Assignment 4

The **due date** for this quiz is **Fri 23 May 2014 8:59 PM PDT**.

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Question 1

Download the following Matlab files:

novak.m : Master program for solving Novak-Tyson model

dydt_novak.m : Function that computes derivatives of Novak-Tyson state variables

novak_cyclin.m : Program to test different levels of cyclin

As noted in the lectures, one of the important results of the Novak-Tyson model was that unreplicated DNA slowed the oscillations of MPF and cyclin. This had been seen experimentally, and the model predicted that the presence of unreplicated DNA changed the location of the bifurcation due to the positive feedback loop. This prediction was later confirmed.

In terms of biochemistry, unreplicated DNA has been shown to make Wee1 more active, and make Cdc25 less active, for a given value of MPF. In the Novak-Tyson simulations, this was achieved by introducing a new variable corresponding to the concentration of unreplicated DNA, and making the rate constants kb and kf depend on this concentration. Do this in your model to reproduce the oscillations with unreplicated DNA shown in the lecture notes. You do not have to exactly match what is shown in the lecture notes, but the oscillations in the presence of unreplicated DNA should be noticeably larger and slower.

Hint 1: You can choose whatever form you like for how kb and kf depend on DNA concentration, but your equations should be such that when DNA = 0, kb and kf are equal to their control values.

Which of the following statements is correct?

○ k kb and Kf gets smaller in presence of unreplicated DNA.

○ Both kb and kf gets bigger in presence of unreplicated DNA.

○ kb gets bigger and kf gets smaller in the presence of unreplicated DNA.

○ kb gets smaller and kf gets bigger in the presence of unreplicated DNA

Question 2

Okadiac acid is an inhibitor of type 1 and type 2A phosphatases such as phosphatases which dephosphorylate Wee1 and Cdc25. What is the effect of okadiac acid on the oscillatory behavior of this system? (Assume that the concentration of the these phosphatases are fixed and just their activity is inhibited)

○ It will suppress the oscillations in Active MPF and Total Cyclin concentrations.

○ It will increase the frequency and amplitude of oscillations of Active MPF and Total Cyclin concentrations.

○ It will increase the frequency and decrease the amplitude of oscillations of Active MPF and Total Cyclin concentrations.

○ It will decrease the frequency and amplitude of oscillations of Active MPF and Total Cyclin concentrations.

Question 3

Lack of which of the following components can suppress the oscillations in concentrations of active MPF and total Cyclin ? (Use the default parameters in the code)

○ Total Cdc25.

○ Total anaphase-promoting complex.

○ Total Wee1.

○ Total intermediate enzyme.

Question 4

For this question, you will reproduce part of the bifurcation plot of $[\text{cyclin}]_{\text{TOTAL}}$ versus [MPF] that was shown in the notes. The file novak_cyclin.m runs simulations over a range of different initial cyclin levels. For each simulation, the program keeps and stores the final value of MPF concentration in the variable MPF_end. When all the simulations are finished, the script generates a plot of initial [cyclin] versus final [MPF]. However, these results are nonsense. This is because the program computes cyclin synthesis and degradation whereas the bifurcation diagram was generated at fixed cyclin concentrations, e.g. both synthesis and degradation were inhibited.

Alter the program so that cyclin synthesis and degradation are inhibited. This will require altering some of the global parameters defined at the top of the script.

Which of the following parameters are needed to be changed to inhibit synthesis and degradation of cyclin?

○ k1 and k3

○ v2_1, v2_2, k1

○ k1, k3, v2_1, v2_2

○ k1

Question 5

With which of the following concentration of total Cdc25, the concentration of total cyclin needs to activate MPF is lower?

○ Total Cdc25=5

○ Total Cdc25=2

○ Total Cdc25=8

○ Total Cdc25=15

Question 6

What will be the effect of presence of unreplicated DNA on this bifucation diagram? (Use the default parameters in the code and then add unreplicated DNA)

○ Higher concentration of total cyclin is needed to turn the switch of the MPF activation on.

○ Lower concentration of total cyclin is needed to turn the switch of the MPF activation on.

○ Unreplicated DNA will cause the system to have more than two stable steady states.

○ There will be no change in the bifurcation diagram.

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