ODE evolution

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An: Stella Maria Sophie Knief <s.knief@uq.net.au>
Cc: Jan Engelstaedter <j.engelstaedter@uq.edu.au>

Hi Stella,

I kept thinking about your model yesterday, the bug, and what it really is telling us. I had a brief meeting with Jan, too going over some aspects of your current model.

Some thoughts for the next round:

1. Each generation an individual gets a genotype alphaA, betaA, K, alphaB, and betaB.
2. These genotypes lead to the ODE system to solve:
    a. dA/dt = alphaA – betaA x A.
    b. dB/dt = ThetaK x alphaB – betaB x B.
        i. Recall that K is the threshold that determines whether ThetaK takes the value of ZERO or if it takes the value of 1. Let's do this approach, which is very similar to a very steep Hill Function.
3. The solution gives you the curves for number of A and B molecules for each time point.
4. You then integrate the area under the curve for B.
5. You then compare the observed value of B (B_obs) against the optimum value of B (B_opt). This value will determine the fitness penalty or gain for everyone. You can use a simple normal distribution here, if you wish, and you can standardise it at any value, like 250, should you wish that. You can also test different fitness functions, should there be time.

Some important notes:

6. The mutational effects must be sampled from a distribution with range [0, large Number].
7. You can use a gamma distribution so you can get a "normal"-like distribution but that does not have negative values.
8. Once you get the value, say 1.1 for alphaA, you **multiply** those times the initial value for alphaA, which you had set at 10, for instance. You do the same for all other four parameters.
9. You can use Latin Hypercube Sampling to create the models.

So, all in all, the goal is to get simulated value of B for everyone every generation and apply a fitness function to all of them to decide the next generation. The simulated values of B arise from the mutational effects accrued in the five genes that control the parameters in the ODE system.

In slim, the genome has five boxes, yes? One for each of the five ODE parameters. So, out of all the possible genotypes that can be produced every generation, some of them will do better than others. Over time, I presume the system will stabilise around the optimum and therefore, you will see a consistent range of values for the different parameters of the ODE system. So, all in all, it is the ODE that evolves, and its evolution relies on how fitness is applied to the amount of B produced.

Once this works you can pursue different questions:

i) How fast do a Forward-Feedback loop stabilises over time?
ii) How variable is the range of ODE solutions once the system approaches equilibrium?
iii) What is the effect of selection strength on (i) and (ii)?
iv) What is the effect of different starting points for the parameters on (i-iii)?
v) What is the effect of recombination between the genetic elements in the ODE system? This will add more parameters to the models, but it seems quite interesting to looked at the effects of linked selection on the evolution of these ODE systems.
vi) Does K converge to a single value? Or are there multiple threshold solutions to approach the B_opt?
vii) What happens if you now do directional selection instead of stabilising selection? This will lead to asking the questions above, and then split the description into “approach to the optimum” versus “staying at the optimum.”

These are some initial questions that when answered will help you characterise the evolution of the FBF-loop.

Let me know if you have questions about this! And look forward to meeting with you on the week of July 12th. Please send an invitation to Jan and I with a clear agenda of what we will accomplish that day. Ideally, the above should be ready? Not the running of all models, but the infrastructure to run it. You can then send the runs middle of July.

Jan, any additional thoughts or clarifications?

Have a great two weeks!
Daniel
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