FBA

$$\frac{d\boldsymbol{c}}{dt} = \mathbf{0} \Rightarrow \mathbf{S} \cdot \boldsymbol{v} = \mathbf{0}. \tag{1}$$

$$\boldsymbol{\ell} \leq \boldsymbol{v} \leq \boldsymbol{u}. \tag{2}$$

$$\tilde{\mathbf{C}} \cdot \boldsymbol{v} \leq \tilde{\boldsymbol{b}}. \tag{3}$$

$$\mathbf{C}\boldsymbol{v} = \begin{pmatrix} \tilde{\mathbf{C}} \\ \mathbf{I_n} \\ -\mathbf{I_n} \end{pmatrix} \boldsymbol{v} \leq \begin{pmatrix} \tilde{\boldsymbol{b}} \\ \boldsymbol{u} \\ -\boldsymbol{\ell} \end{pmatrix} = \boldsymbol{b}, \tag{4}$$

$$Z(\boldsymbol{v}) = \boldsymbol{f}^T \boldsymbol{v}. \tag{5}$$

Summarizing, the following FBA problem is solved using LP:

$$\begin{array}{rl} \max_{\boldsymbol{v}} & \boldsymbol{f}^T \boldsymbol{v} \\ \text{s.t.} & \mathbf{S}\boldsymbol{v} = \mathbf{0} \\ & \mathbf{C}\boldsymbol{v} \leq \boldsymbol{b}. \end{array} \tag{6}$$

Example Network

The stoichiometric matrix of the toy network is given as:

$$\mathbf{S} = \begin{array}{c} \\ A \\ B \\ C \\ D \end{array} \begin{array}{c} \begin{array}{cccccc} v_1 & v_2 & v_3 & v_4 & v_5 & v_6 \end{array} \\ \begin{pmatrix} 1 & 1 & -2 & 0 & 1 & 0 \\ 1 & -1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & -2 & 0 & -1.77 \\ 0 & -1 & 0 & 1 & -1 & 1.38 \end{pmatrix} \end{array} \tag{7}$$

The example network has two degrees of freedom. Hence the choice of two free fluxes (e.g. v_1 and v_6) defines all other fluxes and the following equation holds:

$v_2 = 2 \cdot v_1 + (1.38 - 1.77) \cdot v_6$

$v_3 = (2 \cdot 1.38 - 1.77) \cdot v_6 + 2 \cdot v_1$

$v_4 = v_1 + (1.38 - 1.77) \cdot v_6$

$v_5 = 1.38 \cdot v_6 - v_1$

The reaction rates of the example network (Figure ??) are bounded as follows:

$$\begin{gathered} 0 \leq v_1, v_5 \leq 10 \\ -10 \leq v_2, v_3, v_4 \leq 10 \\ 0 \leq v_6 \leq 20 \end{gathered} \tag{8}$$

The feasible flux space is visualized in Figure ??.

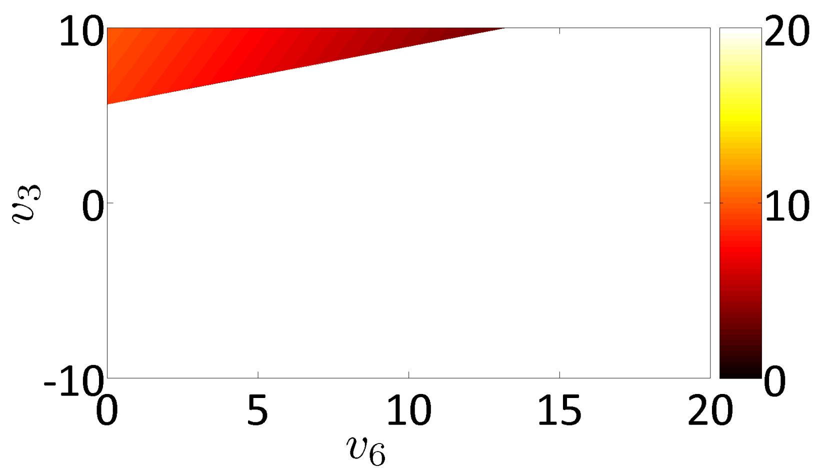

Figure 1: Intersection of a hyperplane with the flux solution space (the uptake is fixed: $v_1 = 8.4$). On the axes the flux range for v_6 (x-axis) and v_3 (y-axis) are shown. Due to the interdependencies between the fluxes the flux polytope is restricted. Thus, the remaining feasible solution space is represented by the colored area. When optimizing reaction v_6 (x-axis), the optimal value can be read off.

For the example network the criterion of optimality might be the maximization of the flux through reaction v_6. Metabolite D represents an artificial biomass metabolite.

The FBA problem is then given by:

$$
\begin{array}{rll}
\max_{\boldsymbol{v}} & Z(\boldsymbol{v}) & = \boldsymbol{v}_6 \\
\text{s.t.} & \mathbf{S}\boldsymbol{v} & = \mathbf{0} \\
& v_{1,5} & \in [0, 10] \\
& v_{2,3,4} & \in [-10, 10] \\
& v_6 & \in [0, 20]
\end{array}
\tag{9}
$$

Solving the LP problem yields a maximal flux of $\frac{40}{3}$ through reaction v_6. The optimal flux solution (given in arbitrary units) is:

$$
\boldsymbol{v} = \frac{1}{15}(126, 24, 150, -102, 150, 200)^T \tag{10}
$$

Comparing the optimal flux distribution with the flux bounds reveals that a further increase of the objective is hampered by v_3 or v_5, because both reactions have the maximal allowed flux.