

- **Project 9**

- Deadlines: For the **REPORT**: 8.01.2022, 18:00; For the **REVIEWS**: 11.01.2022, 18:00
- All files need to be available through your GIT repository, in the directory "Project 9".
- **The report needs to be uploaded to the EduFlow system before the deadline.**

Modeling and Simulation of complex biological systems – using FBA

We will use the COBRApy framework to create a model that represents the lycopene-producing strains of E. coli described in the Nature Biotechnology paper by Alper et al.

- **Recommended Reading**

HINT: Reading and understanding these papers takes a considerable amount of time. Try to work in a team and help each other with understanding them! On the other hand: not everything is really important – try to get a good overview and see what you really need for the project before you try to understand all the details.

- „Construction of lycopene-overproducing E. coli strains by combining systematic and combinatorial gene knockout targets.” by Alper H. et al. (2005) Nat Biotechnol.; 23(5):612-6.
- „Identifying gene targets for the metabolic engineering of lycopene biosynthesis in Escherichia coli.” by Alper H. et al. (2005) Metab Eng.; 7(3):155-64.
- More information about the used E. Coli model can be found here: „A comprehensive genome-scale reconstruction of Escherichia coli metabolism” (2011) by Orth JD; Mol Syst Biol.;7:535. (In particular in the Excel file from the supplementary files: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3261703> HYPERLINK "https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3261703/")

- **Model Building and Analysis**

Build the needed model(s) and use it to answer the following questions:

- What is the theoretical maximum yield of lycopene (mol lycopene/mol glucose)?
- How much lycopene is produced by the wild type strain that has been extended with the lycopene pathway?
- How much lycopene is produced in mutant strains with gene knockouts? (Knockouts are defined in the paper.)
- How much lycopene is produced in mutant strains with genes overexpressed?

(Genes to be overexpressed are defined in the paper.)

- How much lycopene is produced in mutant strains with overexpression and knockouts?

- **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 600-1200 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
 - Background and Modeling
 - Should contain a brief description about the scientific background, the used modeling approach and the model that has been implemented or used / modified.
 - Results
 - Each question should be answered in its respective sub-section.
 - Each sub-section should contain a brief description of the goal, what has been done to reach that goal and what the actual result is.