Bioeng 261 Lecture 1: Basic principles of Reaction modelling.

Idea: The behaviour of cells can (partially) be understood/modelled using **chemical reaction modelling**

Key Principles

General

- conservation/symmetry { mass, energy, momentum
  - [possible]
- direction/asymmetry { entropy
  - [probable]
- constitutive* equations { Here: law of mass action
  - [actual]

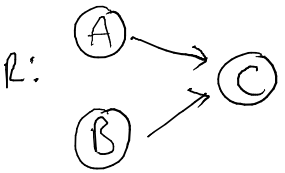
Specific

*→ like 'Hooke's law', $F = kx$
or Newton's gravitational 'law' $F = \frac{GmM}{r^2}$
→ think 'force'/'flux' modelling
→ valid for class of systems but not all.

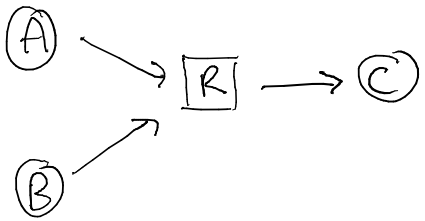
Graphical representations

Reactants $\xrightarrow{\text{rate}}$ Products

R: $A + B \xrightarrow{k} C$ Stoichiometric equation

R: 

Reaction graph

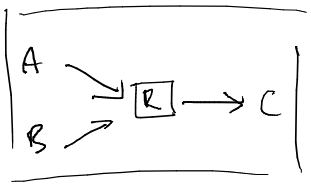


Petri Nets

(explicit rep. of reaction R with square node)

└ helpful to treat reaction as 'object' of interest itself

Example reaction



$$A + B \xrightarrow{k} C$$

1. Conservation of mass

Key: think in terms of the reaction itself:

each 'step', 1 A ↓, 1 B ↓, 1 C ↑

Flux $\tilde{J}$ of reaction

$$\frac{dA}{dt} = -\tilde{J}$$
$$\frac{dB}{dt} = -\tilde{J}$$
$$\frac{dC}{dt} = +\tilde{J}$$

note! (not eg $\tilde{J}/2$)

why $\tilde{J}$ & not J?
- fluxes!
  - see later

2. Specific model for flux $\tilde{J}$

'Law' of mass action.
- for 'elementary' reactions
- will assume more complex reactions built up from simple.

Intuition: collision theory

1A → collide = reaction → 1C

1B

rate ∝ number of collisions

$\approx$ number of A molecules × number of B molecules

$= A \times B$ (for $A+B \to C$)

$$\tilde{J} = k \cdot A B$$

↑

k: reaction rate 'constant'

[also depends on eg temperature
hotter = more collisions]

Finally....

$$\frac{dA}{dt} = -k \cdot A \cdot B$$

$$\frac{dB}{dt} = -k \cdot A \cdot B$$

$$\frac{dC}{dt} = +k \cdot A \cdot B$$

Mass action:

rate $\propto$ number of collisions of reactants

Order of reaction:

number of reactant collisions

Examples

1. $A + A \rightarrow B$ $\quad (2A \rightarrow B)$
2. $A + B \rightarrow C + D$
3. $A + B + C \rightarrow D$.
4. $aA + bB \rightarrow C$
5. Creutzfeldt-Jakob Disease (CJD) (later)

(1.) R: $2A \rightarrow B$

[each step] $\downarrow 2A$, $\uparrow 1B$ } think in terms of reactions (each step)

(conservation (number per step)) $\left\{ \begin{array}{l} \frac{d[A]}{dt} = -2J \\ \frac{d[B]}{dt} = +J \end{array} \right\}$ & $J = \underbrace{k[A]^2}_{\text{rate}}$ ← chance of (collisions)

$$\Rightarrow \frac{d[A]}{dt} = -k \cdot \underbrace{2}_{=} \cdot [A]^{\underbrace{2}_{=}}; \quad \frac{d[B]}{dt} = k[A]^2$$

order = 2

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(4) $\frac{d[A]}{dt} = -a \cdot J$, $\frac{d[B]}{dt} = -b \cdot J$

$\frac{d[C]}{dt} = J$, $J = k[A]^a \cdot [B]^b$

order = $a + b$

Complications

- Units & dimensions
- Reversible/irreversible reactions

Amounts vs concentrations ?

Q: what is conserved ?

A: amount

$$\text{Amount} = \left(\text{Amount}/\text{Volume}\right) \times \text{Volume}$$

$$= [A] \times V$$

($[A]$: concentration)

if Vol = constant

$$\frac{dA}{dt} = V \cdot \frac{d[A]}{dt} = \tilde{J} \quad \leftarrow \text{amount/time}$$

$$\frac{d[A]}{dt} = \frac{\tilde{J}}{V} = J \quad \leftarrow \text{amount/time·vol.} = \text{conc./time}$$

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1 mol : Avogadro's number of molecules (6.022×10^{23})

1 Molar (M) : 1 mol/litre : concentration

↳ typical: μM - mM

$\tilde{J}$: amount/time (eg mol/sec)

$$J = \frac{\tilde{J}}{V} = \text{amount}/\text{volume·time}$$

$$= \text{concentration}/\text{time} \quad (\text{eg } M/\text{sec})$$

Typically $\frac{d[A]}{dt} = J$ } we will often assume in terms of concentrations

But: Careful !

↳ eg if vol. is changing

Order & rate dimensions/units

1st order

$$J = k[A] = \frac{d[A]}{dt} \Rightarrow k : \frac{1}{\text{time}} \quad (\text{eg } \frac{1}{\text{sec}})$$

2nd order

$$J = k[A][B] = \frac{d[A]}{dt} \Rightarrow k : \frac{1}{\text{conc.}} \cdot \frac{1}{\text{time}} \quad (\text{eg } M^{-1}s^{-1})$$

We will look at Dimensional analysis & scaling later

Reversible & irreversible reactions

Microscopic reversibility: [kinetics]

- all elementary reactions can proceed in both directions

- BUT: one direction might be more likely

Possible ≠ Probable { glass breaking / glass spontaneously forming.

$A + B \xrightarrow{k_1} C$ vs $C \rightarrow A + B$ { there are special ways of encouraging one direction

Macroscopic irreversibility: [thermodyn.]

asymmetric { entropy increases (or Gibbs free energy decreases)

Example

Model $A + B \xrightarrow{k} C$

Really should be $A + B \underset{k_-}{\overset{k_+}{\rightleftharpoons}} C$ { key k_+ & k_- possible / BUT $k_+ \neq k_-$ probably

k_+ : forward reaction $A + B \rightarrow C$

k_- : reverse reaction $C \rightarrow A + B$

1. $$\frac{d[A]}{dt} = \frac{d[B]}{dt} = -J_+ + J_-$$

$$\frac{d[C]}{dt} = J_+ - J_-$$

2. $$J_+ = k_+[A][B]$$

$$J_- = k_-[C]$$

$$\Rightarrow \begin{cases} \frac{d[A]}{dt} = \frac{d[B]}{dt} = k_-[C] - k_+[A][B] \\ \frac{d[C]}{dt} = k_+[A][B] - k_-[C] \end{cases}$$

Assume $k_+ \neq k_-$.

BUT: how do we measure/det. $k_+ > k_-$ or $k_- > k_+$

- Equilibrium: reactions balanced
- Steady state: change in concentrations $= 0$

(there: same. But not always!)

Set (eg wait a long time)

$$k_-[C]_{eq} - k_+[A]_{eq}[B]_{eq} = 0$$

$$K_{eq} := \frac{k_-}{k_+} = \frac{[A]_{eq}[B]_{eq}}{[C]_{eq}}$$ } can measure

if K_{eq} { large: $[A]_{eq}[B]_{eq} >> [C]_{eq}$
small: $[A]_{eq}[B]_{eq} << [C]_{eq}$

ie { $\xleftarrow{k_-}$ reverse dominates
$\xrightarrow{k_+}$ forward dominates

If $k_+ >> k_-$ we often approx as

$$A + B \xrightarrow{k} C$$

} 'favours' forward reaction*

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*Thermo: K_{eq} & hence ratios of rates k_+, k_- etc can be related to Gibbs free energy