Adaptability, Adaptedness and Stress-Induced Mutagenesis

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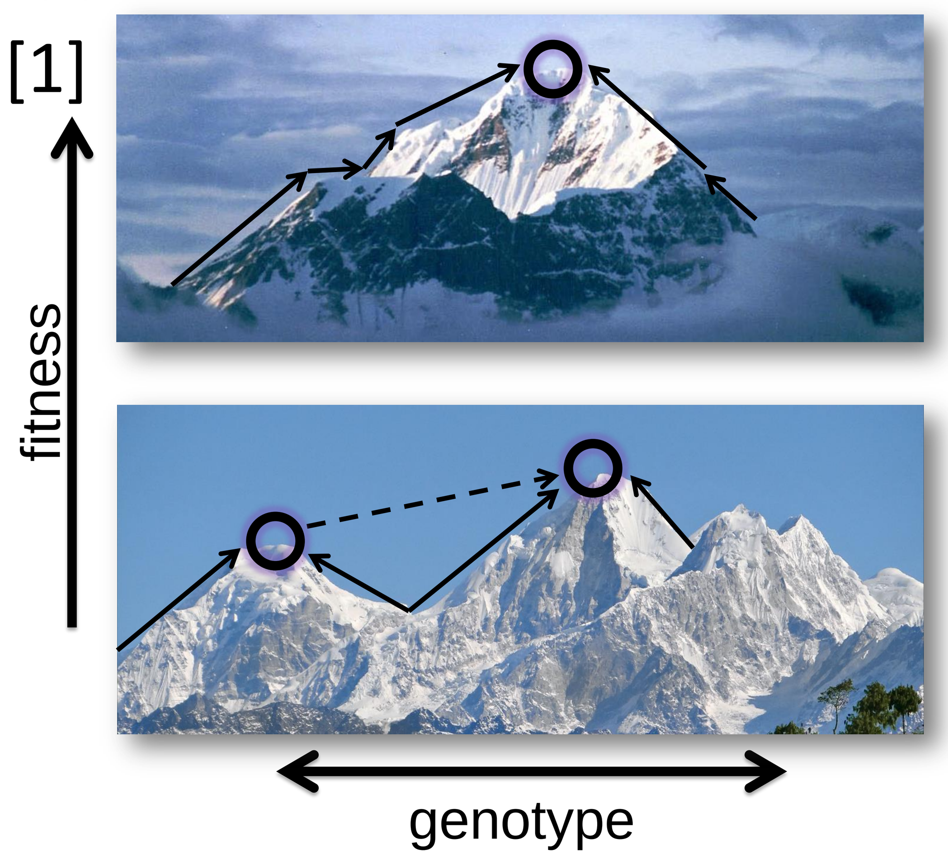
Background

Mutagenesis is induced by stress responses in various species of bacteria and even in eukaryotes (Rosenberg et al. 1998, Galhardo et al. 2007, Bjedov et al. 2003).

In a previous work (Ram & Hadany 2012) we studied the evolution of stress-induced mutagenesis in constant and changing environments. We showed that **stress-induced mutagenesis (SIM) is favored by selection** over constant rate mutagenesis because it generates beneficial mutations when they are most needed.

Complex adaptations require **two or more mutations that are jointly advantageous but separately deleterious**, and therefore presents an open evolutionary question, first described by **Sewall Wright** (1931) and popularized using the **fitness landscape** metaphor:



Sign	Name	Estimate	Citation
s	Selection coefficient	0.001-0.01	6,7
H	Double mutant advantage	1-10	8
U	Genomic mutation rate	0.003-0.0004	8,9
μ	Beneficial site mutation rate	U/5000	7
τ	Mutation rate increase	1-100	10
N	Population size	10^5-10^{10}	11

Table 1. Model parameters and estimated values for bacteria.

Adaptation rate results

The adaptation rate v as a function of the mutation rate fold-increase τ is approximated with normal mutagenesis (NM), constitutive mutagenesis (CM) and stress-induced mutagenesis (SIM) by:

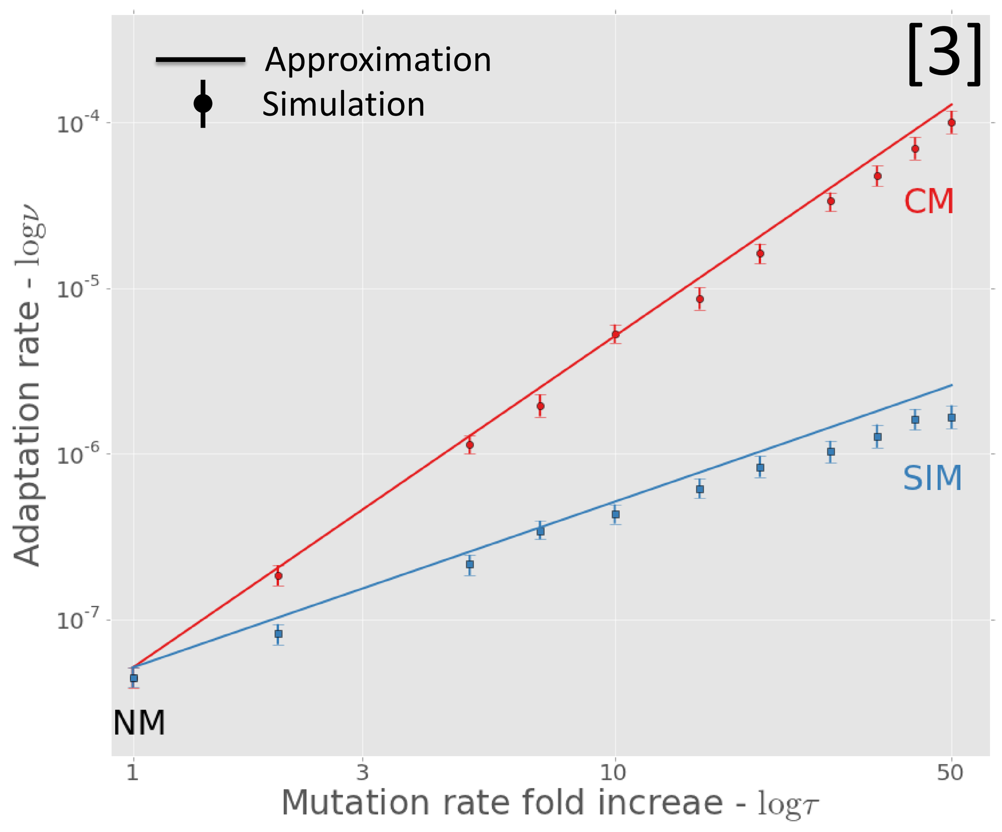
$$v_{NM} \approx 2NH\mu^2(1-U)(2-U) \approx 4NH\mu^2$$

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

$$v_{SIM} \approx v_{NM} \cdot \frac{2\tau}{(2-\tau U)} \approx \tau \cdot v_{NM}$$

SIM increases the adaptation rate of complex traits: solid lines are analytic approximations, markers are results of simulations (see below), error bars are 95% CI. Both axes are in log scale – the slope of the CM line is twice as steep as the slope of the SIM line.

The difference between the approximations and the simulations is explained by appearances of *AB* on deleterious backgrounds in the simulations.



SIM is more efficient than CM

Adaptability

- Constitutive mutagenesis (CM) increases the rate of complex adaptation τ^2-fold (τ: mutation rate fold-increase).
- Stress-induced mutagenesis (SIM) increases the rate of complex adaptation τ-fold.

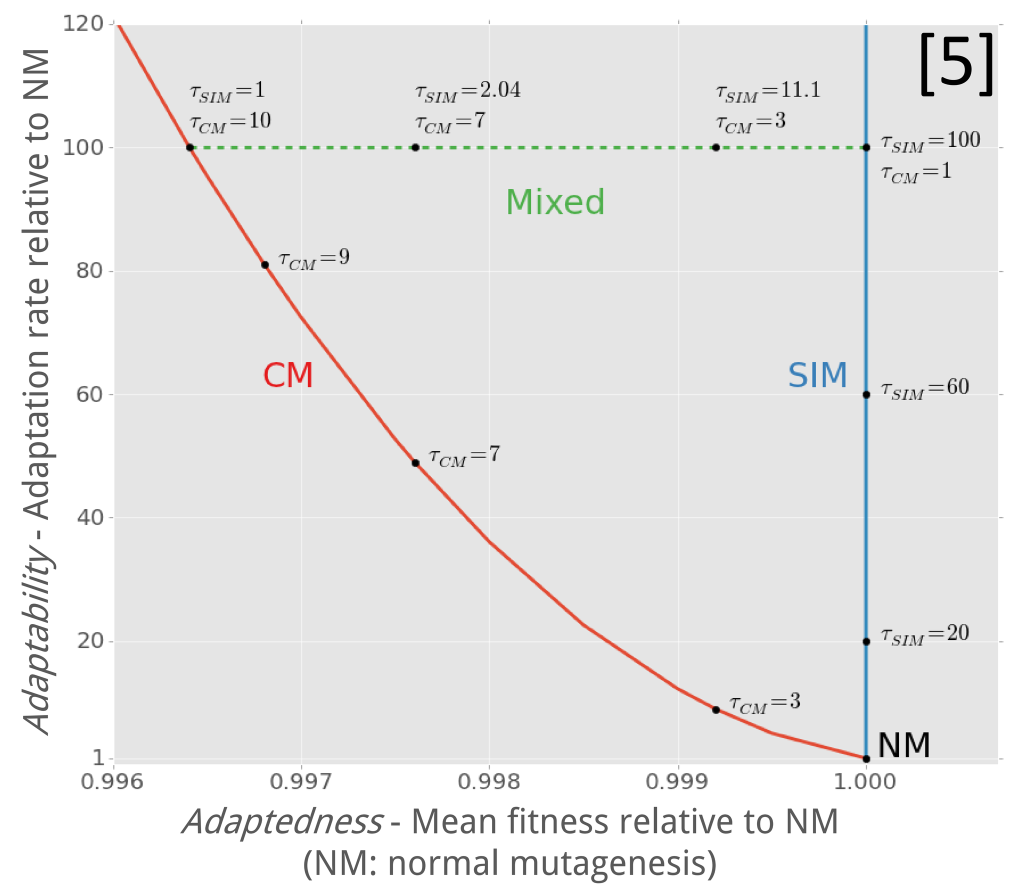
Adaptedness

- CM decreases the population mean fitness $e^{-U(\tau-1)}$-fold due to due to the accumulation of deleterious mutations (Kimura & Maruyama 1966).
- SIM slightly increases the population mean fitness (Ram & Hadany 2012).

Breaking the adaptability-adaptedness trade-off

SIM can achieve the same adaptation rate as CM (by increasing τ), without reducing the fitness of the population.

If τ^2 is too high (*i.e.* $\tau^2 U>s$), a **mixed strategy**, in which all individuals increase their mutation rate τ_{CM}-fold and stressed individuals increase their mutation rate τ_{SIM}-fold, is still more efficient than CM.



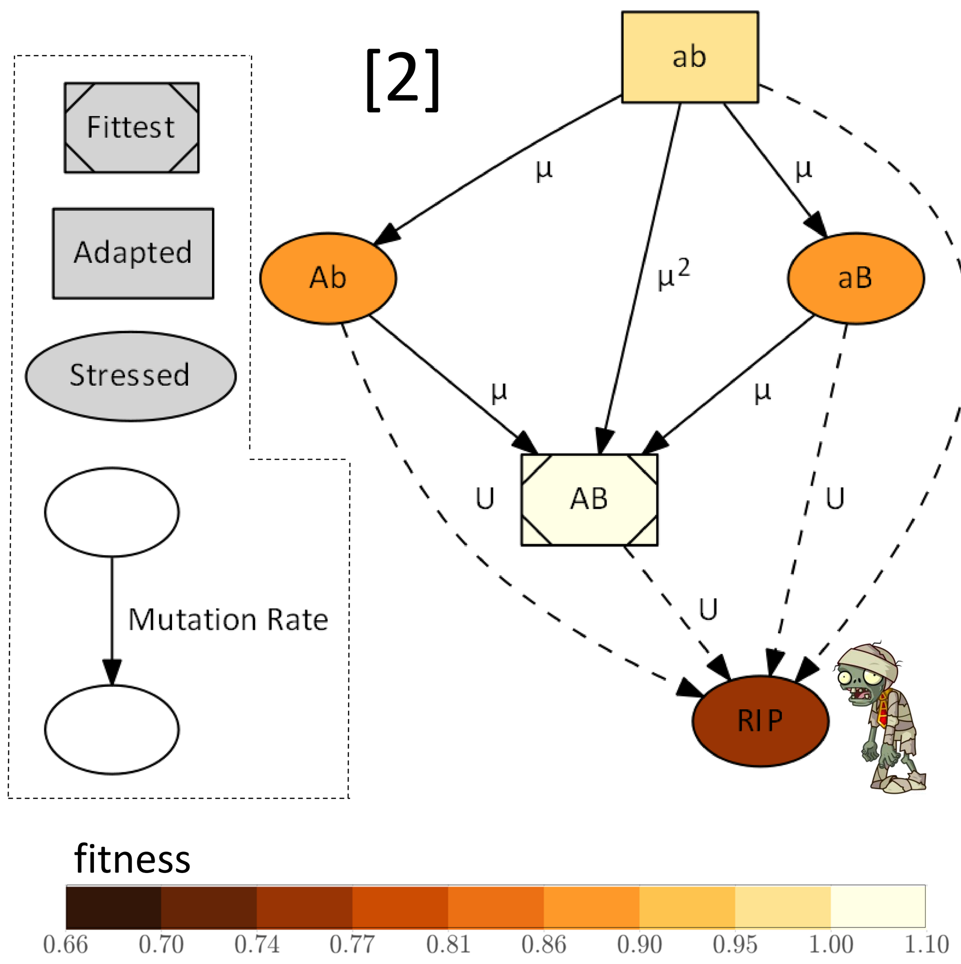
Model

Figure 2 describes are two-locus (*A/a* and *B/b*) model of complex adaptation.

Each node represents a genotype. Genotype ***ab* is the wildtype** local adaptive peak, ***AB* is the global adaptive peak** with the highest fitness, and the single mutants ***Ab* and *aB* are adaptive valleys** with fitness lower than the wildtype - **the darker the color the lower the fitness.**

"RIP" represents genotypes with deleterious mutations that will not contribute to adaptation (**"the living dead"**).

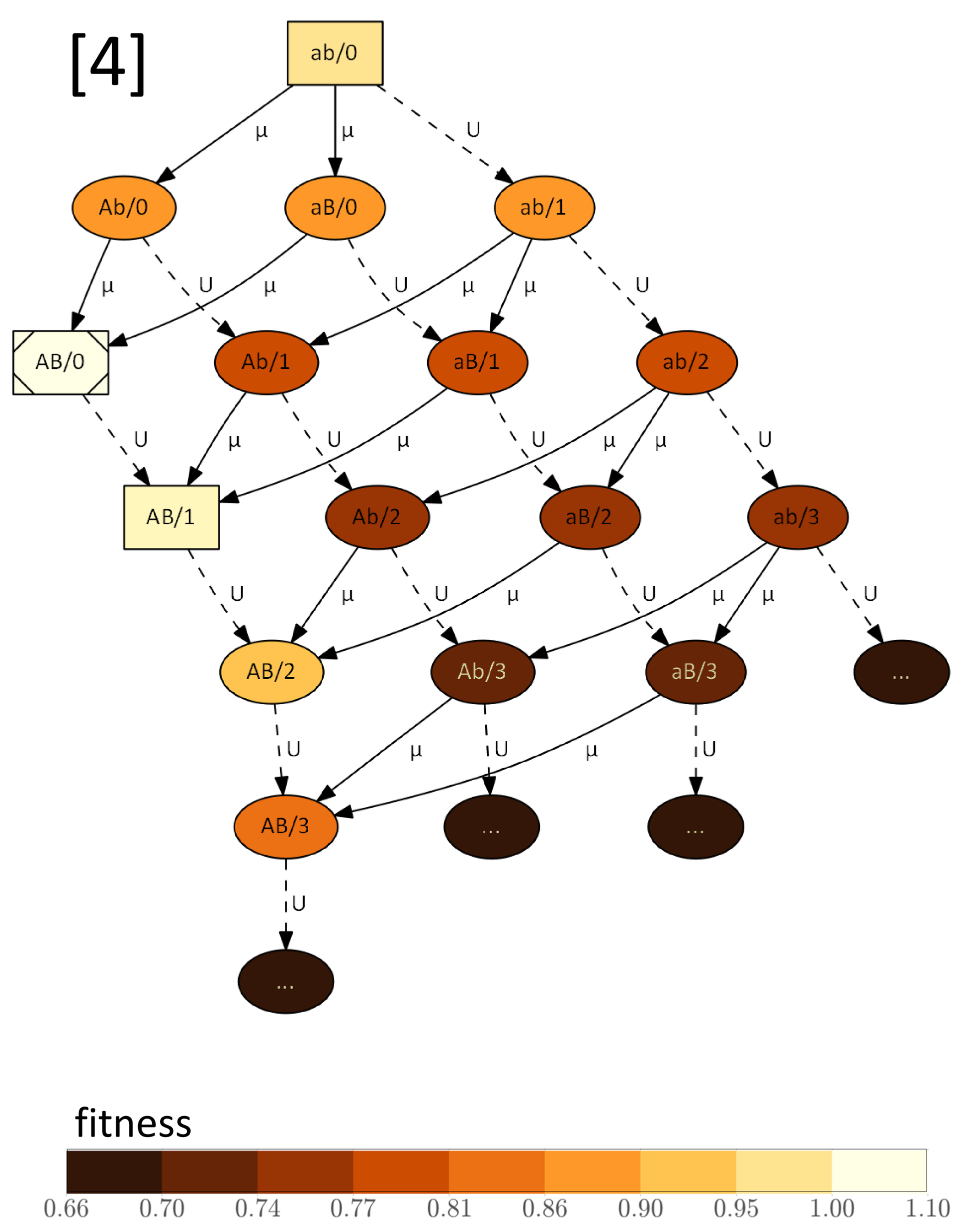
Arrows define the direction of mutation and denote the relevant mutation rate: ***U* for background deleterious mutation** (dashed lines) and ***μ* for mutations in the *A/a* and *B/b* loci** (solid lines).



Simulations

Figure 4 describes our **multi-locus Wright-Fisher simulations**, which also account for **genotypes with deleterious mutations** – denoted by the number after the slash (*ab/2* is *ab* with two deleterious mutations).

The figure shows up to three mutations for simplicity; the simulations has up to 25.



Summary

We compared the **mean fitness** at a mutation-selection balance and the **adaption rate** on a rugged fitness landscape with and without stress-induced mutagenesis.

We showed that **stress-induced mutagenesis increases the rate of complex adaptation**, and that in contrast to constitutive mutagenesis, **it does not jeopardize the fitness of populations** under stable conditions.

Literature cited

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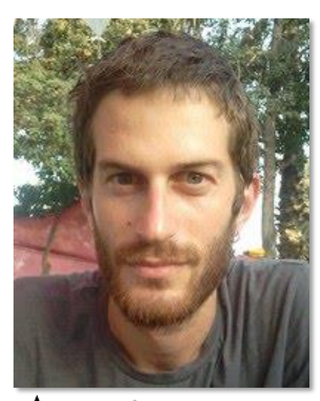

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