On the Role of Stress-Induced Mutagenesis in Evolution

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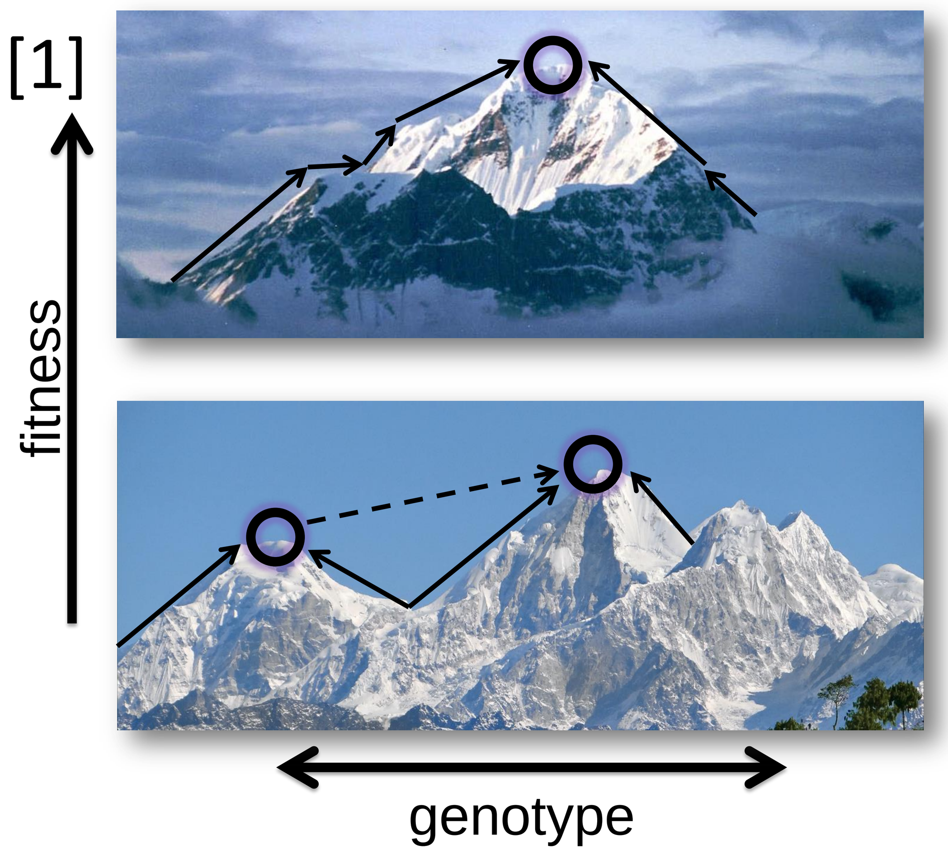
Background

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

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:

[1]



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

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:

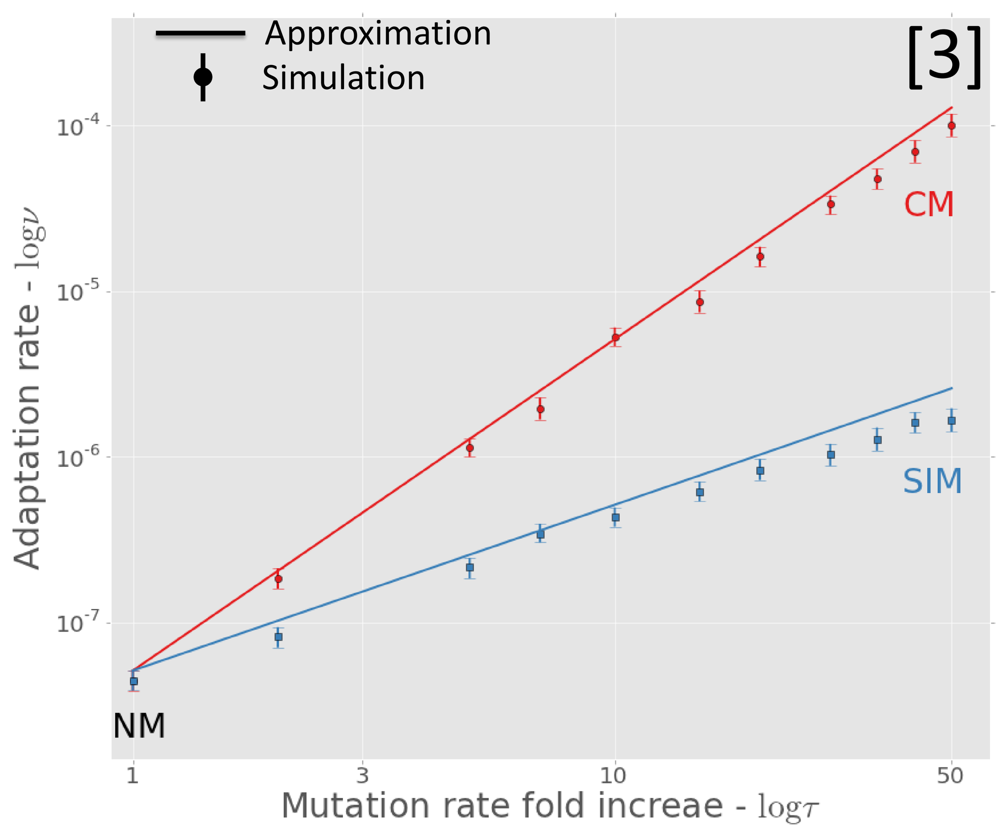
$$v_{NM} \approx 4NH\mu^2\left(1-\frac{U}{s}\right)$$

$$v_{CM} \approx v_{NM}\cdot\tau^2\left(1-\frac{\tau U}{s}\right)$$

$$v_{SIM} \approx v_{NM}\cdot\tau(1-\tau U)$$

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*: adapting to new conditions**

- 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.

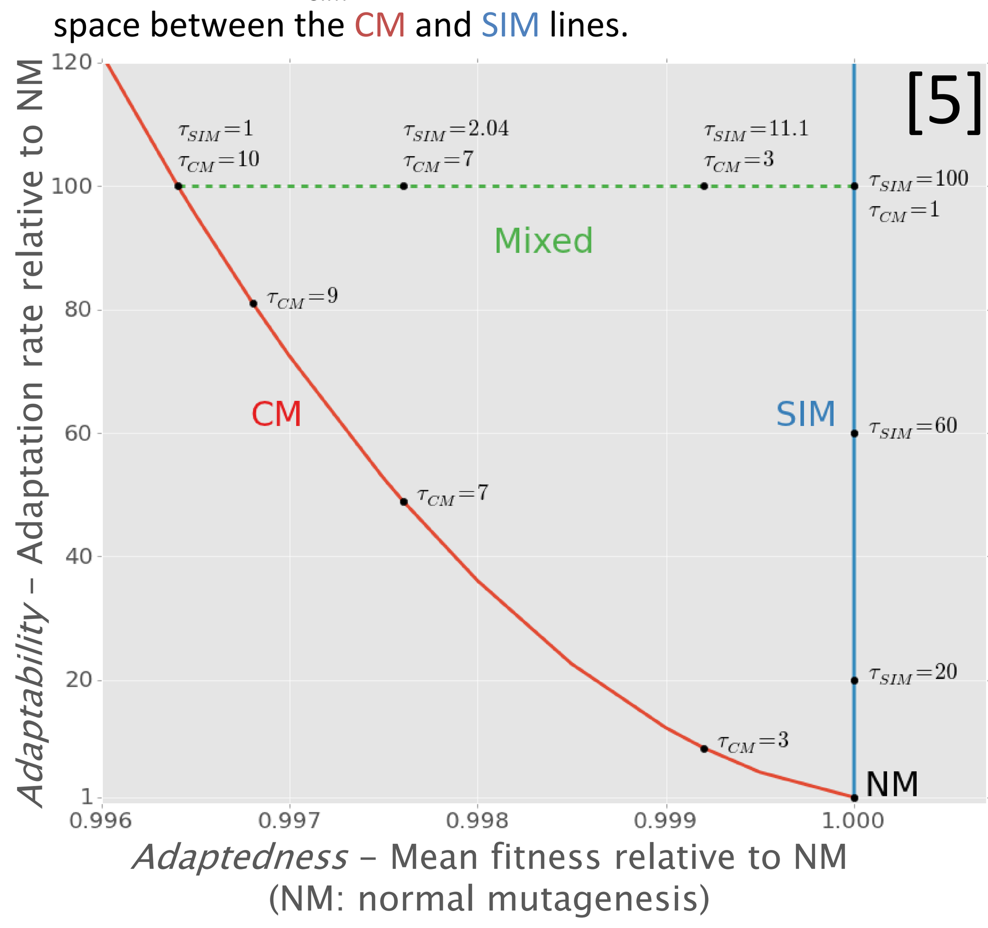
***Adaptedness*: staying adapted to existing conditions**

- CM decreases the population mean fitness in stable environments ≈(1-$U\tau$)-fold 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

Both CM and SIM increase the ***adaptability*** of populations, represented by their adaptation rate. SIM, in contrast to CM, doesn't reduce the ***adaptedness*** of populations, represented by the mean fitness in stable environments.

In mixed strategies all individuals increase their mutation rate τ_{CM}-fold and stressed individuals increase their mutation rate τ_{SIM}-fold. These strategies represent the space between the CM and SIM lines.



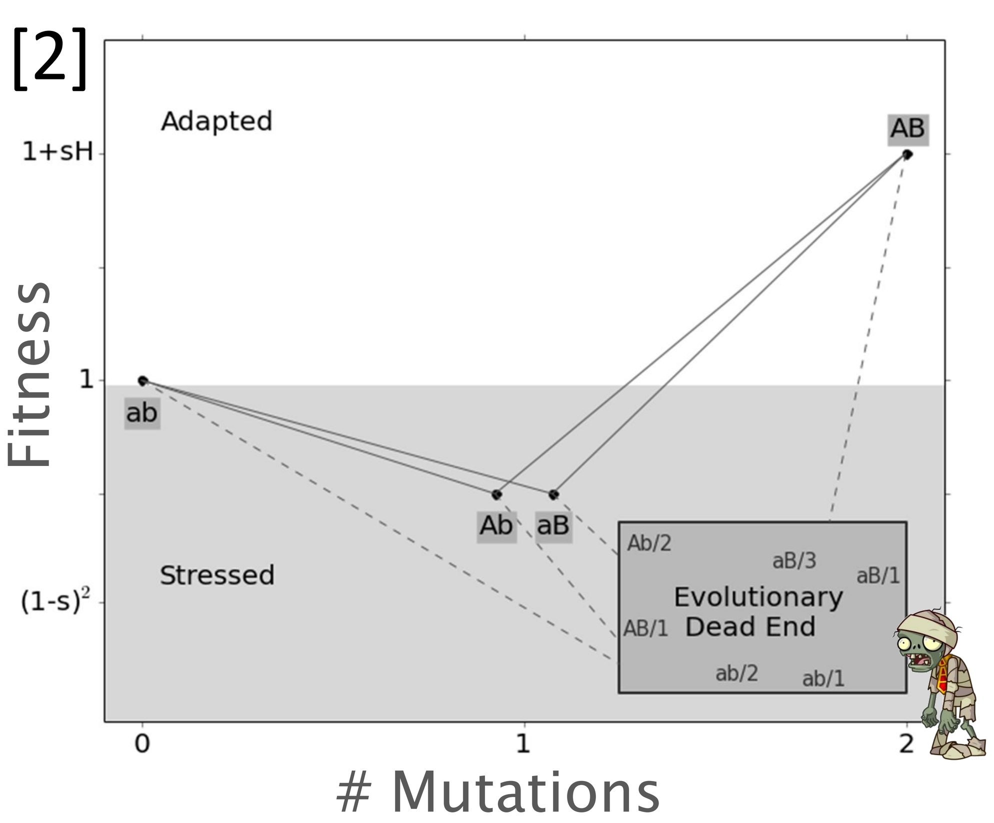
Model

Figure 2 describes a 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. "**Evolutionary Dead End**" represents genotypes with deleterious mutations that will not contribute to adaptation.

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

[2]



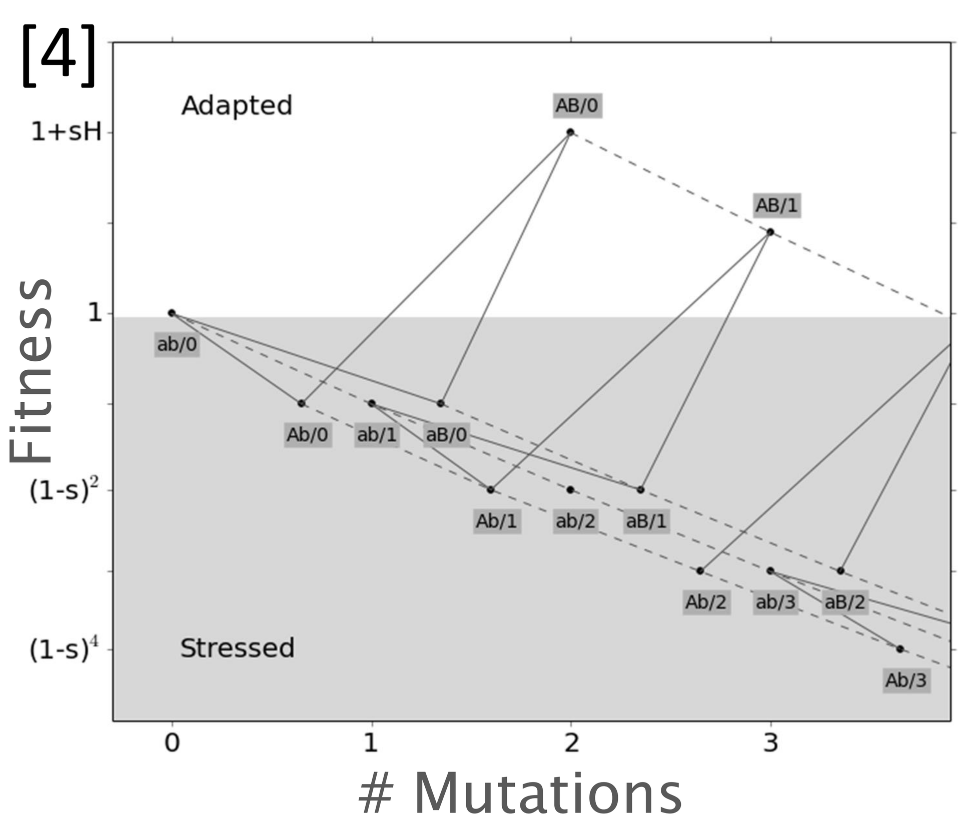
Simulations

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) – so there are no **"Evolutionary Dead Ends"**.

The figure shows up to three mutations for simplicity, the simulations have up to 25.

The simulations do not make assumptions on the distribution of deleterious alleles at the **mutation-selection balance**, but rather allow this balance to evolve before the adaptation process starts.

[4]



Summary

We compared the ***adaptability*** (ability to adapt) and ***adaptedness*** (ability to stay adapted) of populations with and without stress-induced mutagenesis.

We showed that **stress-induced mutagenesis increases the *adaptability*** of a population and that in contrast to constitutive mutagenesis, **it does not jeopardize its *adaptedness***.

Literature cited

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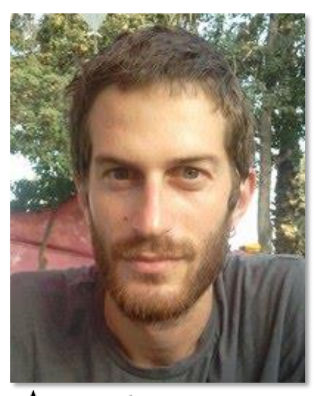

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