Resolution of FBA

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1 Mathematical interpretation of FBA problems

We consider the following mathematical problem:

$$\begin{cases} \max c^T \nu \\ S\nu = b \\ \nu_i \geq 0 \text{ for some arbitrary } i \end{cases}$$

Biologically speaking, ν is the flux vector through metabolic reactions, b the exchange flux vector of metabolites with environment and other cell compartments. S is the stoichiometry matrix of the metabolism. The fact that a $\nu_i \geq 0$ indicates that this specific reaction is irreversible.

Structure of S Let C_1, C_2, ..., C_R be the columns of S. Each column represents a metabolic reaction. Let L_1, L_2, ..., L_M be the lines of S. Each line holds the fluxes of a specific metabolites through each reaction. Note that R is the number of reactions and M the number of metabolites. Generally $R > M$. Here are simple mathematical facts:

- $\mathrm{Im}\,(S) = \mathrm{Vect}\,\{C_1, ..., C_R\}$. There is a solution if and only if $b \in \mathrm{Im}\,(S)$.
- $L_i^T \perp \mathrm{Ker}\,(S)$.
- $\mathrm{Ker}\,(S)$ contains all futile cycles. However these cycles are not necessarily possible if they contain an irreversible reaction. Because $R > M$, the dimension of the kernel is pretty high.

Unicity Straightforward facts:

- If there are no irreversible reactions, the solution structure is $\nu_0 + \mathrm{Ker}\,(S)$, so $\max c^T \nu = \infty$.
- Unicity does not depend on b. The idea is that $\mathrm{Ker}\,(S) \cap \{\nu_i \geq 0\}$ must be bounded in the direction pointed by c.
- Intuitively, unicity is broken if c maximizes the flux of a futile cycle that is thermodynamically possible. By rewriting S and/or c, it should always be possible to warrant unicity.

Properties of a unique solution Let

$$m = \max_{\mathrm{Ker}(S) \cap \{\nu_i \geq 0\}} c^T \nu \geq 0$$

Suppose m is reached for some ν^*. Let $\lambda > 1$. $\lambda\nu^* \in \mathrm{Ker}\,(S)$ and $\lambda\nu^* \in \{\nu_i \geq 0\}$. By definition of m, $c^T(\lambda\nu^*) \leq m$. This leads to $\lambda m \leq m$, hence $m = 0$. This means that if there is a unique solution, it is orthogonal to $\mathrm{Ker}\,(S) \cap \{\nu_i \geq 0\}$. This is consistent with the view that c must points in a direction where $\mathrm{Ker}\,(S) \cap \{\nu_i \geq 0\}$ is bounded.

Duality Let us now emphasize the role of L_i in association with c. Each line of the matrix equation reads

$$L_i^T \nu = b_i$$

This corresponds to a hyperplane orthogonal to L_i. (Fig. 1) (left) shows an example in 2 dimensions with 2 lines L_1 and L_2. The maximal value in the direction of c is bounded if and only if c can be expressed as linear combination of L_1 and L_2. For example, if L_1 and L_2 are colinear, there is a maximal value iff c is colinear to the two vectors. If there is a third dimension, there is a maximal solution iff c is coplanar with L_1 and L_2. Put shortly, there is a solution iff

$$S^T \lambda = c$$

has a solution.

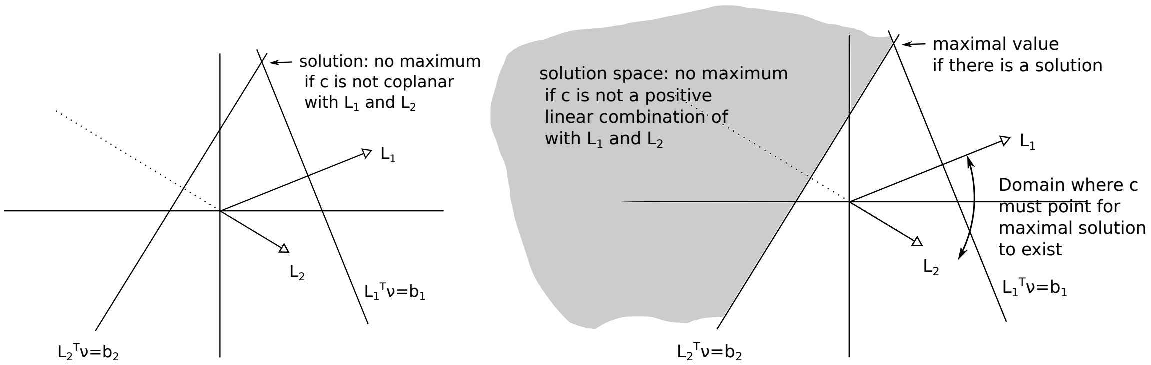

Figure 1: 2D illustration. (Left) Solution space of $S\nu = b$. (Right) Solution space of $S\nu \leq b$.

Inequalities instead of equalities I feel like the example above generalizes to inequalities except there is a solution iff there is a solution to

$$S^T \lambda = c, \quad \lambda \geq 0$$

Figure 1 (right) sums up this idea.