① Metabolism
Signaling
Gene Expression

② Models of Metabolism

③ Basics: Chemical Kinetics / Physical Chemistry

$$\underbrace{2A}_{\text{Reaktanten}} \xrightarrow{v_1} \underbrace{B}_{\text{Produkte}}$$

v_1: Reaktionsgeschw.

Substrate

$$\frac{d[A]}{dt} = -2v_1 \qquad \frac{d[B]}{dt} = +v_1$$

also:

$$\frac{d[B]}{dt} = -\frac{1}{2}\frac{d[A]}{dt}$$

Stöchiometrische Koeffizienten
-2 $\quad +1$

Beispiel

$$2A + B \rightarrow A + C$$

	A	B	C	Σ
Stöch. Koeff	-1	-1	$+1$	

} enthält nicht die komplette Info

④ Reaktionsraten

$$v = f([A], [B], \text{etc.} \ldots)$$

hier: intensive

⑤ Massenwirkungsgesetz

Massenwirkungsgesetz

$A \to B$ $\quad \frac{d[A]}{dt} = -V$

$V = K \cdot [A]$

$n_A \cdot A + n_b \cdot B + \ldots \to n_p P + n_q Q + \ldots$

$V = K^+ \cdot [A]^{n_A} \cdot [B]^{n_B} \cdot \ldots$

Mass-action kinetics!

Rück reaction: $V = K^- \cdot [P]^{n_p} \cdot [Q]^{n_q} \ldots$

Bsp $\quad 2\,ADP \to ATP + AMP$

$v^+ = K^+ \cdot [ADP]^2$

$v^- = K^- [ATP][AMP]$

Chemical equilibrium

Bsp $\quad A \to B$ $\quad v^+ = K^+ \cdot [A]$

$v^- = K^- \cdot [B]$

$v = v^+ - v^- \overset{!}{=} 0$

$\Rightarrow K^+ [A]^0 = K^- [B^0]$

$\Rightarrow \frac{K^+}{K^-} = \frac{[B^0]}{[A]^0} = \underline{\underline{K_{eq}}}$

für

$$K_{eq} = \frac{[P]^{n_p} \cdot [Q]^{n_q}}{[A]^{n_a} \cdot [B]^{n_b}} = \frac{k^+}{k^-}$$

(6) Detailed Balance ("detailliertes Gleichgewicht")

$$A \overset{①}{\rightleftharpoons} B \overset{②}{\rightleftharpoons} C \overset{③}{\rightleftharpoons} A$$

$$\frac{k_1^+}{k_1^-} = \frac{B^0}{A^0} = K_{eq1} \qquad \frac{k_2^+}{k_2^-} = \frac{C^0}{B^0} = K_{eq2} \qquad \frac{k_3^+}{k_3^-} = \frac{A^0}{C^0} = K_{eq3}$$

$$K_{eq1} \cdot K_{eq2} \cdot K_{eq3} = 1 = \frac{k_1^+}{k_1^-} \frac{k_2^+}{k_2^-} \frac{k_3^+}{k_3^-}$$

for any cycle: product of forward rate constant = prod of rev. rate constants

$$\prod k_i^+ = \prod k_i^- \quad \text{or} \quad \prod K_{eq} = 1$$

"Wegscheider condition"

<u>gilt auch für metabolische Netzwerke!</u>

Mass-action ratio

$$v = v^+ - v^- = v^+ \left(1 - v^-/v^+\right)$$

$$\frac{v^-}{v^+} = \underbrace{\frac{k^-}{k^+}}_{K_{eq}} \underbrace{\frac{[P]^{n_p}[Q]^{n_q}\cdots}{[A]^{n_a}[B]^{n_b}}}_{\text{mass-action ratio} = \Gamma}$$

$$v = v^+\left(1 - \frac{\Gamma}{K_{eq}}\right)$$

Thermodynamic

⑦ Slides: Models of Metabolism

...umatik RN Gleichg

Stöchiometrische Matrix

$$\frac{dx}{dt} = N \cdot V$$

<u>Bsp</u> glycolyse

- Eigenschaften von N
- ~~Massenverhalten~~

  lin. depend. rows!

  rank(N)

  <u>linker Nullraum</u> $E \cdot N = 0$

$$[0\ 0\ 0\ \cancel{1}\ 1] \cdot N = 0$$

$$E \cdot \dot{x} = \cancel{N} E \cdot N \cdot v = 0$$

$$E \cdot \begin{bmatrix} \dot{x} \\ \vdots \\ \dot{ATP} \\ \dot{ADP} \end{bmatrix} = \frac{d}{dt}(ATP + ADP) = 0$$

Beispiel

$A + B \to C$
$C \to 2B$
$B \to A$

	r_1	r_2	r_3
A	-1	0	$+1$
B	-1	$+2$	-1
C	$+1$	-1	0

$\mathrm{rank}(N) = 2$

$E = (1 \;\; 1 \;\; 2) \qquad E \cdot N = 0$

$$\Rightarrow \underbrace{\frac{d}{dt}\begin{bmatrix} A \\ B \\ C \end{bmatrix} = N \cdot v}$$

$$\dot{A} = -r_1 + r_3$$
$$\dot{B} = -r_1 + 2r_2 - r_3$$
$$\dot{C} = +r_1 - r_2$$

$$\Rightarrow \cancel{E} \cdot (\;) = E \cdot N \cdot v = 0$$

$$\frac{d}{dt}(A + B + 2C) = 0 \Rightarrow A + B + 2C = \mathrm{const}$$

$$-r_1 + r_3 - r_1 + 2r_2 - r_3 + 2(r_1 - r_2) = 0$$

Rechts Nullraum

$$N \cdot K \Leftrightarrow N \cdot v^0 = 0$$

$r - \mathrm{rank}(\cancel{N})$

typisch $r > m$