Constraint-based Modeling of Cellular Networks

Exercise 13 – EFM

26. 1. 2023

Identifying EFMs

- Find the maximal number of reactions that can have a 0 flux while the remaining active reactions still satisfy the steady state constrain

Identifying EFMs

Find the maximal number of reactions that can have a 0 flux while the remaining active reactions still satisfy the steady state constrain

Step 1: Split reversible reactions into two irreversible

Step 2: Introduce binary variable y_i for each reaction in the network such that

If $y_i = 0 \Leftrightarrow v_i = 0$

If $y_i = 1 \Leftrightarrow \varepsilon \leq v_i \leq v_i^{max}$

Next: Write the appropriate objective function

The LP

$$\min \sum y_i$$

$s.t.$

$$Nv = 0$$
$$v_i \leq y_i v_i^{max}$$
$$y_i \varepsilon \leq v_i$$
$$y_i \in \{0,1\}$$

Next: Add a constraint that exclude trivial solution

(no reaction carrying flux)

The LP

$$\min \sum y_i$$

$s.t.$

$$Nv = 0$$

$$v_i \leq y_i v_i^{max}$$

$$y_i \varepsilon \leq v_i$$

$$y_i \in \{0,1\}$$

$$\sum y \leq 1$$

Next: Enforce directionality of reverse reactions

The LP

$$\min \sum y_i$$

$s.t.$

$$Nv = 0$$
$$v_i \leq y_i v_i^{max}$$
$$y_i \varepsilon \leq v_i$$
$$y_i \in \{0,1\}$$
$$\sum y \leq 1$$

For paired reactions R_j

$$y_{jFw} + y_{jBw} \leq 1$$

Alternative Solution – integer cut

$$\begin{bmatrix} v \\ y^d \\ y^u \end{bmatrix}$$

$$\begin{bmatrix} 1 \\ 0 \\ \vdots \\ 1 \end{bmatrix}_{r\times 1}$$

$$\begin{bmatrix} 1 \\ 1 \\ \vdots \\ 0 \end{bmatrix}_{r\times 1}$$

(1) Find zeros from these two vectors (e.g. using `find(...)`)

For instance: $y_2^d = y_{12}^d = y_{25}^d = y_{51}^d = y_3^u = y_{10}^u = y_r^u = 0$

Take into account that there is integer tolerance `options.IntegerTolerance`

(2) Add an additional constraint:

$$y_2^d + y_{12}^d + y_{25}^d + y_{51}^d + y_3^u + y_{10}^u + y_r^u \geq 1$$

(at least one of them must be equal to one)

How to modify if $y_i = 1$ means that a reaction is in the previous solution?