How does demography affect adaptation?

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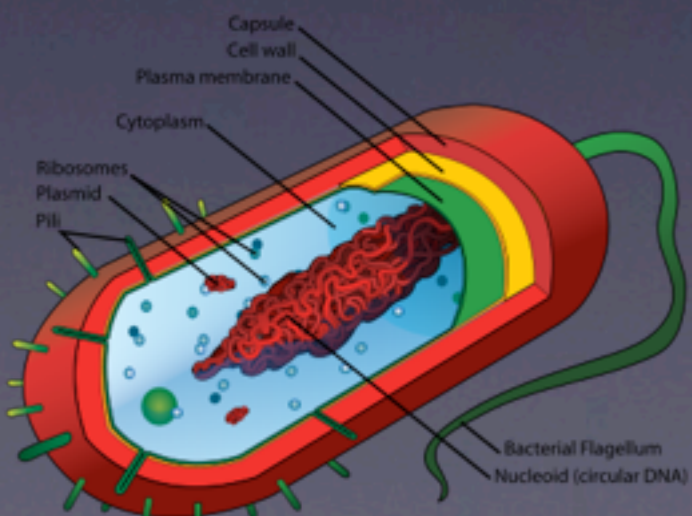
Desai Lab

Harvard University

11 Jan 2011

Microbial and Viral Evolution
KITP

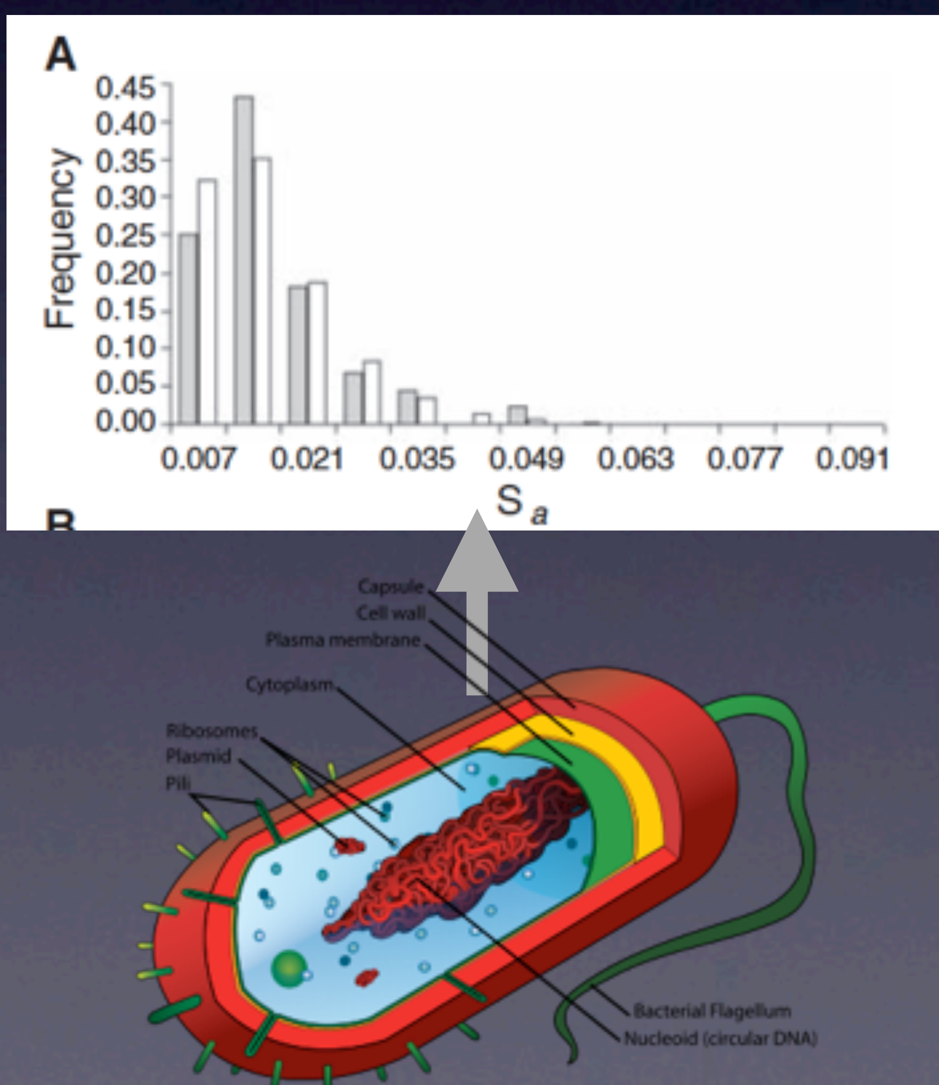
Adaptation



Environment + cellular architecture

- Regulatory networks
- Proteins

Adaptation



Fitness landscape:
- Mutation rates
- Distribution of fitness effects
- Epistasis

Environment + cellular architecture
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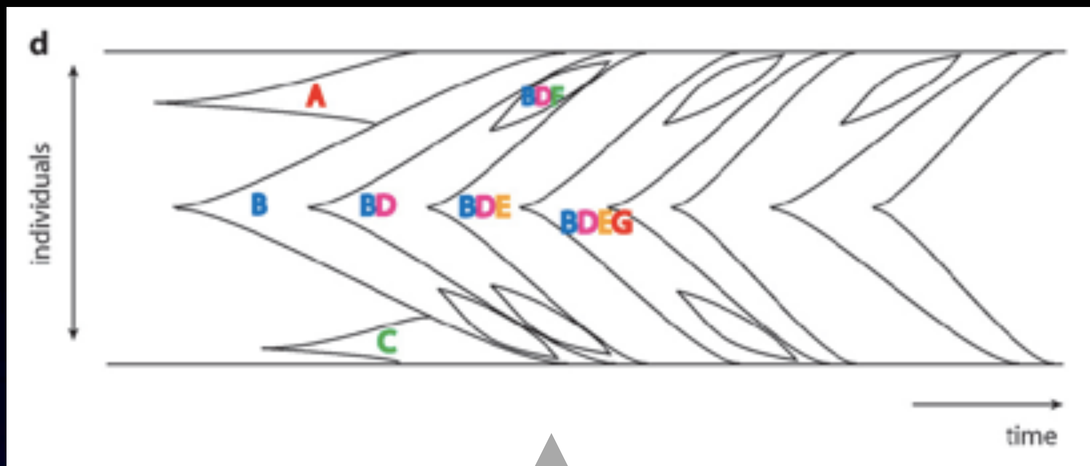
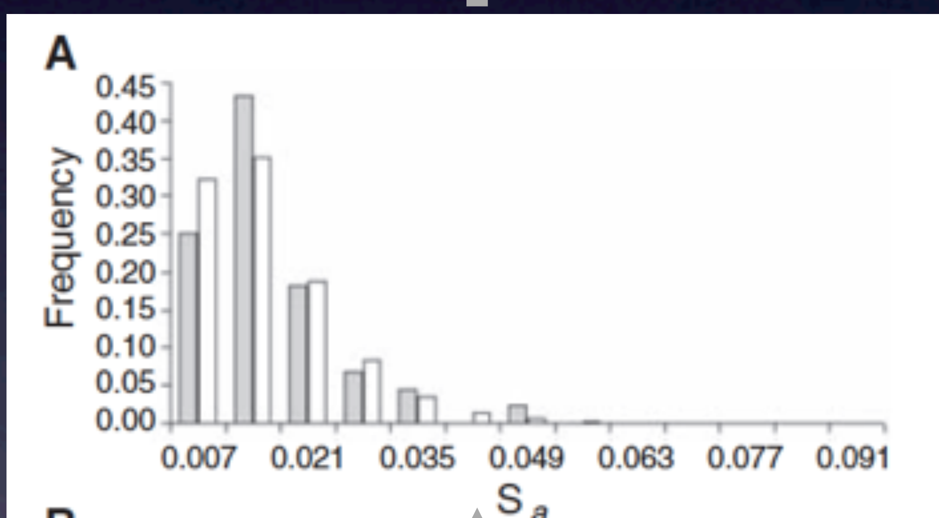
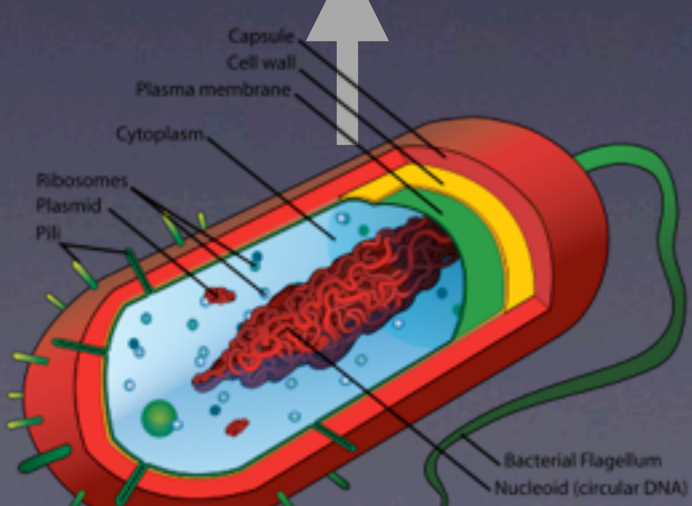
Adaptation







Dynamics of adaptation:

- Population structure
- Clonal interference
- Multiple mutations

Fitness landscape:

- Mutation rates
- Distribution of fitness effects
- Epistasis

Environment + cellular architecture

- Regulatory networks
- Proteins

Simplest case

- Well-mixed asexual population of size N
- Beneficial mutations are rare

Fixation probability of a mutation with selective advantage s

$$\pi(s) = \frac{1 - e^{-2s}}{1 - e^{-2Ns}} \approx 2s$$

Population fitness F increases as

$$\frac{dF}{dt} = \mu N r(F), \;\; F(0) = 1$$

r is the expected fitness increment of a mutation

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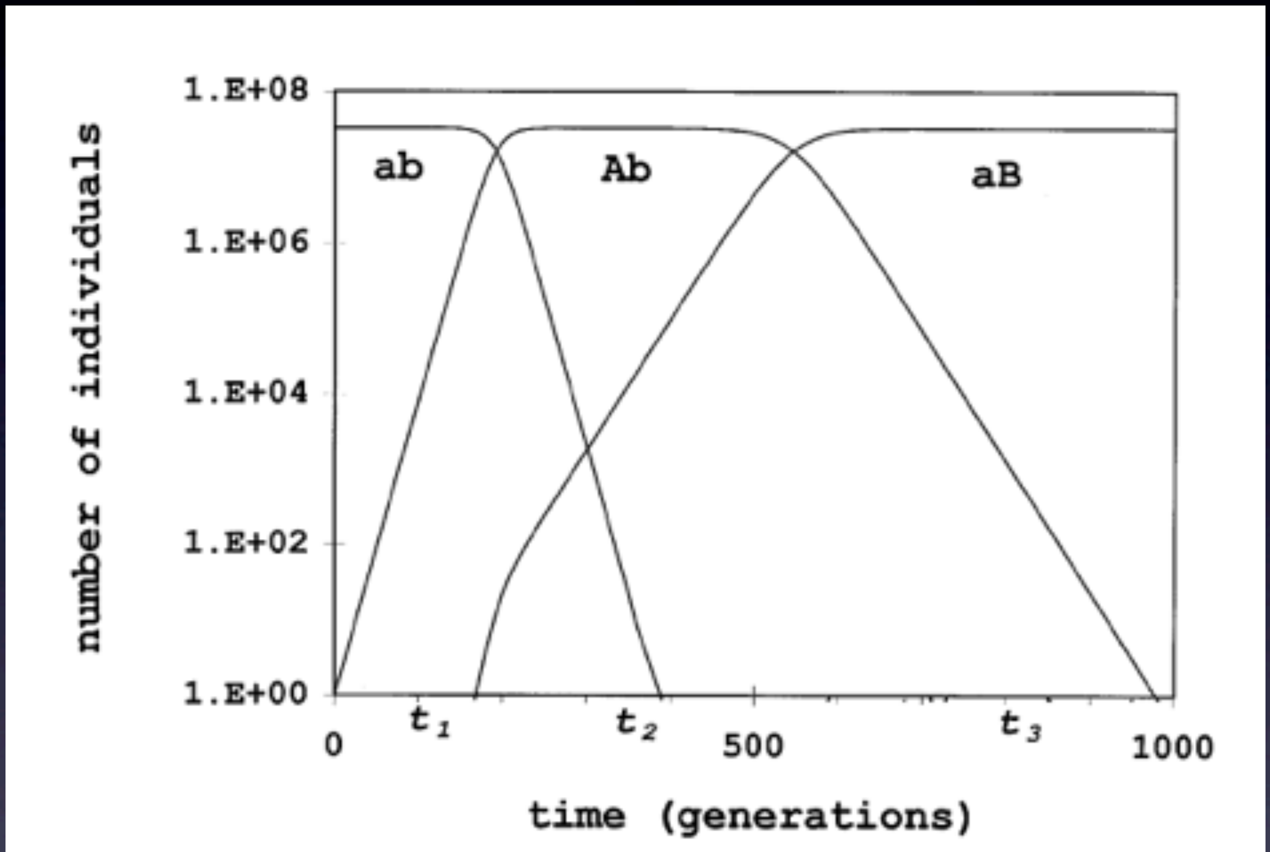
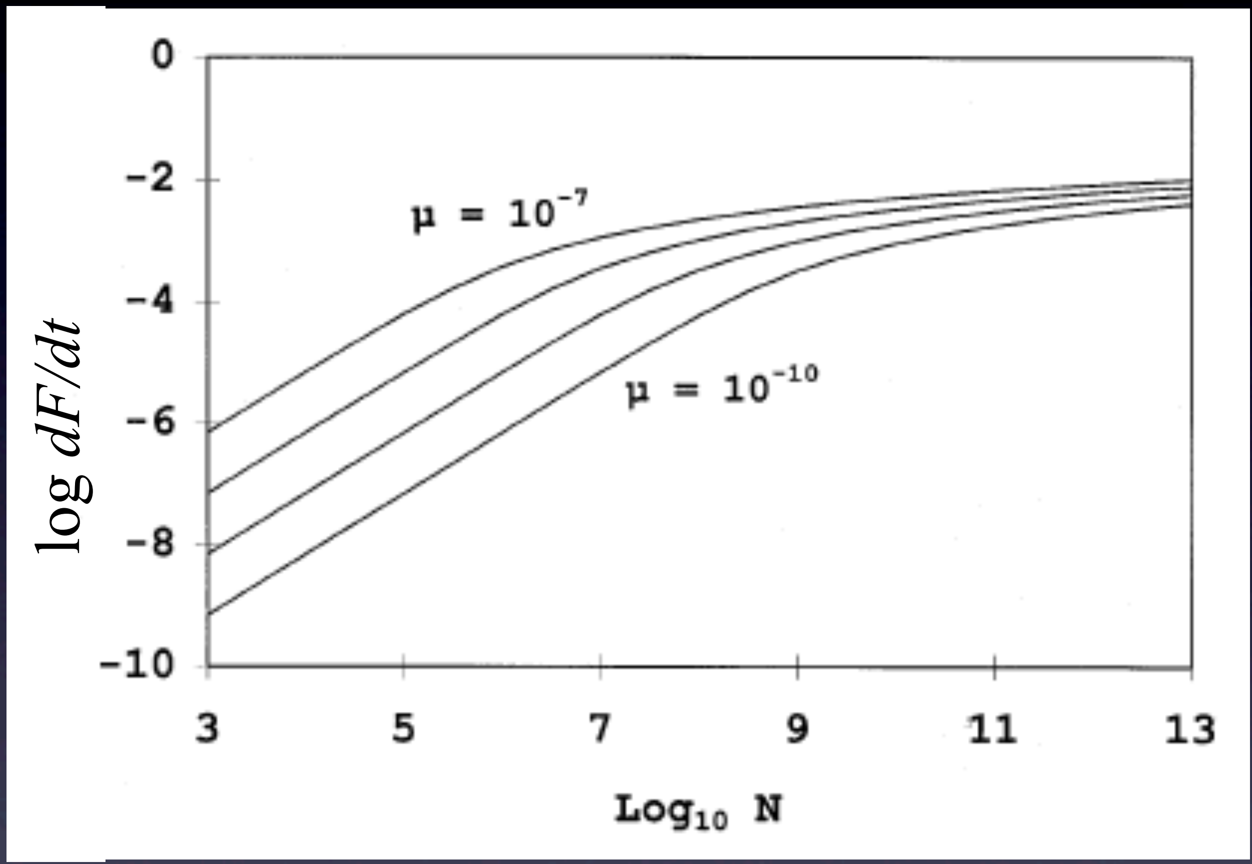
Complication: clonal interference





$$\frac{dF}{dt} = \alpha\mu N \int_0^\infty s\pi(s)e^{-\lambda(s,\alpha,\mu,N)-\alpha s} ds$$

Gerrish and Lenski et al, Genetica 1998

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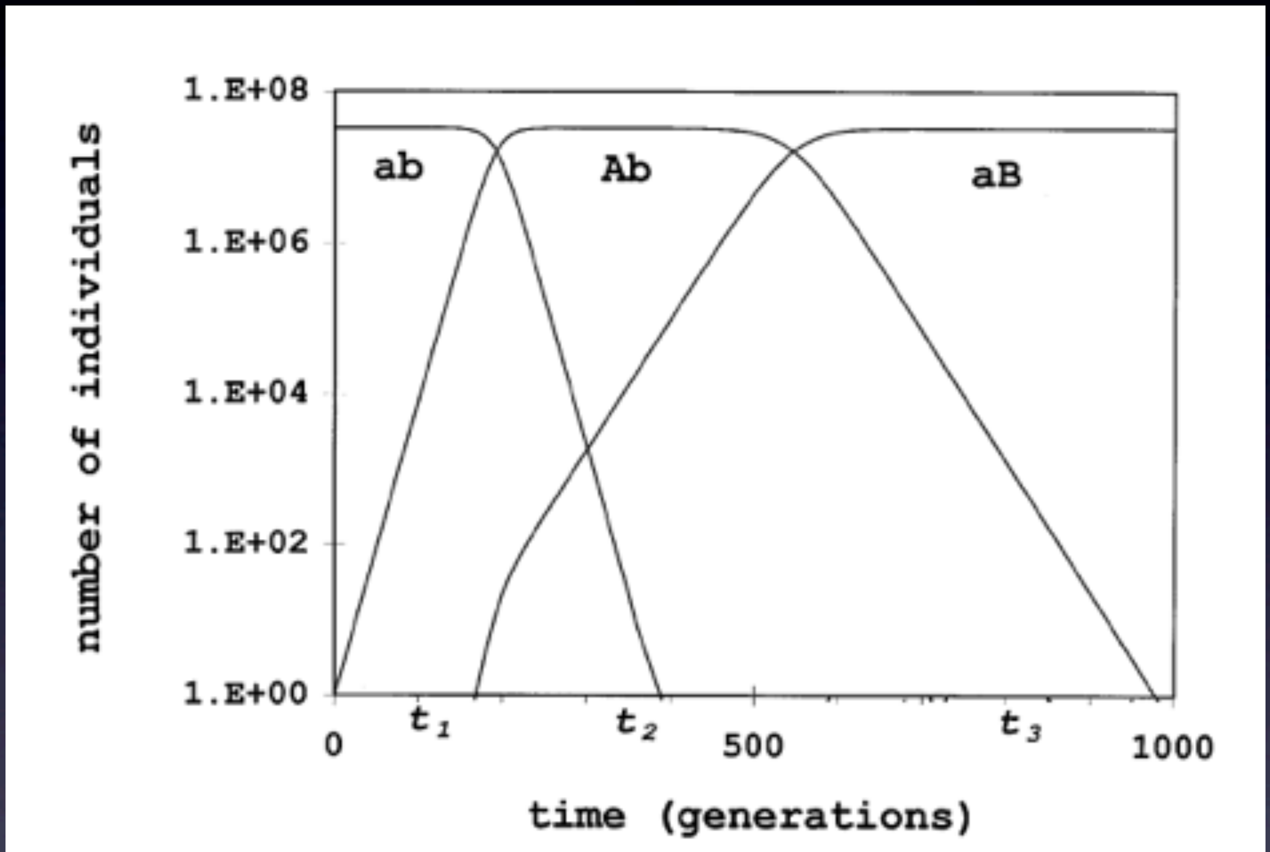

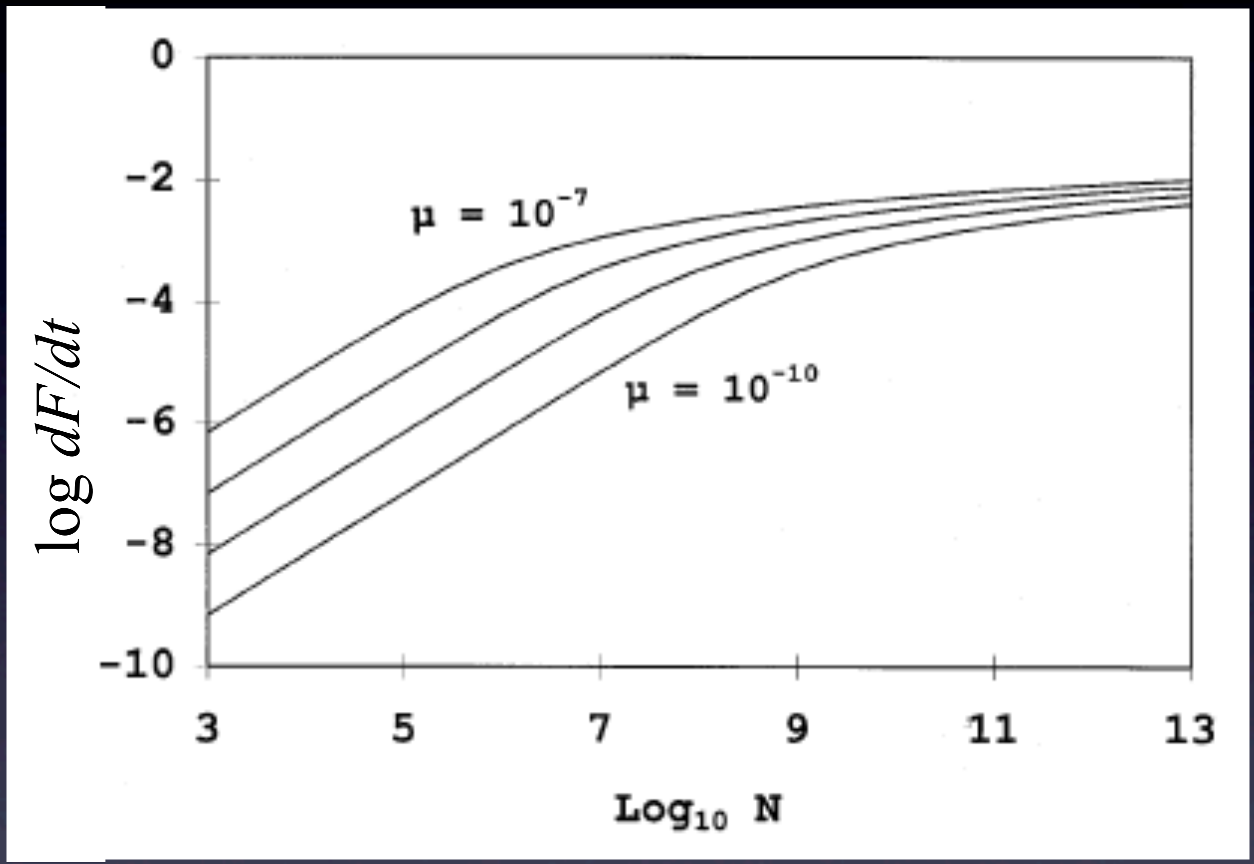

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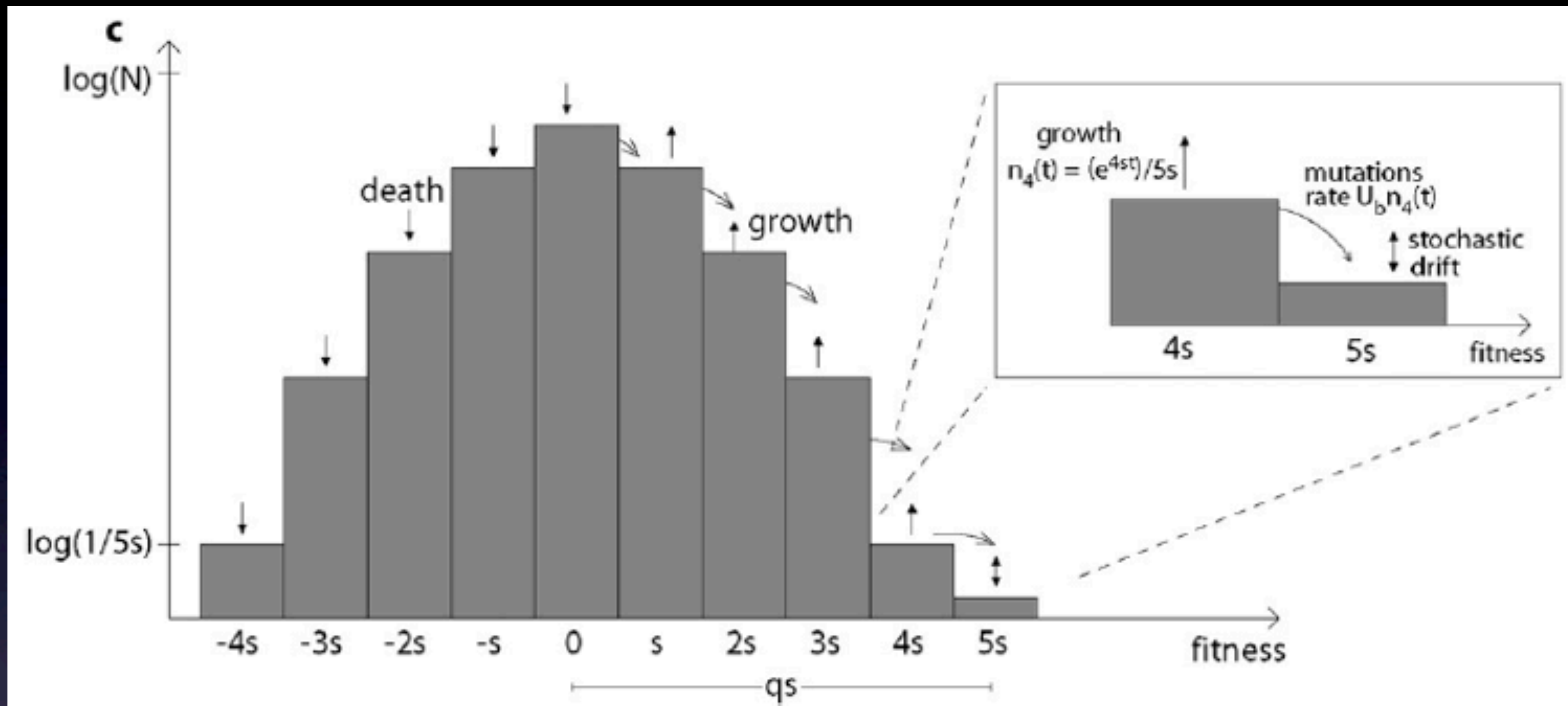
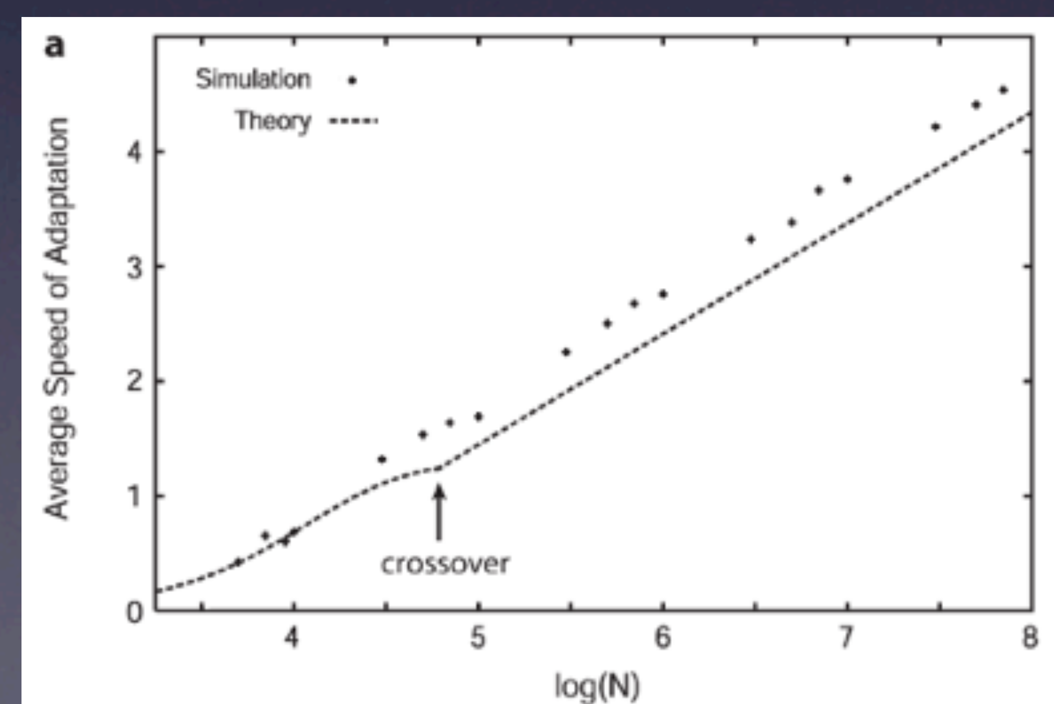
Complication: piggybacking





$$\frac{dF}{dt} = s^2 \frac{2 \log Ns - \log s/\mu}{\log^2 s/\mu}$$

Desai and Fisher, Genetics 2007

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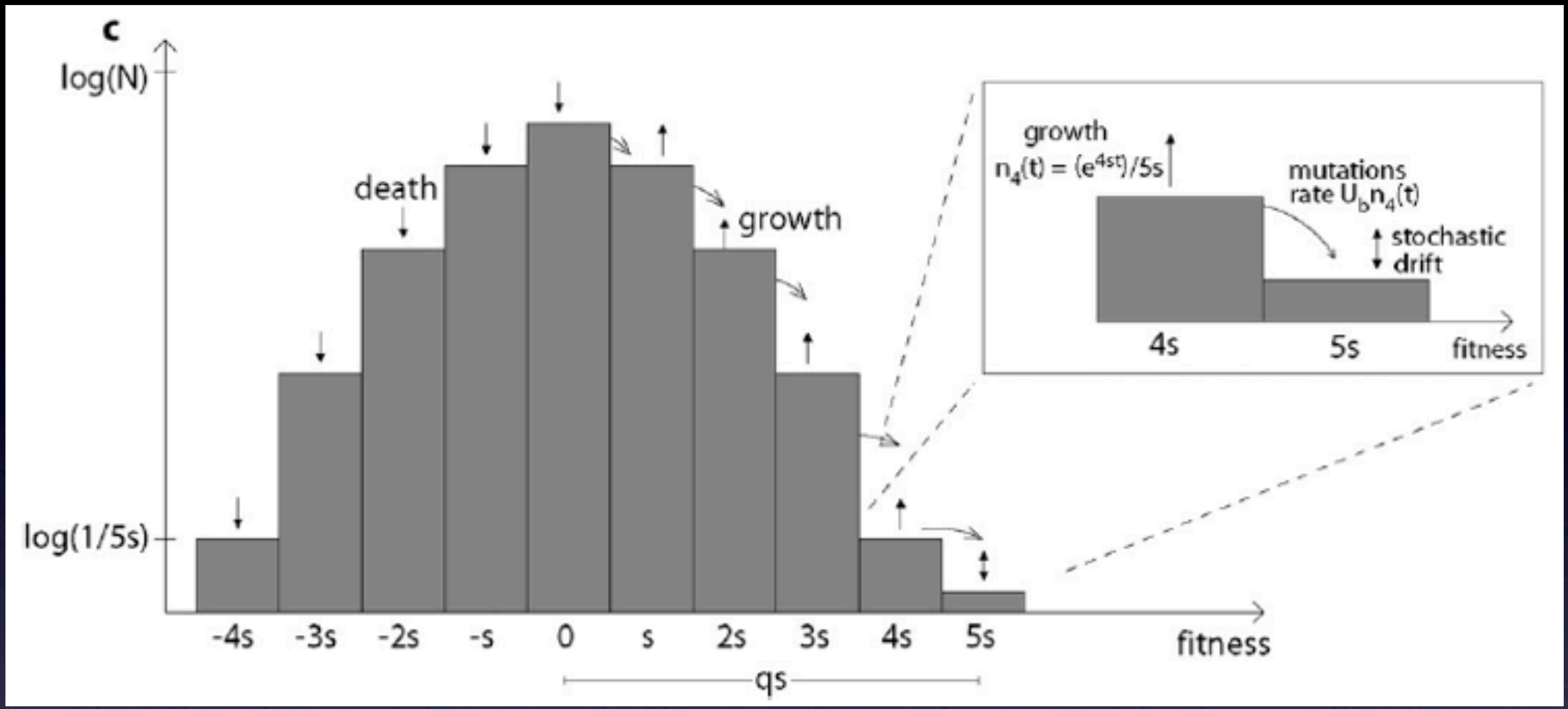

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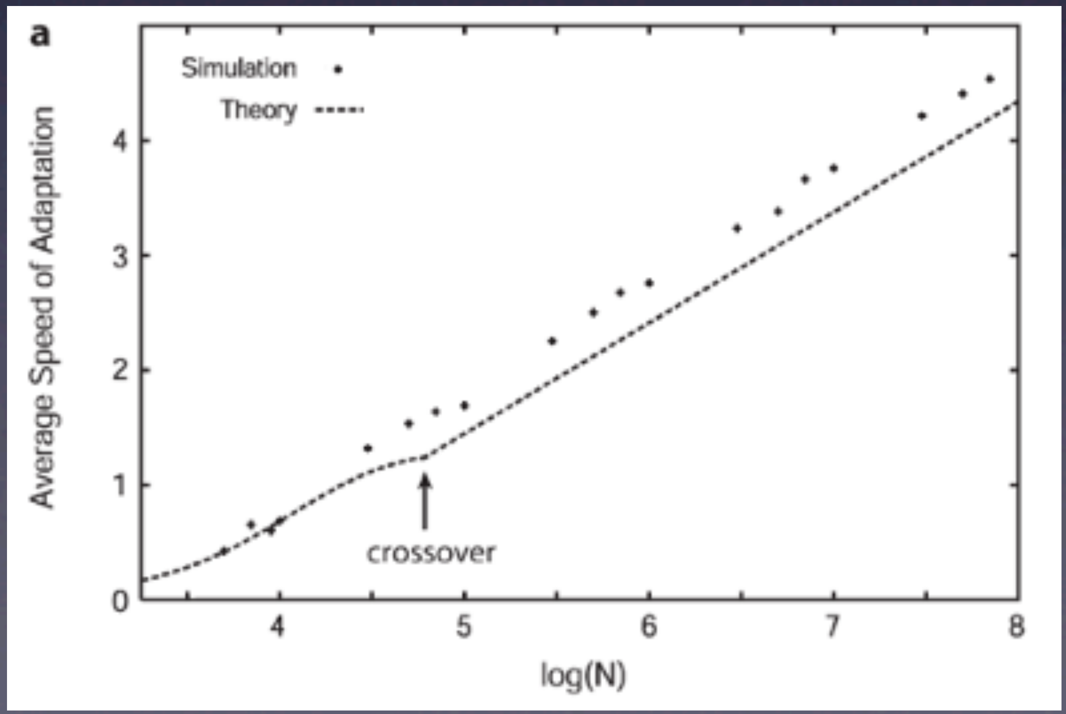

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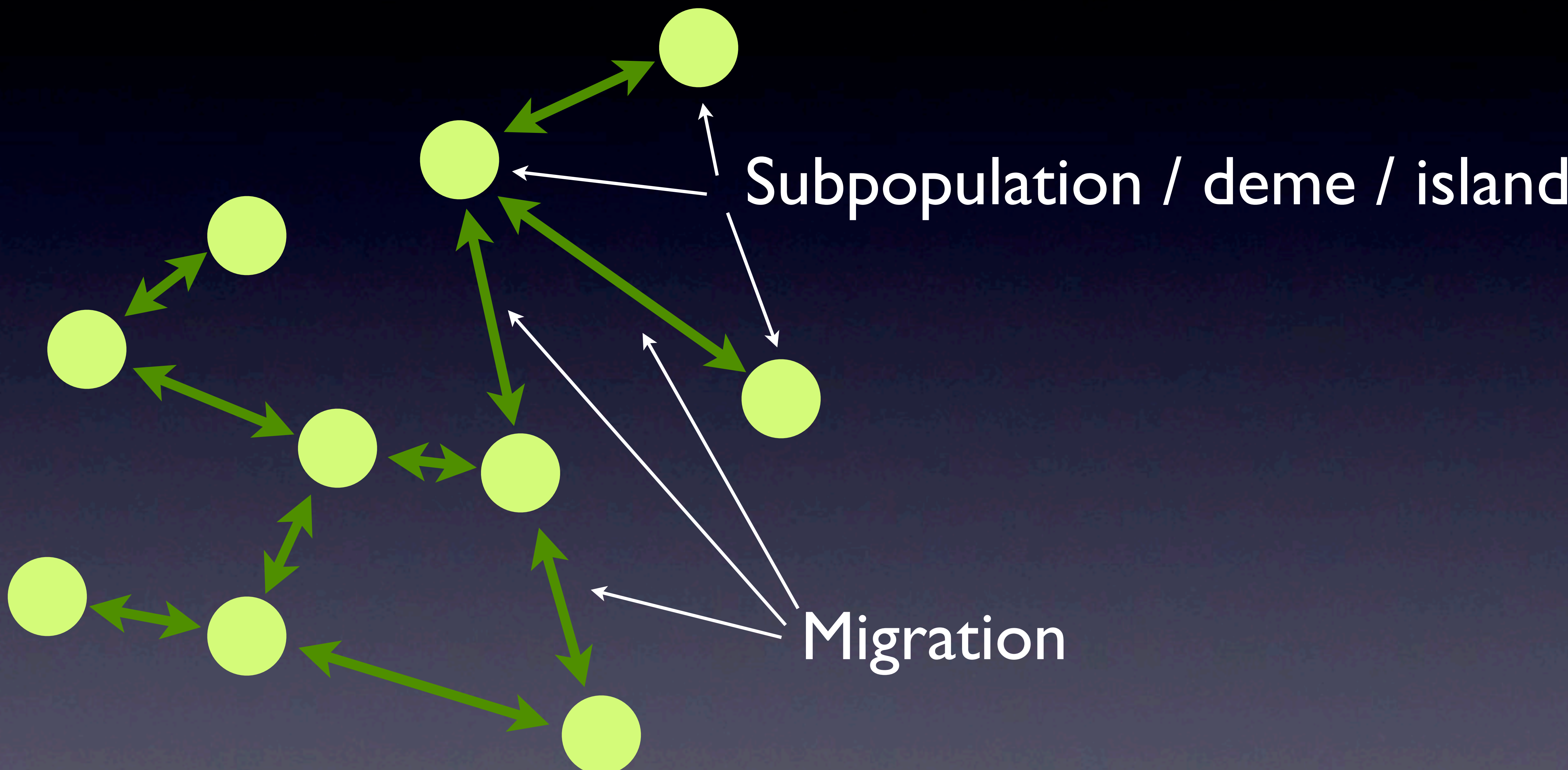
Complication: population subdivision



Shifting balance theory (S. Wright)

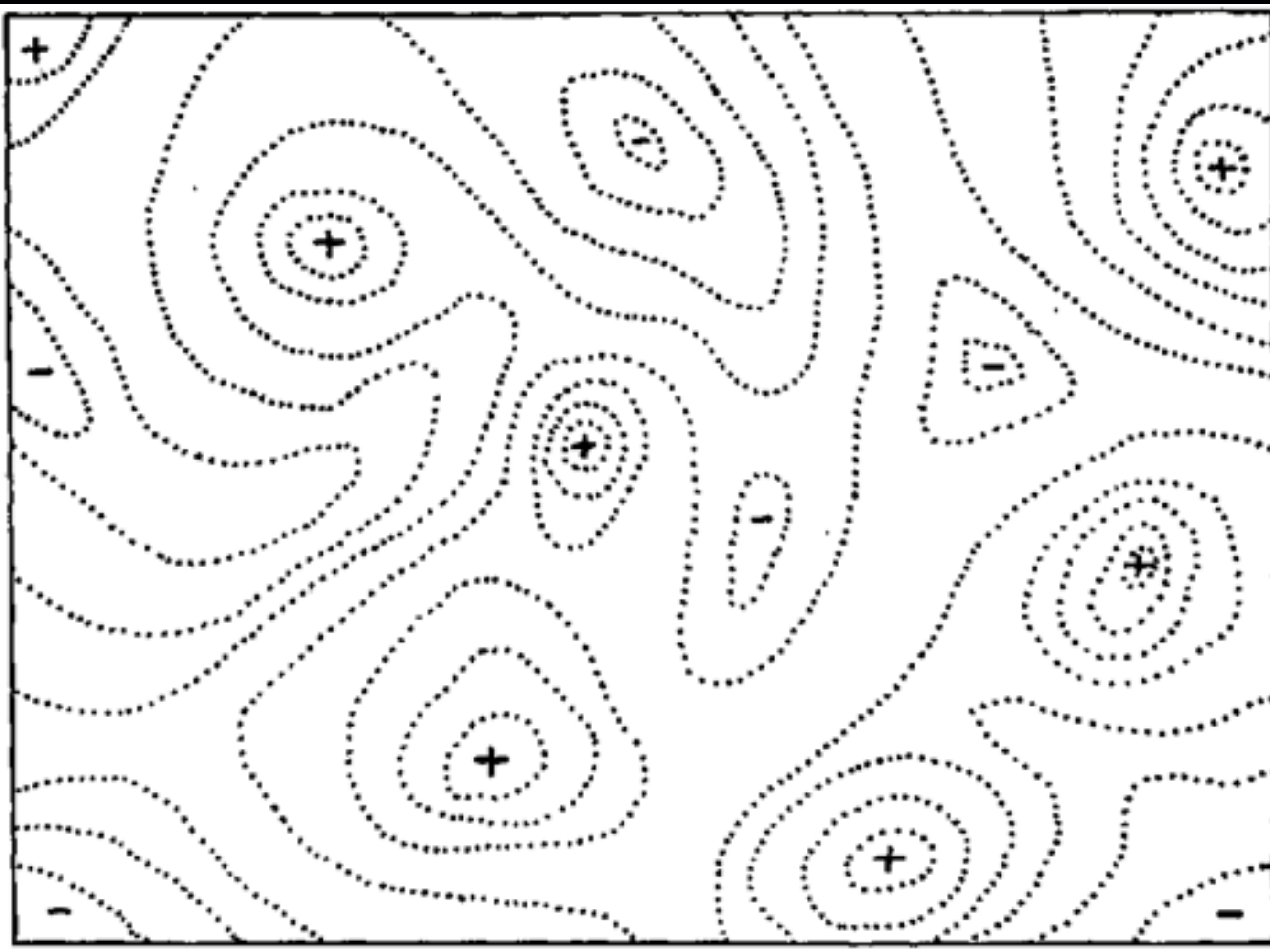


FIGURE 2.—Diagrammatic representation of the field of gene combinations in two dimensions instead of many thousands. Dotted lines represent contours with respect to adaptiveness.

"With 10^{1000} possibilities it may be taken as certain that there will be an enormous number of widely separated harmonious combinations. <...> In a rugged field of this character, selection will easily carry the species to the nearest peak, but there may be innumerable other peaks which are higher but which are separated by "valleys". The problem of evolution as I see it is that of a mechanism by which the species may continually find its way from lower to higher peaks in such a field."

Sewall Wright (1932)

Wright, 6th Int Congr Genet, 1932

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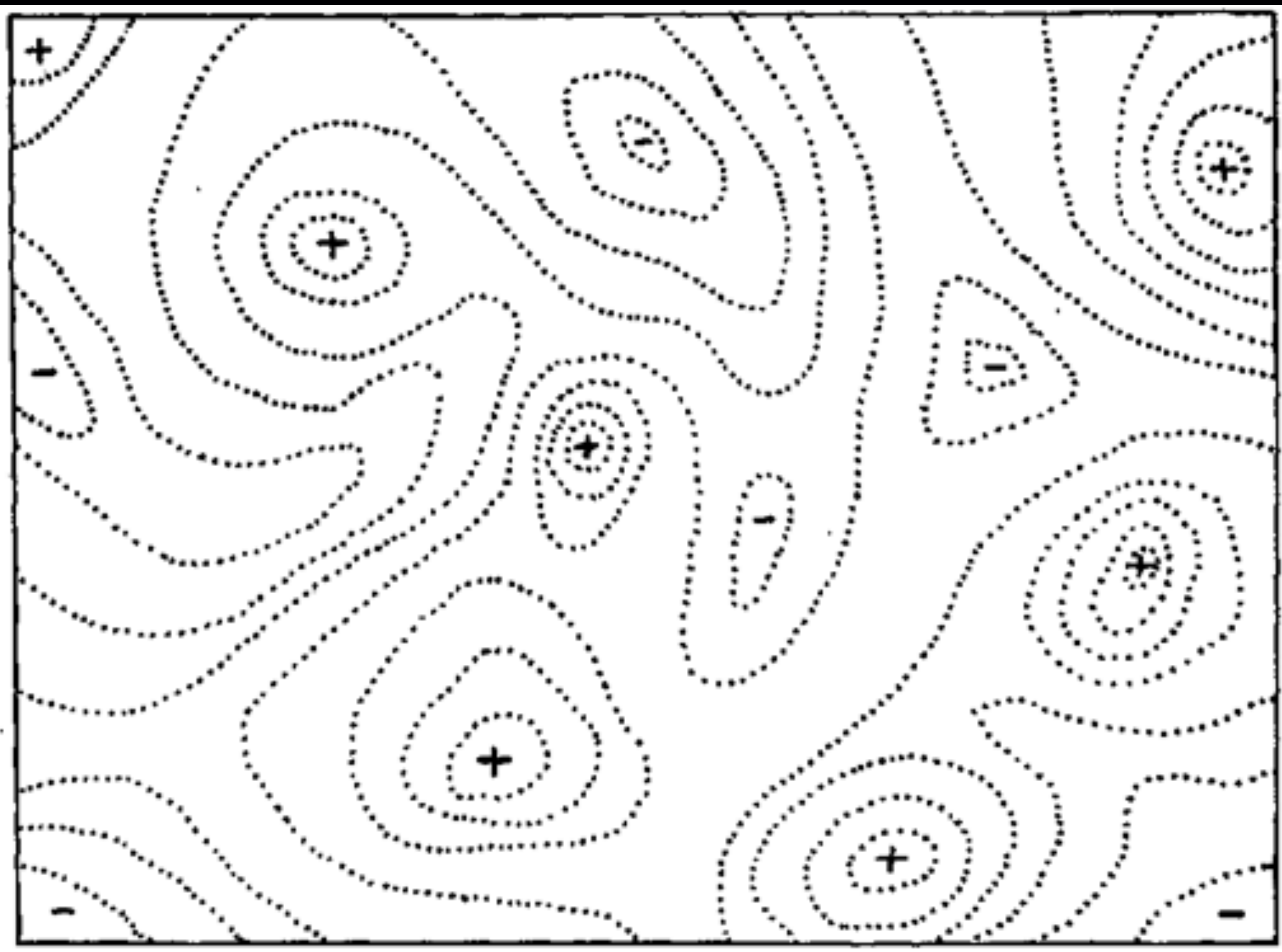

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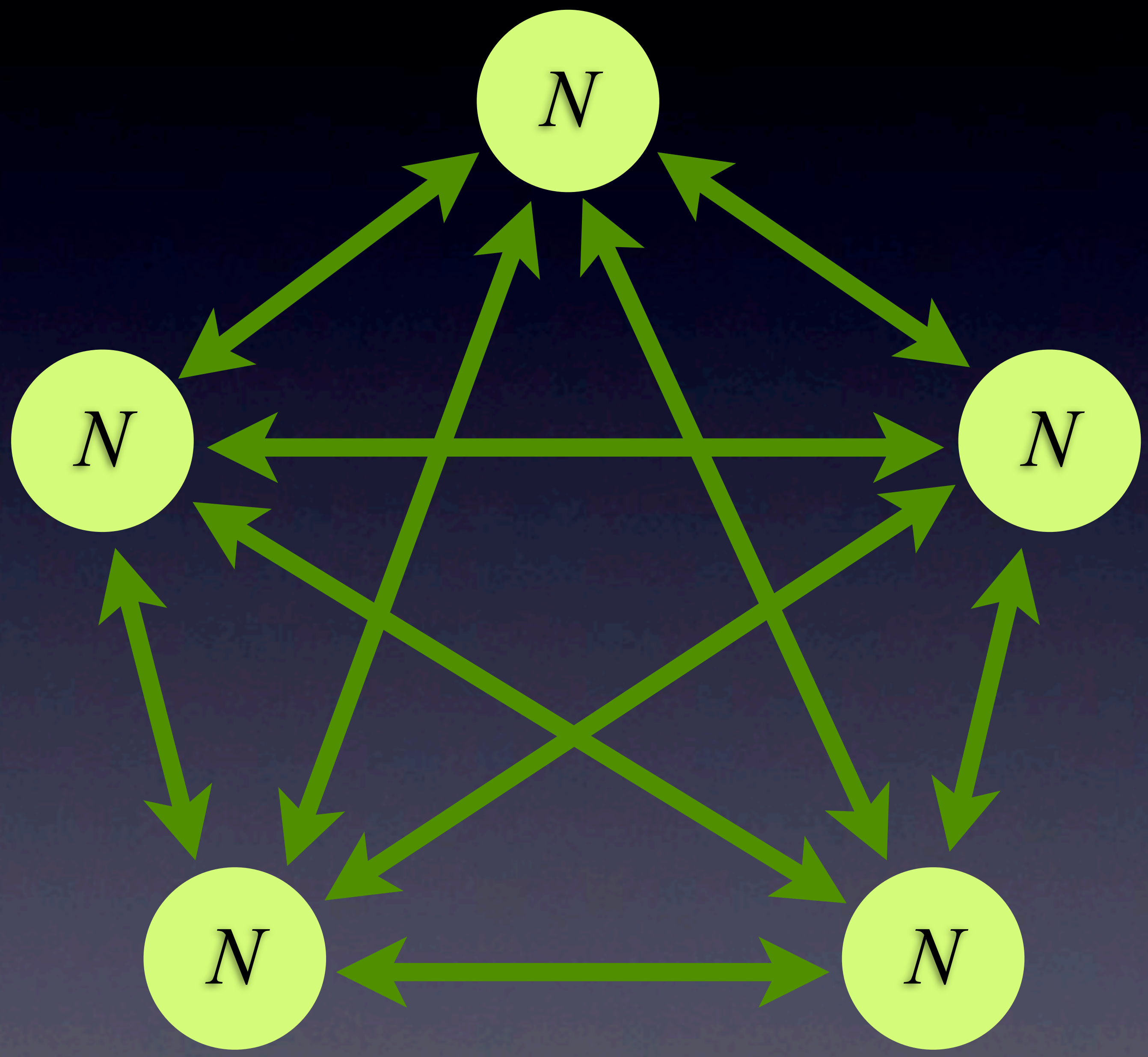
Shifting balance theory (S. Wright)

Phase I	extensive local differentiation with stochastic variability in each locality
Phase II	occasional crossing of a saddle leading to a higher selective peak in a subpopulation
Phase III	excess proliferation and dispersal from local populations in which peak shift has occurred

The island model



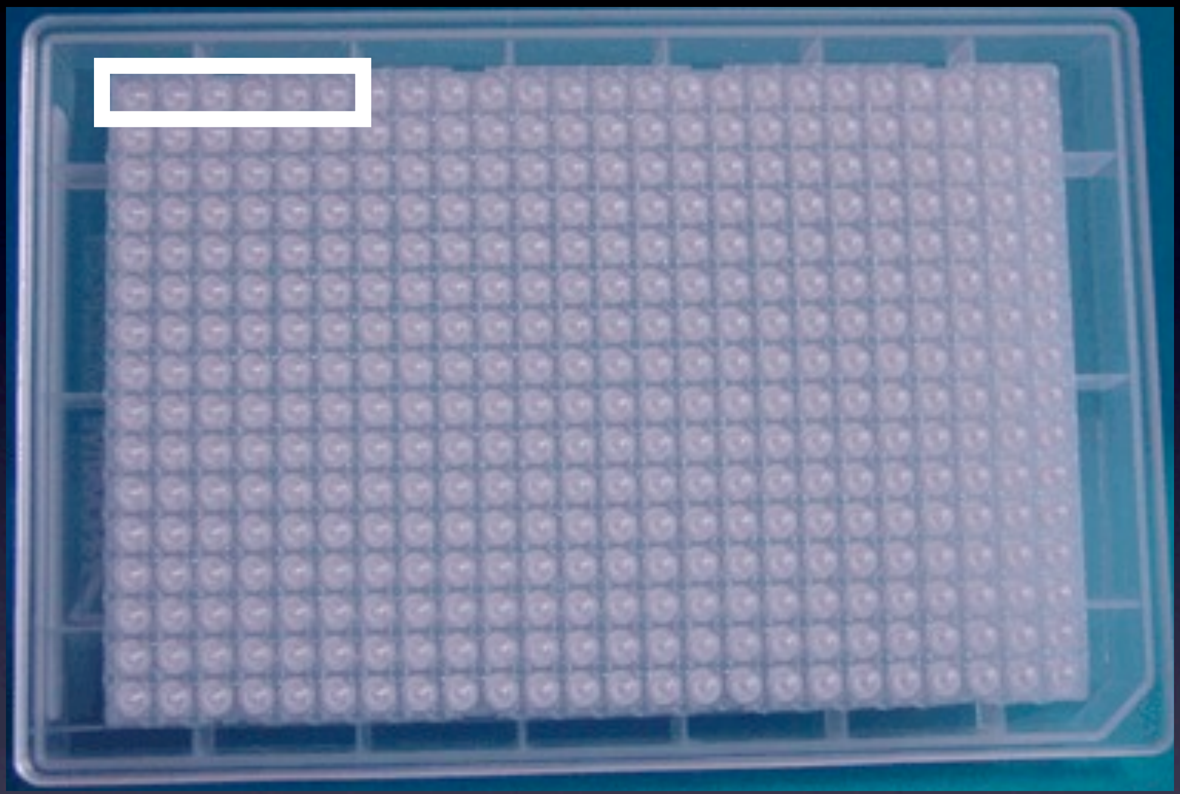
Deme size N

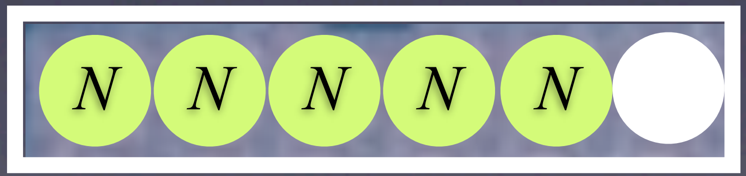
Number of demes d

Migration rate m

Experimental design

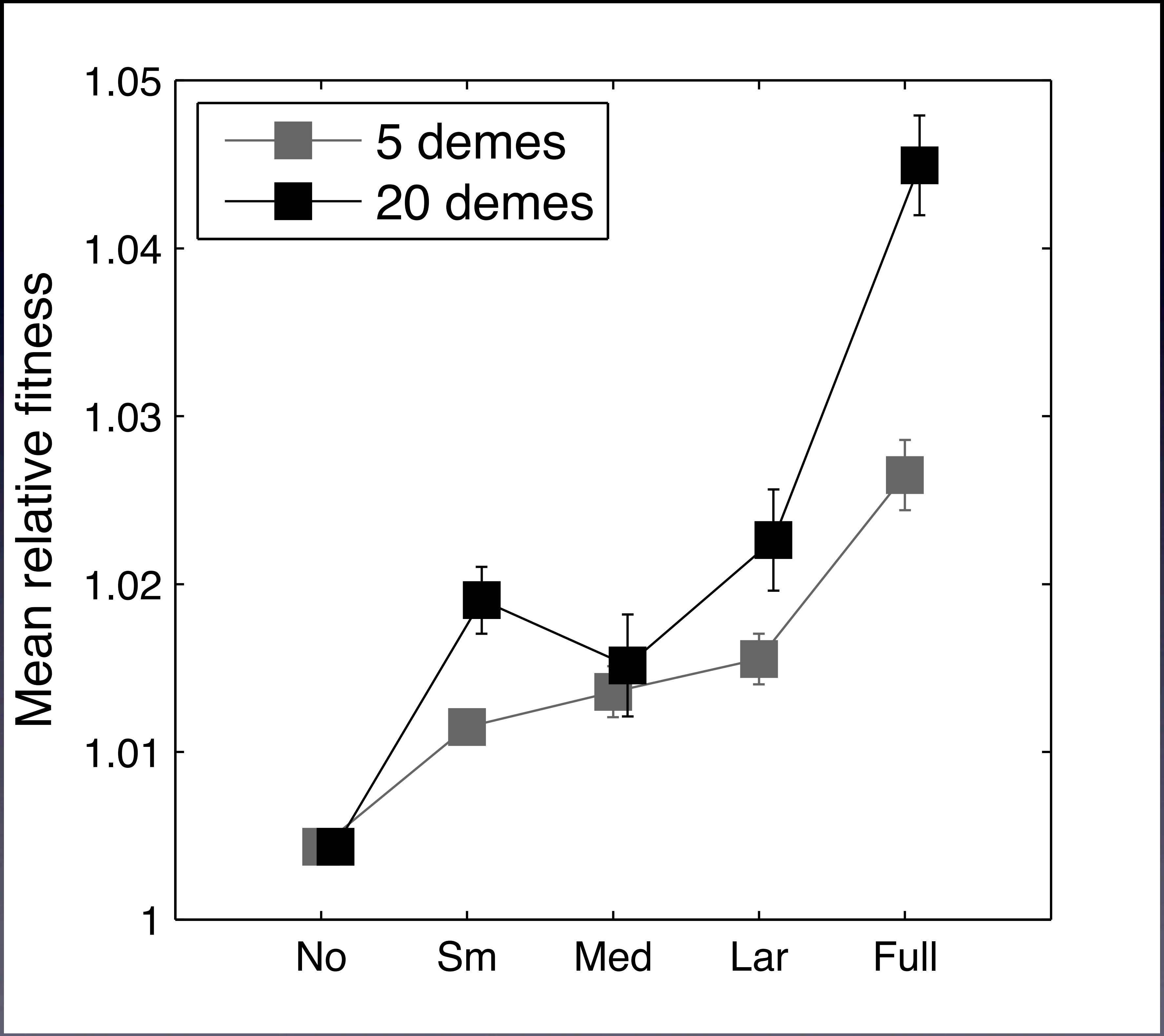
- Haploid yeast, asexual growth
- YPD
- 384-well plates, well volume 64μl
- Serial transfer every 24h, dilution 1:1000
- 550 generations (2 months)





$$N_b = 1000$$

Mean fitness

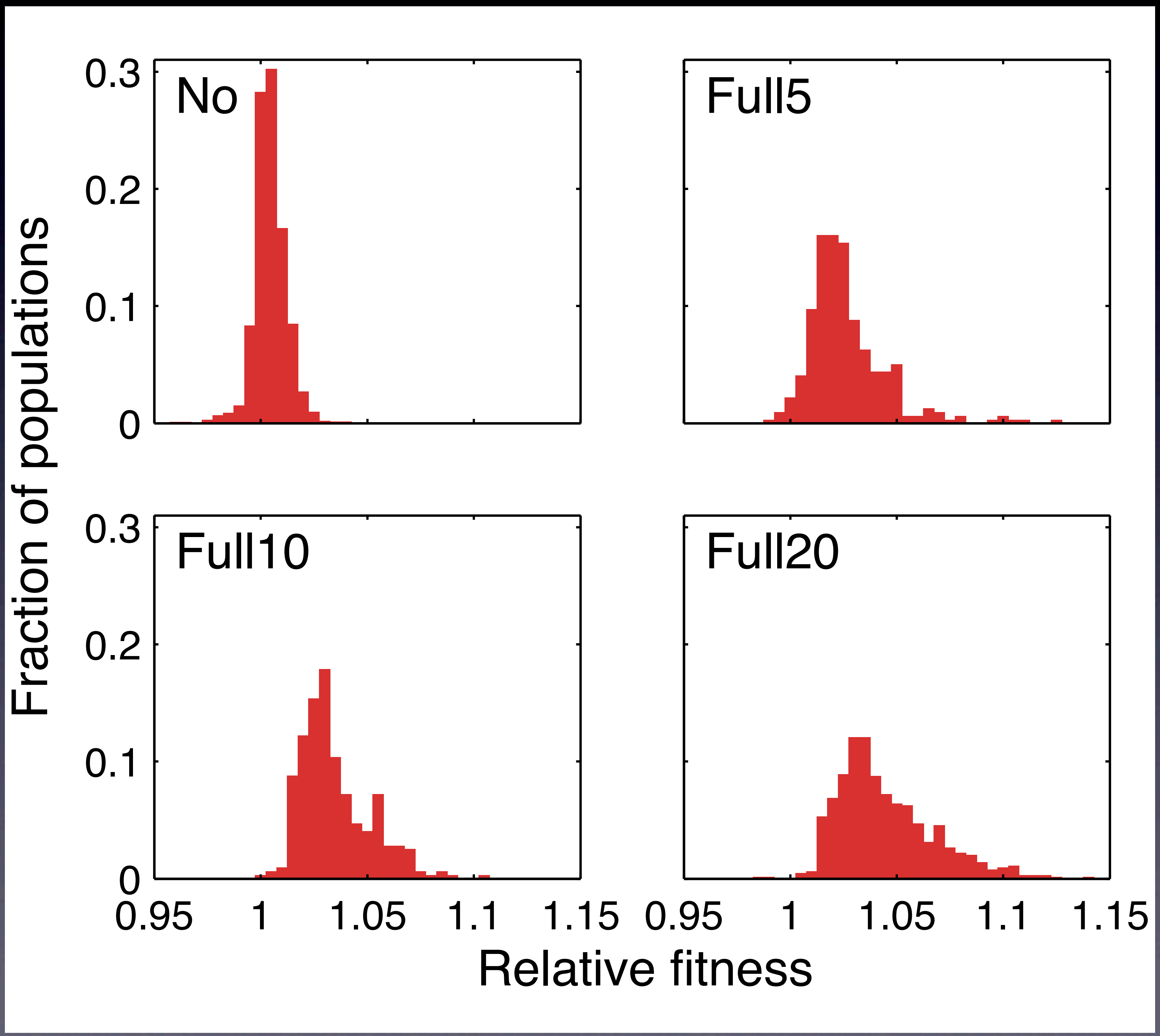


	m imm/gen
No	0
Sm	5
Med	20
Lar	80

$N_b = 1000$

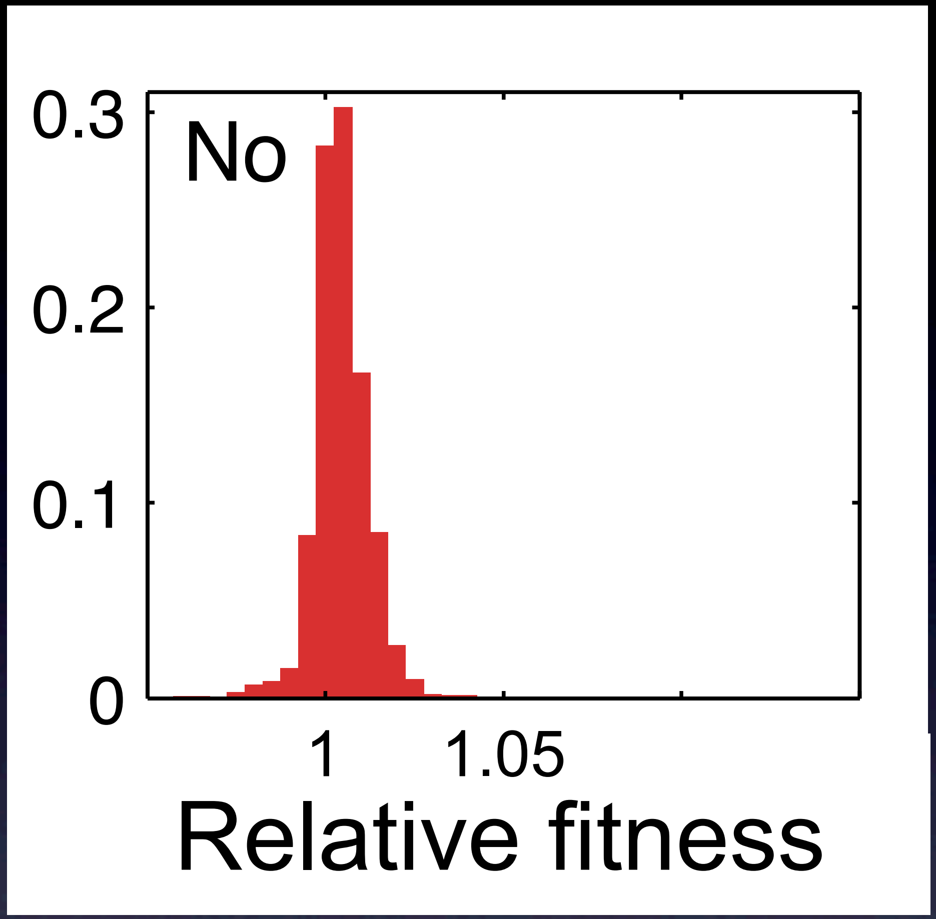
Well-mixed populations

Well-mixed populations. Distribution of mean fitnesses



	N_b
No	10^3
Full5	5×10^3
Full10	10^4
Full20	2×10^4

Well-mixed populations



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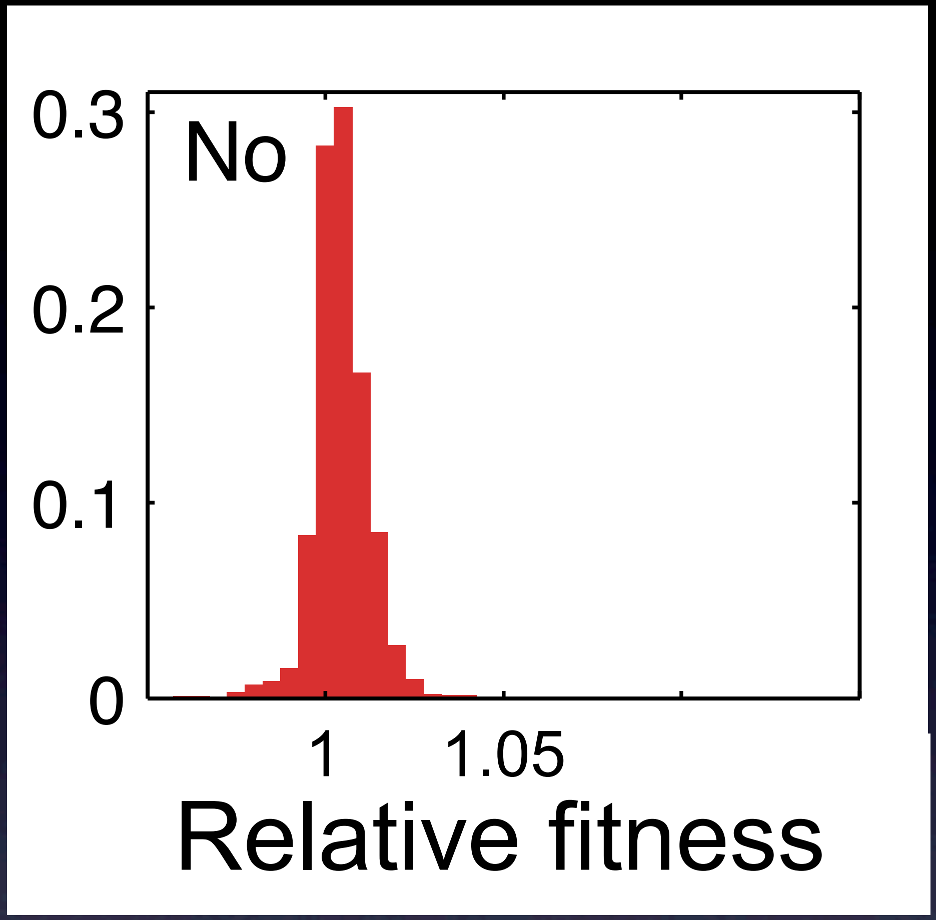
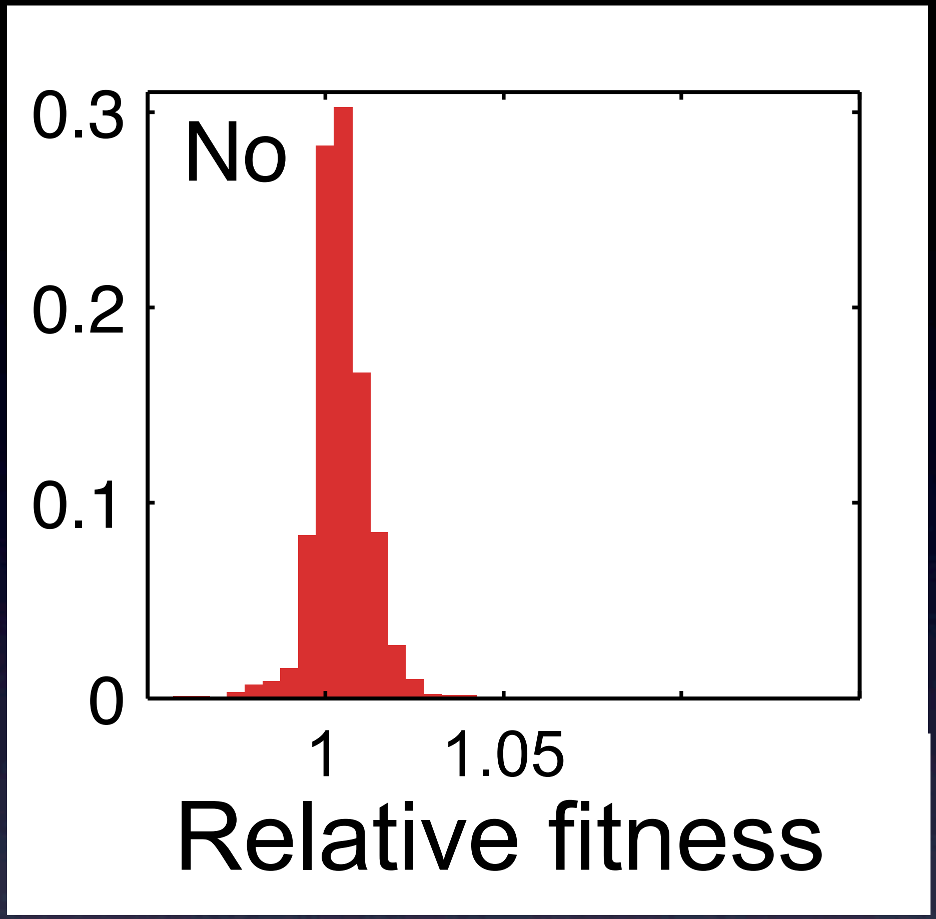


Fraction of populations that got one beneficial mutation

Well-mixed populations



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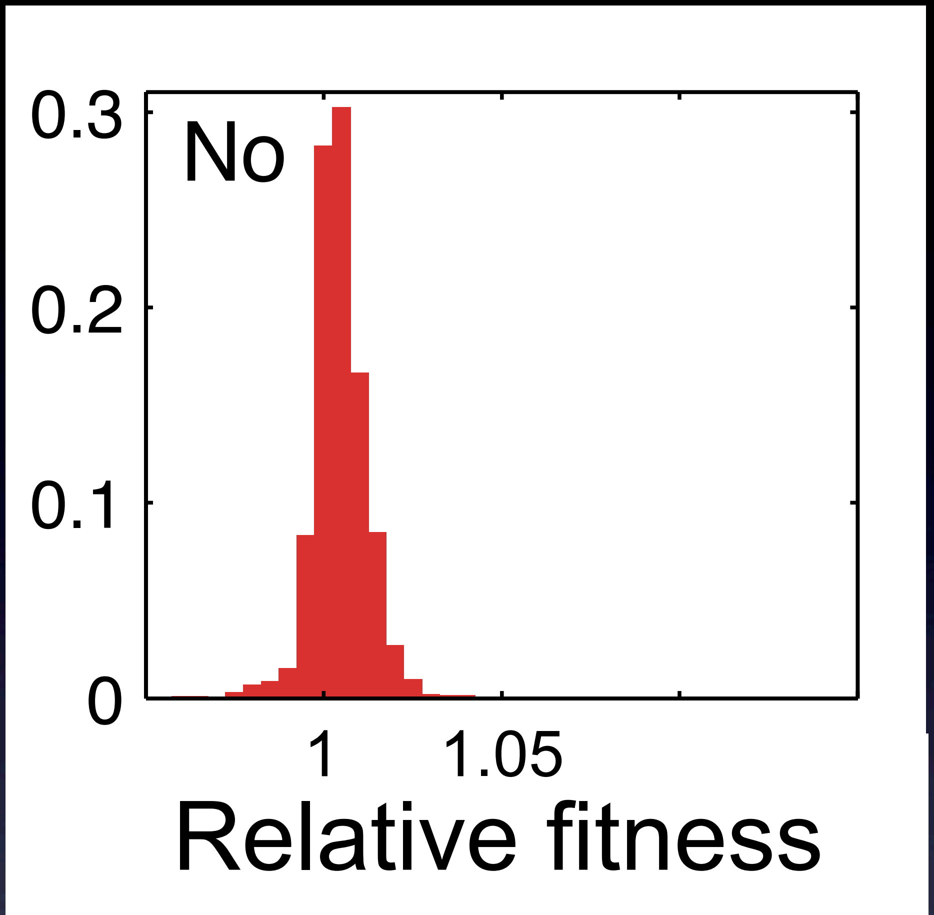
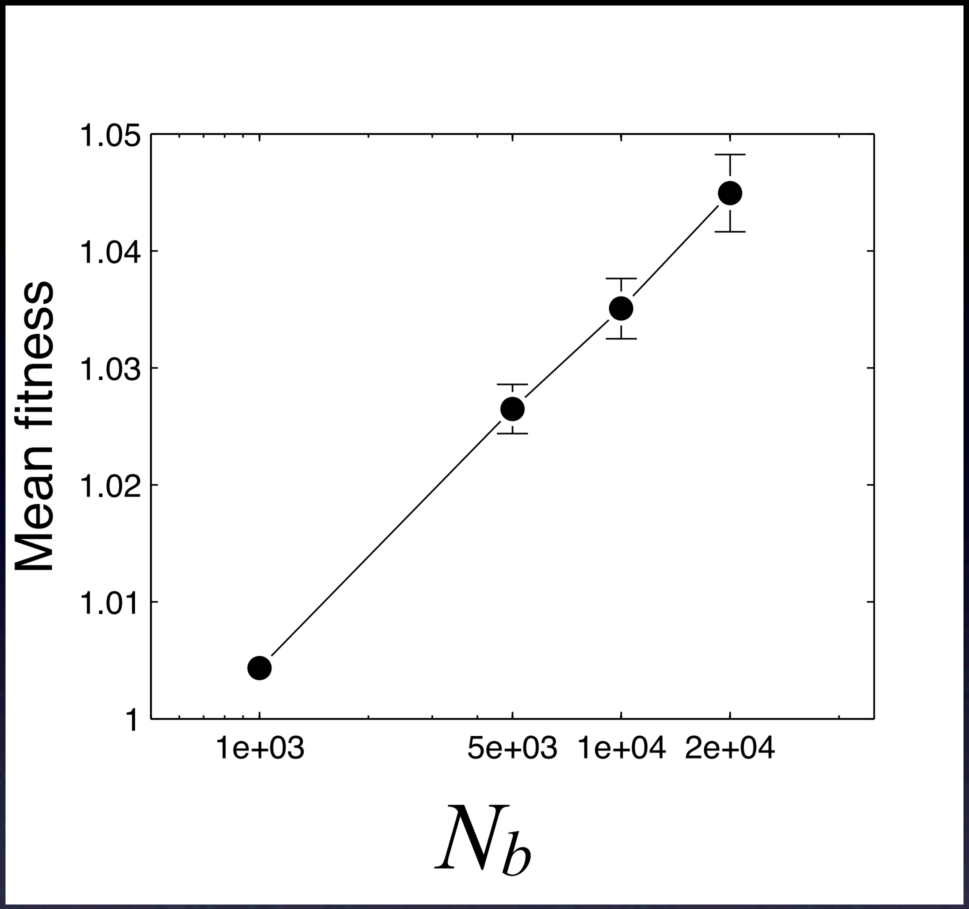
$$P_1 = 2sN\mu T \approx 0.67$$

Well-mixed populations





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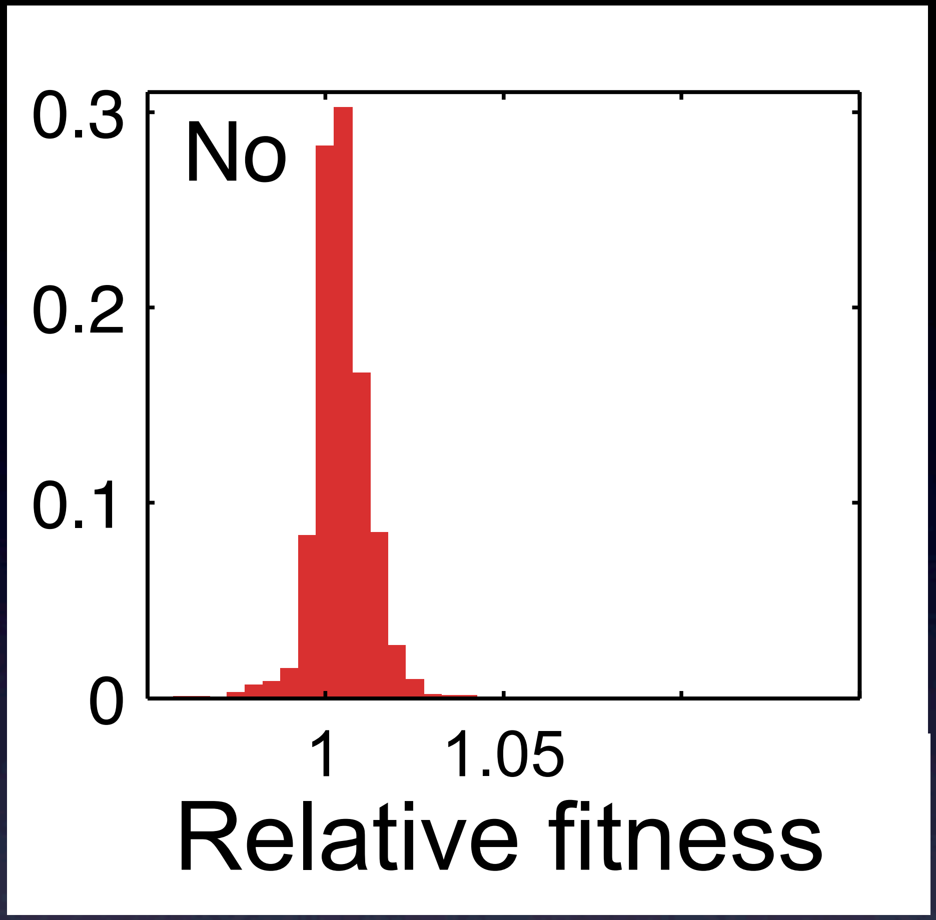

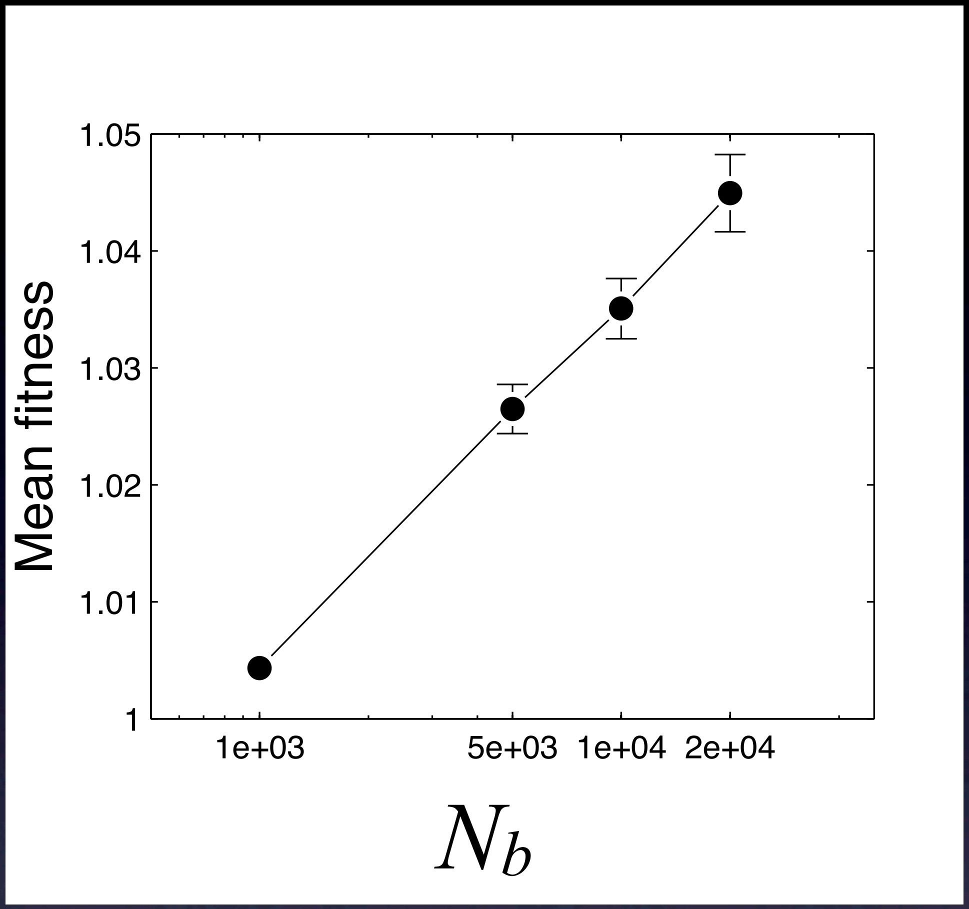

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Slope of mean fitness

$$k = \frac{2s^2 T}{\log^2 s/\mu} \approx 0.013$$

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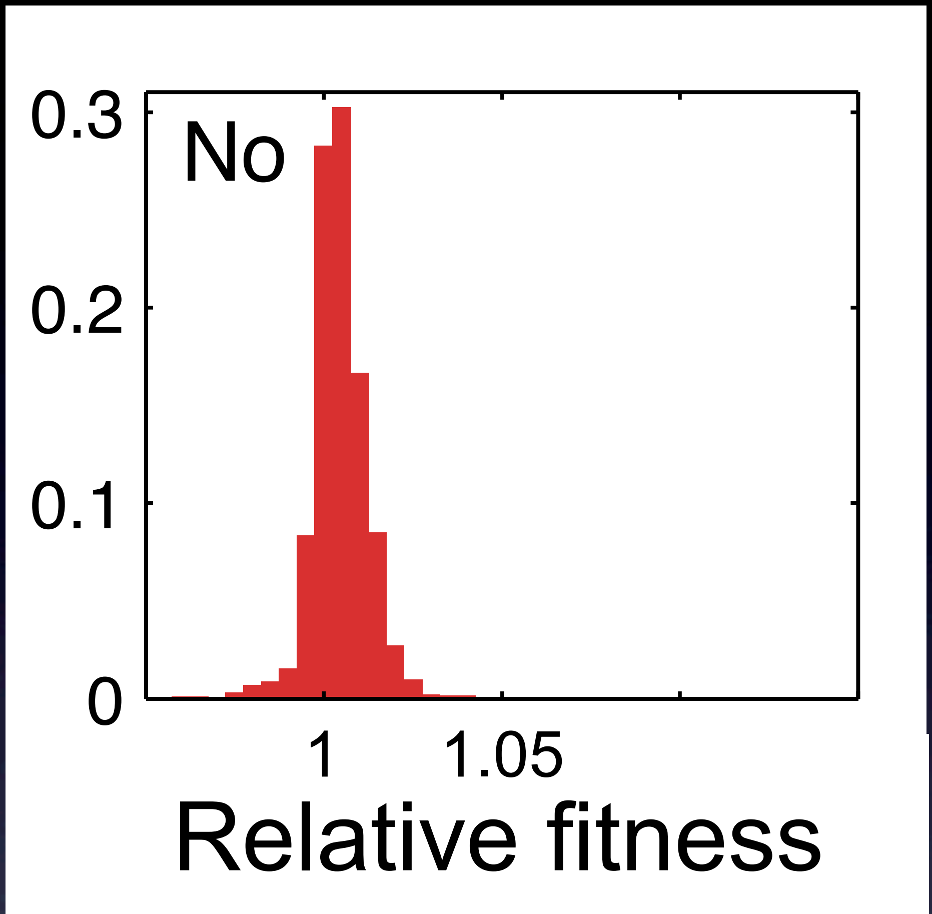

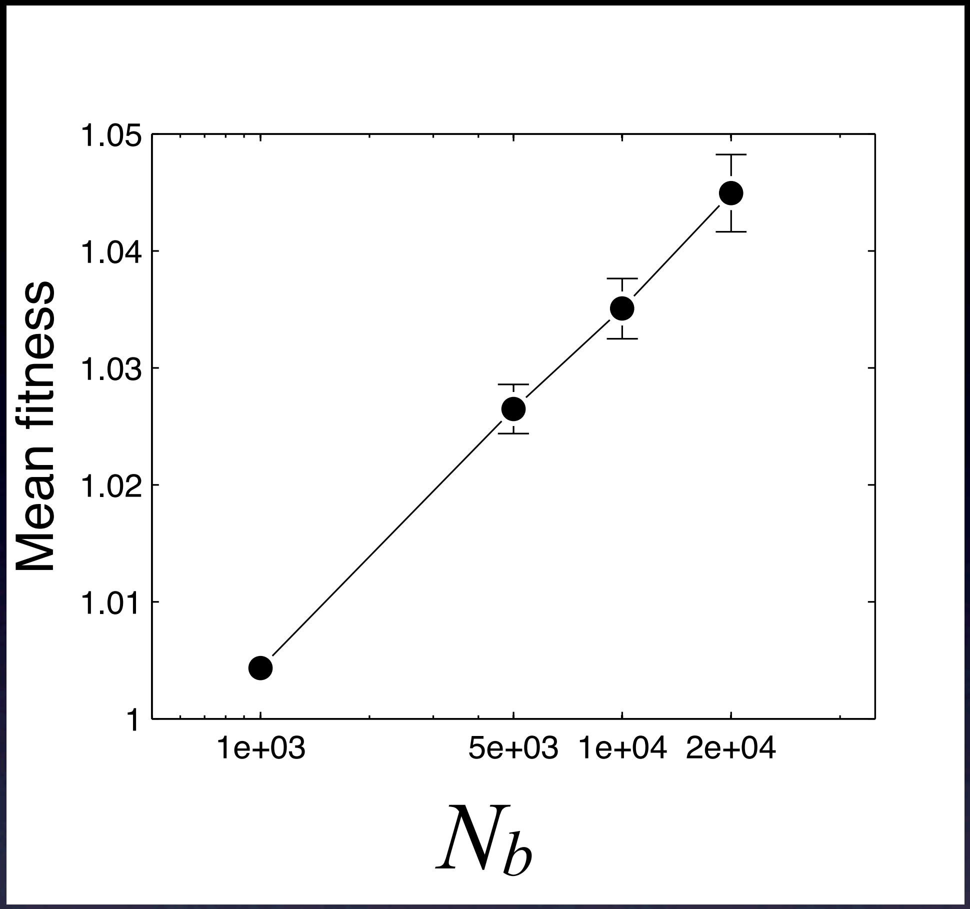

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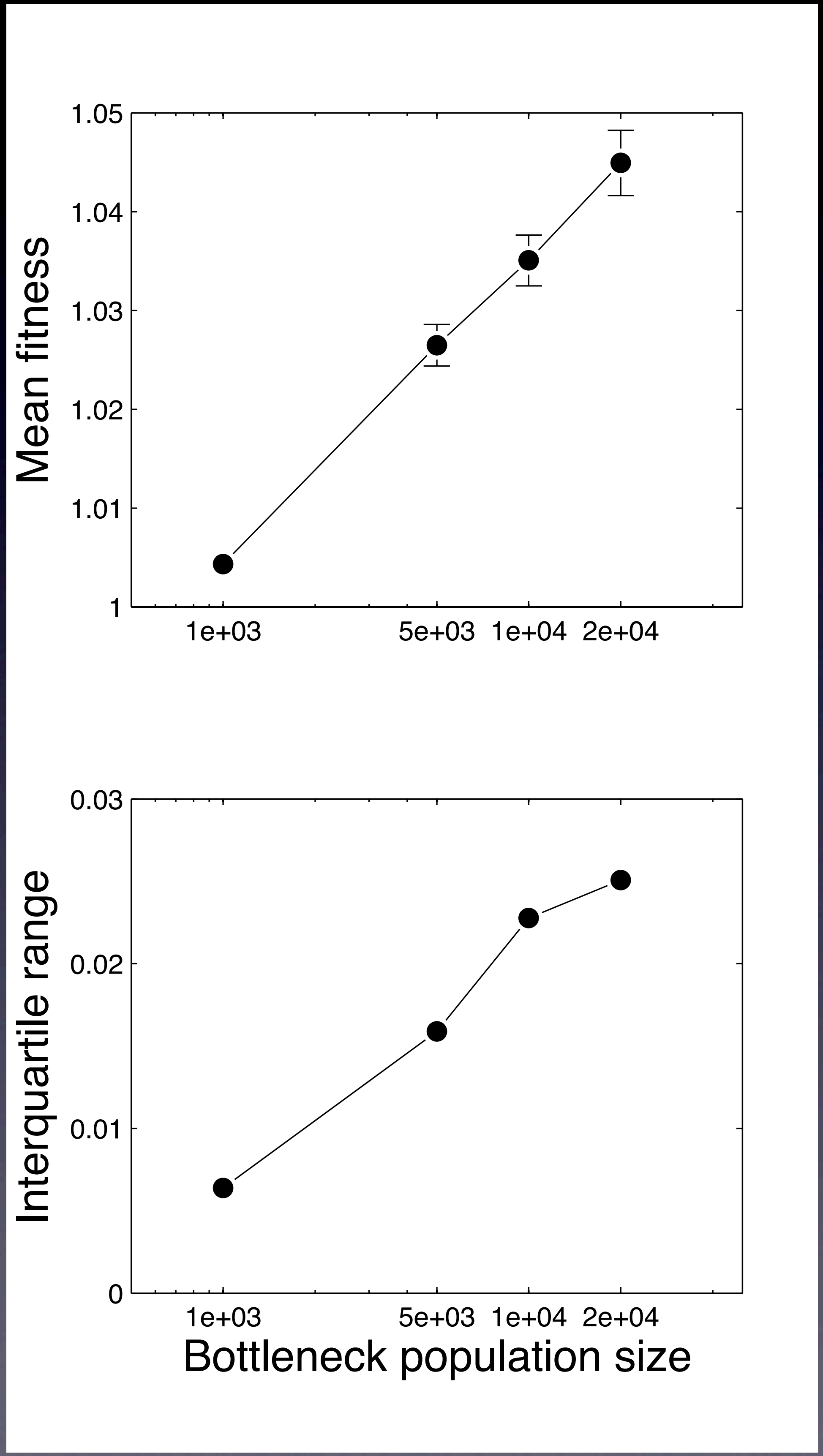
$$\mu \approx 2\times10^{-6}$$
$$s \approx 0.03$$

Well-mixed populations



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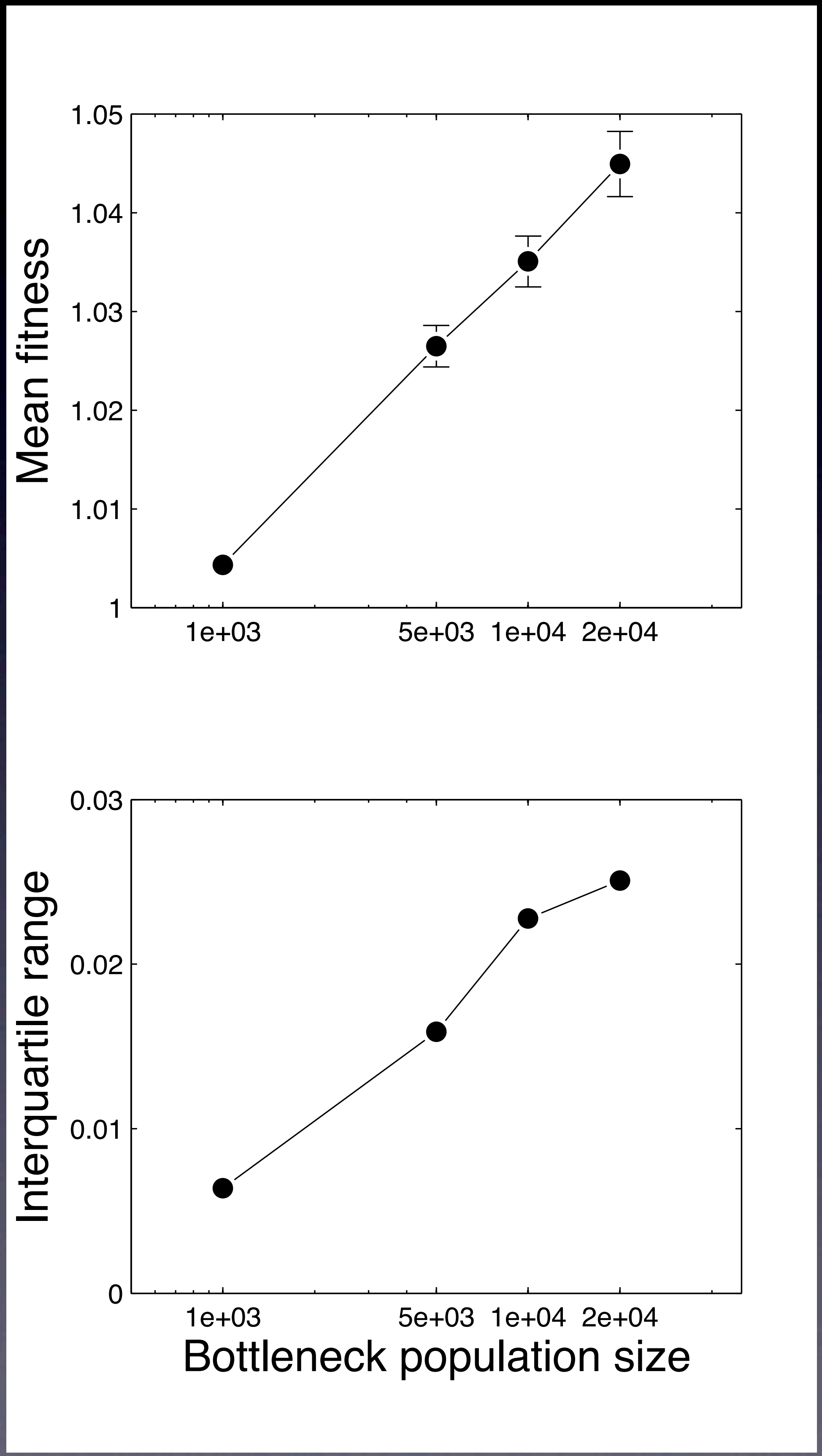

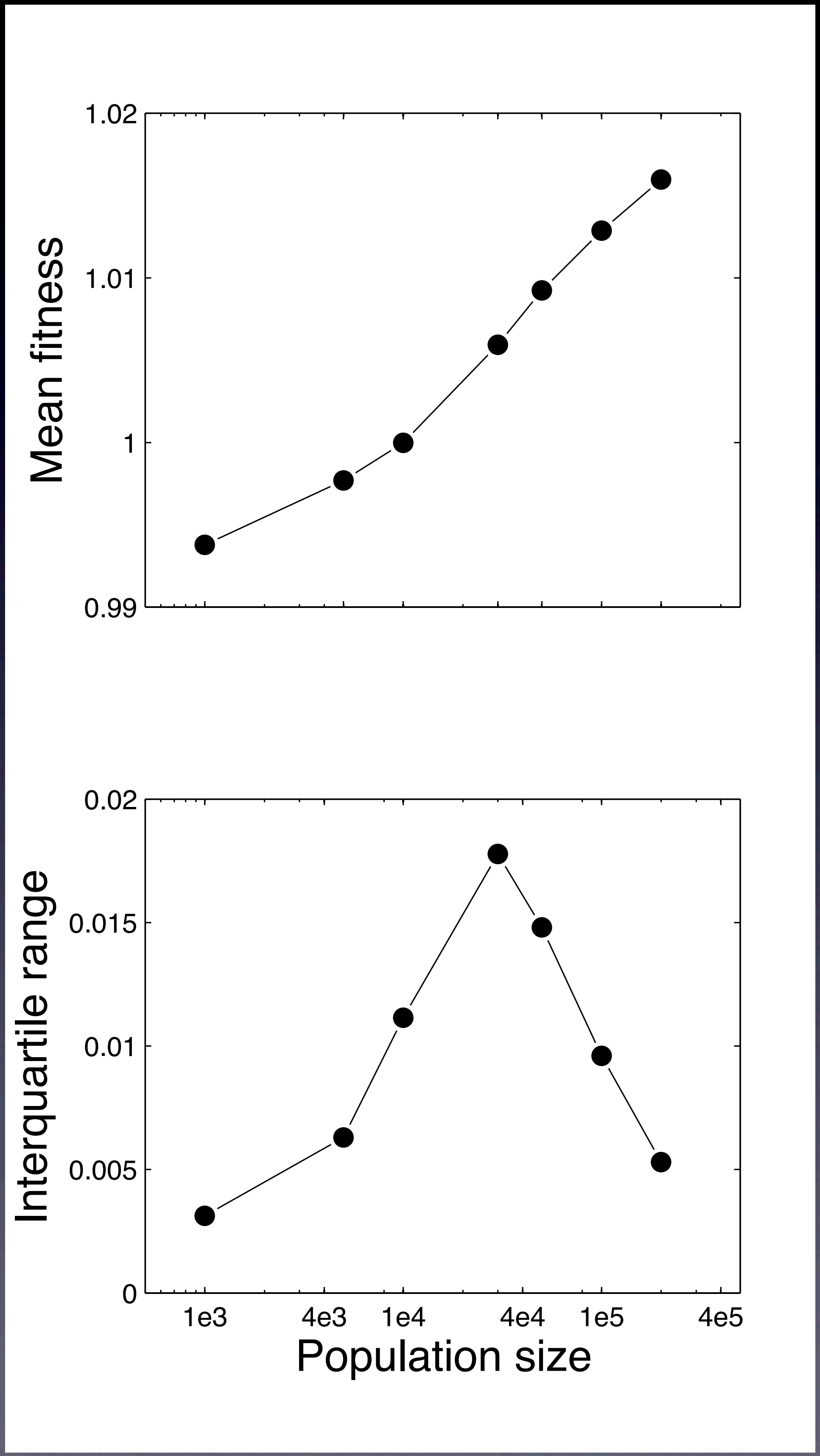

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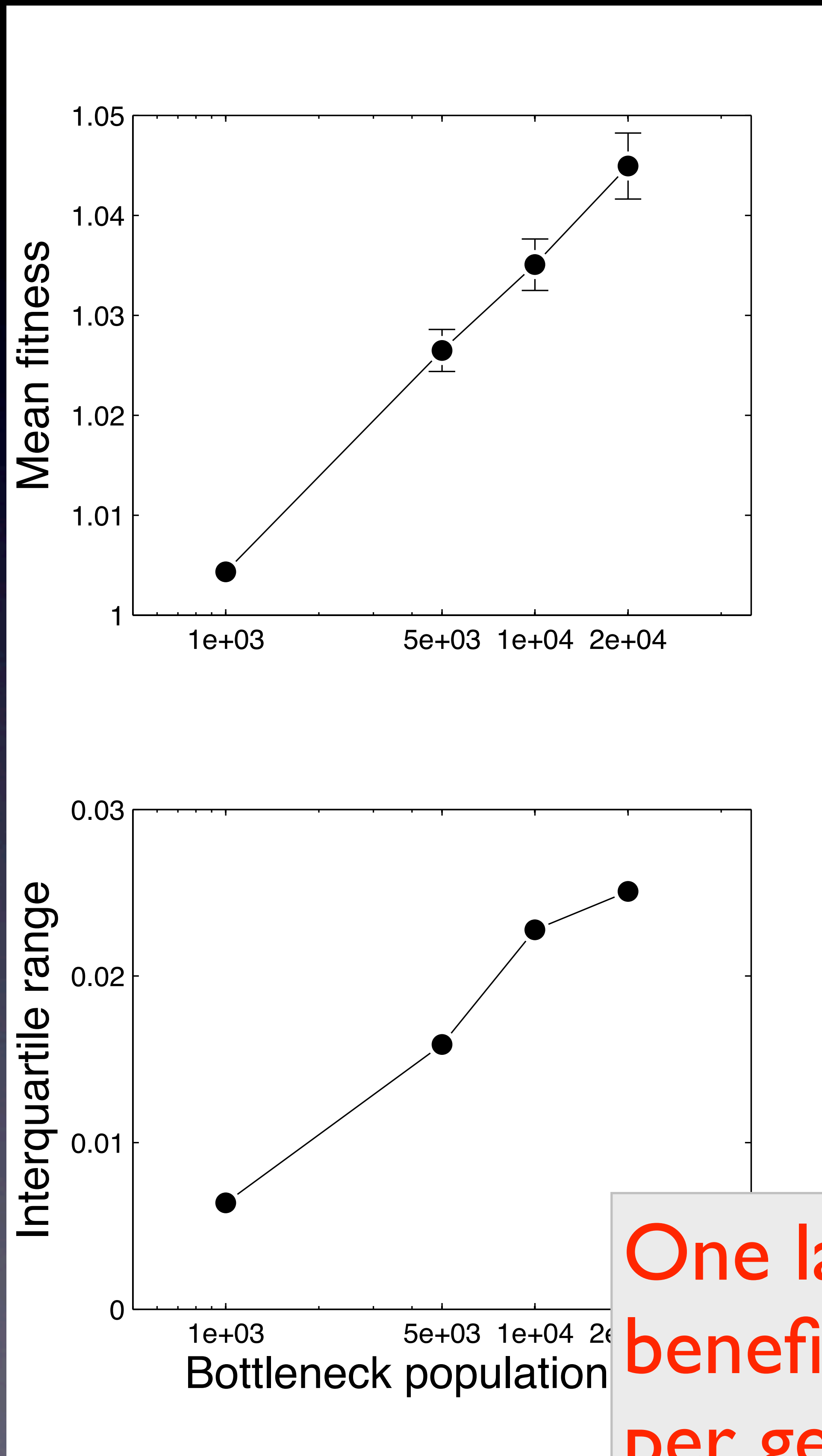
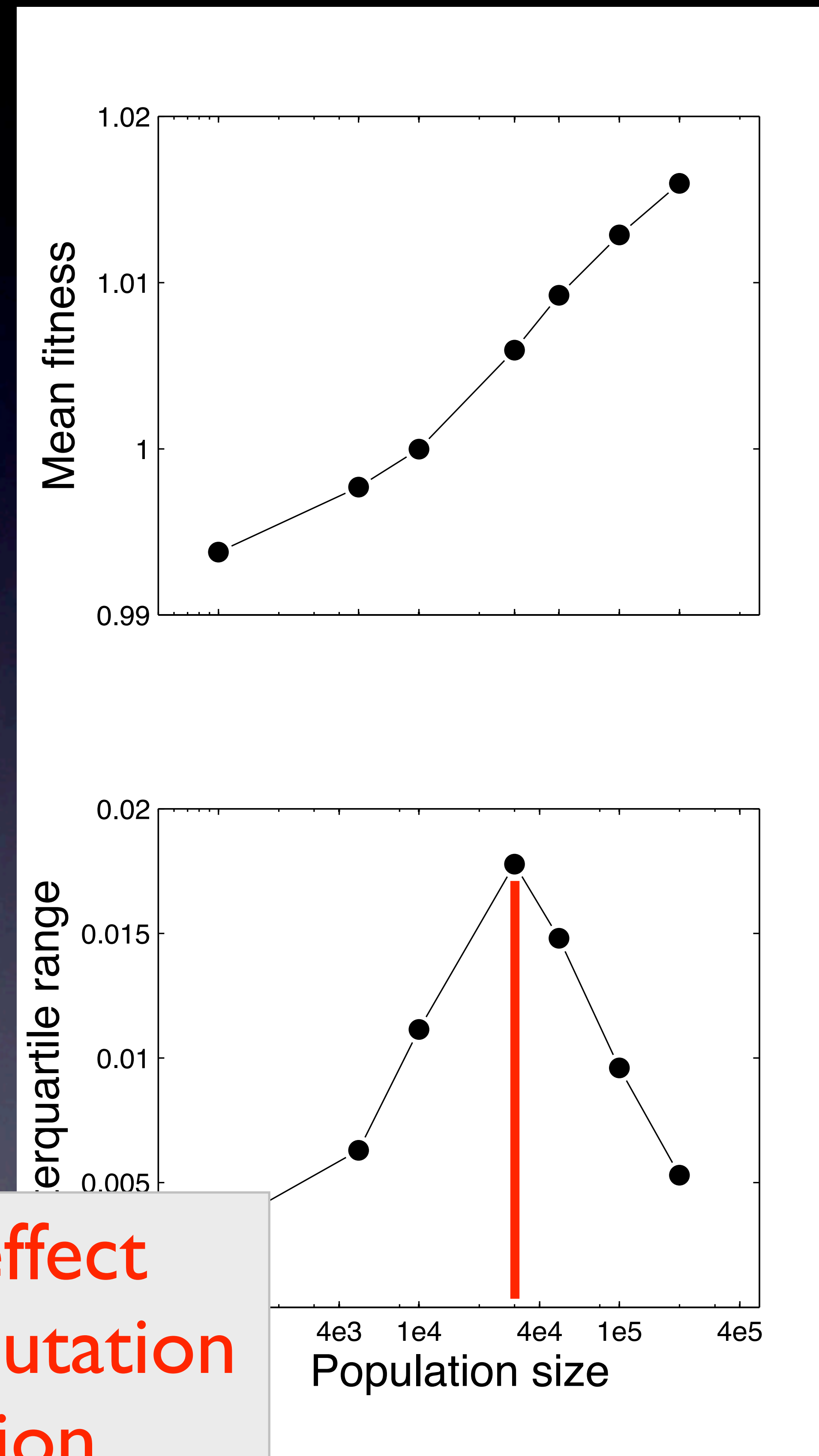
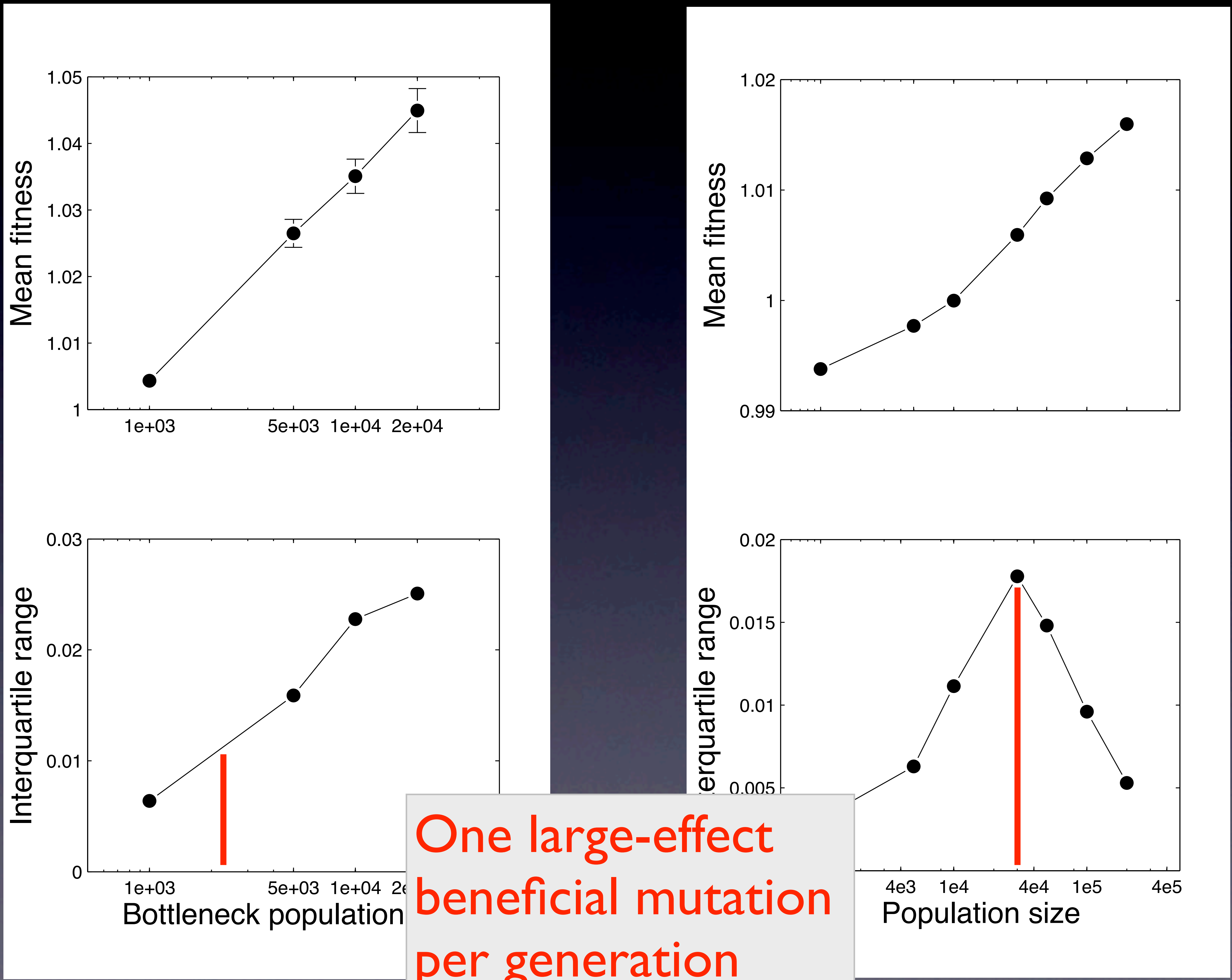




One large-effect beneficial mutation per generation

Well-mixed populations



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Thanks

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Dan Rice

Desai Lab

Core facilities at Princeton University and Harvard University