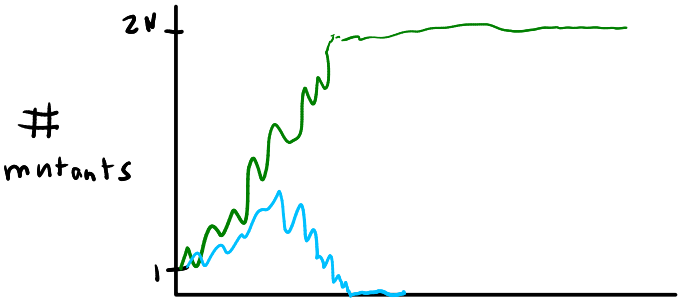
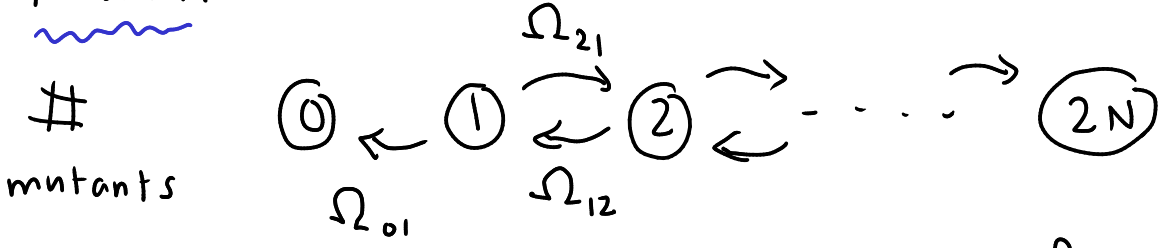



overall rate at which new mutants appear & fix:

$$K = 2N\mu\,\pi_{fix}$$

Moran:




$$i \to i+1: \quad \Omega_{i+1,i} = \frac{2N-i}{2N}\,\frac{f_i}{f_i + g(2N-i)}$$

$$i \to i-1: \quad \Omega_{i-1,i} = \frac{i}{2N}\,\frac{g(2N-i)}{f_i + g(2N-i)}$$

$$\Omega_{1,0} = 0 \qquad \Omega_{2N-1,2N} = 0$$

sidenote: Moran can be mapped onto WF

look at this in neutral case $f = g$

mut. fitness, WT fitness

$$s = \frac{f}{g} - 1 = 0 \quad \text{(neutral)}$$

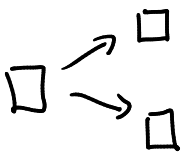
quantity: prob. that two lineages have not coalesced going back time $t$

neutral WF

$$U_c(t) \approx \exp\left(\frac{-t}{2N t_g}\right)$$

$t_g$ = gen. time

Moran version: in prev. time step, prob. that a pair did coalesce



$$= \frac{1}{\#\text{ pairs}} = \frac{1}{\binom{2N}{2}} = \frac{2}{2N(2N-1)}$$

prob. not to coalesce $= 1 - \frac{2}{2N(2N-1)}$

go back $n$ time steps: $t = n\,\delta t$ (↳ single Moran step)

$$U_c(t) = \left(1 - \frac{2}{2N(2N-1)}\right)^{\frac{t}{\delta t}}$$

$N \gg 1$

$$\approx \left(1 - \frac{1}{2N^2}\right)^{\frac{t}{\delta t}}$$

$$\approx \exp\left(-\frac{t}{2N^2\,\delta t}\right)$$

neutral Moran result

$\Rightarrow$ map Moran by setting $t_g = N\,\delta t$

$N$ Moran steps $\approx$ one WF generation

---

Goal: find $\pi_i$ = prob. that if you start w/ $i$ mutants you reach $2N$

$\pi_{fix} \equiv \pi_1$ (starting w/ 1 mutant)

Let's say we are at state $i$

$$1 \leq i \leq 2N-1$$

Before reaching $2N$ we have to pass thru either $i-1$ or $i+1$:

$$\pi_i = \left(\begin{matrix}\text{prob. to}\\ \text{jump to } i-1\end{matrix}\right)\pi_{i-1} + \left(\begin{matrix}\text{prob. to}\\ \text{jump to } i+1\end{matrix}\right)\pi_{i+1}$$

$$= \frac{\Omega_{i-1,i}}{\Omega_{i-1,i}+\Omega_{i+1,i}}\pi_{i-1} + \frac{\Omega_{i+1,i}}{\Omega_{i-1,i}+\Omega_{i+1,i}}\pi_{i+1}$$

$$\pi_i = \frac{(1+s)}{(2+s)}\pi_{i+1} + \frac{1}{2+s}\pi_{i-1}$$

boundary cond: $\pi_{2N} = 1 \quad \pi_0 = 0$

exact solution: $\pi_i = \dfrac{1-(1+s)^{-i}}{1-(1+s)^{-2N}}$

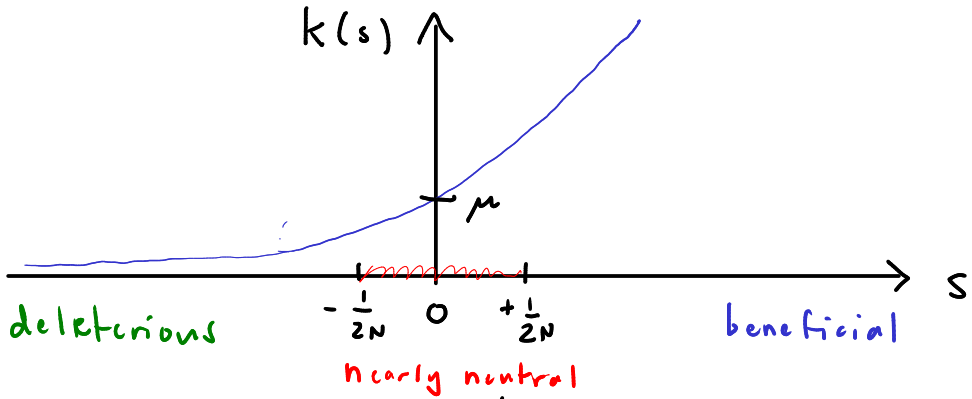
$|s| \ll 1 \quad \approx \dfrac{1-e^{-is}}{1-e^{-2Ns}}$

$$\pi_{fix} = \pi_1 \approx \frac{1-e^{-s}}{1-e^{-2Ns}}$$

Substitution rate $k = 2N\mu \dfrac{1-e^{-s}}{1-e^{-2Ns}}$

Motoo Kimura 1962

$$s = \frac{f}{g} - 1 \qquad \begin{cases} s > 0 & \text{beneficial mutant} \quad f > g \\ s = 0 & \text{neutral} \quad f = g \\ s < 0 & \text{deleterious mutant} \quad f < g \end{cases}$$




$|s| \ll 1$

regimes: $|s| \ll \frac{1}{2N}$ : $k \approx 2N\mu \frac{1-(1-s)}{1-(1-2Ns)} \approx \mu$

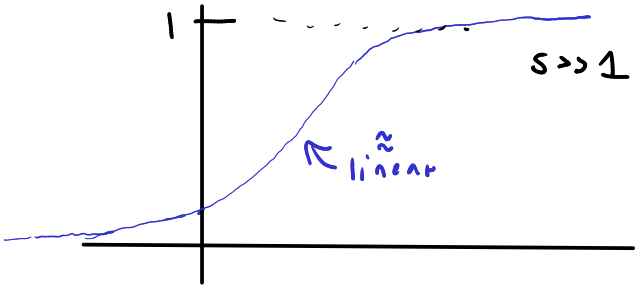
for neutral mutations, rate of substitution $= \mu$ indep. of $N$

(Kimura, Ohta 1971) : "molecular clock"

Strongly beneficial: $s \gg \frac{1}{2N}$ + $|s| \ll 1$

$$\pi_1 \approx s$$

$$k = 2N\mu|s| \gg \mu$$




Strongly deleterious $s \ll -\frac{1}{2N}$

$$\pi_1 \approx |s| e^{-2N|s|}$$

$$k \approx 2N\mu|s| e^{-2N|s|} \ll \mu$$

The bigger $N$ is, the stronger the $e^{-2N|s|}$ term becomes, the less likely a deleterious can take over.