Metabolic Networks

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Mathematics for key technologies

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Importance

- Biology
  - Cell metabolism
  - Catabolism, anabolism
- Medicine
  - Metabolic disorders
  - Cancer
- Biotechnology
  - Biofuel
  - Bioleaching

Mathematical representation
Algebraic description

- Stoichiometric matrix $S \in \mathbb{R}^{m \times n}$
  - Rows $\sim$ internal metabolites $i = 1, \ldots, m$
  - Columns $\sim$ internal and external reactions $j = 1, \ldots, n$
  - $S_{ij}$: stoichiometric coefficient of reactant $i$ in reaction $j$

- Set of irreversible reactions $Irr$

- Metabolic model $\mathcal{M} = (S, Irr)$

1. Kinetic modeling

- Metabolites $i$ and reactions $j$
- $C_i(t)$: metabolite concentrations at time $t$
- $v_j = v_j(C, k)$: reaction rates, depending on kinetic law and kinetic parameters $k$
- $S_{ij}$: stoichiometric coefficient

$$\frac{dC_i}{dt} = \sum_{j=1}^{n} S_{ij} v_j \quad \text{or} \quad \frac{dC}{dt} = S \cdot v(C, k)$$

- System of ordinary differential equations (ODEs)

2. Constraint-based modeling

- Steady-state assumption:
  Assume metabolite concentrations $C_i$ and reaction rates $v_j$ are constant $\sim$ flux vector $v \in \mathbb{R}^n$

- Stoichiometric constraints (mass balance):
  $$\sum_{j=1}^{n} S_{ij} v_j = 0, \text{ for all } i = 1, \ldots, m$$

- Thermodynamic irreversibility constraints:
  $$v_j \geq 0, \text{ if } j \text{ is irreversible}$$

$\leadsto$ system of linear equations and inequalities in $\mathbb{R}^n$
Steady-state flux cone

Set of all possible steady-state flux distributions

\[ C = \{ v \in \mathbb{R}^n \mid Sv = 0, \; v_i \geq 0, \; i \in \text{Irr} \} \]

\( \rightsquigarrow \) polyhedral cone