Bio-PEPA Tutorial: Part I

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Main exercise: model construction

The first part of this tutorial focuses on familiarising oneself with the Bio-PEPA language and supporting software tools. You should have a small printed out manual for the Bio-PEPA software, a more complete manual is available online at the following address: http://homepages.inf.ed.ac.uk/aclark6/biopepa-manual/

1 The MapK models

- MAPK BioModels 09
 - Does this model reach a steady-state and if so at what time? A. Yes, around time 120, 80 for most species other than MAPKK_PP.
 - Can you explain why this model takes so long to simulate? **A. The population numbers are very high.**
 - Does this model conserve mass? A. Yes
- MAPK BioModels 10
 - Does this model conserve mass? A. Yes
 - Perform a Gillespie simulation of the model up to time 10000. Does this model oscillate? A.
 Yes it does oscillate, but you need to do up to about time 10000 to see this.
 - What about multiple independent Gillespie simulation runs A. The oscillations seem to dampen.
 - Now try with ODEs
 - Is there any difference between a stochastic simulation of this model and an ODE analysis?
 A. Well, yes and no, the oscillations dampen when we do ultiple replications, this is due to non-synchronicity.
 - Does the oscillation continue indefinitely? A. see below
 - Is the answer to the above question the same whether we use stochastic simulation or ODE analysis? Does it matter how many replications we do for stochastic simulation. Can you explain these results? A. Continues indefinately with SSA 1 run, or ODEs but not SSA 1000 runs.
 - Is the system sensitive to initial populations? Try setting all the populations to the same value, this sometimes has the effect of breaking an oscillation since it exactly hits a steady-state which in reality won't be found. A. Yes and No, setting everything equal to 50 doesn't break it, setting everything to 10 does break the oscillations.

- Which reactions, when knocked out, do not completely break the oscillations? Hint, perform an experiment knocking out each reaction in turn. A. Alpha_{5,9}, so Alpha_{0,1,2,3,4,6,7,8} do not, although they do for some species.
- Describe the affect of increasing the value of parameter "k4" from its default of 0.025 to 0.5.
 We suggest that you incrementally increase this using a step-size of around 0.025. oscillations?
- Possibilities: difference between stochastic simulation, stochastic simulation with many replications and finally ODE analysis.

2 Neurospora

- Note: this model's time points are in days, so you most likely wish to stop your timeseries analysis around time point 100.
- The given model has light turned off, change this so that we have a 12 hour cycle, for example dawn at 6am and dusk at 6am.
- Can you display the light function? Try displaying the time-since-start-of-day (hint: multiply it by a factor in order to see it clearly on the same scale as the species' populations).
- Can we break the oscillations? On which parameter do the oscillations most depend? (We may have to give some choices for this, rather than any of the parameters in the model since there are 37).
- What happens when we alter the light-dark cycle in the following ways:
 - Always light generally known as light-light **A. Breaks the oscillations**
 - Always dark, generally known as dark-dark **A. The is the default and the oscillations are fine.**
 - Very short light A. Oscillations essentially unaffected.
 - Very short dark A. This breaks the oscillation, no idea how long the dark must be in order to not break the oscillations.
- Does this model conserve mass? Some reactions create/destroy mass deliberately because the scope of the model is finite (we can't model everything). But is the model otherwise self-consistent? (Hint: try ignoring those reactions which create/destroy mass. Further Hint: the outline view will tell you those reactions.) A. No, but yes if you ignore all the source and sink reactions which are everything but the 'transformation' reactions.

3 Extra exercises

- 1. Other than the fact that Model 09 does not oscillate, what is the major difference between Model 09 and Model 10?
- 2. Can you modify Model 09 to oscillate using a similar mechanism to that of Model 10?
- Can you make a skeleton light function? That is two periods of light per day? There are two ways this can be done, but suppose we wish for the two periods of light to be of different lengths.
 A. The cheaty way is simply to halve the period. The other way is simply more H function conditions.
- 4. Explore any of these models using the Traviando trace analyser which can be downloaded from: www.dcs.ed.ac.uk/pepa/group/TraviandoReleaseMarch2011.tar.gz

5. Explore any of these models using the PRISM model checker.