EVOLUTION WITH A STRESS-INDUCED MUTATION RATE

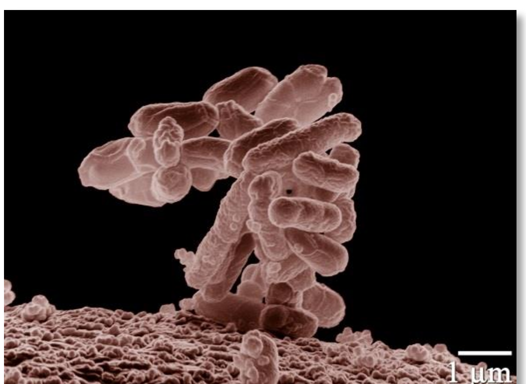
YOAV RAM
HADANY LAB – THE EVOLUTIONARY THEORY LAB
MOLECULAR BIOLOGY AND ECOLOGY OF PLANTS
LIFE SCIENCES FACULTY
TEL-AVIV UNIVERSITY
4 NOVEMBER 2013

VARIABILITY IN MUTATION RATES

Between species

Rates are in average number of measurable mutations per genome per generation

Bacteria: 0.0004
Wielgoss et al. G3 2011



Flies: 0.455
Keightley et al. Gen Res 2009

Humans: 41
Lynch, PNAS 2010

2

EVOLUTION IN A STATIC ENVIRONMENT

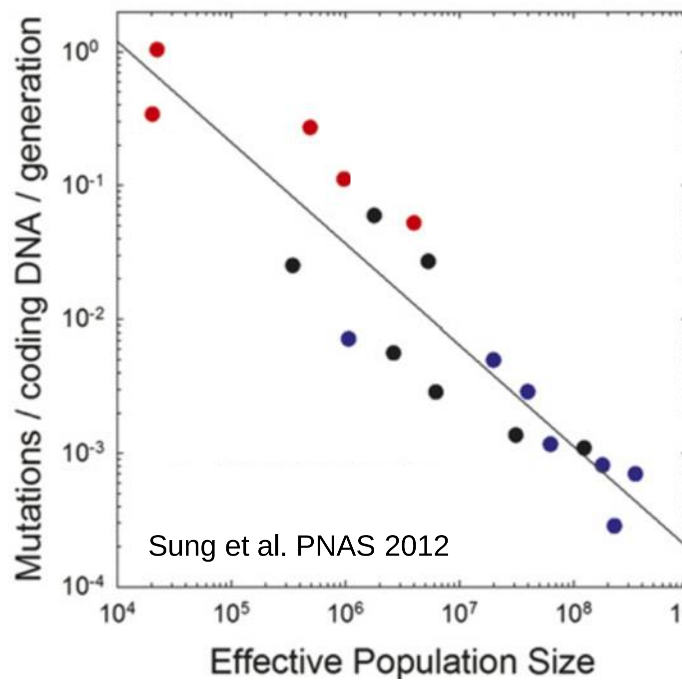
- Directional selection without change
- A balance between mutation and natural selection

MUTATION RATE IN STATIC ENVIRONMENTS

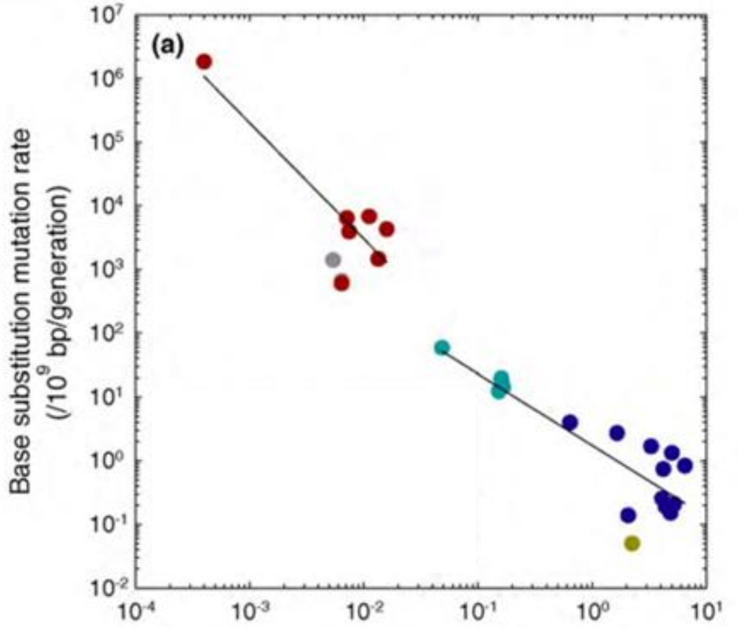
$$\overline{\omega} = e^{-U}$$

High mutation rates reduce *adaptedness* of populations

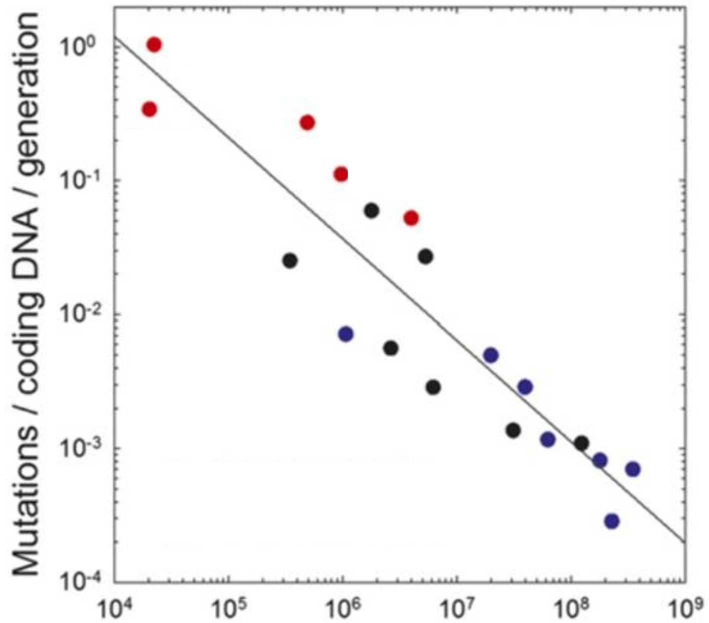
- Selection will **reduce** the mutation rate to it's lowest attainable level
- What sets this level?
- Kimura 1967 - physical or physiological
- Dawson 1999 – "cost of fidelity"
- Lynch 2010 – "Drift barrier hypothesis"



NON-ADAPTIVE HYPOTHESES



Genome size (Mb)



Effective population size

Sung et al. PNAS 2012

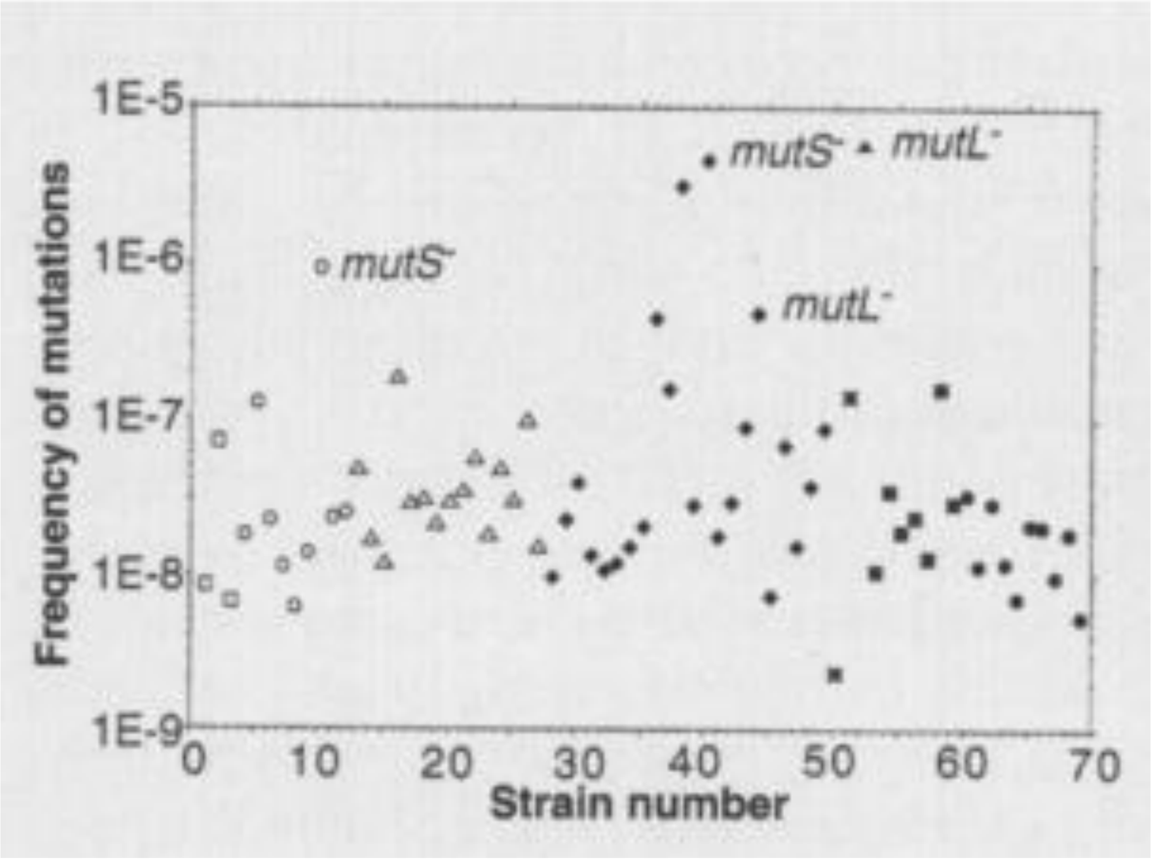
EVOLUTION IN A DYNAMIC ENVIRONMENT

- In changing environments rapid adaptation can be favored by natural selection (*adaptability*)
- The mutation rate must balance between *adaptability* and *adaptedness*

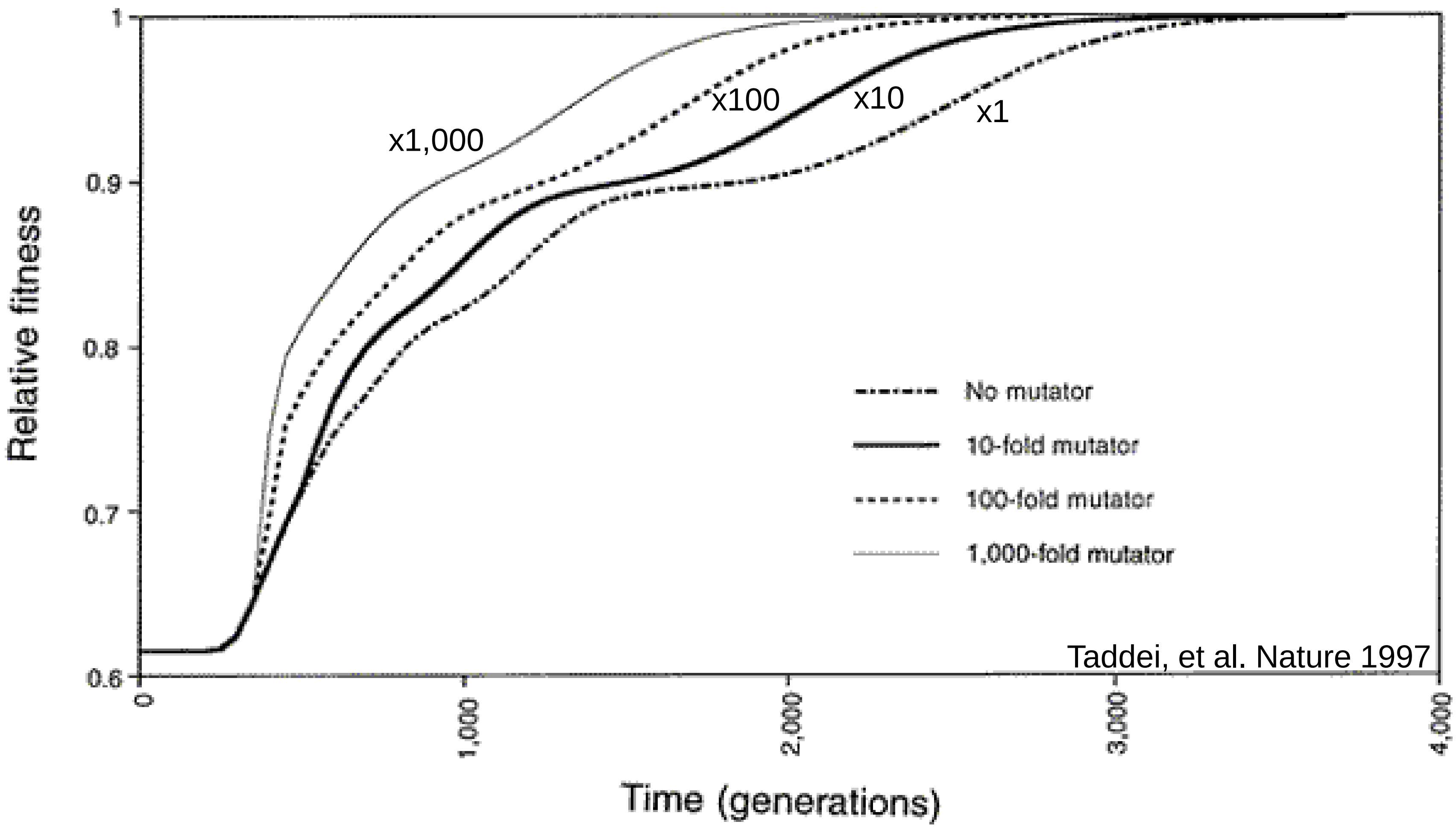
VARIABILITY IN MUTATION RATES

Within species

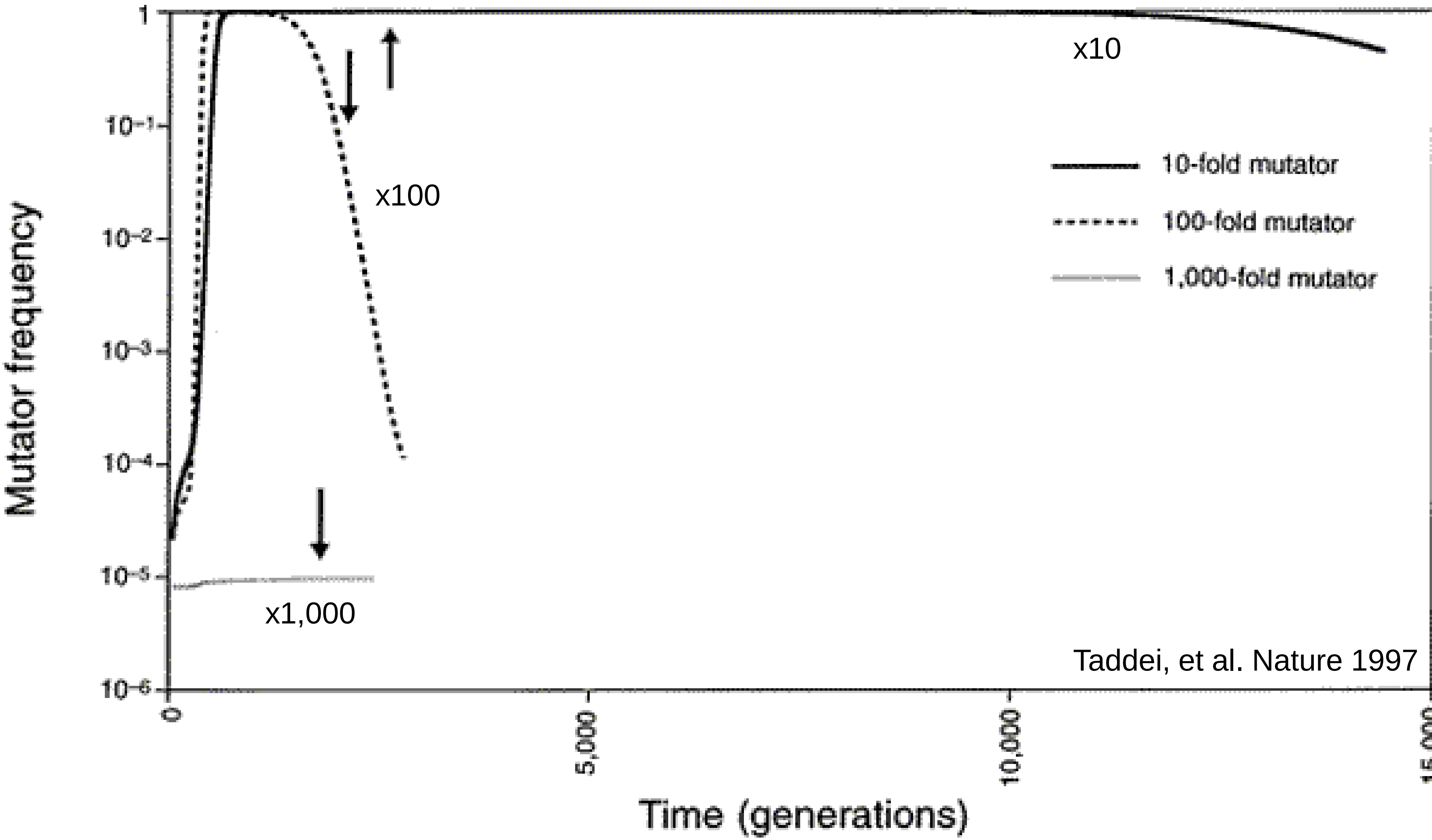
Mutation rate in 69 natural populations of *E. coli* – Matic et al. 1997



ADAPTATION WITH MUTATOR ALLELES



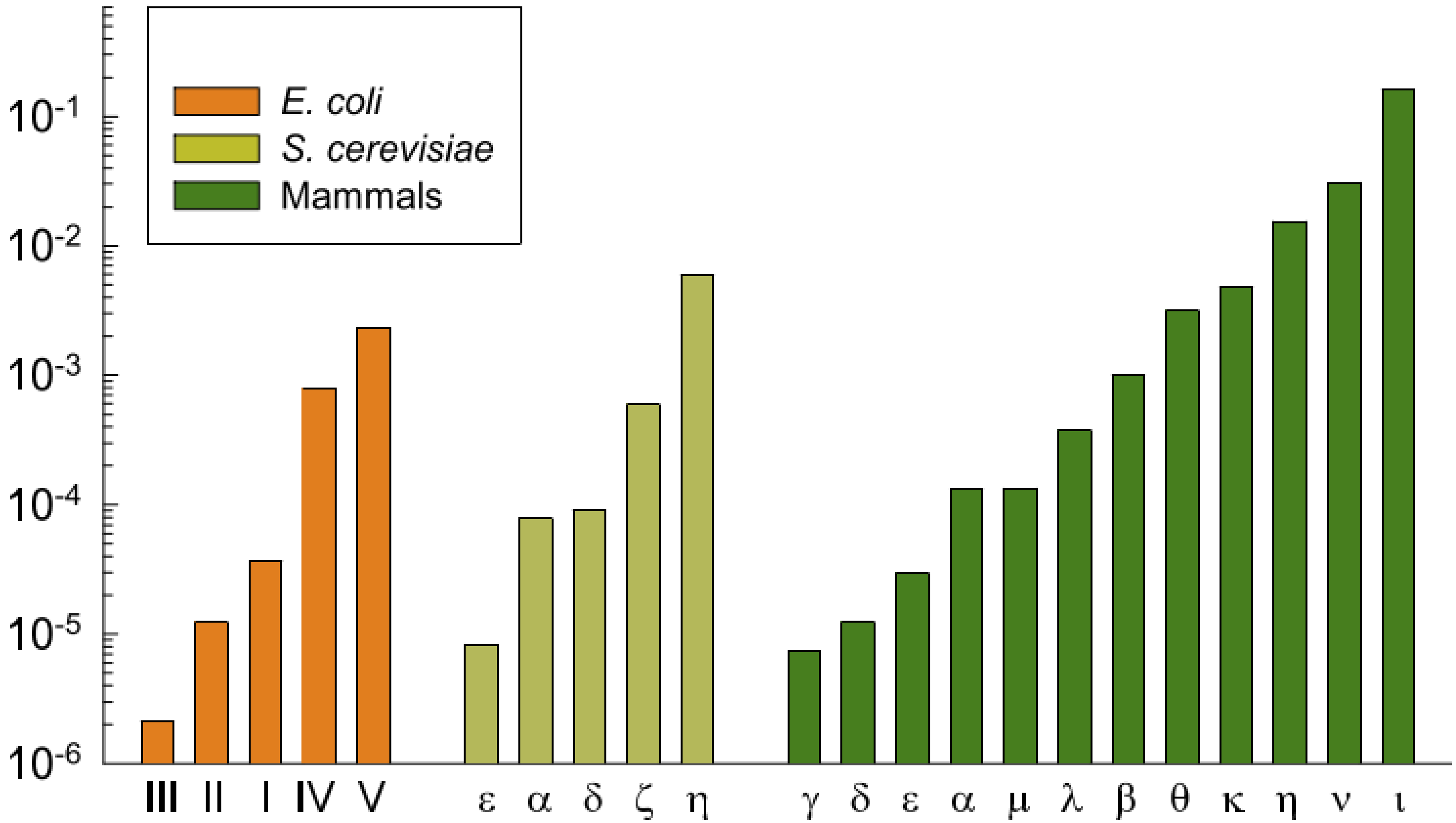
RISE AND FALL OF THE MUTATOR ALLELE



VARIABILITY IN MUTATION RATES

Within individuals

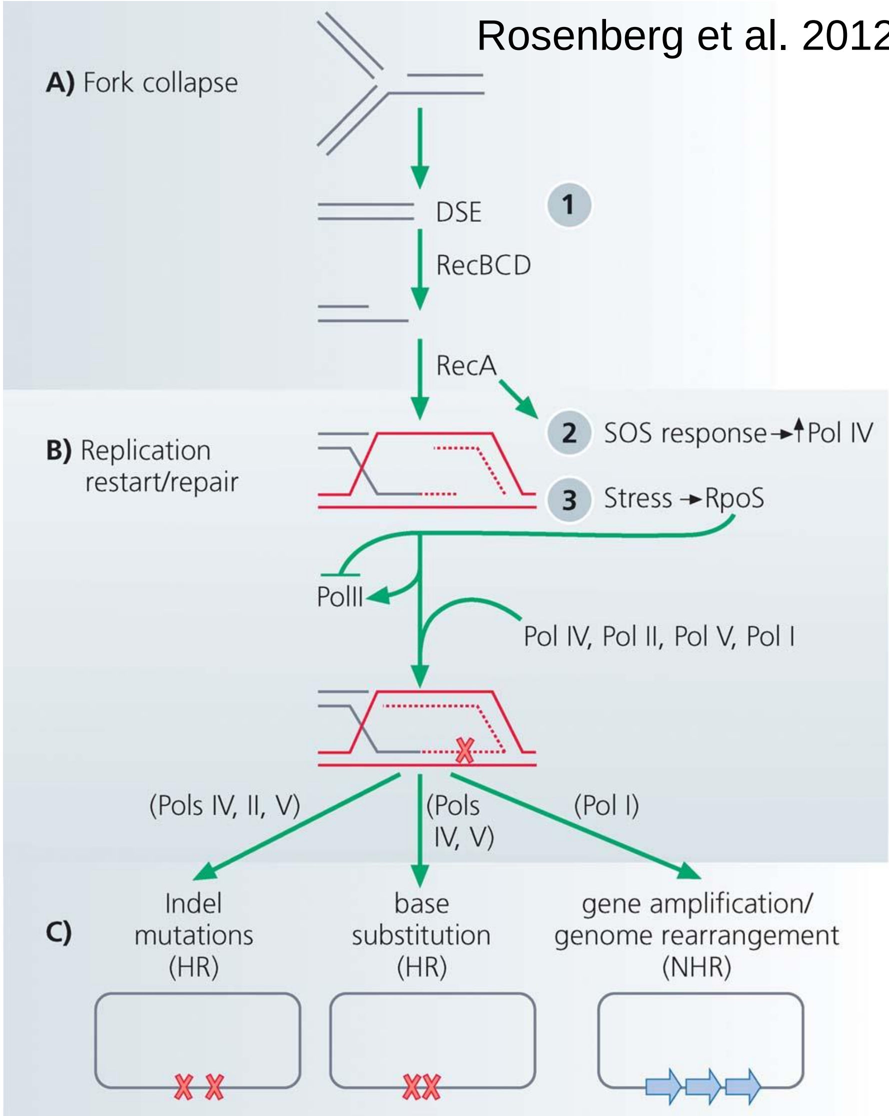
DNA polymerase error rate – Lynch 2011

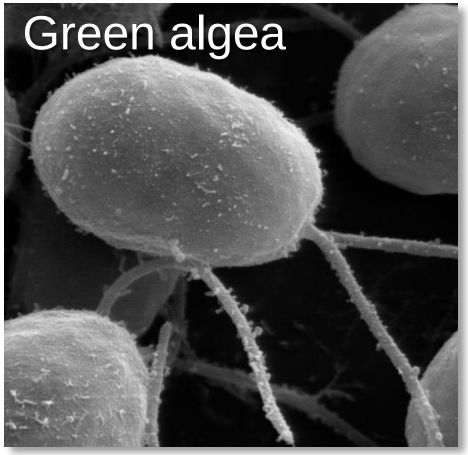


STRESS-INDUCED MUTATION

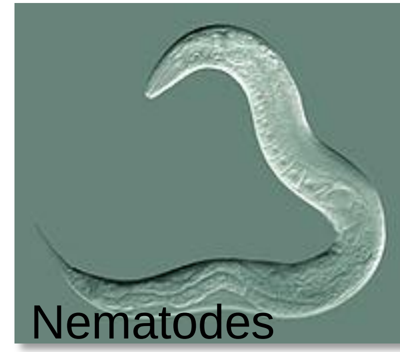
In *E. coli:*

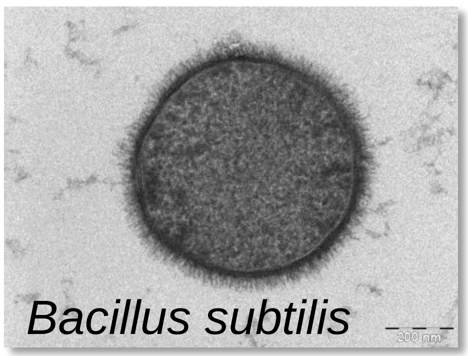
- Error prone polymerase induced by stress responses:
  - SOS response
  - DNA damage
  - Starvation
- Mismatch repair system
- Other mechanisms:
  - Galhardo et al. 2007
  - Al Mamun, Science 2012



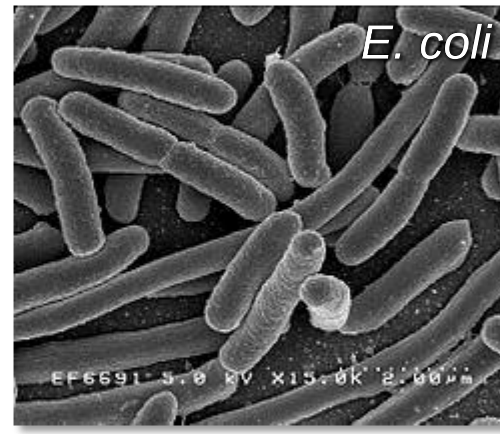

Green algea

EVIDENCE

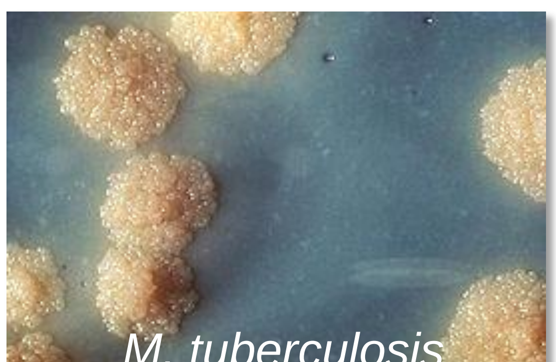

Nematodes

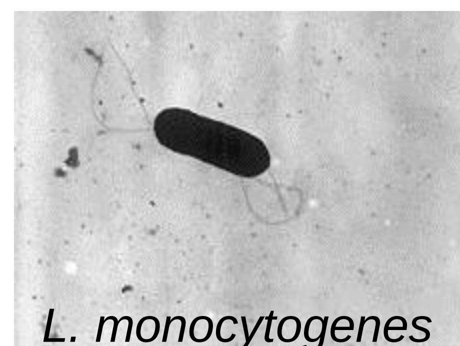

Bacillus subtilis


Breast cancer cell


E. coli


D. Melanogaster


M. tuberculosis


L. monocytogenes

EVOLUTION OF STRESS-INDUCED MUTATION

Null hypothesis

Mutagenesis is the by-product of stress

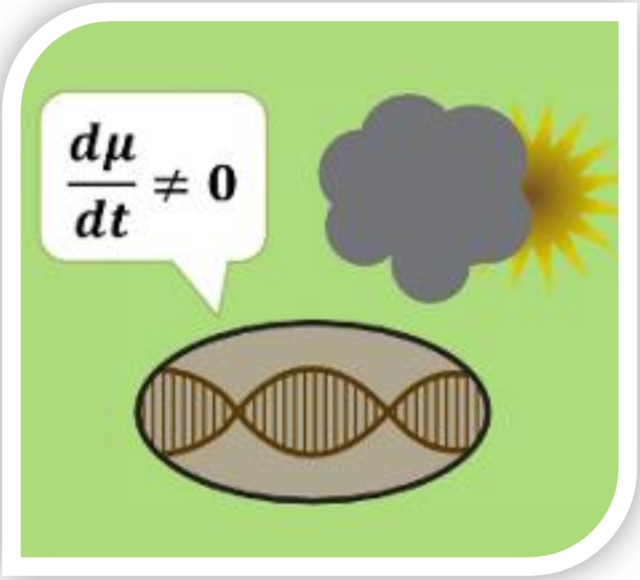
Alternative non-adaptive hypotheses

Cost of fidelity

Drift barrier hypothesis

Adaptive hypothesis

Second order selection



STATIC ENVIRONMENT

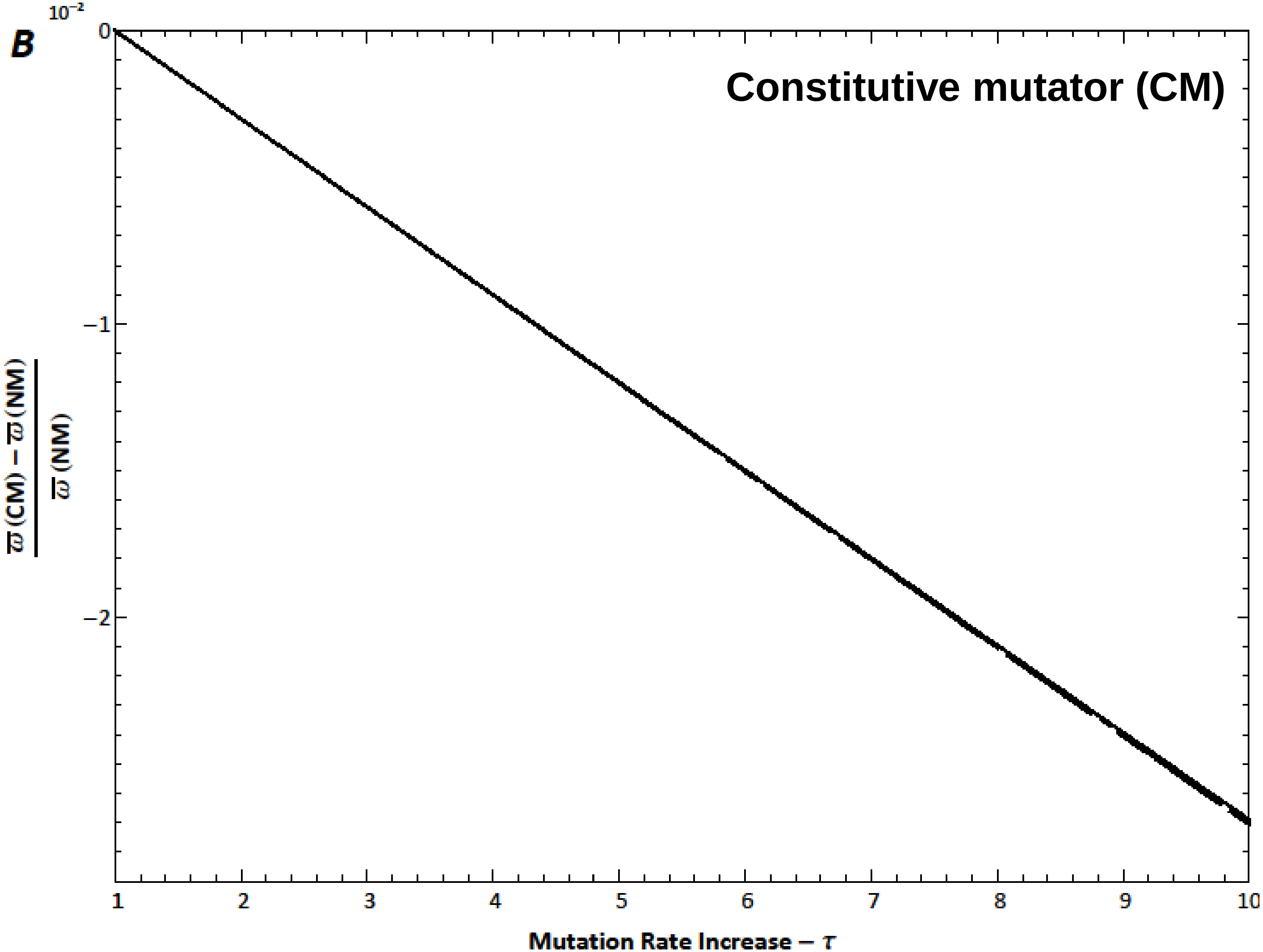
General solution

$$sign\frac{\partial\overline{\omega}}{\partial U_x} = sign\,(\overline{\omega} - \omega_x)$$

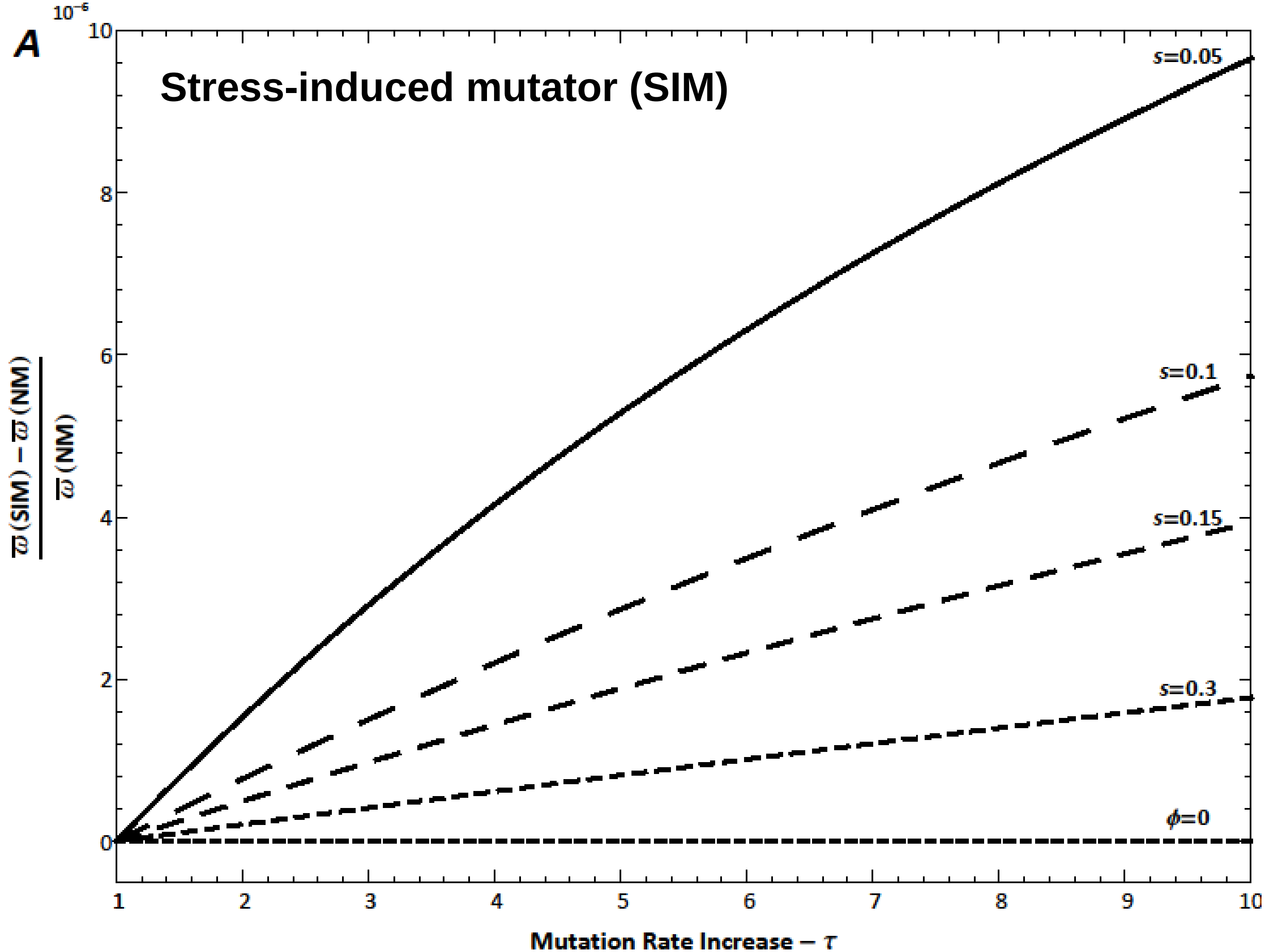
“Increasing the mutation rate of individuals with below average fitness increases the population mean fitness”

Selection doesn’t reduce the mutation rate!

STATIC ENVIRONMENTS



STATIC ENVIRONMENTS



RAPIDLY CHANGING ENVIRONMENTS

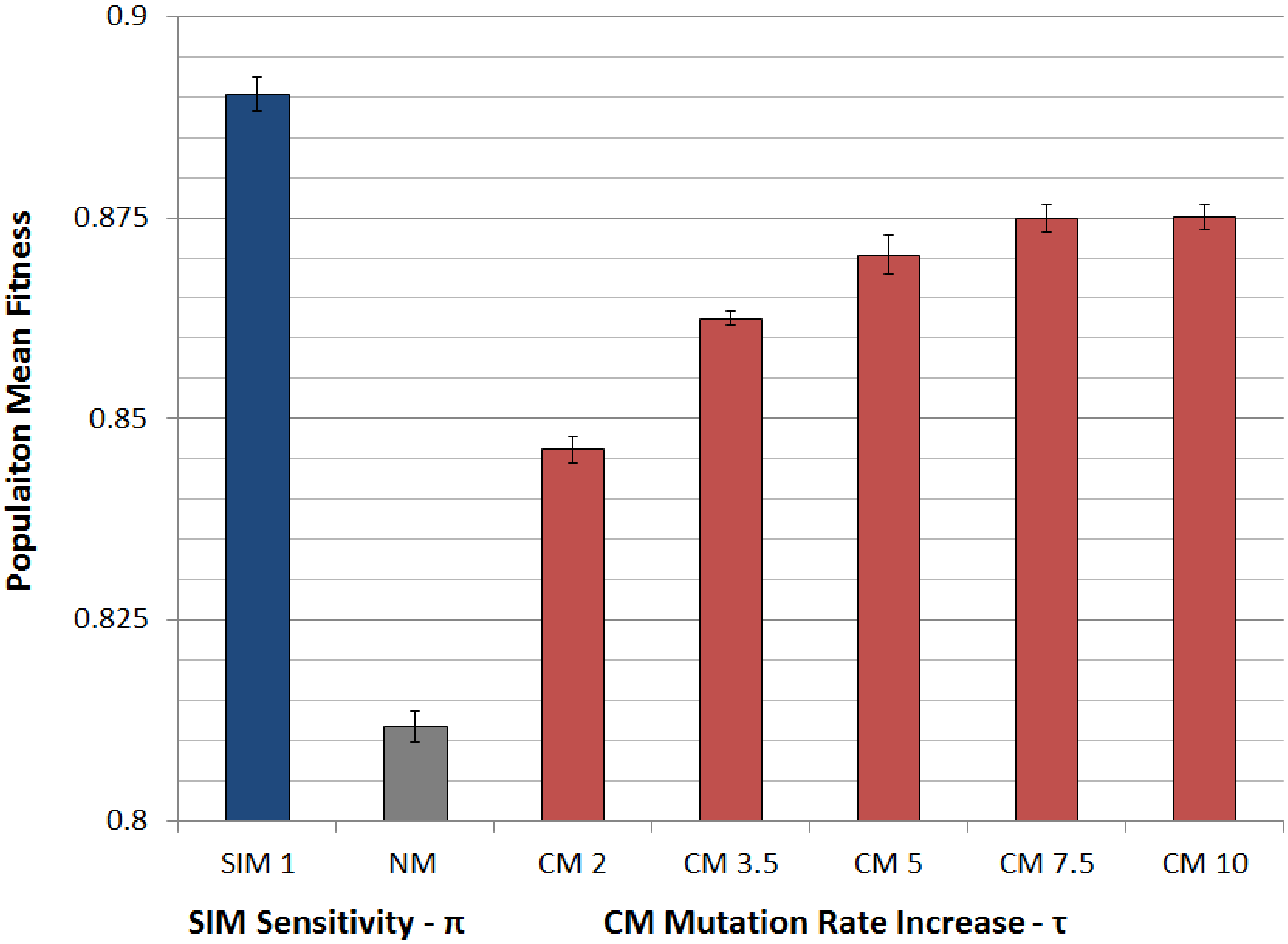
The Red Queen hypothesis (van Valen, 1973):

"It takes all the running you can do, to keep in the same place."

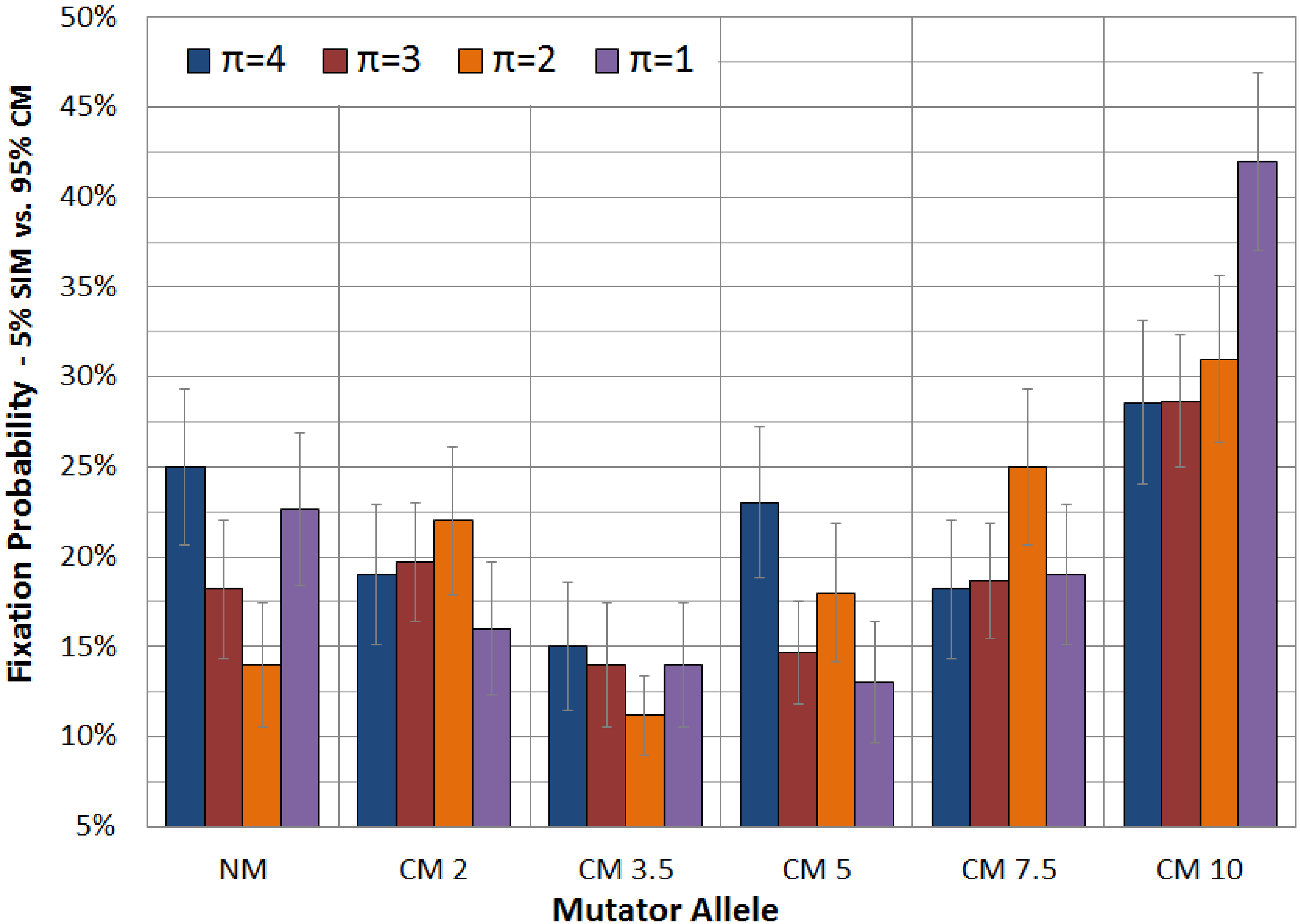
- Lewis Carrol, Through the Looking Glass

What happens when the environment changes frequently?

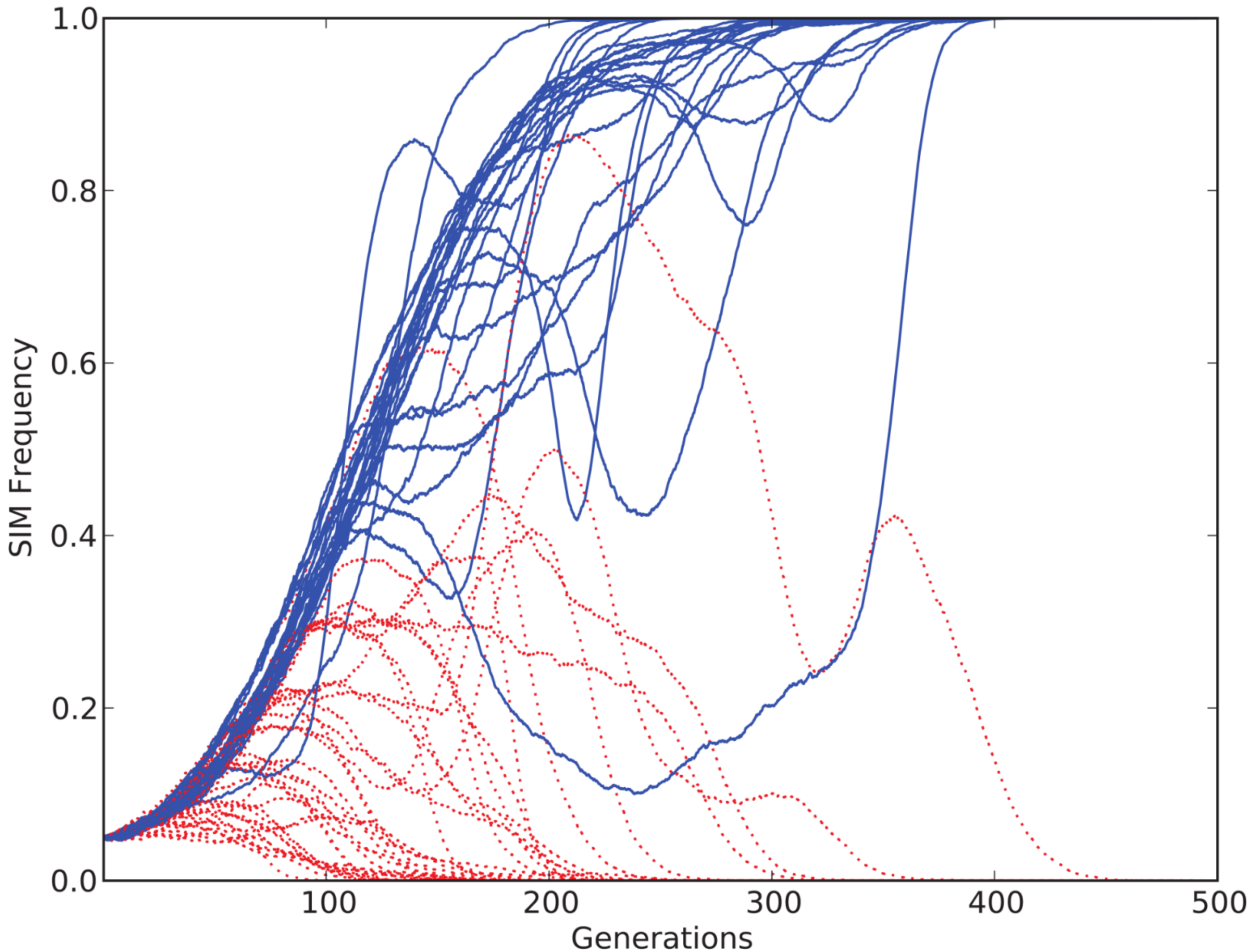
POPULATIONS WITH SIM ARE FITTER



SIM WINS COMPETITIONS



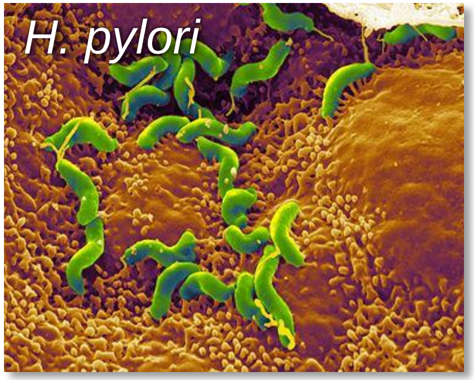
SIM WINS COMPETITIONS



SUMMARY: EVOLUTION OF STRESS-INDUCED MUTATION

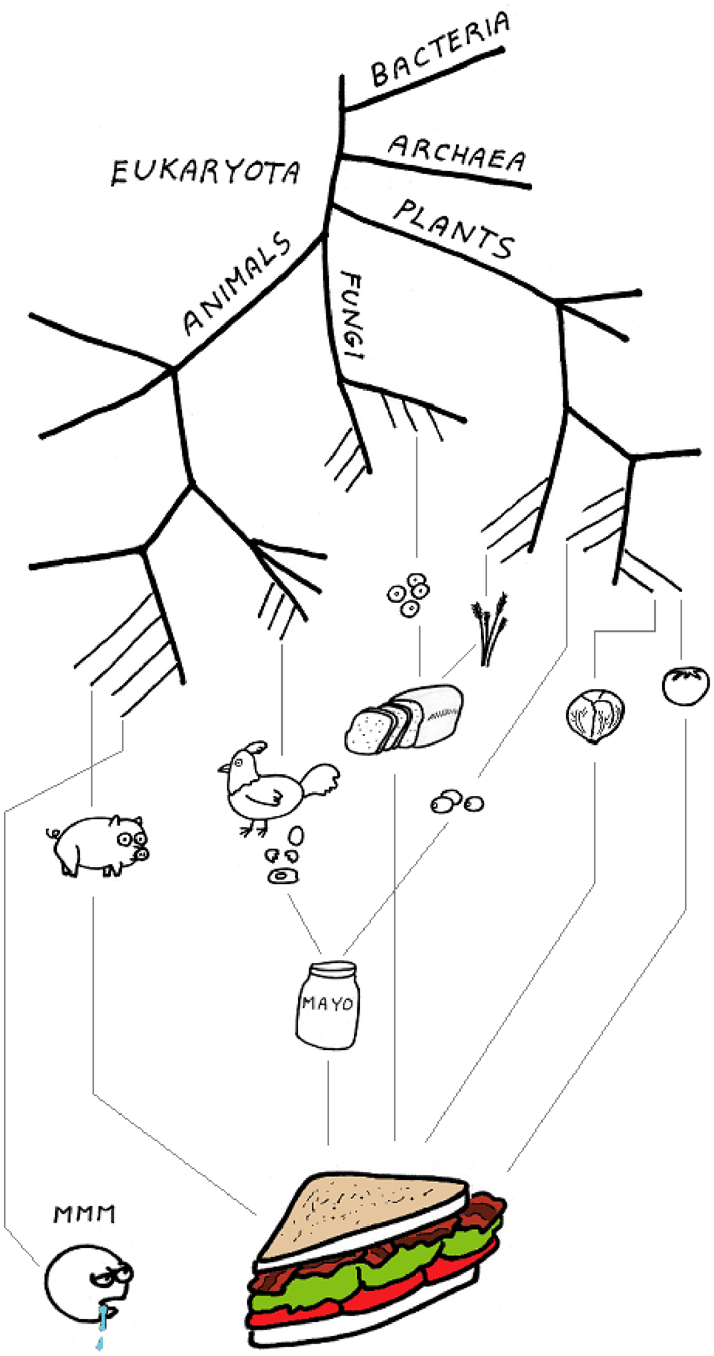
- Stress-induced mutators evolve:
  - In finite & infinite populations
  - In constant & changing environments

- **Second-order selection** can lead to the evolution of stress-induced mutagenesis in asexual populations
- Selection for evolvability



CONSEQUENCES OF STRESS-INDUCED MUTATION RATE

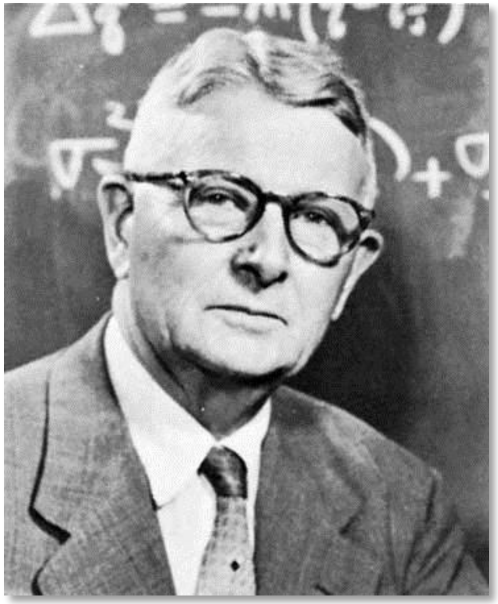
How does SIM affect evolution?



ADAPTIVE PEAK SHIFTS

This problem was introduces by Sewall Wright in 1931:

If a new adaptation requires several, separately deleterious mutations, how can it evolve?



EXAMPLES

Criteria

- Adaptation requires a change in two or more traits
- Change in only one trait causes reduced fitness

Wings and bones

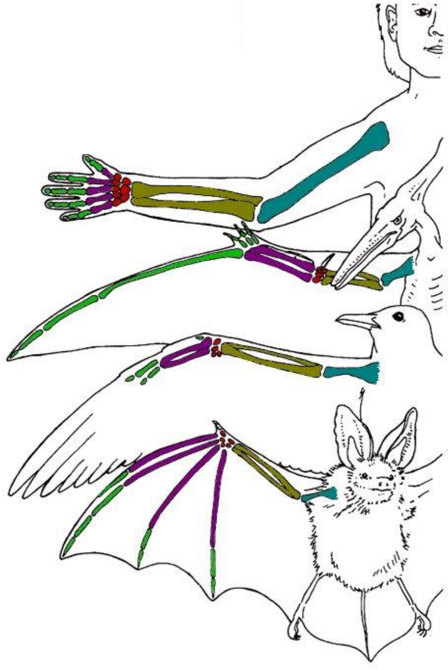
- Flying with heavy bones is costly
- Walking and climbing with light bones is dangerous

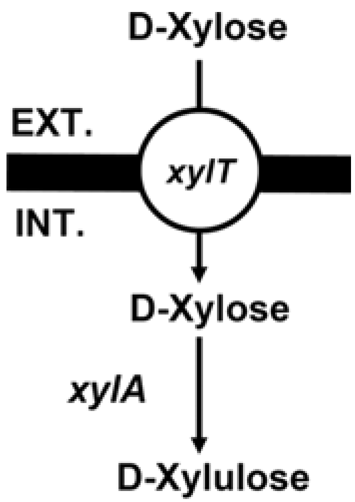
New metabolic pathway

- Two new proteins required – pump and enzyme
- each is wasteful without the other

Adaptation to high UV (Haldane 1932, p. 175)

- Dark skin – increased pigmentation
- Vitamin D storage in the liver

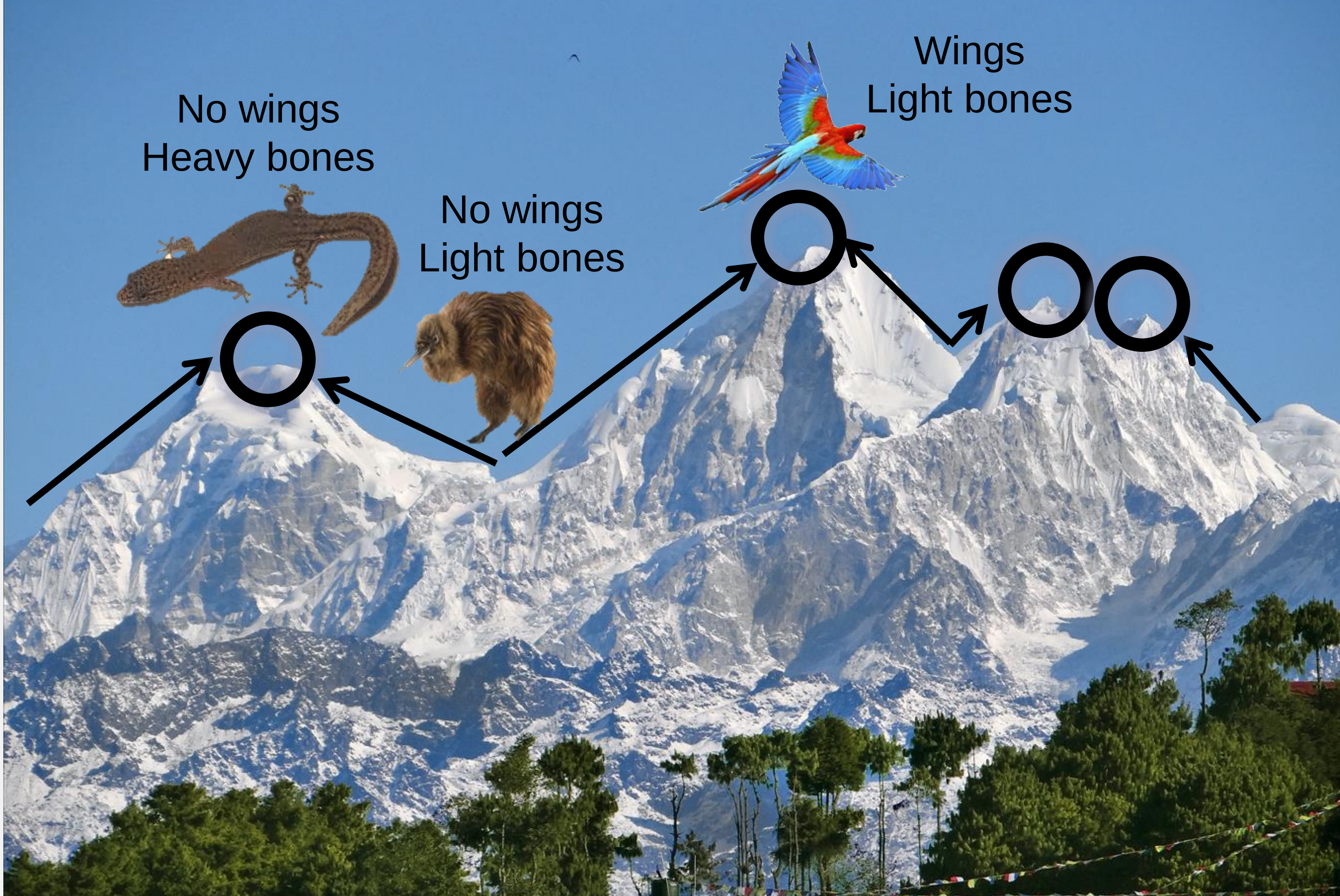




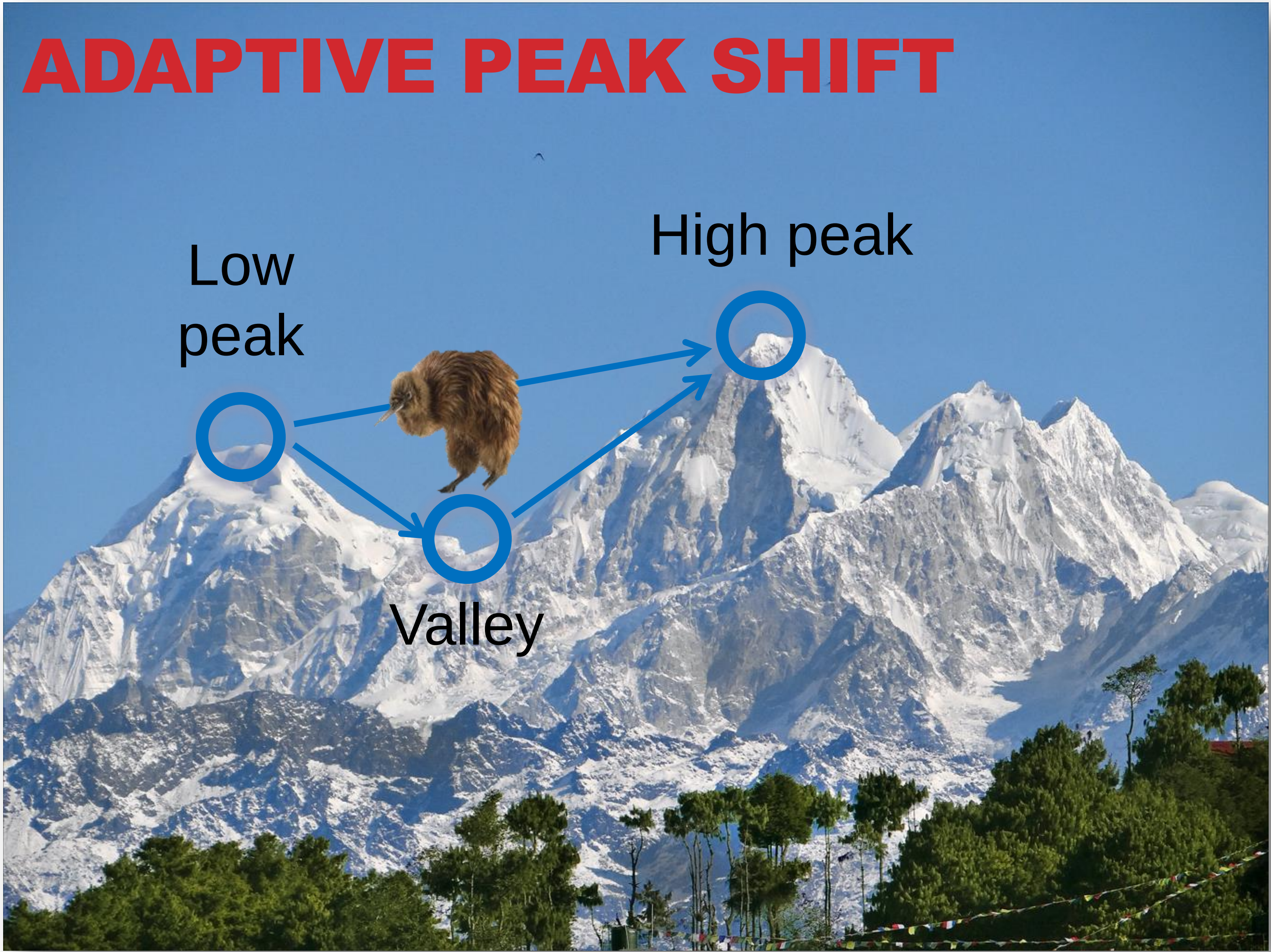
Xiao et al. 2011

SIMPLE LANDSCAPE

RUGGED LANDSCAPE

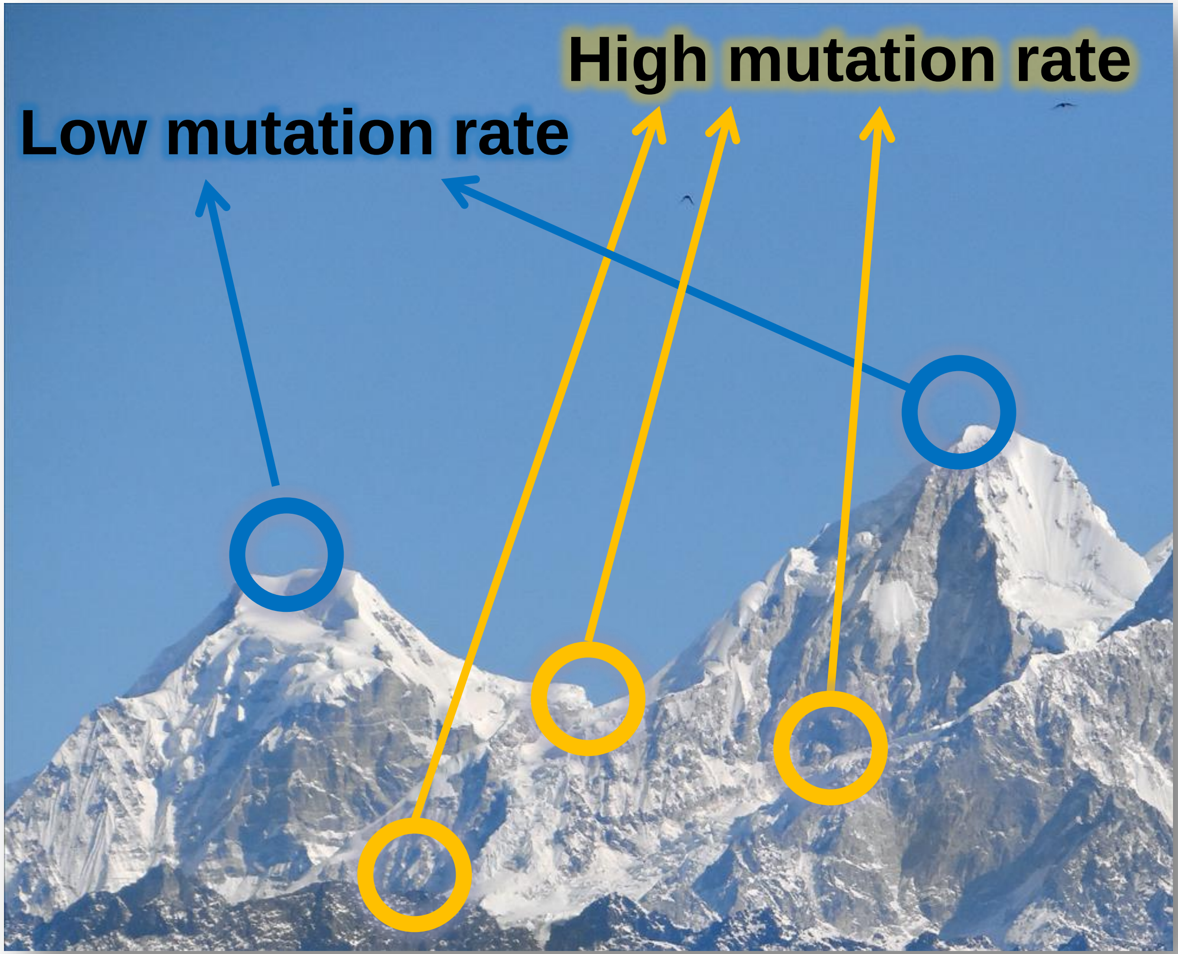


ADAPTIVE PEAK SHIFT

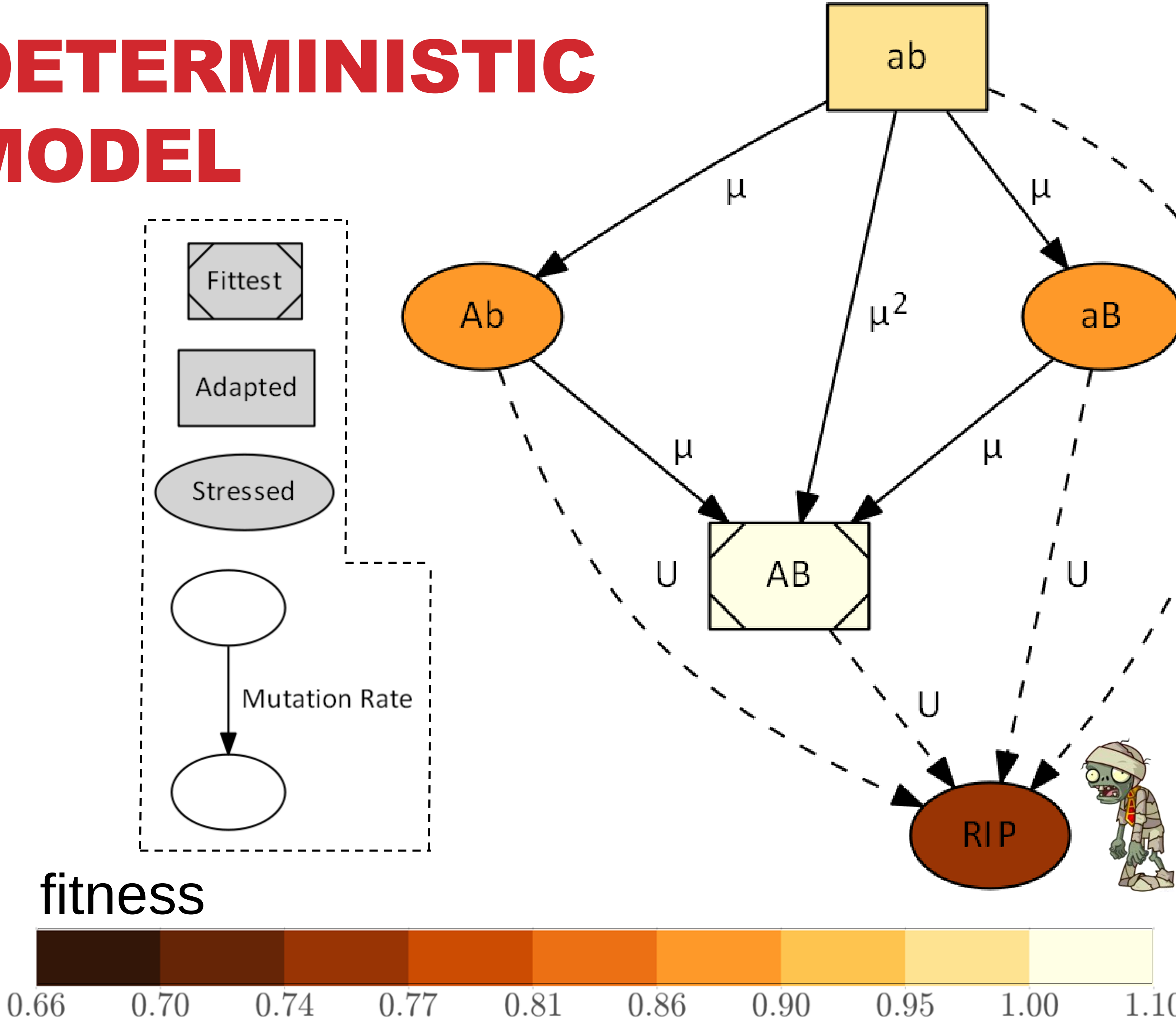


SIM & RUGGED LANDSCAPE

Increasing the mutation rate in individuals below **both** peaks



DETERMINISTIC MODEL



DETERMINISTIC RESULTS

The rate of adaptation without **normal mutation**:

$$\nu_{NM} \approx 4NH\mu^2$$

The rate of adaptation without **high mutation**:

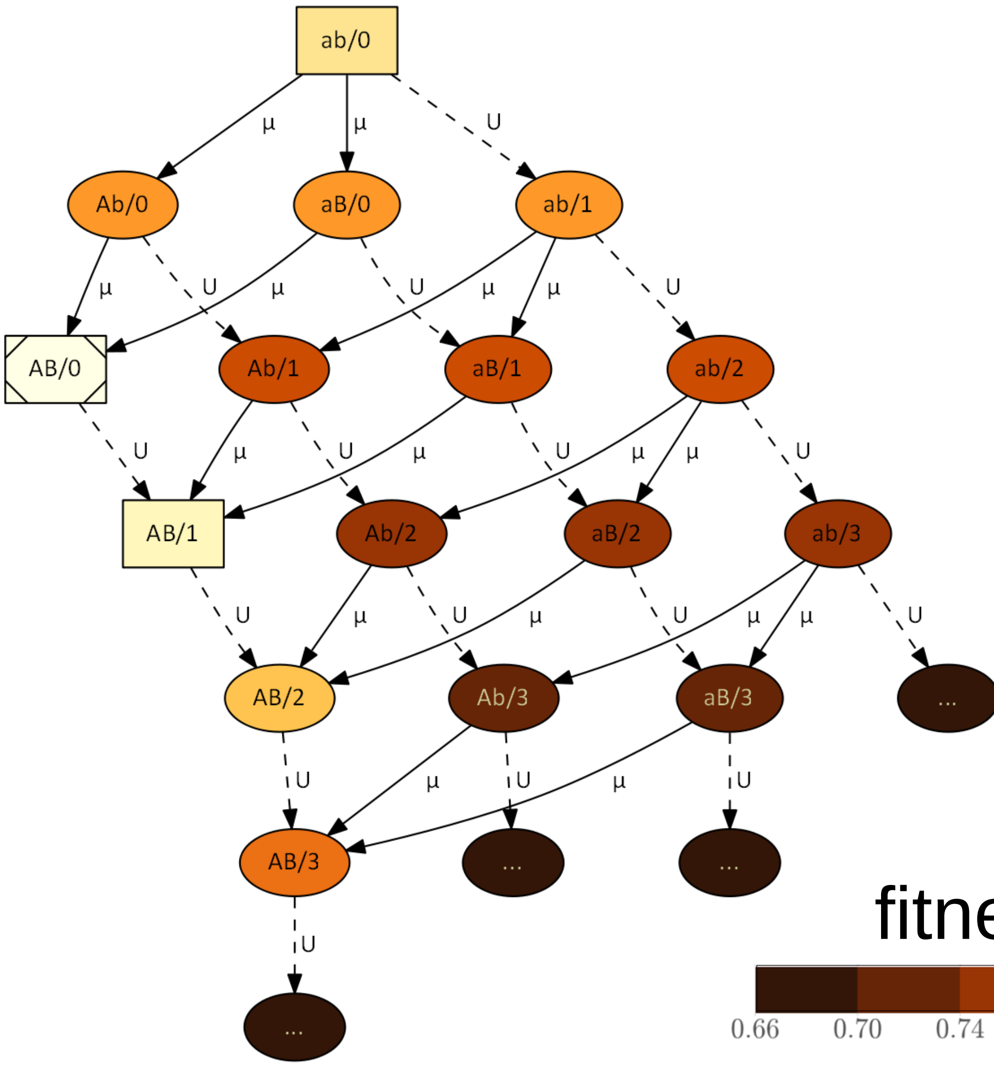
$$\nu_{CM} \approx \tau^2 \cdot \nu_{NM}$$

The rate of adaptation without **stress-induced mutation**:

$$\nu_{SIM} \approx \tau \cdot \nu_{NM}$$

ν – adaptation rate; N – population size; τ – mutation rate increase; H – double mutant advantage; μ – beneficial mutation rate

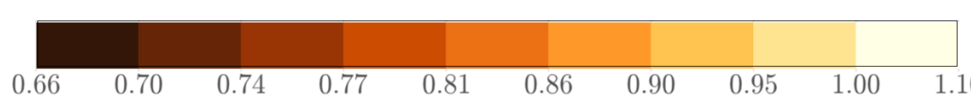
STOCHASTIC MODEL



No MSB assumption

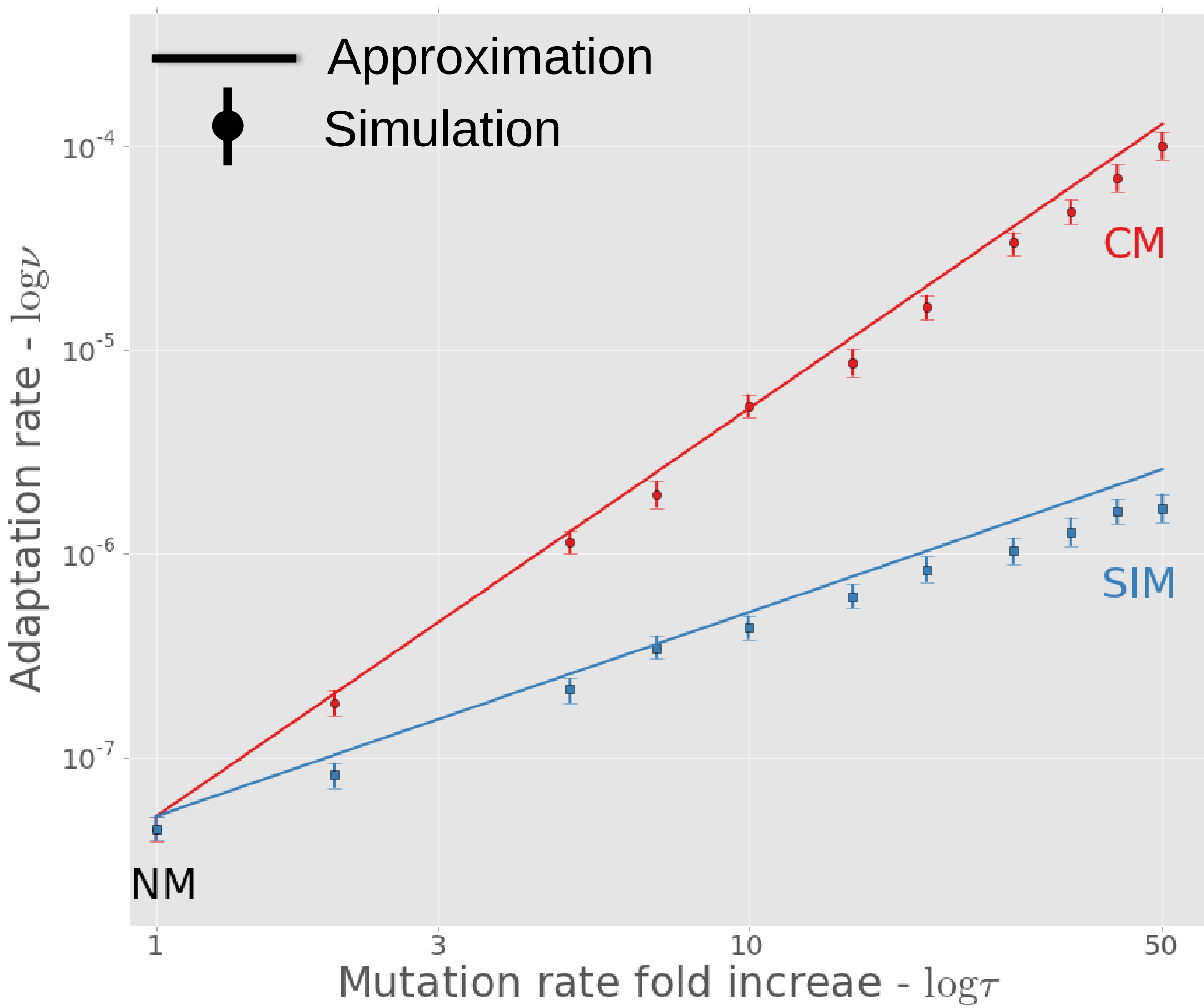
No 

fitness

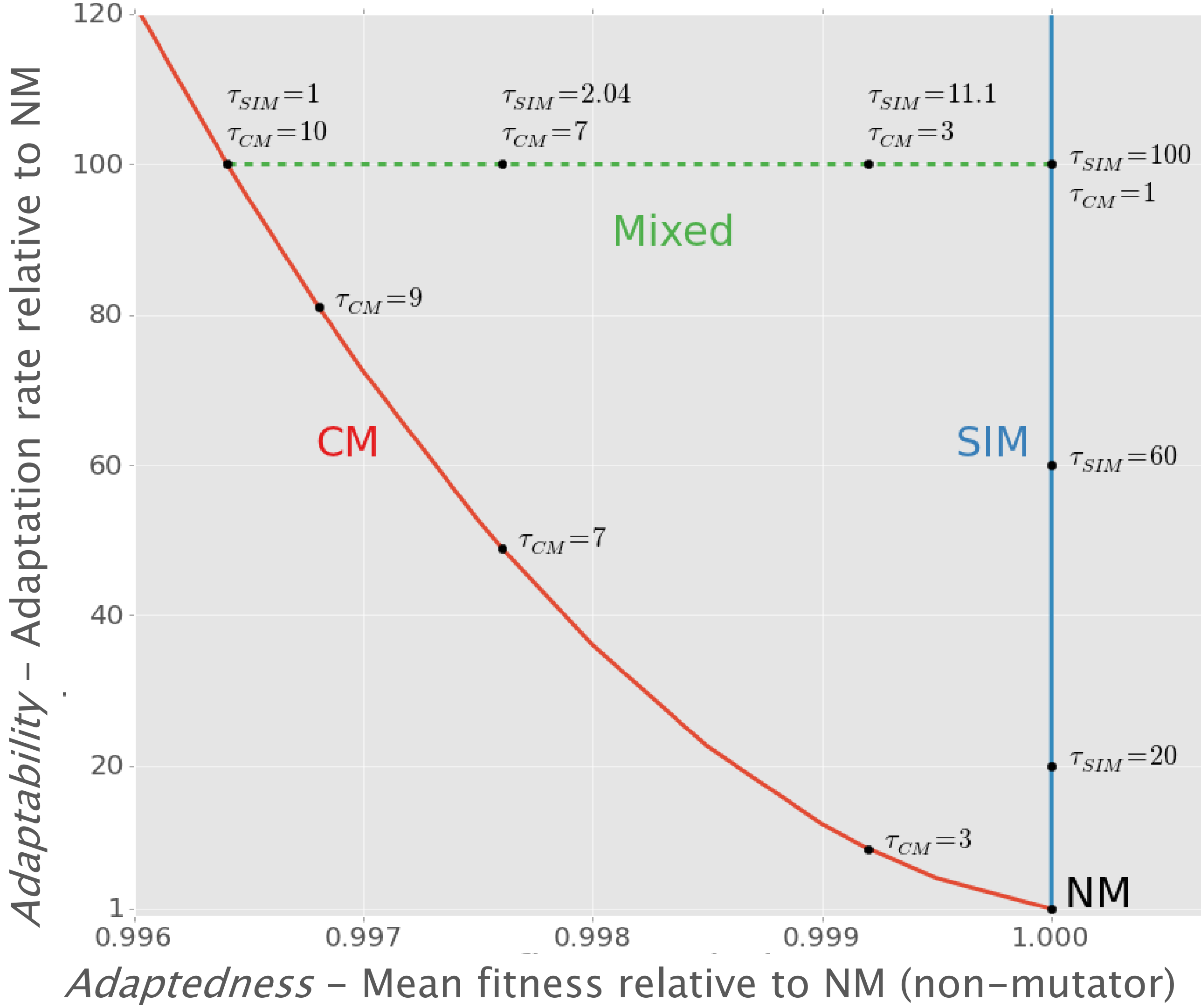


$$\nu_{CM} \approx \tau^2 \cdot \nu_{NM}$$
$$\nu_{SIM} \approx \tau \cdot \nu_{NM}$$

ADAPTATION RATE



SIM BREAKS THE *ADAPTABILITY-ADAPTEDNESS* TRADE-OFF



CONCLUSION

- **Evolution of Stress-induced mutagenesis:**
  - SIM can evolve due to second order selection
  - In constant and changing environments
- **Effects of stress-induced mutagenesis:**
  - SIM increases the adaptation rate without reducing the population mean fitness
  - Breaks the trade-off between *adaptability* and *adaptedness*

yoavram@post.tau.ac.il

@yoavram

http://www.yoavram.com