Introduction to mathematical modelling with ODEs

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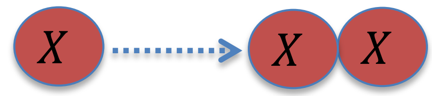
1. Reactions

Biochemistry is the science of life. All our life processes - walking, talking, moving, feeding - are essentially chemical reactions. So biochemistry is actually the chemistry of life, and it's supremely interesting.
Aaron Ciechanover

Thinking reactions

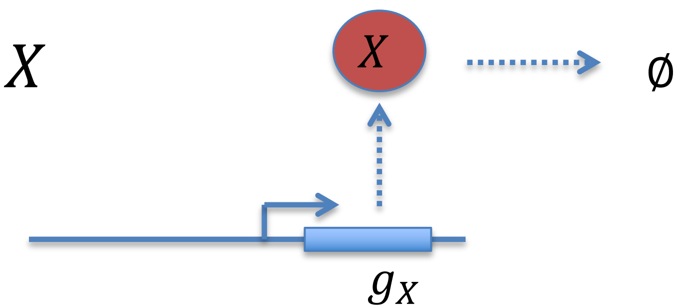
Many biological processes can be modelled as reactions, for example:

- Bacterial growth $X \rightarrow 2X$

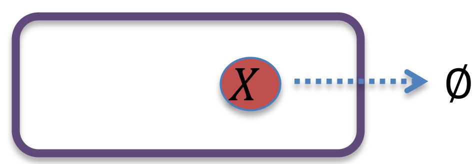


- Gene expression $g_X \rightarrow g_X + X$

$X \rightarrow \emptyset$



- Ions leaving a cell $X \rightarrow \emptyset$



Reactions and rates

Each reaction has a rate constant (k) that relates the concentration of the reactants to the rate of the reaction.
Increasing the concentration of the reactants will increase the rate of the reaction according to k.
Note: k can dependent on environmental factors, such as temperature and pressure in a chemical reaction

$$X \xrightarrow{k} Y$$

$$X + Y \xrightarrow{k} Z$$

$$2X \xrightarrow{k} X_2$$

$$\emptyset \xrightarrow{k} X$$

Task 1.1

Think about the following questions

1. What is a rate?

2. How might we measure it? (think of an experiment)

3. What are the units of a reaction rate

4. Consider the reaction $A + B \rightarrow X$
5. What happens to the rate if we increase A, or B?

Task 1.1: answers

1. What is a rate?
   – Rate ≈ change in concentration / change in time

2. How might we measure it? (think of an experiment)
   – Rate ≈ $\frac{\Delta[Y]}{\Delta t}$

3. What are the units of a reaction rate
   – Measured in Ms^{-1} (or mols per litre per second)

Reaction rates

- How might we model the rate of reaction $ES \xrightarrow{k_2} E + P$?

  - Rate is proportional to $[ES]$ (concentration [ ])
  - Rate = $k_2\ [ES]$

- Rate constant k_2, units?

  - Reaction rate has units of concentration per second
  - Ms^{-1}
  - Units of $k_2 = s^{-1}$

Reaction rates

- How do we model reaction $E + S \xrightarrow{k_1} ES$?
- Rate constant k_1, units?

- How do we model the reverse reaction $ES \xrightarrow{k_{-1}} E + S$?
- Rate constant k_{-1}, units?

Reaction rates

- How do we model reaction $E + S \rightarrow ES$?
- Rate constant k_1, units?

  - Rate = $k_1 [E] [S]$
  - k_1 units $M^{-1}s^{-1}$

- How do we model reaction $ES \rightarrow E + S$?
- Rate constant k_{-1}, units?

  - Rate = $k_{-1} [ES]$
  - k_{-1} units s^{-1}

Common assumption: dynamic equilibrium

- Constant temperature, pressure and volume

- Reactants and product are well mixed (no spatial gradients), homogeneous

- Reactants and products are at sufficiently high concentrations so that reactions are occurring all the time

- Note that even when these assumptions are not satisfied (almost always) we can still use the tools we will develop

Law of mass action

Definition

The law of mass action Given a chemical reaction involving two reactant A and B with stochiometries m and n

$$mA + nB \xrightarrow{r} C$$

the rate of the reaction r is given by

$$r = k[A]^m[B]^n$$

where $[A]$ and $[B]$ denote the concentrations of the species A and B respectively and k denotes the rate constant.

Order of reactions

The order of a reaction summarizes the relationship between concentration of reactants and the reaction rate

- Zero order

$$\emptyset \xrightarrow{k_3} S \qquad \text{Rate} = k_3$$

No dependence on reactants

- First order

$$ES \xrightarrow{k_2} E + P \qquad \text{Rate} = k_2\,[ES]$$

Dependent on one reactant

- Second order

Dependent on two reactants

$$E + S \xrightarrow{k_1} ES$$

$$\text{Rate} = k_1\,[E][S]$$

Dependent on two reactants

$$2X \xrightarrow{k_4} X_2$$

$$\text{Rate} = k_4\,[X]^2$$

Task 1.2: what are the rate laws?

$$X \xrightarrow{k} Y$$

$$X \xrightarrow{k} 2X$$

$$X + Y \xrightarrow{k} Z$$

$$2X \xrightarrow{k} X_2$$

$$\emptyset \xrightarrow{k} X$$

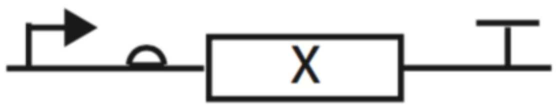
$$\mathrm{X} \xrightarrow{k} \emptyset$$

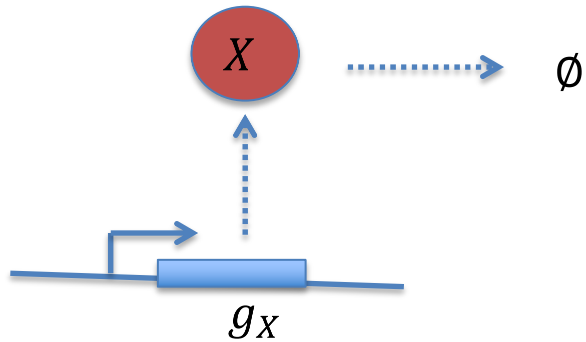
Task 1.2: answer

$X \xrightarrow{k} Y$	Rate $= k[X]$
$X \xrightarrow{k} 2X$	Rate $= k[X]$
$X + Y \xrightarrow{k} Z$	Rate $= k[X][Y]$
$2X \xrightarrow{k} X_2$	Rate $= k[X]^2$
$\emptyset \xrightarrow{k} X$	Rate $= k$
$\mathrm{X} \xrightarrow{k} \emptyset$	Rate $= k[X]$

Task 1.3

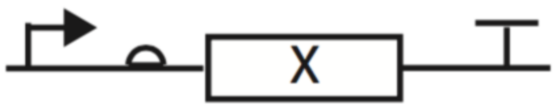
- Can you write down some reactions that model simple gene expression in a bacterial cell:





- Can you do this for two abstractions:
  - Protein level
  - Protein + RNA level

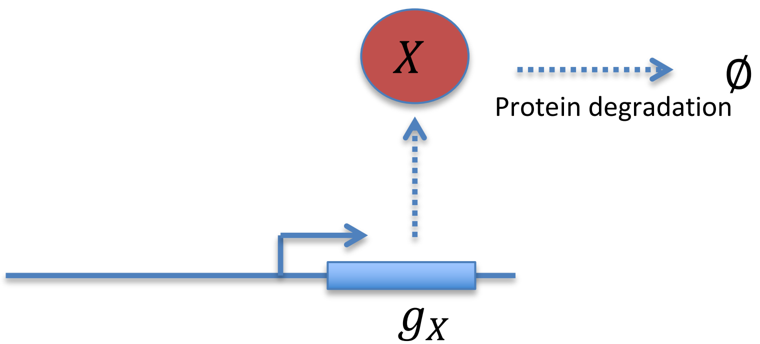
Task 1.3: answer (1)



- Can you do this for two abstractions:
  - Protein level

$$g_X \rightarrow g_X + X$$

$$X \rightarrow \emptyset$$



  - Protein + RNA level

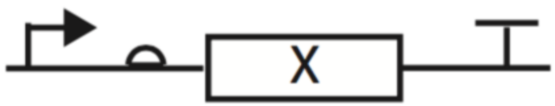
$$g_X \rightarrow g_X + X_{rna}$$

$$X_{rna} \rightarrow X + X_{rna}$$

$$X \rightarrow \emptyset$$

$$X_{rna} \rightarrow \emptyset$$

Task 1.3: answer (2)



- For the protein + RNA level we can also simplify

$$g_X \to g_X + X_{rna}$$
$$X_{rna} \to X + X_{rna}$$
$$X \to \emptyset$$
$$X_{rna} \to \emptyset$$

- Under certain assumptions about the dynamics (next section) namely decay of RNA much quicker than protein

$$g_X \to g_X + X_{rna}$$
$$X_{rna} \to X$$
$$X \to \emptyset$$