MATH1070

Enzyme Kinetics

Compartments

- A dynamic entity such as a level, concentration or number.
- Value in compartment is controlled by a differential equation:

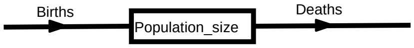
$$\frac{dCompartment}{dt} = f()$$

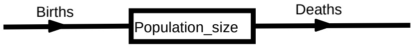
Or usually…

$$\frac{dx}{dt} = \Sigma \text{ inflows} - \Sigma \text{ outflows}$$

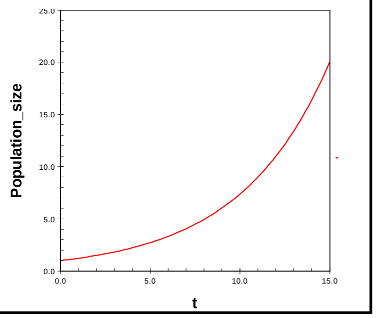
Compartments: Population Growth

- $\frac{dPopulation\_size}{dt} = Births - Deaths$
- Births = birth_rate * Population_size
  - birth_rate is a constant based on the biology of individuals
- Deaths = death_rate * Population_size
  - death_rate is a constant based on the biology of individuals





- Initial size = 1
- birth_rate = 0.3
- death_rate = 0.1



Mass Action

- Law of mass action states that the rate of a reaction is proportional to an integral power of the concentrations of all the substances taking part in the reaction.
- E.g., for $A + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C$ the differential equ for C is:

$\frac{dC}{dt} = k_1AB - k_{-1}C,$ where k_1 is the constant relating to the rate of production of C when A binds with B; and k_{-1} is the constant relating to rate of release of A and B from C.

Mass Action

- E.g., for $A + 2B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C$ the differential equ for C is:

$\frac{dC}{dt} = k_1AB^2 - k_{-1}C,$ where *B* is raised to the power of 2 because there are 2 molecules of *B*.

Enzyme activity or Protein transfer

- Concentration of Substrate (S),
- Concentration of Enzyme (X_0),
- Enzyme bound to substrate (X_1),
- Concentration of Product (P).

$$S + X_0 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1 \xrightarrow{k_2} P + X_0$$

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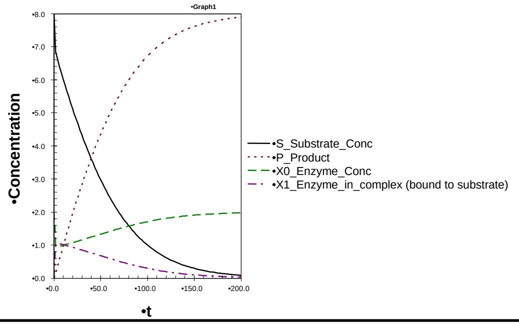
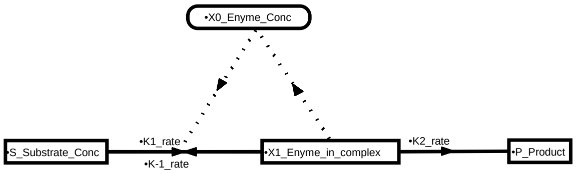


$$S + X_0 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1 \xrightarrow{k_2} P + X_0$$

$$\frac{ds}{dt} = -k_1 s x_0 + k_{-1} x_1$$

$$\frac{dx_1}{dt} = +k_1 s x_0 - k_{-1} x_1 - k_2 x_1$$

$$\frac{dp}{dt} = +k_2 x_1$$



Enzyme Kinetics

- In our previous problem of enzyme and substrate, let us assume two molecules of substrate are required by the enzyme. In this case, our reaction becomes the following with the corresponding differential equation below:

$$2S + X_0 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1 \xrightarrow{k_2} 2P + X_0$$

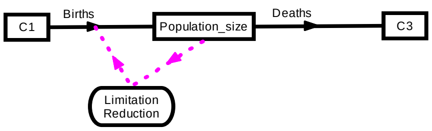
$$\frac{dc}{dt} = -k_1 s^2 x_0 + k_{-1} x_1$$

$$\frac{dx_1}{dt} = +k_1 s^2 x_0 - k_{-1} x_1 - k_2 x_1$$

Feedback & Homeostasis

- Positive feedback (less common than negative feedback) is where an increased value enhances further increases. (e.g. limitless population growth; early pioneer species growth).
- Negative feedback occurs where the rate of the process is limited for positive values of the control variable (or variable combination). This leads to homeostatic control.
  - Self-inhibition
  - Extrinsic
  - Saturation

Self-Inhibition



Limitation = $1 - \frac{\text{Population\_size}}{K}$,where K is the carrying capacity

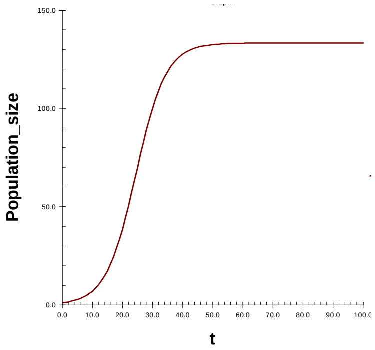
Births = birth_rate * Population_size*Limitation

$$\frac{dN}{dt} = [b(1 - \frac{N}{K})]N - dN$$

N = Population_size
b = birth_rate
d = death_rate

Self-Inhibition

- limited population growth



Extrinsic Inhibition

- An extrinsic or external factor may limit a process. E.g.,
  - a beaker of cold water warming to room temperature.
  - diffusion across a membrane
  - blood flow (between organs) driven by pressure differences

Example - Beaker of water warming to Room Temp.

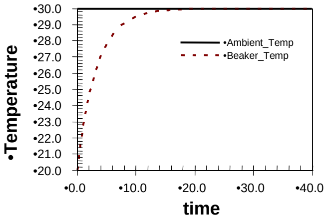
- FACTS:
  - The water is initially below ambient temperature.
  - The rate of temperature change is initially large and decreases over time.
- This is consistent with the rate of temperature rise being a function of the difference between the current temperature and the ambient temperature. Newton's law of cooling describes this:

$$\frac{dT}{dt} = k(T_a - T)$$

T_a = ambient temp
k = constant dependent on characteristics of the liquid

Extrinsic Feedback

$$\frac{dT}{dt} = k(T_a - T)$$

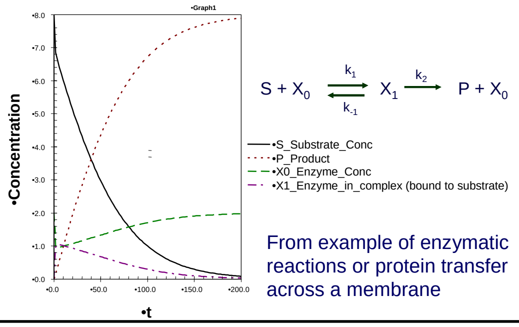


T_a = ambient temp
k = constant dependent on characteristics of the liquid

Saturation Feedback

- Negative feedback through the interaction between the quantity of donor available and the ability of the recipient to convert the donor substance.
- Commonly used in describing enzyme substrate kinetics/dynamics.
- Negative feedback puts bounds on the rates by saturating the recipient.
- Has elements of positive and negative feedback because the rate does not decrease to 0, nor increase infinitely.

Saturation Feedback



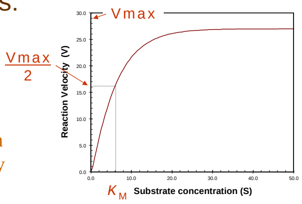
$$S + X_0 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1 \xrightarrow{k_2} P + X_0$$

From example of enzymatic reactions or protein transfer across a membrane

Saturation Feedback

- E.g., Transfer of a protein across a membrane via a receptor:
- Basic equation Michaelis-Menten equation applies:

$$V = Vmax \cdot \frac{S}{Km + S}$$



V = rate of product formation
Vmax = max reaction velocity
S = substrate concentration
Km = half saturation constant; low Km is a rapidly rising curve

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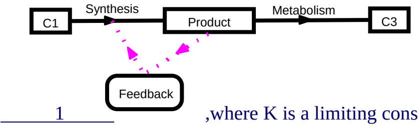
Homeostatic Self-Inhibition

- The products of enzymatic reactions often inhibit the activity of the same enzyme or transcription (DNA to RNA).



$$\text{Feedback} = \frac{1}{1+(\text{Product}/K)^n}$$,where K is a limiting constant

Synthesis = synthesis_rate * Product*Feedback

$$\frac{dP}{dt} = \left[s\left(\frac{1}{1+(P/K)^n}\right)\right]P - mP$$

P = Product_concentration
s = synthesis_rate
m = metabolism_rate