Exercise for Constraint-based Modeling of Cellular Networks
8 December 2022

Homework should be sent to Anika (ankueken@uni-potsdam.de)

Hand in your commented code / answers for all exercise tasks as homework.

Exercise

Step by step to implement ROOM

1. Solve the LP

$$\max_{w} w_{bio}$$
$$s.t.$$
$$Nw = 0$$
$$lb \leq w \leq ub$$

2. Use the equations below to determine the significance thresholds for the flux changes (w^u and w^l). Set $\delta = 0.05$ and $\varepsilon = 0.001$
for $1 \leq i \leq r$

$$w_i^u = w_i + \delta|w_i| + \varepsilon$$
$$w_i^l = w_i - \delta|w_i| - \varepsilon$$

3. Form all following inequality constraints in a matrix form for the optimization problem. Here the variables for the optimization problem are the vectors of v and y.
for $1 \leq i \leq r$ (*r* is the number of reactions in the model)

$$v_i - y_i(v_{max,i} - w_i^u) \leq w_i^u$$
$$v_i - y_i(v_{min,i} - w_i^l) \geq w_i^l$$

4. In the *E. coli* core model, we aim to knock out the reaction NAD transhydrogenase. Use the information from the GPR-rules to find the genes that knocked out lead to blocking flux through this reaction.

5. Form the MILP based on the following constraints and the objective function. Remember that y is a Boolean vector that can be presented by an integer vector in which $y_i \in \{0,1\}$.

$$\min_{y,v} \sum_{i=1}^{r} y_i$$
$$\text{s.t}$$
$$Nv = 0,\ v_{min} \leq v \leq v_{max}$$
$$v_j = 0, for\ \forall j\ blocked\ by\ gene\ knock-out$$
$$\text{for } 1 \leq i \leq n$$
$$v_i - y_i(v_{max,i} - w_i^u) \leq w_i^u$$
$$v_i - y_i(v_{min,i} - w_i^l) \geq w_i^l$$
$$y_i \in \{0,1\}$$

6. Find the Euclidean distance between *v* and *w*.

MOMA

Suppose we obtained wild type flux distribution w from solving the LP

$$\max_{w} w_{bio}$$
$$s.t.$$
$$Nw = 0$$
$$lb \leq w \leq ub$$

In MATLAB you can solve quadratic problems (QP) using function X = quadprog(H,f,A,b,Aeq,beq,LB,UB) solving QP of the form

$$min\ 0.5 * x' * H * x\ +\ f' * x$$
$$subject\ to\text{:}\ A * x\ <=\ b$$
$$Aeq * x\ <=\ beq$$
$$LB\ <=\ x\ <=\ UB$$

Write down the QP that minimize the Euclidean distance between the flux distribution in the wild-type and the NAD transhydrogenase knockout mutant. (no implementation needed! Write it the way the problem of ROOM is written above)

Explain what would be the variables entering vector x, how would H look like, what are the boundaries on the variables?