

Adaptive fixations

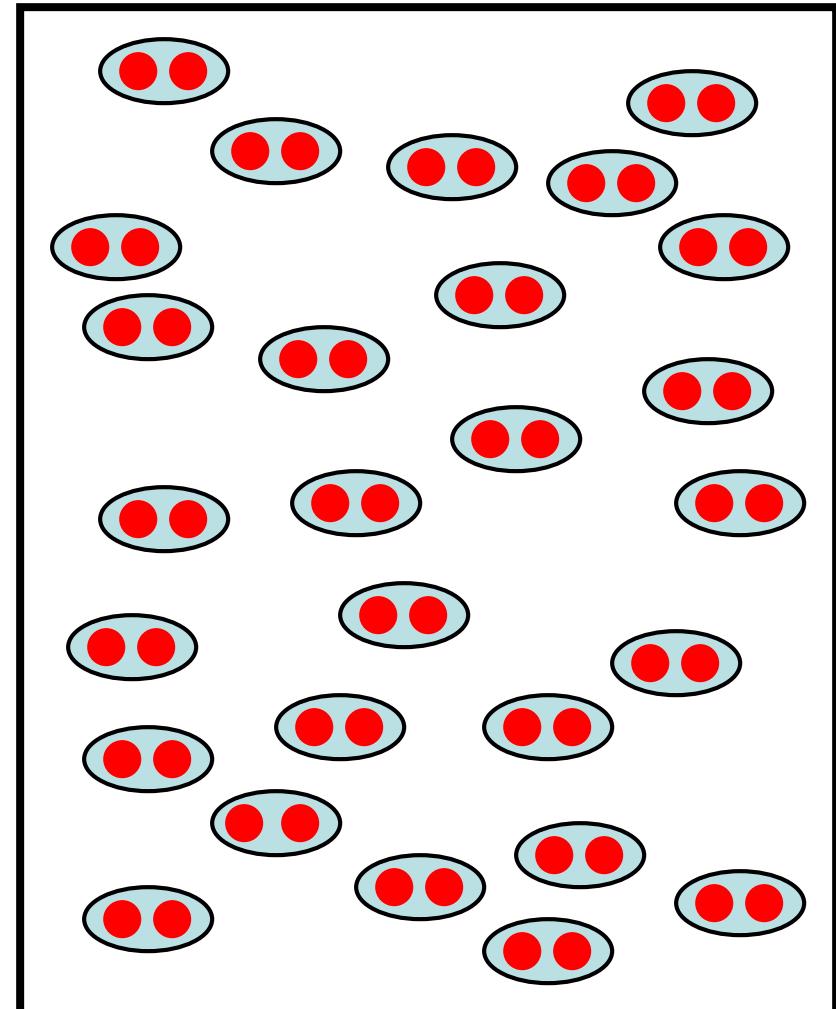
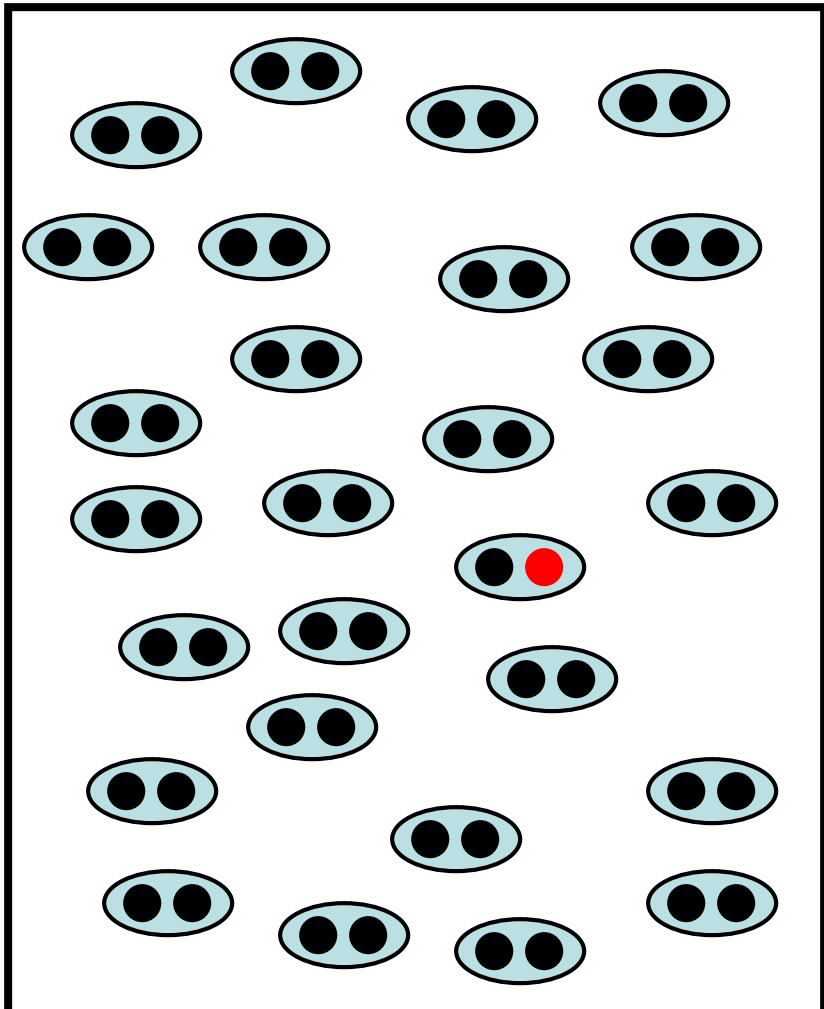
In the beginning ...

$$p = 1/2N$$

... then after substitution

What's the chance this happens?

If neutral? If beneficial?



How selection biases drift (The Book)

Intuition suggests that if the random allele frequency change caused by drift is much larger than the directional change caused by selection, then drift might overpower selection and allow deleterious mutations to fix in the population.

In 1962, Motoo Kimura showed that

$$P_{fix} = (1-e^{-4Nsq})/(1-e^{-4Ns})$$

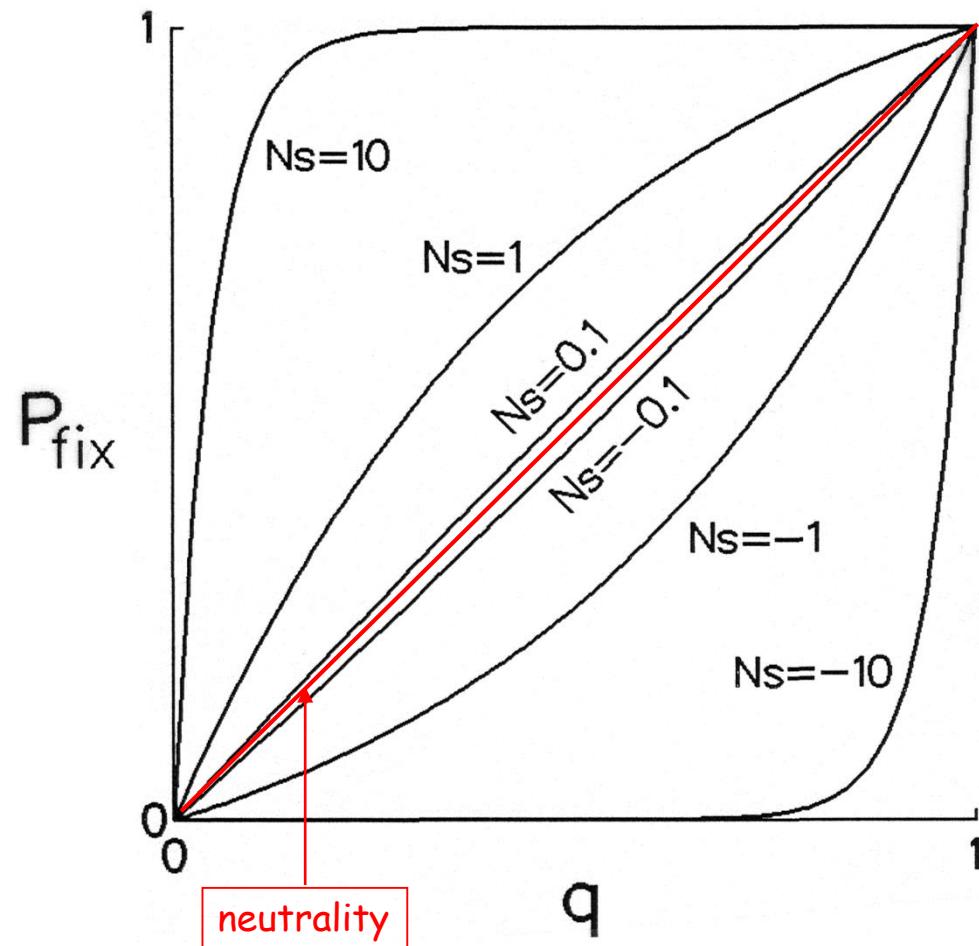
where the fitnesses of the AA, Aa and aa genotypes are 1, $1+s$, and $1+2s$, and q is the current frequency of a.

Note that the population size (N) and the selection coefficient (s) always appear as their product -- never separately!

When $s = 0$ (neutral), then the probability that a will ultimately fix is simply its present frequency, q .

When $Ns > 1$ in absolute value, then selection tends to determine the outcome.

But when $Ns < 1$ the alleles act almost as if they are neutral, regardless of s .



Thus small fitness differences will determine the evolutionary fates of alleles in larger populations, but larger fitness differences are required to overcome drift in smaller populations.

How selection biases drift (The Movies)

Each panel shows 100 allele-frequency histories for a given N , s , and initial frequency q_0 .

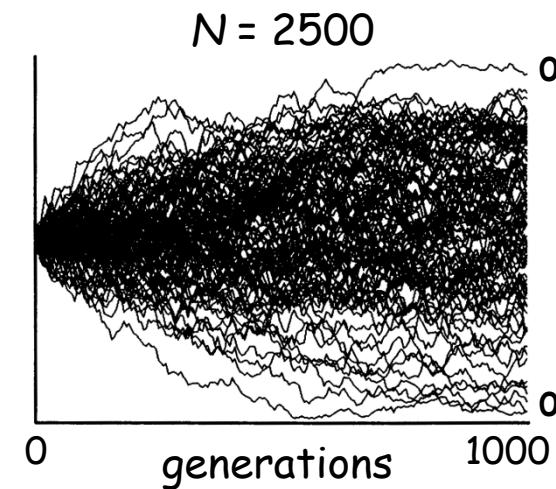
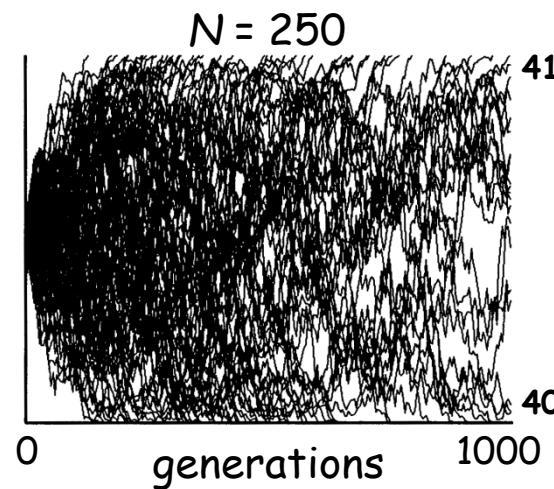
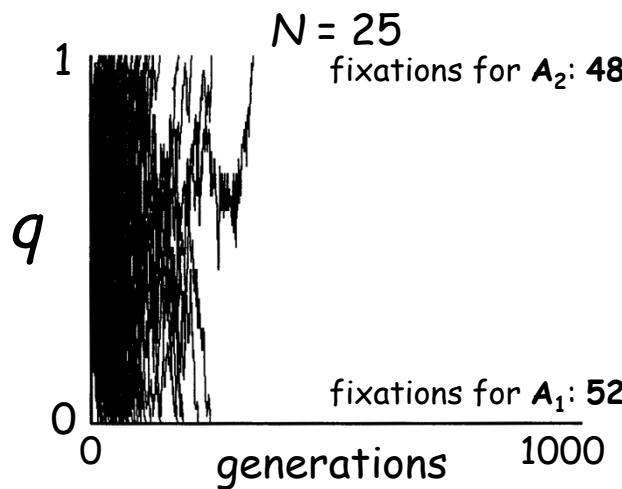
Each history runs for 1000 generations or until fixation occurs.

Within each row of three panels, the population sizes are 25, 250, and 2500.

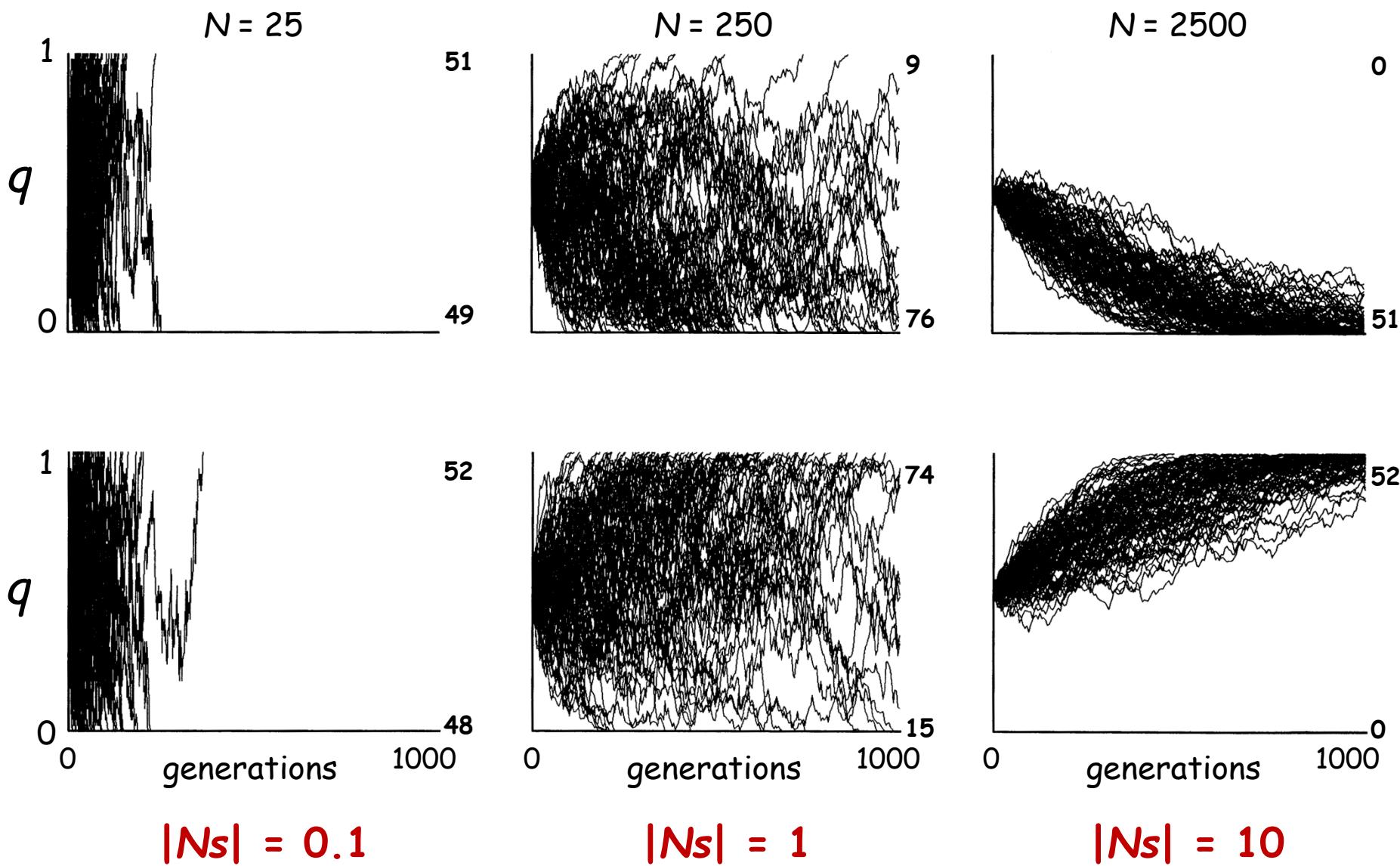
$W(A_1A_1) = 1$, $W(A_1A_2) = 1 - \frac{1}{2}s$, and $W(A_2A_2) = 1 - s$.

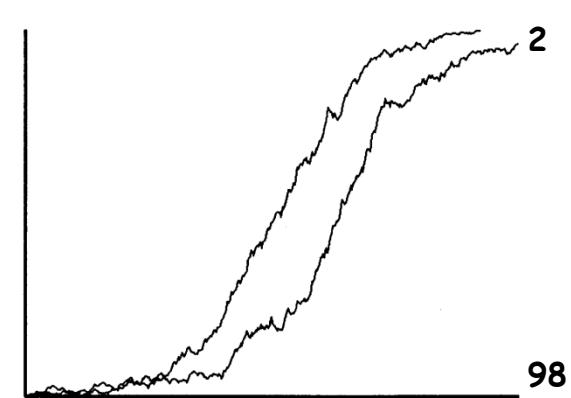
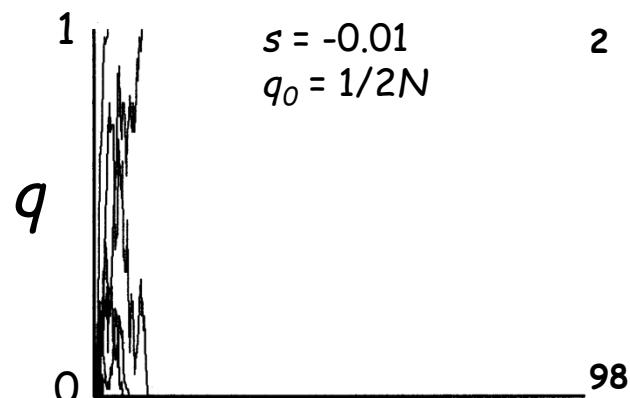
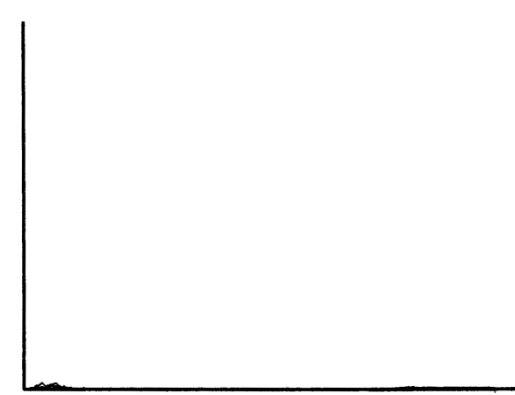
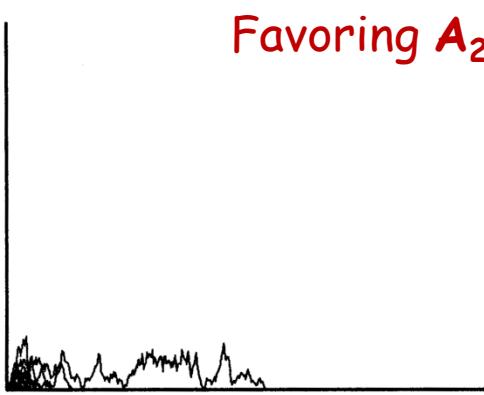
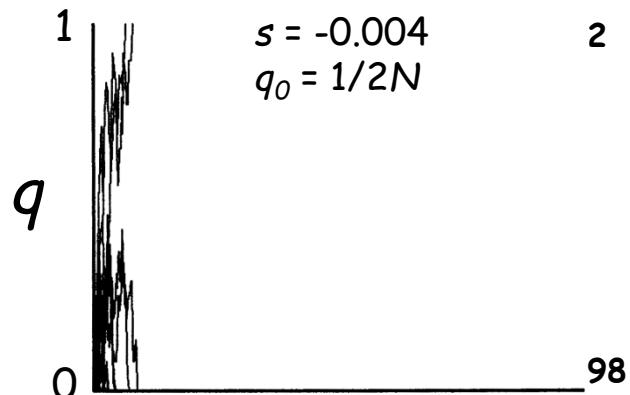
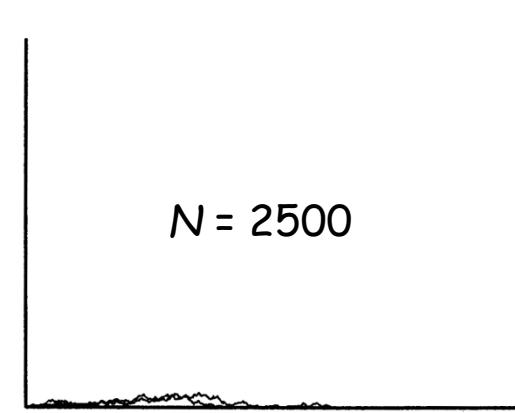
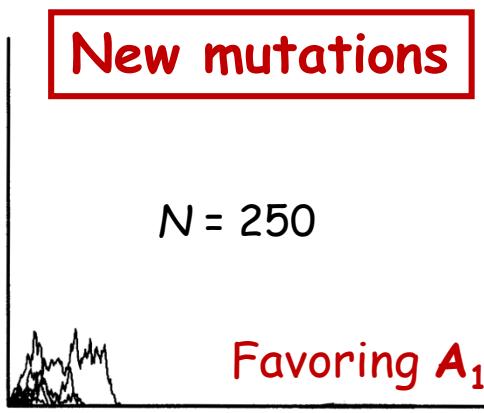
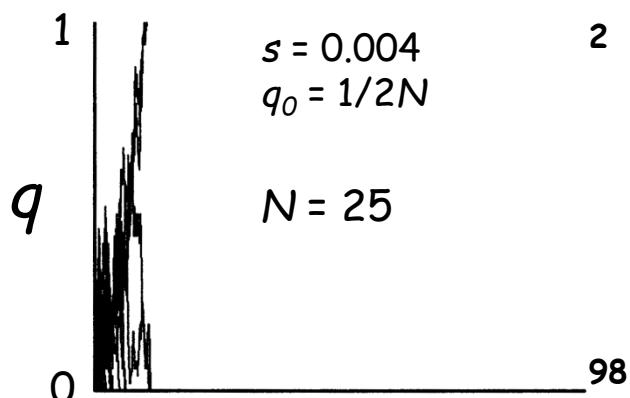
The first set of cases (below) is a neutral "control" for the experiments in subsequent slides.

$s = 0$, $q_0 = \frac{1}{2}$ (neutral case, pure drift)



Selection against A_2 (upper row, $s = 0.004$) and for A_2 (lower row, $s = -0.004$)





Gillespie's notation differs from Kimura's!

$$W(A_1 A_1) = 1 + s$$

(positive s means A_1 is advantageous)

$$W(A_1 A_2) = 1 + \frac{1}{2}s$$

(we assume additive allelic interactions: $h = \frac{1}{2}$)

$$W(A_2 A_2) = 1$$

Then the fixation probability for A_1 is $\pi_1(p) = (1 - e^{-2Ns p}) / (1 - e^{-2Ns})$.

For a new mutation (where $p = 1/2N$), $\pi_1(1/2N) = (1 - e^{-s}) / (1 - e^{-2Ns})$.

What are the fates of NEW weakly advantageous mutations?

If s is small, then $(1 - e^{-s}) \approx s$.

And if N is large enough that $2Ns \gg 1$, then $(1 - e^{-2Ns}) \approx 1$.

In this limit, then, $\pi_1(1/2N) \approx s$, regardless of N !

For other values of h , $\pi_1(1/2N) \approx 2(1-h)s$

In other words, **the fixation probability is roughly twice the fitness advantage of heterozygotes for the new mutation.**

Implications for rates of evolution at the genomic level

When $s = 0$, the rate of evolution (ρ) is *independent* of N .

$2N\mu$ mutations/generation, each with probability $1/2N$ of fixing

$$\rho = (2N\mu)(1/2N) = \mu \quad [\rho/\mu = 1]$$

When $s > 0$ and N is large, the rate of evolution *increases* with N .

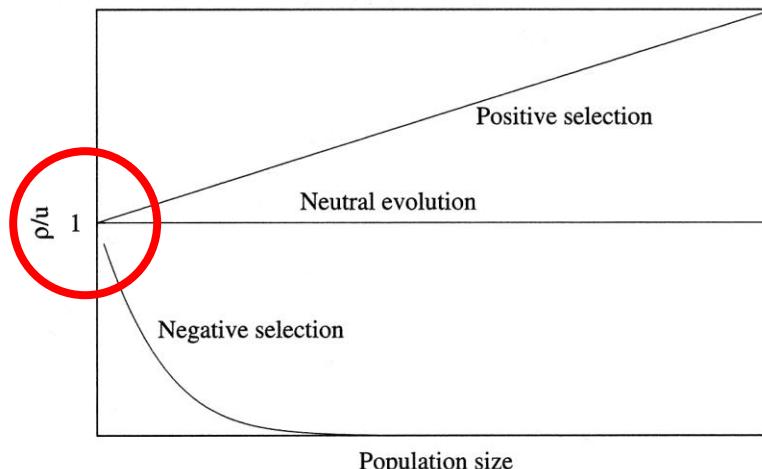
$2N\mu$ mutations/generation, each with probability $\sim s$ of fixing

$$\rho = (2N\mu)(s) = 2N\mu s \quad [\rho/\mu = 2Ns]$$

When $s < 0$ and N is large, the rate of evolution *decreases* with N .

$2N\mu$ mutations/generation, each with probability $|s|/(e^{2N|s|} - 1)$ of fixing

$$\rho = (2N\mu)(|s|/[e^{2N|s|} - 1]) = 2N\mu|s|/(e^{2N|s|} - 1) \quad [\text{see Fig. 3.11, below}]$$

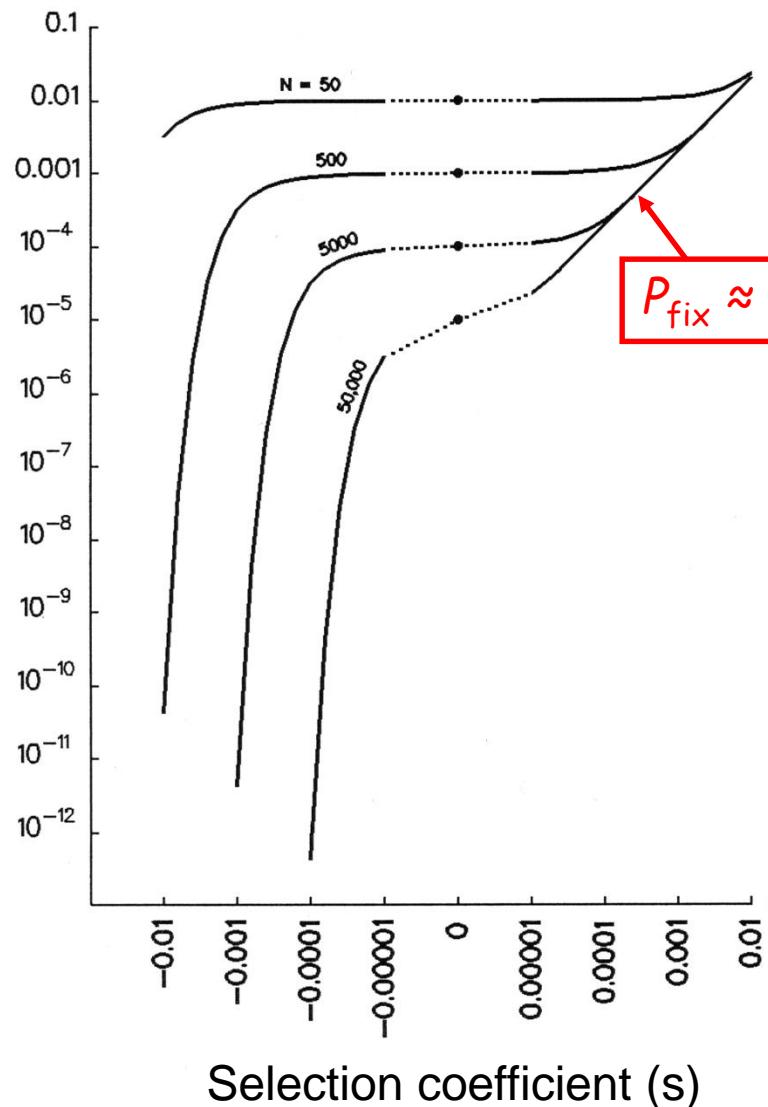


See Gillespie
pp. 94-96

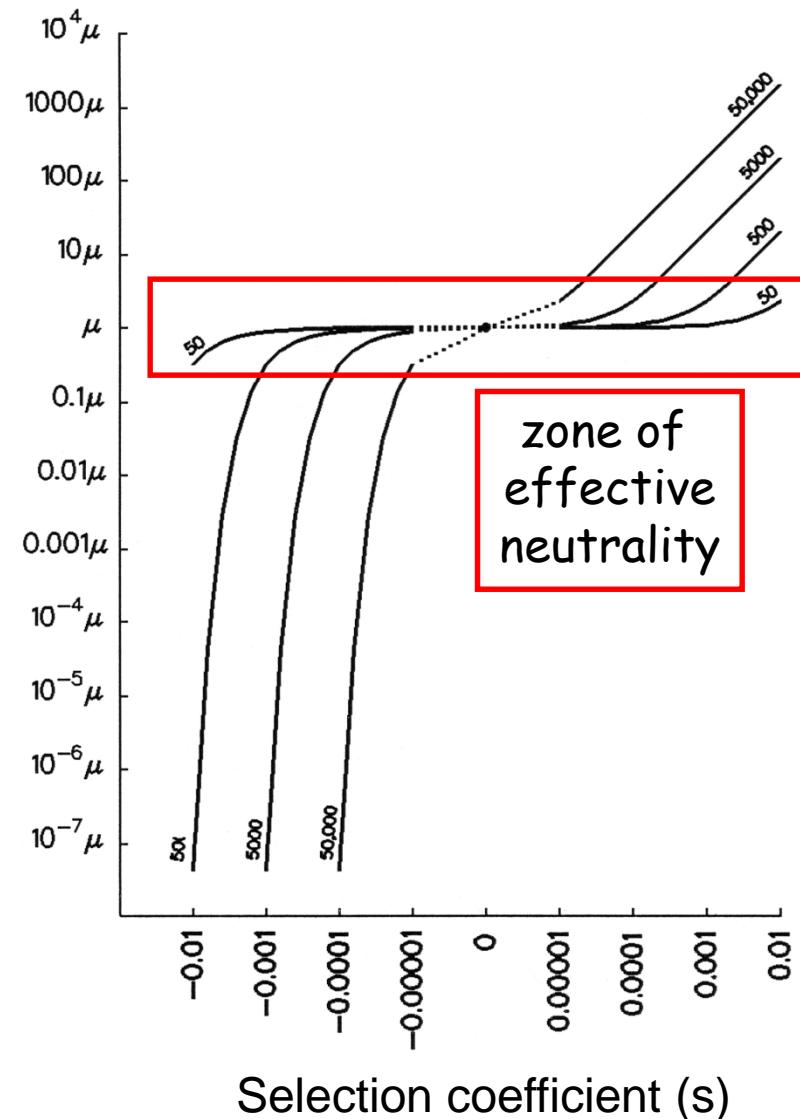
Figure 3.11: The rate of substitution divided by the mutation rate for three models of molecular evolution.

But remember, "large" means $N_s \gg 1$ and "small" means $N_s \ll 1$!

Probability of fixation
(per mutation)



Rate of fixation
(per generation)



The Islands model: drift versus selection

Each island is a closed population with 18 breeding adults ($N=18$, $2N=36$).

The A allele is green, a is yellow.

AA homozygotes have fitness $W = 1-s$.

Aa heterozygotes have fitness $W = 1-\frac{1}{2}s$.

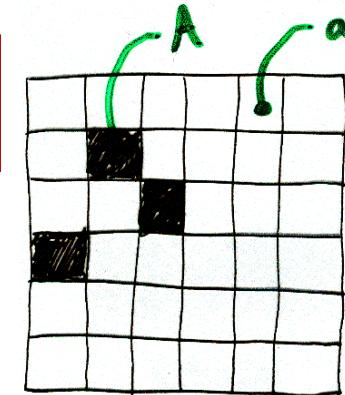
aa homozygotes have fitness $W = 1$.

Individuals are chosen at random, then they contribute a gamete to the next generation with probability W .

There are 100 identical islands, each beginning with the same frequencies of A and a (which we set) and the same selection coefficient s (which we also set).

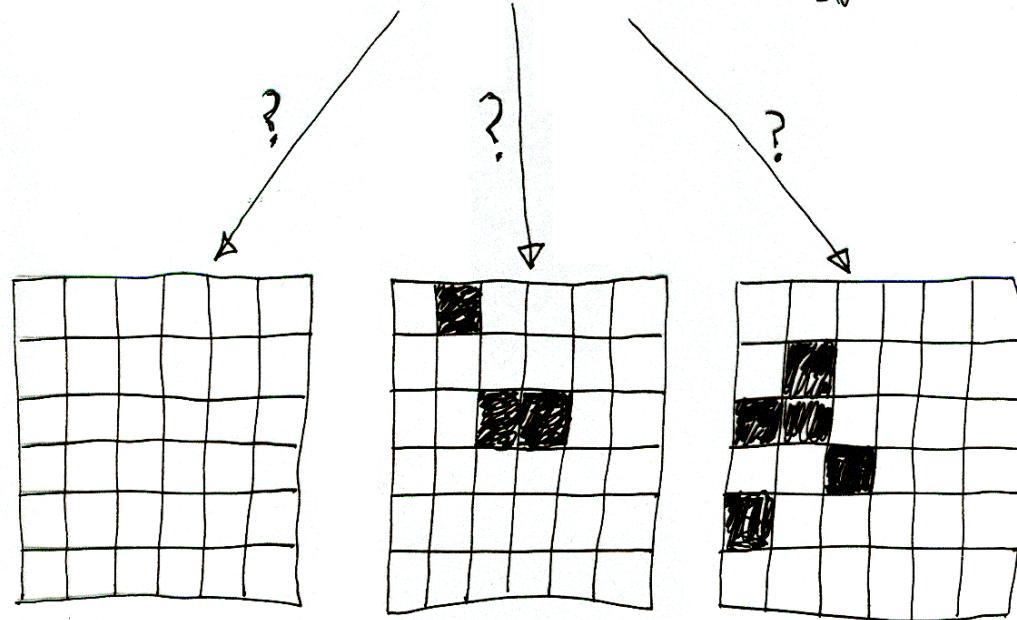
Kimura's model predicts that selection will strongly affect the fates of alleles for which $|Ns| \gg 1$ (here, $|s| \gg 0.05$), but not those for which $|Ns| \ll 1$ ($|s| \ll 0.05$).

Similar to Buri's experiment!



$$P(A) = \frac{3}{36} = 0.083$$

$$P(a) = \frac{33}{36} = 0.917$$



$$P'(A) = 0$$

$$P'(A) = 0.083$$

$$P'(A) = 0.139$$