

Chapter 8 – Selection in a Finite Population

Fixation Probabilities of New Mutations
Rates of Substitution of Selected Alleles
Genetic Hitchhiking

Simulating Drift and Selection

- ❖ see Box 8.1
- ❖ Step 1: calculate new allele frequency due to viability selection

$$f'_A = \frac{v_{AA}f_A^2 + v_{Aa}f_A(1-f_A)}{\bar{v}}$$

- ❖ Step 2: randomly draw $2N$ gametes for next generation

with $s = 0$

- ❖ probability of fixation = initial frequency
 - ❖ $1/2N$ for a new mutation
- ❖ the “gambler’s ruin” paradox

with $s \neq 0$

- ❖ $w_{AA} = 1+2s$; $w_{Aa} = 1+s$ (additive fitness)

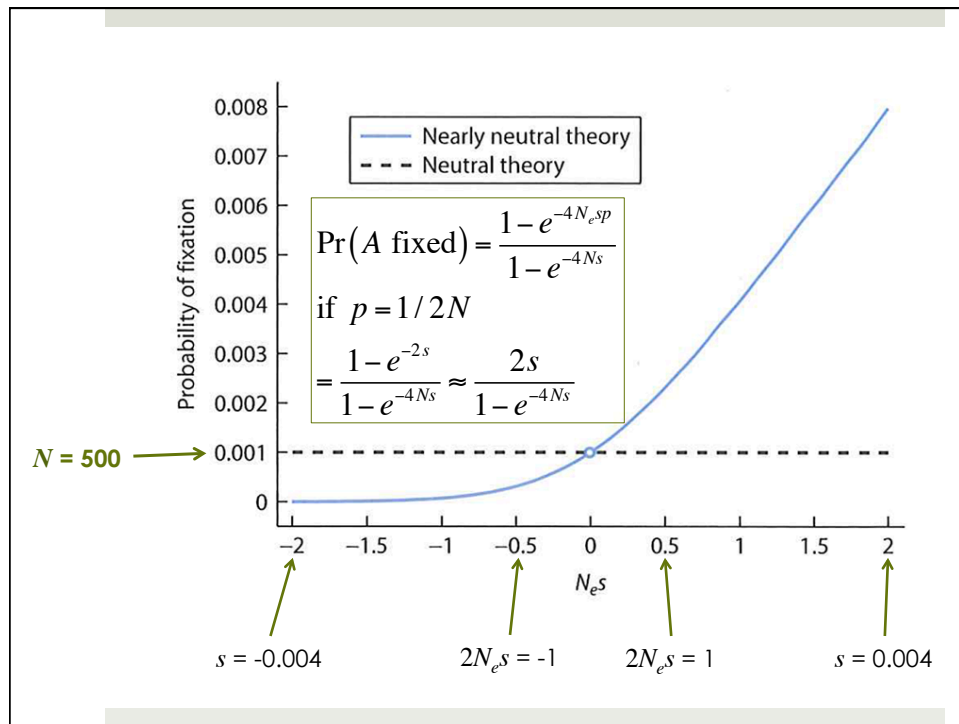
- ❖ $Pr(\text{fixation})$ for a new mutation = u

$$u(s, N) = \frac{1 - e^{-2s}}{1 - e^{-4Ns}}$$

- ❖ fixation probability for “strongly selected” alleles

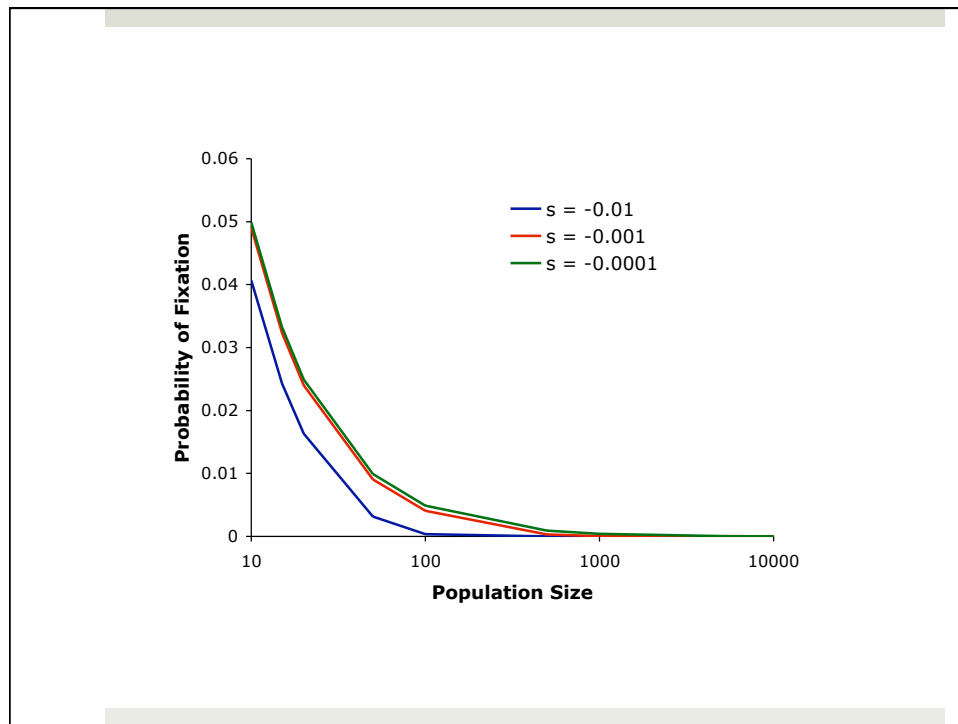
$$u \approx 2s$$

- ❖ “strongly selected” if $2Ns > 1$
- ❖ “nearly neutral” if $-1 < 2Ns < 1$



Nearly Neutral Theory

- ❖ what happens in small populations when selection is weak?
 - ❖ changes in allele frequency due to drift and selection are approximately equal $|2N_e s| \approx 1$



What qualifies as nearly neutral?

- ❖ Hamilton: $2s = 1/2N_e$ or $4N_e s = 1$
 - ❖ value at which “the processes of genetic drift and selection are **equal**”
- ❖ Hartl & Clark: $|2Ns| \approx 1$
- ❖ Hedrick: $s < 1/(2N)$ or $2Ns < 1$
- ❖ Ohta & Gillespie (1996): $s \approx 1/N$ or $Ns \approx 1$
- ❖ Nielsen & Slatkin (2013): $-1 < 2Ns < 1$

Nearly Neutral Theory - Summary

- ❖ the rate of neutral evolution is independent of population size

- ❖ substitution rate equals mutation rate

$$2N\mu \times \frac{1}{2N} = \mu$$

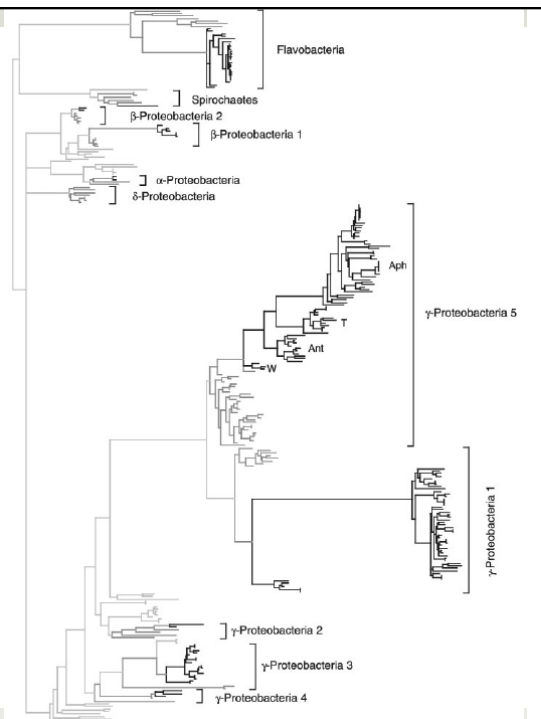
- ❖ in contrast, the fate of nearly neutral mutations depends on population size

$|2Ns| \approx 1$ ❖ when N is small, the effect of genetic drift can be comparable to that of selection, making slightly deleterious mutations "effectively neutral"

- ❖ thus, lineages experiencing small population size should accumulate both neutral and nearly neutral mutations, leading to a faster rate of sequence evolution

Woolfit & Bromham
2003 Increased rates
of sequence evolution
in endosymbiotic
bacteria and fungi
with small effective
population sizes. *MBE*
20:1545-1555.

- higher rate in endosymbiotic bacteria interpreted as a consequence of nearly neutral evolution



Substitution Rate for Selected Alleles

❖ substitution rate for neutral allele = μ

❖ for selected alleles: $r(s, N) = 2N\mu u(s, N)$

$$= 2N\mu \left(\frac{1 - e^{-2s}}{1 - e^{-4Ns}} \right)$$

❖ substitution rate from data:

❖ where d/L is proportion of sites that differ between two sequences

$$r = \frac{d}{2LT}$$

Neutral Rate from Synonymous Sites?

TABLE 8.1 Universal genetic code

Ala/A	GCU, GCC, GCA, GCG	Leu/L	UUA, UUG, CUU, CUC, CUA, CUG
Arg/R	CGU, CGC, CGA, CCG, AGA, AGG	Lys/K	AAA, AAG
Asn/N	AAU, AAC	Met/M	AUG
Asp/D	GAU, GAC	Phe/F	UUU, UUC
Cys/C	UGU, UGC	Pro/P	CCU, CCC, CCA, CCG
Gln/Q	CAA, CAG	Ser/S	UCU, UCC, UCA, UCG, AGU, AGC
Glu/E	GAA, GAG	Thr/T	ACU, ACC, ACA, ACG
Gly/G	GGU, GGC, GGA, GGG	Trp/W	UGG
His/H	CAU, CAC	Tyr/Y	UAU, UAC
Ile/I	AUU, AUC, AUA	Val/V	GUU, GUC, GUA, GUG
START	AUG	STOP	UAA, UGA, UAG

Neutral Rate from Synonymous Sites?

- ❖ E.g., *β-globin*
 - ❖ 78 four-fold degenerate sites
 - ❖ 30 differ between mouse and human
 - ❖ synonymous mutations
 - ❖ divergence time: ~80MY
 - ❖ $r = 2.4 \times 10^{-9}$

Neutral Rate from Synonymous Sites?

TABLE 8.2 Synonymous and nonsynonymous substitution rates estimated by comparing genes in humans and mice

Gene	Codons	Synonymous rate	Nonsynonymous rate
Histone <i>H3</i>	101	6.38	0.0
Histone <i>H4</i>	135	6.13	0.027
Growth hormone	189	4.37	0.95
Prolactin	197	5.59	1.29
<i>α</i> -hemoglobin	141	3.94	0.56
<i>β</i> -hemoglobin	144	2.96	0.87
<i>γ</i> -interferon	136	8.59	2.80
HPRT	217	2.13	0.13
Fibrogen- <i>γ</i>	411	5.82	0.55
Albumin	590	6.72	0.92

Source: Li et al. (1985). All rates are in units of 10^{-9} per site per year.

Purifying Selection

- ❖ proportion of non-synonymous mutations strongly selected against? α

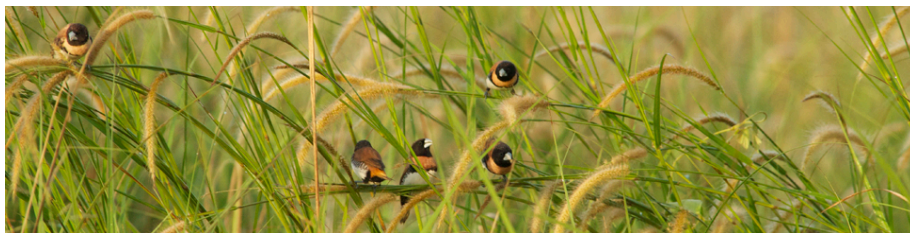
$$r_N = (1 - \alpha)\mu$$

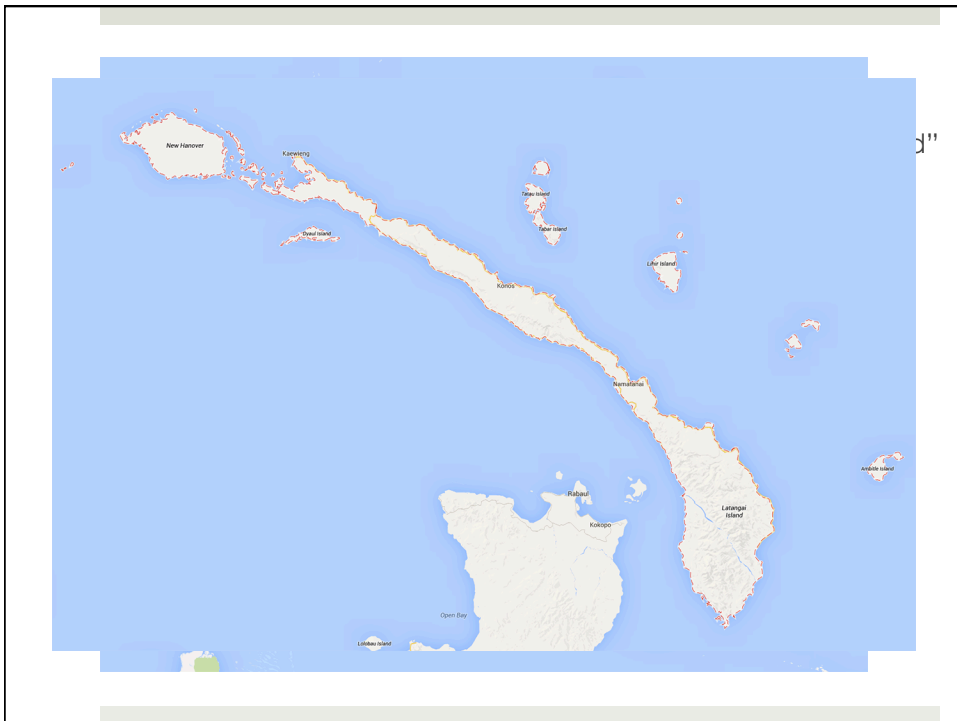
- ❖ e.g., prolactin

$$(1 - \alpha) = \frac{r_N}{\mu} = \frac{1.29}{5.59} = 0.23$$

$$\alpha = 0.77$$

An extraordinary avian radiation: the *Lonchura munias* of Papua New Guinea







New Ireland
Lonchura
hunsteini
hunsteini



New Hanover
Lonchura
hunsteini
nigerrima

Data Set

- ❖ 6,146 autosomal RAD-seq loci with 10+ reads per locus for 36 individuals (19 on New Ireland, 17 on New Hanover)
 - ❖ 770,864 base pairs per sample
- ❖ 250 Z-chromosome RAD-seq loci (10+ reads per locus for all 36 individuals)
 - ❖ 32,172 base pairs per sample
- ❖ plus comparable data for 16 samples representing the other munia species

