LD with Mutator state Switching

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We have 2 distinct states (mutator and non mutator) where rates of switching are r_{ij} and growth rate is identical λ. Say state 2 is the mutator state.

Equilibrium fraction of state 2:

$$\hat{f}_2 = \frac{r_{12}}{r_{12} + r_{21}}; \hat{f}_1 = 1 - \hat{f}_2$$

The absolute number of bacteria:

$$N(t) = N_1(t) + N_2(t) = N_0 e^{\lambda t}$$

Where λ is growth rate, assumed to be identical for both states.

Assume we sample N individuals, and make each the origin of a distinct colony. The time dependent fraction of state 2 in a colony is:

$$f_i(t) = \frac{N_i(t)}{N(t)}$$

The rate equation for it:

$$\frac{df_2(t)}{dt} = r_{12}(1 - f_2(t)) - r_{21} f_2(t)$$

Solutions depend on the IC of state of originator:

$$f_2(t) = \begin{cases} \hat{f}_2 + (1 - \hat{f}_2)e^{-(r_{12}+r_{21})t} & p = \hat{f}_2 \\ \hat{f}_2(1 - e^{-(r_{12}+r_{21})t}) & p = 1 - \hat{f}_2 \end{cases}$$

$$\langle f_2(t) \rangle = \hat{f}_2 \left(\hat{f}_2 + (1 - \hat{f}_2)e^{-(r_{12}+r_{21})t} \right) + \left(1 - \hat{f}_2 \right) \hat{f}_2(1 - e^{-(r_{12}+r_{21})t}) = \hat{f}_2$$

As can be expected. As in LD, average number of mutants at time t:

$$\frac{d \langle m(t) \rangle}{dt} = \mu N_2(t) + \lambda \langle m(t) \rangle = \mu f_2(t)e^{\lambda t} + \lambda \langle m(t) \rangle$$

We can see that this solution gives the above equation:

$$\langle m(t) \rangle = \mu e^{\lambda t} \int f_2(t) dt$$

The full solution:

$$\langle m(t) \rangle = \mu e^{\lambda t} \times \begin{cases} \hat{f}_2 t + \frac{1-\hat{f}_2}{r_{12}+r_{21}}\left(1 - e^{-(r_{12}+r_{21})t}\right) & p = \hat{f}_2 \\ \hat{f}_2\left(t - \frac{1}{r_{12}+r_{21}}\left(1 - e^{-(r_{12}+r_{21})t}\right)\right) & p = 1 - \hat{f}_2 \end{cases}$$

Now average again on IC to get the true average across colonies:

$$\langle m(t) \rangle = \mu e^{\lambda t} \times \left(\hat{f}_2^{\,2} t + \hat{f}_2 \frac{1 - \hat{f}_2}{r_{12} + r_{21}}\left(1 - e^{-(r_{12}+r_{21})t}\right) + \hat{f}_2(1 - \hat{f}_2)\left(t - \frac{1}{r_{12} + r_{21}}\left(1 - e^{-(r_{12}+r_{21})t}\right)\right) \right)$$

$$= \mu \hat{f}_2 t e^{\lambda t}$$

Now lets say we run an experiment to time t_f. The expected number of survivors at time t_f originating from mutations that happened at time t is instantaneous mutants at time t minus the growth from mutants that already exist:

$$\langle S(t) \rangle = \left(\frac{d\langle m(t) \rangle}{dt} - \lambda \langle m(t) \rangle \right) e^{\lambda(t_f - t)} = \mu f_2(t) e^{\lambda t_f}$$

So it seems the addition to the mean relative to the standard LD process is a trivial factor of $\hat{f}_2$, and the average number of survivors originating from time t does not depend on t, exactly as in the original setting.

Now we calculate the variance of the number of mutations.