Plan of attack

Project D: Understanding metabolic network models

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Step 1 (Easy Goal)

1. Understand the basic concept of metabolic network

   (a) Read through modules 1 & 4 to obtain basic knowledge of

      i. Biological Networks
         - Application of different models
         - Network interactions
         - different constraints in biology
      ii. Process of Metabolic Reconstruction
         - Mathematical Representation of a Biochemical Network
         - Obtaining the Stoichiometric Matrix
         - S links metabolites and reactions
         - Dynamic Mass Balance

2. Environment setup for COBRA toolbox

3. Understand the basic functionality of COBRA

   - Read COBRA documentation on data analysis:
     https://opencobra.github.io/cobratoolbox/stable/modules/analysis.html
   - Read the paper:
     Quantitative prediction of cellular metabolism with constraint-based models: the COBRA Toolbox [1]
   - Read paper:
     The effects of alternate optimal solutions in constraint-based genome-scale metabolic models [2]

4. Follow lab 4 exercises to obtain basic knowledge of

   - Basic model (stochiometric matrix) analysis for question 1
   - **Flux Balance Analysis** for question 2,3
   - **Flux Variability Analysis** for question 4
   - Genome wide single deletion analysis using the FBA for question 5

Step 2 (Hard Goal)

1. Environment setup for MONGOOSE

   - Need to be discussed with Dr. Chindelevitch

   > You can use the GUI: github.com/WGS-TB/MongooseGUI3, and the instructions for using it at www.overleaf.com/read/cmyvwrrmykkx

2. Understand how MONGOOSE works

   - Refer to web-page: http://cb.csail.mit.edu/cb/mongoose/
   - Read Paper:An exact arithmetic toolbox for a consistent and reproducible structural analysis of metabolic network models [3] https://www.nature.com/articles/ncomms5893
   - Any further documentation if its available

3. Use the same data set on MONGOOSE and get the output

4. Analyze in general the difference between MONGOOSE and COBRA

5. Apply the analysis in 4 to tell why the results are different and which tool gives better solution in terms of accuracy/comprehensiveness/efficiency.

   Obtain a basic knowledge about

   > Accuracy is going to be difficult to evaluate without gold standard data, so you might consider doing this on yeast.

   - Analysis using floating-point arithmetic in COBRA toolbox
   - Analysis using exact arithmetic in MONGOOSE toolbox

Step 3 (Stretch Goal)

- Collect datasets in http://sbrg.ucsd.edu/InSilicoOrganisms/OtherOrganisms
- Repeat step 1 & 2 for each dataset above

Tentative Schedule

1. Easy Goal: Nov 12th - Nov 16th
2. Hard Goal: Nov 16th - Nov 23rd
3. Stretch Goal: Nov 23rd - Dec 4th

References

[1] Becker, S. A., A. M. Feist, M. L. Mo, G. Hannum, B. O. Palsson, and M. J. Herrgard. 2007. Quantitative prediction of cellular metabolism with constraint-based models: the COBRA Toolbox. Nature Protocols 2:727-738.

[2] Mahadevan, R. and C. H. Schilling. 2003. The effects of alternate optimal solutions in constraint-based genome-scale metabolic models. Metab Eng 5:264-276.

[3] Leonid Chindelevitch, Jason Trigg, Aviv Regev Bonnie Berger, 2014, An exact arithmetic toolbox for a consistent and reproducible structural analysis of metabolic network models, Nature Communications 5: 4893.