Consider outer descriptions of the flux cone $\mathcal{C}$.

Characterize $\mathcal{C}$ directly by its minimal proper faces and the lineality space.

The lineality space $\text{lin}_{sp}(\mathcal{C}) = \{ v \in \mathcal{C} \mid v_i = 0, \text{ for all } i \in \text{Irr} \}$ has a natural description by equality constraints $\sim$ reversible metabolic space.

Each minimal proper face can be characterized by a unique set of inequality constraints ($\neq$ irreversible reactions) $\sim$ minimal metabolic behaviors (MMBs).

The resulting outer description is both minimal and unique.

A metabolic behavior is a set of irreversible reactions $D \subseteq \text{Irr}, D \neq \emptyset$, such that there exists a flux vector $v \in \mathcal{C}$ with

$$D = \{ i \in \text{Irr} \mid v_i \neq 0 \}.$$

A metabolic behavior $D$ is minimal, if there is no metabolic behavior $D' \subsetneq D$ strictly contained in $D$.

If $v \in \mathcal{C}$ is an elementary flux mode, then the set

$$\text{supp}(v) = \{ i \in \{1, \ldots, n\} \mid v_i \neq 0 \}$$

is a minimal set of active reactions.

Similarly, a minimal metabolic behavior

$$\{ i \in \text{Irr} \mid v_i > 0 \} = \{ i \in \text{Irr} \mid v_i \neq 0 \},$$

for some $v \in \mathcal{C}$, is a minimal set of active irreversible reactions.
**Characteristic set of a minimal face**

- **Lemma** Given a minimal proper face \( G \) of \( C \) and an irreversible reaction \( j \in \text{Irr} \), the following are equivalent:
  1. \( \forall v \in G \setminus \text{linsp}(C) \), \( v_j > 0 \).
  2. \( \forall v \in G \setminus \text{linsp}(C) \), \( v_j > 0 \).

- Call \( D = D_G = \{ j \in \text{Irr} \mid v_j > 0, \forall v \in G \setminus \text{linsp}(C) \} \) the characteristic set of \( G \).

- \( D \) is a minimal metabolic behavior.
- There exists a minimal proper face \( G \) of \( C \) whose characteristic set is \( D \).

**MMBs and minimal faces**

- **Theorem**
  Let \( C = \{ v \in \mathbb{R}^n \mid Sv = 0, v_i \geq 0, i \in \text{Irr} \} \) be the flux cone of a metabolic network.
  For any set of irreversible reactions \( D \subseteq \text{Irr} \), the following are equivalent:
  1. \( D \) is a minimal metabolic behavior.
  2. There exists a minimal proper face \( G \) of \( C \) whose characteristic set is \( D \).

**MIP to enumerate shortest MMBs/GFMs**

\[
\min \ W \cdot \sum_{j \in \text{Irr}} z_j + \sum_{j \notin \text{Irr}} z_j
\]

- \( Sv = 0, \ v_{irr} \geq 0 \),
- \( -Mz_j \leq v_j \leq Mz_j \), for \( j = 1, \ldots, n \),
- \( \sum_{j \in \text{Irr}} v_j \geq 1 \),
- \( v \in \mathbb{R}^n, z \in \{0,1\}^n \)

Forbidding the \( k \)-th solution \((v^k, z^k)\): Let \( D^k = \{ j \in \text{Irr} \mid z_j^k = 1 \} \).

\[
\sum_{j \in D^k} z_j \leq |D^k| - 1, \text{ for } k = 1, \ldots, K - 1.
\]

\( v^k \) is called the \( k \)-th generating flux mode (GFM)

**EFMs vs. GFMs in E. coli**

(thickness of arrows proportional to the number of times a reaction appears in the 100 shortest EFMs / GFMs)
### EFMs vs. GFMs in *E. coli* (2)

| NoR, number of reactions; LI, length interval; OvR, overlapping percentage of reactions of the 100 shortest EFMs (GFMs) in the shortest GFMs (EFMs); AHD, average hamming distance; No EFMs, number of EFMs emerging from the network formed by the 100 shortest EFMs (GFMs); No EFMs (R), number of EFMs emerging from the network formed by the 100 shortest EFMs (GFMs) and the reversible metabolic space (RMS); Lys, L-lysine. |
|---|---|---|---|---|---|
| EFMs | 100 shortest | 54 | 25–26 | 90.74% | 1665 | 5398 | Lys: 1636 | Lys: 3960 |
| GFMs | 100 shortest | 132 | 25–37 | 37.12% | 354238 | 5 × 10^10 | Lys: 25007 | Lys: * |

NoR, LI: No. of reactions, length interval; OvR, overlapping percentage; AHD, average hamming distance; No EFMs, No. of EFMs; No EFMs (R), No. of EFMs (R)