BT4110: Computational Biology Laboratory

Assignment on Dynamic modeling

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Prerequisite: Download MATLAB and COPASI (https://copasi.org/Download/)

PART A - Solving differential equations

1. Integrate the given differential equation from 0.01s to 1s with a time interval of 0.01s with the following methods:
    a) Simple Euler method
    b) Runge - Kutta method (fourth order method)
    y(1) = 0.1 and dy/dt = (y+1)

a) Plot the solution over time for these two methods in a single plot.
b) Experiment with five different ranges of time intervals and comment on your observations. What happens in each of the solving methods as the interval is increased?

PART - B Dynamic modeling of TCA cycle

2. Download the dynamic model (both .m and .xml format) of TCA cycle in *M. tuberculosis* from this site: (https://www.ebi.ac.uk/biomodels/BIOMD0000000219#Files)

The central idea: Persistent tuberculosis bacteria survive on fatty acids, through the glyoxylate bypass. The flux through the bypass is aided by isoform enzymes (Isocitrate lyase) (ICL - 1) and (ICL - 2), and the objective in this paper is to reduce the flow through this pathway, and for the bacteria depend only on the main TCA cycle. This is involved with (Isocitrate dehydrogenase) (ICD -1) and (ICD-2), and these enzymes are deactivated by ICD kinase (so that the glyoxylate bypass is activated). The reduction in the deactivation of ICDS will serve as a possible strategy for targeting drug resistant *M. tuberculosis*.

a) Can you use the equations given in the pdf (given on the website, same link), but use a simple euler method to integrate the same? Observe what happens if you use the code as compared to the euler method.
b) Based on the above results, can you differentiate between a stiff system and a non - stiff system?
c) Run the code in MATLAB as well as COPASI (.xml) , are there any differences between the results?
d) Can you come up with an interesting experiment to determine the effect of corresponding enzymes on the pathway, and how to possibly prevent bacteria from taking up the path of resistivity?