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 mutation events m:

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

Integrating:

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

And we can approximate:

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

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

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

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

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:

$$\langle S(t)\rangle = \langle m(t)\rangle\, e^{\lambda(t_f-t)} = \frac{\mu}{\lambda}\hat{f}_2 e^{\lambda t_f}$$

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.