Kimura and Ohta (1971) found

  $$k_s = 1.6 \times 10^{-9} \frac{\text{amino acid substitutions}}{\text{site year}}$$

- Laboratory experiments determine $u_s = \frac{\text{amino acid mutations}}{\text{site year}}$
  and $u_s \approx k_s \Rightarrow$ evidence for neutral theory

- $H \approx 0.1$ in humans $\Rightarrow \frac{4Nu}{1+4N\boxed{u}} \approx 0.1$ ← rate in units of generations

  $$\Rightarrow 4Nu \approx 0.1 + 0.4Nu$$
  $$\Rightarrow 3.6Nu \approx 0.1$$
  $$\Rightarrow 4Nu \approx \frac{0.4}{3.6} \approx 0.1$$

<u>2.10</u>: $4Nu = 4N \cdot \frac{10^{-7}}{1/20} = 0.1$

$$\Rightarrow \boxed{N = \frac{0.1}{80} \cdot 10^{7}}$$

Issues

1.) But $\rho = u$ for <u>generations</u>, they say years.
substitution rate should be larger in mice than humans, but this is not observed in practice in proteins (But is seen in noncoding DNA)

2.) Heterozygosity is relatively stable b/t species

$0.05 \leq H \leq 0.15$

So if $H = \frac{4Nu}{1+4Nu}$ and u is same accross species (b/c neutral theory) then N is relatively stable

↑ this is weird

(Maybe smaller populations in past?)

3.) $Var(N_t) > E(N_t)$ in practice

↑ # substitutions over time t

But Poisson says $Var(N_t) = E[N_t]$