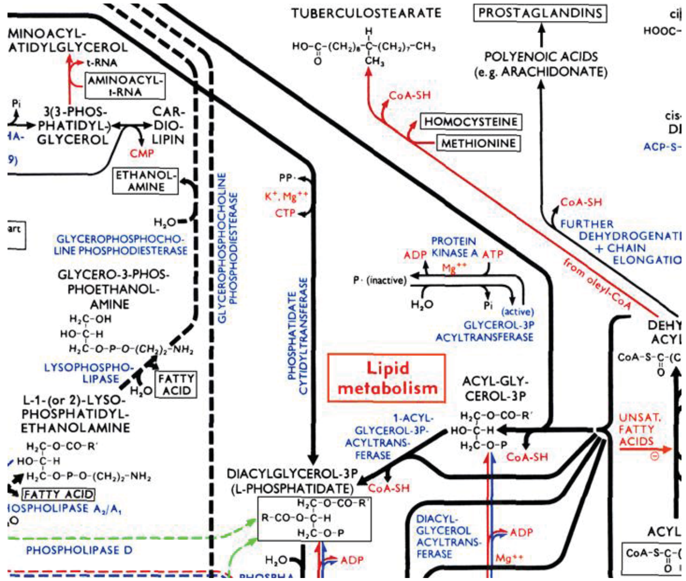
Metabolic Networks

Alexander Bockmayr
Freie Universität Berlin

Research Center MATHEON
Mathematics for key technologies

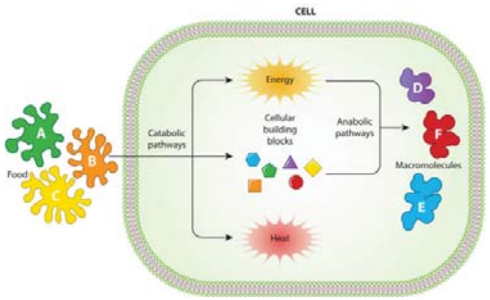
Metabolic networks



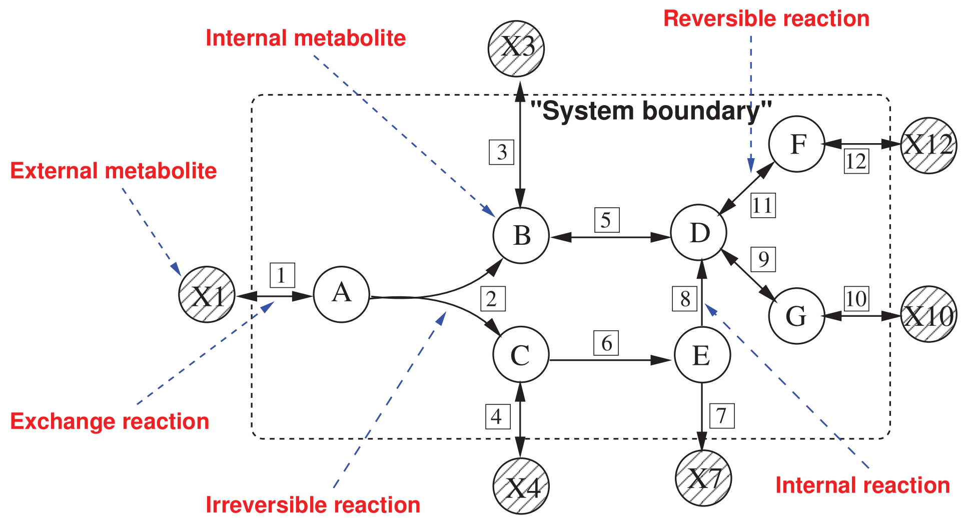
http://web.expasy.org/pathways/

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 $\rightsquigarrow$ internal metabolites $i = 1, \ldots, m$
  - Columns $\rightsquigarrow$ internal and exchange reactions $j = 1, \ldots, n$
  - S_{ij}: stoichiometric coefficient of reactant i in reaction j
- Set of irreversible reactions Irr
- Metabolic model $\mathscr{M} = (S, Irr)$

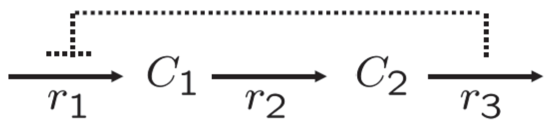
1. Kinetic modeling

- Metabolites i and reactions j
- $C_i(t)$: metabolite concentrations at time t
- $v_j(t) = v_j(C(t), k)$: 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)

Example



$$\begin{pmatrix} dC_1/dt \\ dC_2/dt \end{pmatrix} = \begin{pmatrix} 1 & -1 & 0 \\ 0 & 1 & -1 \end{pmatrix} \cdot \begin{pmatrix} v_1(C,k) \\ v_2(C,k) \\ v_3(C,k) \end{pmatrix}$$

$$\begin{aligned} v_1(C,k) &= v_{m1}/(1+(C_2/k_i)^p) \\ v_2(C,k) &= v_{m2} \cdot C_1/(k_1+C_1) \\ v_3(C,k) &= v_{m3} \cdot C_2/(k_2+C_2) \end{aligned}$$

Which kinetic laws?

Which kinetic parameters?

2. Constraint-based modeling

- Steady-state assumption
  Assume metabolite concentrations C_i and reaction rates v_j are constant (over some time interval)
  $\rightsquigarrow$ steady-state 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:

$$v_j \geq 0, \text{ if } j \text{ is irreversible}$$

$\rightsquigarrow$ system of linear equations and inequalities in $\mathbb{R}^n$