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 (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:

[1]

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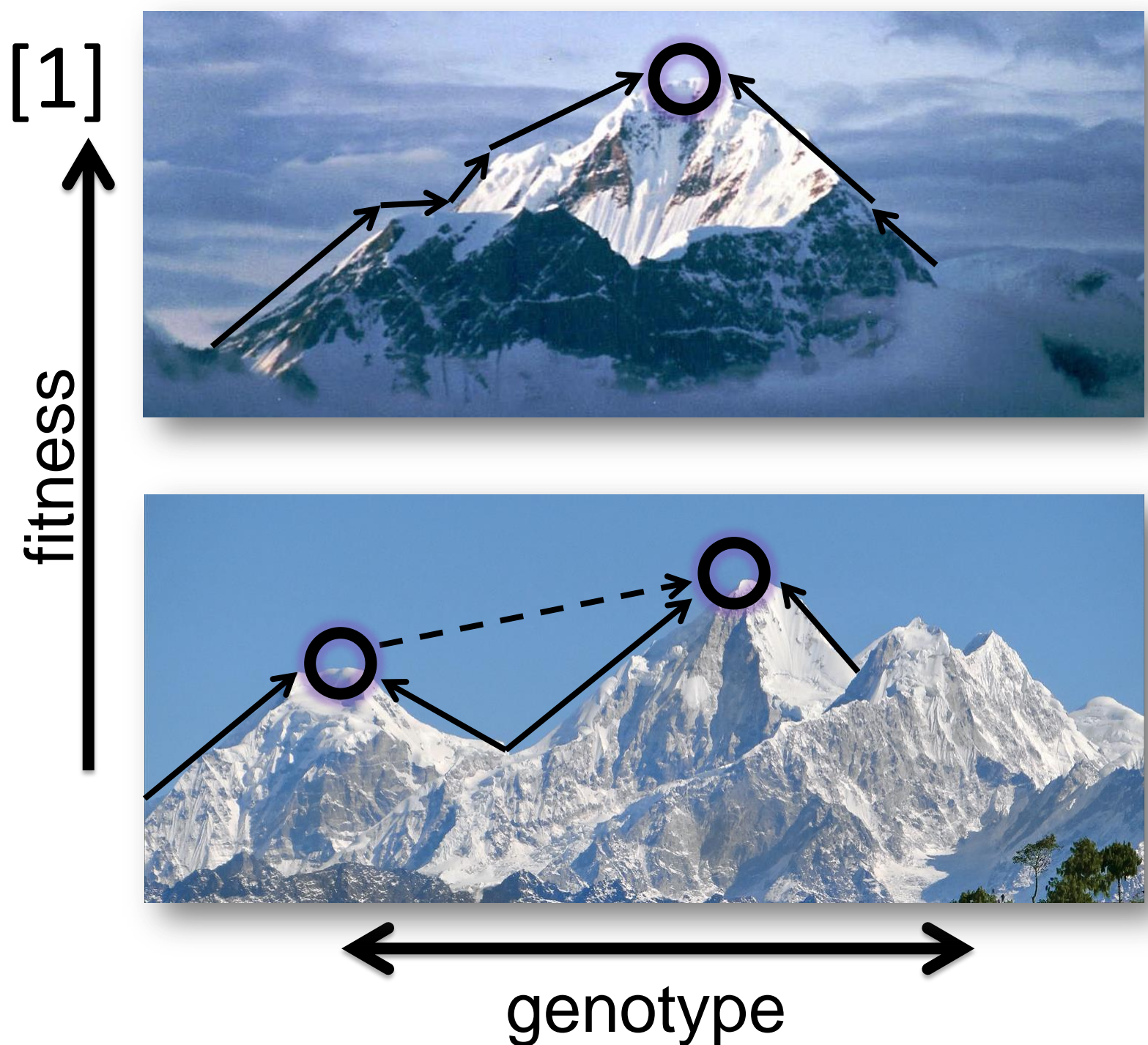
Sign	Name	Estimate	Citation
s	Selection coefficient	0.001-0.01	5,6
H	Double mutant advantage	1-10	7
U	Genomic mutation rate	0.003-0.0004	7,8
μ	Beneficial site mutation rate	U/5000	6
τ	Mutation rate increase	1-100	9
N	Population size	10^5-10^{10}	10

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:

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

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

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

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 ("rise of the living dead").

[3]
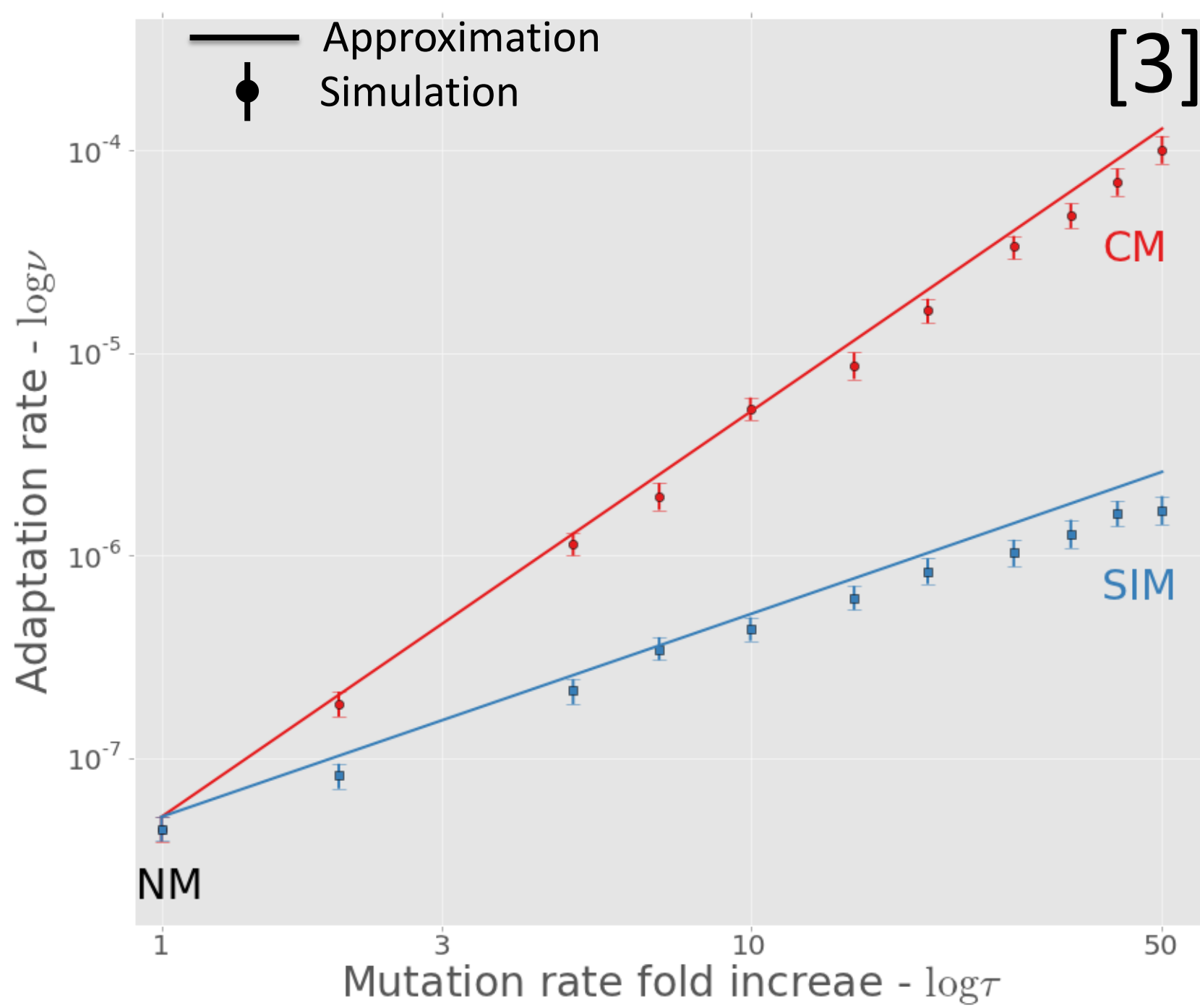
SIM is more efficient than CM

***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 $\approx(1-U\tau)$-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.


[5]
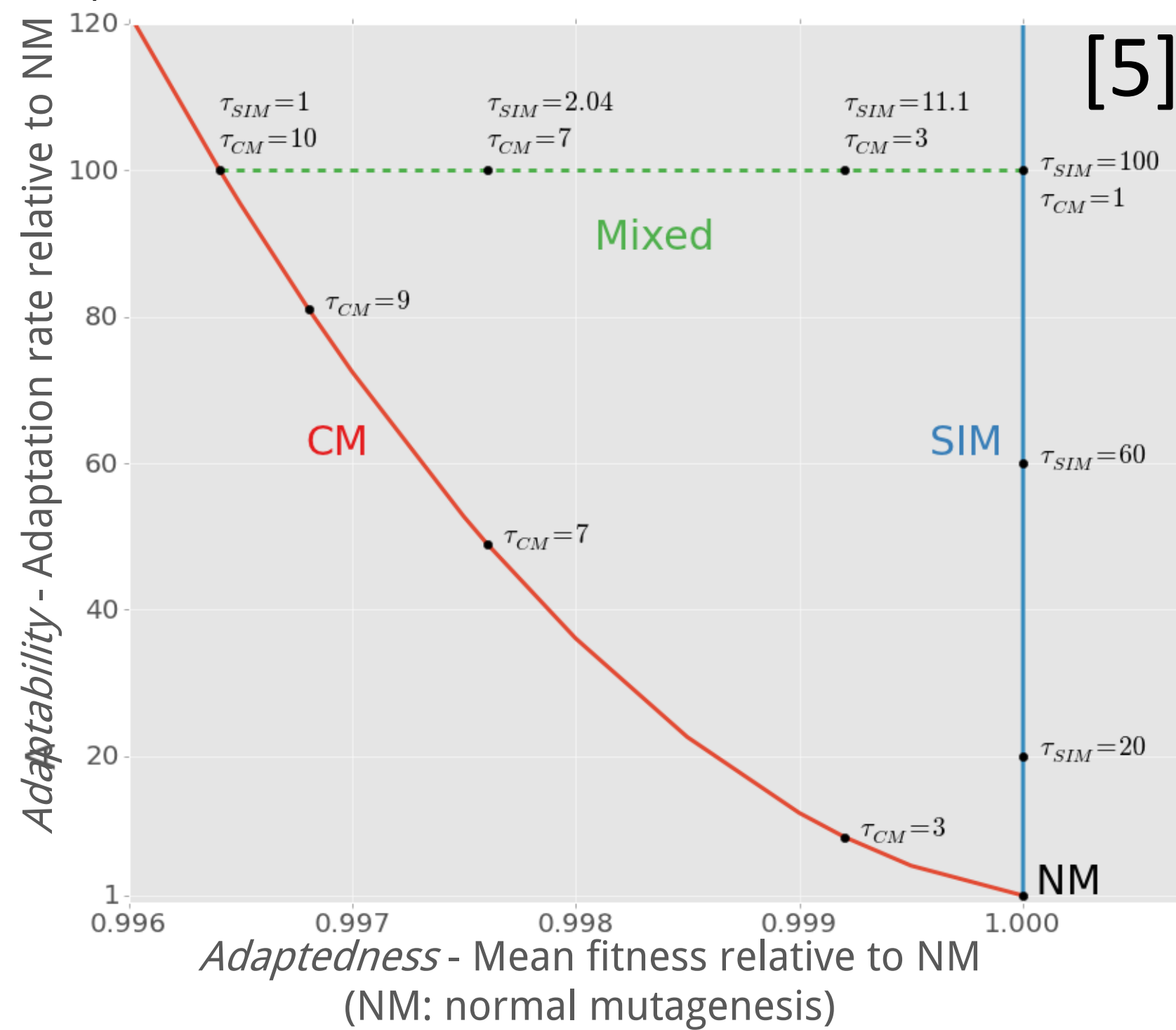
Model

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 mutations (dashed lines) and *μ* for mutations in the *A/a* and *B/b* loci (solid lines).

[2]
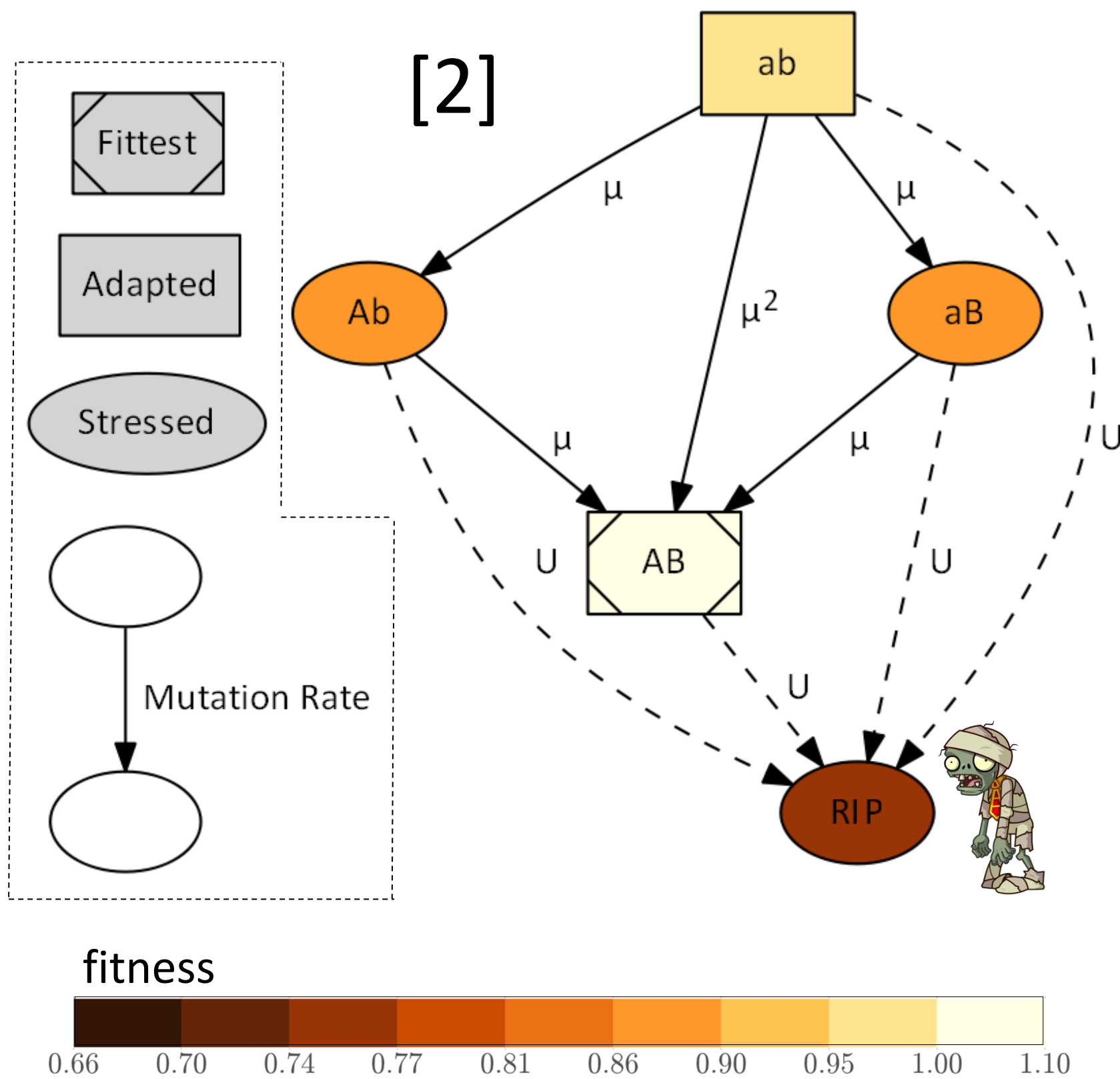
Simulations

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 "living dead".

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

[4]
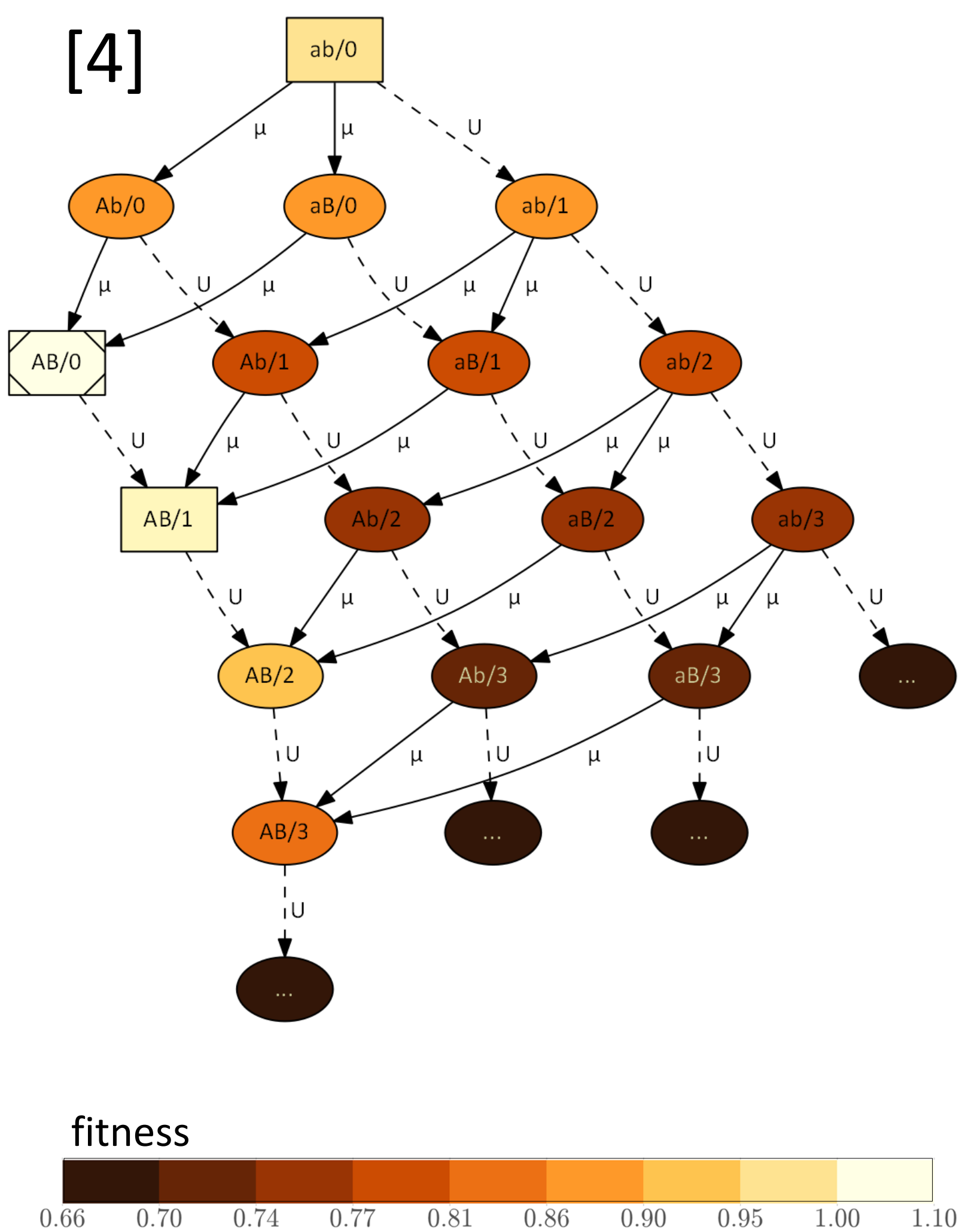
Summary

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***.
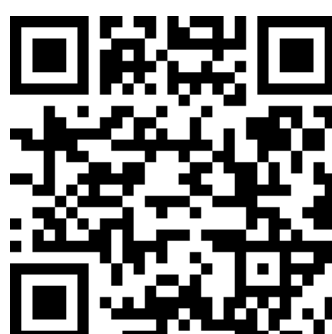
Literature cited

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