Simple Simulation Model

Using the terminology from the SI, a stressful environment is defined as follows:

> ***Definition***:
>
> An environmental sequence $\vec{e} = \langle e_{s_1}, e_{s_2}, e_{s_3}, \dots, e_{s_Z} \rangle$ is **stressful** to genotype $\vec{g}$, if
>
> $$\Omega\left[\vec{g}, e_{s_j}\right] > \Omega\left[\vec{g}, e_{s_{j+1}}\right],$$
>
> for all $j \in \{1,2,3, \dots Z\}$. That is, the fitness of $\vec{g}$ monotonically decreases over the sequence of environments.

If the environmental state has no effect on the fitness of a genotype, we have the following definition:

> ***Definition***:
>
> We will define the environment sequence $\vec{e} = \langle e_{s_1}, e_{s_2}, e_{s_3}, \dots, e_{s_Z} \rangle$ as **neutral** to genotype $\vec{g}$ if
>
> $$\Omega\left[\vec{g}, e_{s_j}\right] = \Omega\left[\vec{g}, e_{s_k}\right],$$
>
> for all $j, k \in \{1,2,3, \dots Z\}$.

Consider a wild-type genotype (denoted $\vec{g}_w$) and every mutant genotype differing from the wild type at exactly one of L loci. Given the environmental sequence $\vec{e} = \langle e_{s_1}, e_{s_2}, e_{s_3}, \dots, e_{s_Z} \rangle$, we consider a system with the following properties (see Supplementary Figure 5):

1) The sequence $\vec{e}$ is stressful to the wild type and neutral to every mutant.
2) Each mutant has a unique fitness (which is constant across environments). That is, $\Omega\left[F_i[\vec{g}_w], e_{s_k}\right] \neq \Omega\left[F_j[\vec{g}_w], e_{s_k}\right]$, where $i \neq j$ and $i, j \in \{1,2,3, \dots L\}$.
3) The wild-type has the highest fitness of all genotypes in the least stressful environment (i.e., $\Omega\left[\vec{g}_w, e_{s_1}\right] > \Omega\left[F_i[\vec{g}_w], e_{s_1}\right]$ for all $i \in \{1,2,3, \dots L\}$) and the lowest fitness of all genotypes in the most stressful environment (i.e., $\Omega\left[\vec{g}_w, e_{s_Z}\right] < \Omega\left[F_i[\vec{g}_w], e_{s_Z}\right]$ for all $i \in \{1,2,3, \dots L\}$).

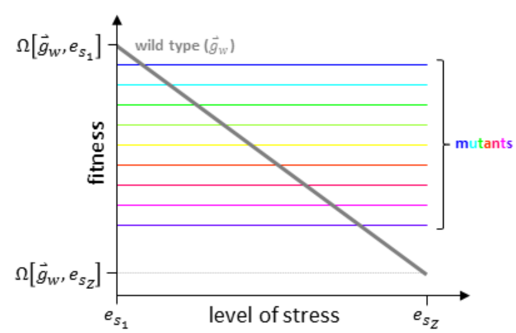

Figure 1: A graphical representation of the assumptions.

For our simple simulation, we use the following life cycle:

I) A finite population of size M is initialized with the wild-type genotype at fixation.
II) Every discrete generation a Wright-Fisher process with selection is used:
   a. M offspring are generated.
   b. Parents are chosen proportional to their fitness in the current environment.
   c. If the parent is a mutant, the genotype of the offspring will be identical (i.e., no back mutation).

d. If the parent is wild type, the offspring will be a mutant with probability μ (where the specific locus of mutation is chosen with uniform probability) and wild type with probability $1 - \mu$.
e. The parents are discarded.

III) The environment can change and then step II is repeated.

Under this life cycle, with the above assumptions, simulations show that a lower rate of increase in the level of stress leads to a higher mean fitness and a smaller variance in fitness in the evolved population (Figure 2). This can be understood roughly by imagining moving along the wild type fitness function of Figure 1 (by increasing the level of stress) at different speeds. At very low speeds, when a mutant first arises, it will spread by selection only if it is very fit (as the fitness of the wild type will be relatively high). At extremely high speeds, when a mutant first arises it can spread by selection despite its fitness (as the fitness of the wild type will be lower). If the first beneficial mutant to arise fixes, then gradual change should tend to favor higher mean fitness and lower variance in fitness.

The results from our evolution experiment do ***not*** agree with these simulation results. As we show, some of the basic assumptions of this simulation model (e.g., the assumption that the fitness of each mutant does not change with environment and the assumption that only single mutations occur) do not hold for our bacterial system.

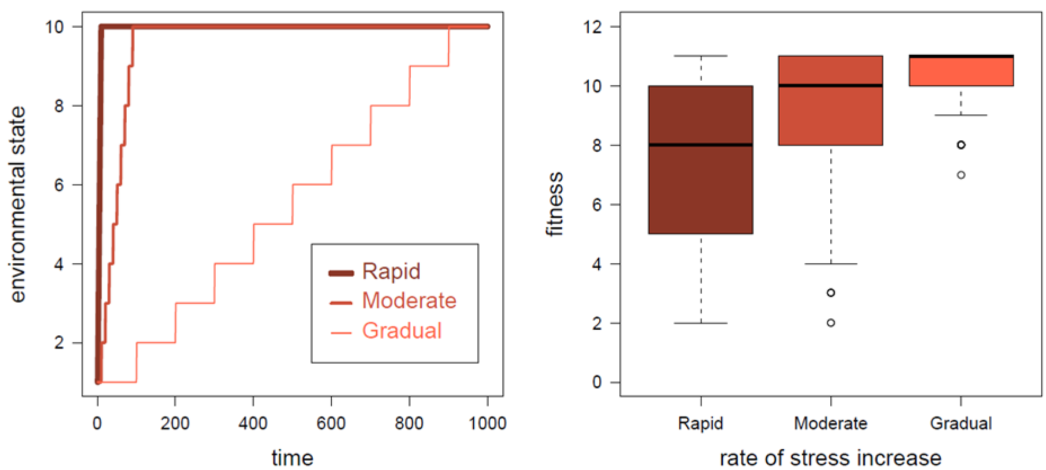

Figure 2: We consider a genetic system with $L = 10$ loci. We label each mutant with the index of the locus where it differs in allelic state from the wild type. Thus, mutants are labeled 1, 2, 3, … 10. We focus on a case with $Z = 10$ environmental states ordered in terms of the level of stress (1 is the least stressful and 10 is the most stressful). Each mutant is assigned an environment-independent fitness equal to its index plus one. The wild type has fitness equal to 1+11(10-E)/9, where E is the state of the environment. The population size is 1000 and the probability of mutation is 10^{-4}. (Left) Here we consider three rates of stress increase over a period of 1000 time steps. Rapid increase involves spending a single time step in each successively more stressful environmental state and then remaining in the most stressful environment for the remainder of the time. Moderate increase involves spending 10 time steps in each successively more stressful environmental state and then remaining in the most stressful environment thereafter. Gradual increase involves spending 100 time steps in each successively more stressful environmental state. (Right) The final fitness of 1000 replicate populations at each environmental change rate is shown. Each box is drawn from the first to third quartile with the median as the thick horizontal line.