# Stochastic Simulations of Gavrilov and Gavrilova's 'High Initial Damage Load' Hypothesis of Aging

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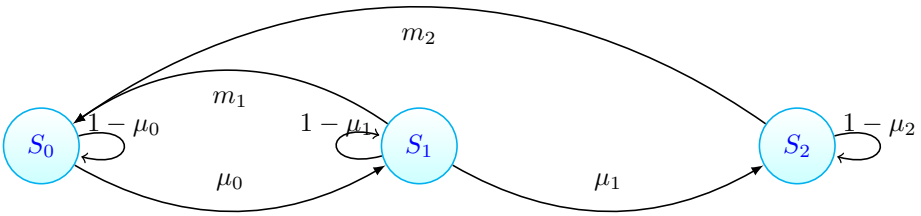
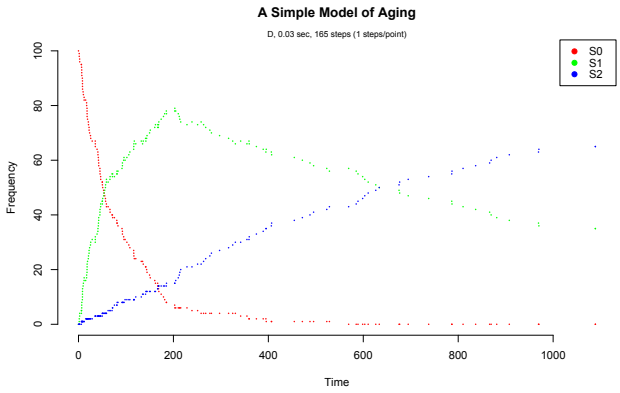



A matrix population model was used to study how mutation rates affect the fitness of a population of organisms with 3 stage-classes in their life cycle. The life-cycle graph can be used to derive the following matrix:

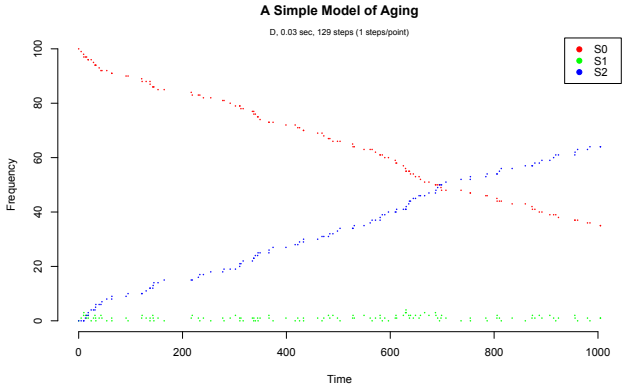
$$\begin{pmatrix} m_0 + 1 - \mu_0 & m_1 & m_2 \\ \mu_0 & 1 - \mu_1 & 0 \\ 0 & \mu_1 & \mu_D \end{pmatrix}$$

$\mu_i$ equals a mutation rate individuals experience as they move from one stage-class to the next (e.g., grow older), 1 - $\mu_i$ equals the rate at which individuals grow but do not accumulate any mutations, and each $m_i$ equals the fecundity of the respective stage-classes. Finally, $\mu_D$ is the probability of individuals that have survived to the last stage-class dying. The population matrix can be used to calculate the leading eigenvalue for a given set of initial conditions. The logarithm of the leading eigenvalue is the instantaneous population growth rate. The leading eigenvalue can then be used to find the stable age distribution vector and the reproductive value vector.

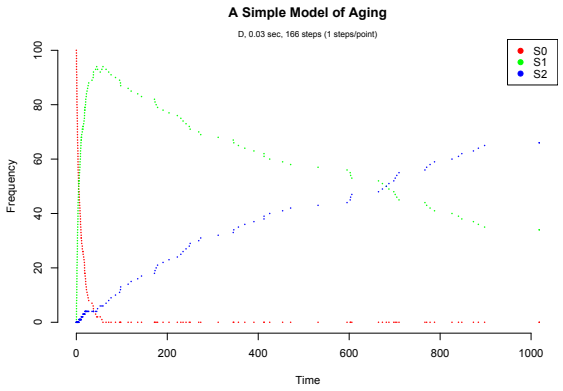
Simulations of the model's long-term population dynamics were performed in R. The simulations revealed a trade-off between the mutation accumulation rate (referring only to the rate of *somatic* mutation accumulation) and the fitness of the population (where fitness is measured as the annual per-captia growth rate of the population, $\lambda$). For some parameter regimes, aging faster and having more offspring go hand in hand. Here, I show simulated stochastic solutions to the model, using the Gillespie algorithm. The cases in Figure 1 encapsulate 3 three different scenarios of how the rate of damage per time-step, $\mu$, can affect both the amount of post-mitotic cells of different types over time (for simplicity this set of simulations included only 3 different cell types) and the transition rates between cell life-stages. The first graph shows something like normal aging, where cells are in early and middle-life for a reasonably long number of generations (up around 600 generations), but old cells, those in $S_3$ eventually dominate the population and take over. $\mu_0 = \mu_1$ in this simulation. The second plot shows what happens when middle-age doesn't exist: all cells are either young or old, but nowhere in between. This is what happens when $\mu_1 \gg \mu_0$. Finally, the third plot shows something like a long middle-age. This is due to $\mu_0 \gg \mu_1$.




(a) M




(b) C




(c) F

Figure 1: Results