Introduction to Focus Areas in Bioinformatics – WS21/22
Lecturer: Heike Siebert

Project 7

- Deadlines: For the REPORT: 11.12.2021, 18:00; For the REVIEWS: 14.12.2021, 18:00
- All files need to be available through your GIT repository, in the directory "Project 7".
- The report needs to be uploaded to the EduFlow system before the deadline.

We will use the software GINsim (https://ginsim.org/) and WebMaBoSS (https://webmaboss.vincent-noel.fr/) to model and simulate complex biological systems.

The model

In this project we want to investigate a model of a molecular network underlying tumor cell invasion and migration. The model is described and analyzed in the paper „Mathematical Modeling of Molecular Pathways Enabling Tumour Cell Invasion and Migration" by D. Cohen at al. and can be found here: https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1004571

The task

Using the computational tools linked to above you are supposed to reproduce the results of the mentioned paper and garner some insights in typical questions, analysis steps and capabilities of logical modeling.

- Read the paper. Focus in particular on: modeling assumptions, model building, read-outs and validation; stable state analysis; matching data and model outputs; robustness analysis; model reduction
- Load the model found here http://ginsim.org/node/191 and reproduce the nine stable states of the wild type model and the stable states of the PTEN LoF as described in the paper. Do another stable state analysis for a genetic perturbation with one LoF and one GoF of your choice and determine its phenotypes.
- Load the model in WebMaBoSS. It can be imported from CellCollective (Tumour Cell Invasion and Migration from Cohen DP et al.). Reproduce the results for the probabilities for reaching each phenotype for the wild type and the mutants p53 LoF, NICD GoF and NICD GoF / p53 LoF. Pick another double mutant not discussed in the paper, run the simulation and compare the probabilities to the wild type. Repeat the simulation for the wild type several times for different choices for Max time and Sample count for values between 10 and 1000 (for Max time) and 100 and 10000 (for sample count) and compare the results.
- Watch the video of Laurence Calzone's talk available in the resources in the Whiteboard (Week7_Talk_Calzone.mp4). Extract the framework and software extensions suggested in the talk and discuss their advantages and drawbacks.

Deliverables

You need to upload all source codes and a report to your GIT repository **and to the EduFlow system**.

- The report should be about 1000-1500 words in length, include the main points of the paper and a full description of your own additional analysis and results

- 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
    - Scientific background
    - Model building and tools
    - Validation and analysis
        - stable states and phenotypes
        - robustness
        - mutants
    - Conclusion: What insights can be gained from the analysis?
    - Discussion I : discuss the possible extensions of the framework presented in the talk by L. Calzone in the context of the study presented in the paper
    - Discussion II: discuss why (or why not) the use of a mathematical model is fruitful here
    - Appendix: Who did what