Introduction to Focus Areas in Bioinformatics WS21/ 22

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Project 8
Modeling and Simulation of Complex Biological Systems

- Deadlines: For the **REPORT** 18.12.2021 6pm, for the **REVIEWS** 04.01.2022 6pm.
- All files need to be available through your GIT repository, in the directory 'Project 8'
- The reports need to be uploaded to the EduFlow system before the deadline.

Model: The 'Repressilator' Model
A synthetic oscillatory network of transcriptional regulators, MB Elowitz, S Leibler , Nature, 335–338, (2000).

Modeling and simulation software: COPASI

Tasks
- Read the paper by Elowitz and Leibler Nature 2000 [available on the Whiteboard site].
- Understand the mathematical model of the 'repressilator' (what are the variables, what are the parameters of the system).
- Download COPASI from http://copasi.org
- Go to https://www.youtube.com/user/CopasiTutorials/videos for an introduction and watch the following three short videos: Introduction to COPASI, Basic Plotting with COPASI, COPASI Time Course Simulation (among the last four videos of that page).
- Have a look at the User Manual: http://copasi.org/Support/User_Manual/
- Load the repressilator model, which is available in on the whiteboard site as an SBML file and can be imported (-> File/ Import SMBL: week8-project_BIOMD0000000012_url).
- Simulate the model (with the deterministic method LSODA, that is the standard setting) and plot the time courses of the variables (for a sufficient time and with a small interval size that give a smooth output).
- Plot the concentrations of LacI protein and TetR protein in a Phase Plane plot. (One can see the limit cycle best by suppressing an initial time span).
- Perform simulations from different initial conditions and see how this effects the time course.
- Investigate how changes in parameters, especially those affecting the protein half lifes, affect the time course of the variables.
- Investigate whether you can change the kinetic parameters to find stable steady states.
- Simulate the model with a stochastic method (method: stochastic: Gibson + Bruck) and observe the differences to the deterministic solution.

Deliverables

Write a report:

- The report should be about 1000-1500 words in length.
- The report must be delivered in PDF format using the usual template.

- The following sections must be present (you can add more if needed):
  - Abstract
  - Introduction
    - Biological background
    - Description of the mathematical model (including a brief discussion, why this is a complex model)
  - Results: a short description of your simulations including the main produced figures. Show the impact of the protein half lifes on the model dynamics.
  - Discussion:
    - Discuss your simulation results in terms of biology.
    - Highlight differences between the Boolean modelling used last week and the ODE modelling approach.
  - Appendix: Who did what.