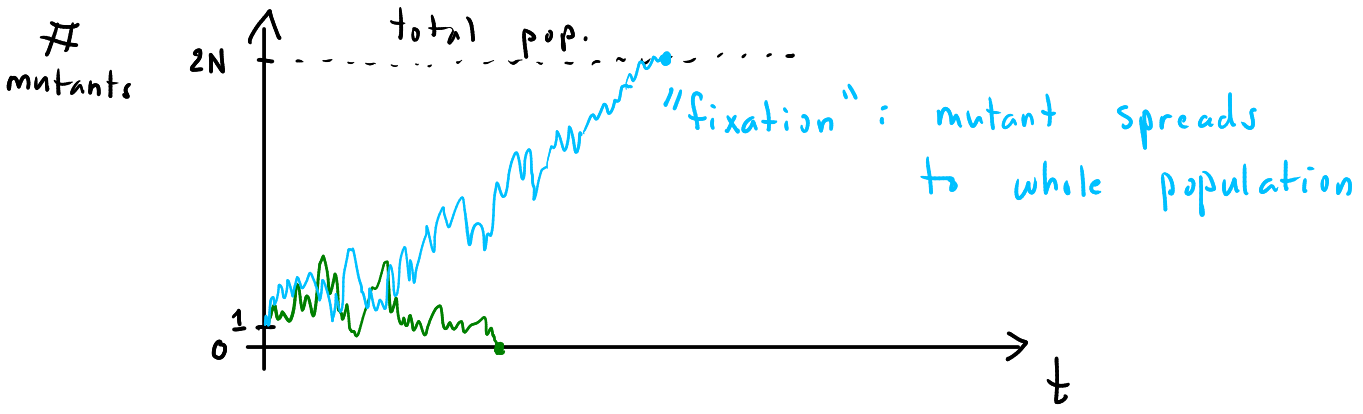
Dynamics of mutations



Keep track of single mutant type.

⇒ assume mutation rate μ is small such that a new mutant appears rarely, it either goes extincts or takes over before another mutant appears at that locus.

For larger μ ⇒ multiple mutants competing simultaneously

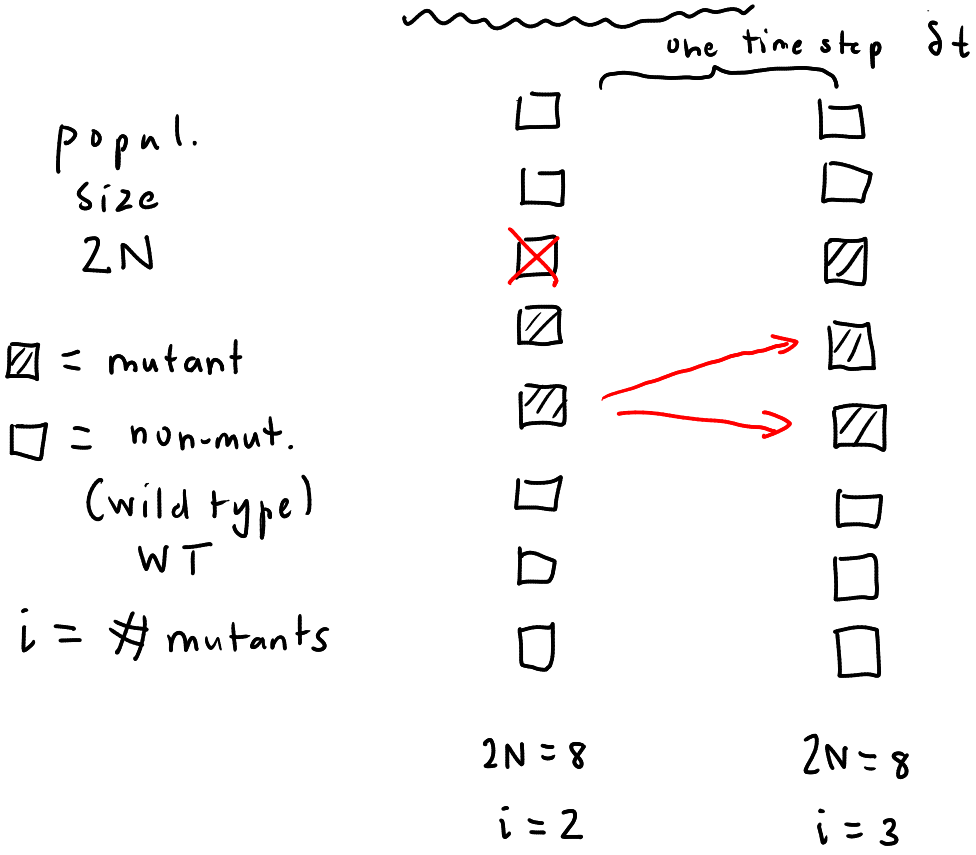
⇒ "clonal interference"

Quantity to calculate: "speed of evolution"

substitution rate = $K = \underbrace{2N\mu}_{\text{rate at which mutant alleles appear}} \cdot \underbrace{\pi_{fix}}_{\text{prob. that mutation gets fixed}}$

= rate at which new mutants appear & get fixed in popul.

Consider a "microscopic" version of WF model: Moran model



every δt:

- one allele at random dies
- one gets chosen to reproduce & everyone else survives

rules for reproduction:

either WT or mutant reproduces first, moving system to next time step

g = repr. rate of wild type

f = " " of mutant

	prob.
WT first $\Rightarrow$	$\frac{g(2N-i)}{fi + g(2N-i)}$

note: if $f = g \Rightarrow$

prob: $\frac{2N-i}{2N} \propto$ frac. of WT in popul.

mutant first $\Rightarrow$	$\frac{fi}{fi + g(2N-i)}$

define: $s = \frac{f}{g} - 1$ selection coefficient

typically:

$|s| \ll 1$

i.e. $s \approx .07$
for lactose tolerance when it initially arose

$s > 0$ beneficial mutant ($f > g$)

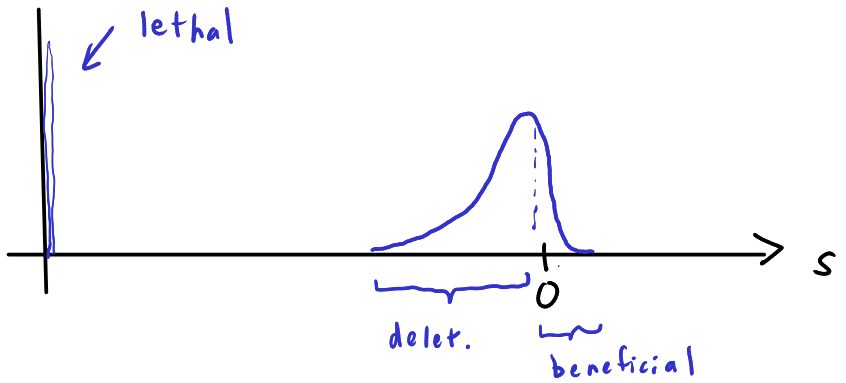
$s = 0$ neutral mutant ($f = g$)

$s < 0$ deleterious mutant ($f < g$)

in principle s can vary in time as environment fluctuates, but for now assume it is constant

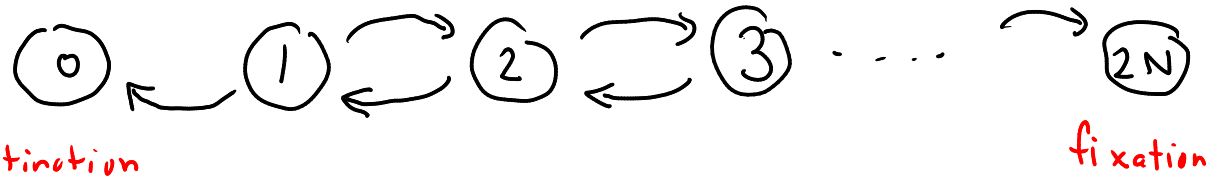
$s = -1$ is minimum: lethal mutation w/ $f = 0$

typical distrib. of s values when you mutate a particular locus:
(distrib. of fitness effects = DFE)



Put all details together:

mutants i = state



$$i \to i+1: \quad \Omega_{i+1,i} = \underbrace{\frac{2N-i}{2N}}_{\text{prob. WT dies}} \cdot \underbrace{\frac{f_i}{f_i + g(2N-i)}}_{\text{prob. mut. gives birth first}}$$

$$i \to i-1: \quad \Omega_{i-1,i} = \underbrace{\frac{i}{2N}}_{\text{mut. dies}} \cdot \frac{g(2N-i)}{f_i + g(2N-i)}$$

$$\Omega_{1,0} = 0 = \Omega_{2N-1,2N} \qquad i=0 \text{ \& } i=2N \text{ are traps (no escape)}$$

Moran $\Rightarrow$ Markov model w/ matrix Ω