Summary on 3 state simulations

“Method”

I originally computed the optimal parameters as in the two state case, that is by analytically computing the average time it would take to consume all the nutrients (T_S). However, to isolate T_S I had to make an assumption that I did not trust on close inspection. Now I have redone the calculations, and computed the optimal parameters without the previous assumption, but instead by numerically determining T_S. For a given set of antibiotic parameters (p, T_0, T_{ab}) I determine T_S for every set of bacterial parameters (λ_d, λ_r, δ). The optimal combination of (λ_d, λ_r, δ) is the one that minimizes T_S.

In addition to the theoretical optimal parameters, I have also computed the competition average parameters. This is done by evolving several species according to the differential equations and using a solver to find T_S for 20 000 consecutive cycles. The different species have parameters $\lambda_{d/r} \in [0.01, T]$ with $d\lambda = 1$ and $\delta \in [0, 0.05]$ with $d\delta = 0.001$.

The mutation simulations are done like the competition simulations, but with a mutation rate between the different species. Every simulation is started from a single species with a specific set of bacterial parameters (min and max?)

- What about mutation from λ_d=0? Create exception?
- Extinction?

Coupled nutrients and antibiotics, $T_0 = 0$

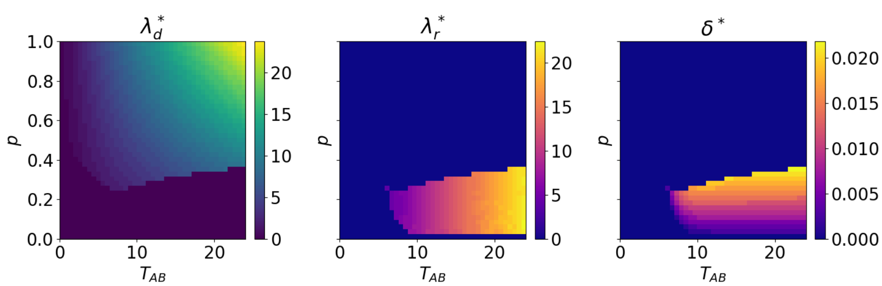


Figure 1: Optimal parameters for $T_0 = 0$

I still get same result as before: optimal strategy is either only triggered persistence, or only spontaneous persistence (see Fig. 1). The result is confirmed by a competition simulation in Fig. 2, where the dashed lines represent the theoretical optimals from Fig. 1. For $p > 0.1$ the optimal is to have only triggered persistence, whereas for $p = 0.1$ spontaneous persistence is the optimal. $p = 0.3$ is very close to the phase transition, and is therefore fluctuating slightly between the two optimals.

For λ_d the competition average is not perfectly consistent with the theoretical optimal, which I think is because the resolution of the parameters in Fig. 1 is much higher (The competition average is much more computationally heavy to compute). The behaviour of δ for $p = 0.3$ is a bit weird. What I think happens is that when this weakly bistable system jumps from a low risk state (only spontaneous persistence) to a high risk state (only triggered persistence), it also benefits from the marginal additional protection from having $\delta = \delta_{max} = 0.05$. With time δ decreases toward 0, but since $\lambda_r = 0.01$ the penalty for having non-zero δ is very small, hence the decrease is very slow. The parameter combination of $\lambda_r \approx 0$ and $\delta > 0$ is probably not very realistic. Having very small fraction of spontaneous persistence affects the growth very little, however after very many cycles the loss is significant.

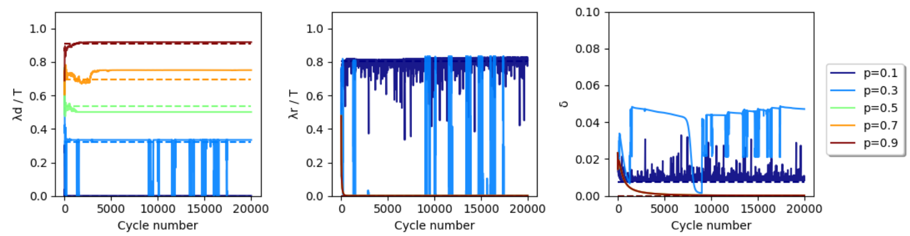
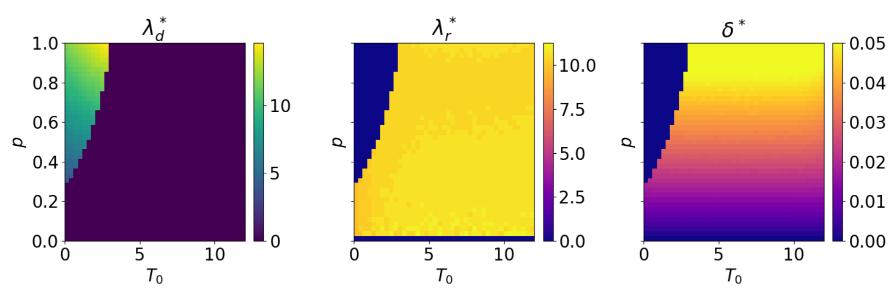


Figure 2: Interspecies competition at $T_0 = 0$, $T_{ab} = 12$

10 example feast-famine cycles

Figure 3: 10 example feast-famine cycles

Decoupled nutrients and antibiotics, $T_0 > 0$



Also when the antibiotics are decoupled from the addition of nutrients the two strategies are separated.

Mutation

Redo competition simulations with mutation.

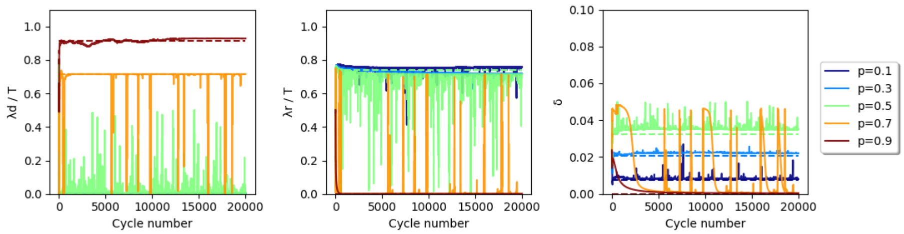


Figure 4: Interspecies competition at $T_0 = 2$, $T_{ab} = 12$

10 example feast-famine cycles

Figure 5: 10 example feast-famine cycles

To do

3) Modify to add mutation
4) Run mutation

weird delta values for p=0.3, because it doesn't matter what delta is as long as lambda=0? But why suddenly more fluctuations than earlier??