Bioinformatics: Network Analysis

Reaction Kinetics

COMP 572 (BIOS 572 / BIOE 564) - Fall 2013
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- Reaction kinetics is the study of how fast chemical reactions take place, what factors influence the rate of reaction, and what mechanisms are responsible.

- Many variables can affect the reaction rate, including temperature, pressure, and composition.

- A chemical reaction is usually depicted in the form of a chemical equation which describes the transformation of one or more reactants into one or more products.

$$A \rightarrow B$$

reactant product

$$2\mathrm{ADP} \rightarrow \mathrm{ATP} + \mathrm{AMP}$$

Two molecules of ADP are transformed into one molecule of ATP and one molecule of AMP

- Sometimes, a double arrow is used to explicitly indicate that a reaction is reversible:

$$2\mathrm{ADP} \rightleftharpoons \mathrm{ATP} + \mathrm{AMP}$$

- If a reaction is reversible (as almost all reactions are, to some extent), then the reaction rate can be positive or negative.
- By convention, a positive rate means that the reaction progresses from left to right, whereas a negative rate indicates a right to left reaction.

Stoichiometric Amount

- The <u>stoichiometric amount</u> (or, molecularity) is defined as the number of molecules of a particular reactant or product taking part in a reaction.

- Stoichiometric amounts are always positive numbers.

$$\begin{array}{ccccc} 2\mathrm{ADP} & \rightleftharpoons & \mathrm{ATP} & + & \mathrm{AMP} \\ 2 & & 1 & & 1 \end{array}$$

Stoichiometric Amount

- If the same species occurs on the reactant and product side of a reaction, then it must be treated separately.

$$\begin{array}{ccccccccccccc} 2A & + & B & + & C & \rightarrow & 3A & + & D & + & 2B \\ 2 & & 1 & & 1 & & 3 & & 1 & & 2 \end{array}$$

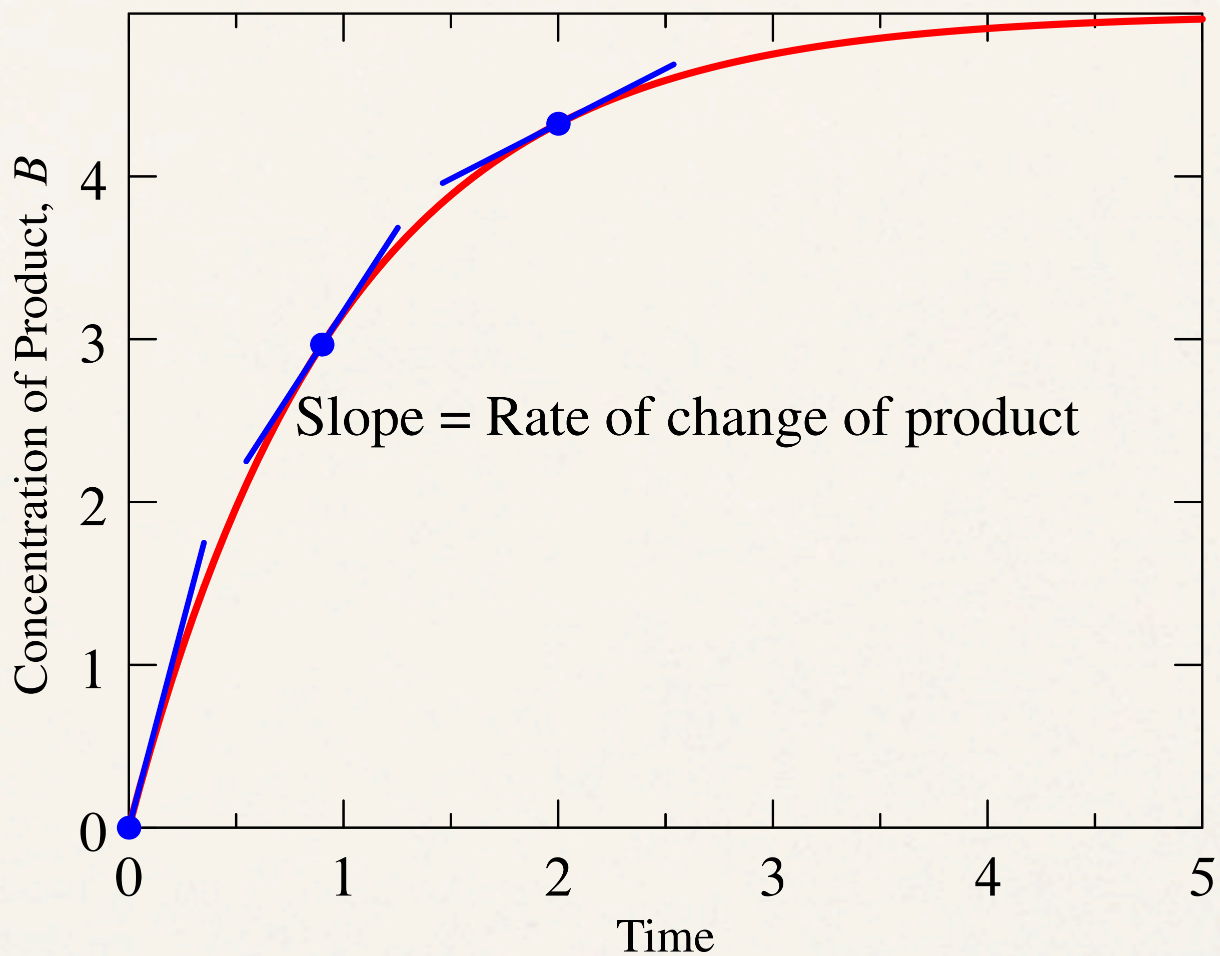
Rates of Change

- The rate of change can be defined as the rate of change in concentration or amount (depending on units) of a designated species.

- If S is the species, then the rate of change is given by

$$\text{Rate} = \frac{dS}{dt}$$

Rates of Change



$$A \rightarrow B$$

(initial concentration of A is 5 units)

Rates of Change

- If concentrations are measured in moles per liter (L) and time in seconds (sec), then the rate of reaction is expressed in mol L^{-1} sec^{-1}.
- When reporting a rate of change, it is important to give the name of the species that was used to make the measurement.

Rates of Change

$$2A \rightarrow B$$

- The rate of change of A is twice the rate of change of B.

- The rate of change of A is negative because it is consumed, whereas the rate of change of B is positive because it is being made.

Stoichiometric Coefficients

- Stoichiometry deals with static information about the amounts of substances involved in a chemical reaction, whereas kinetics relates rates of change that occur in these amounts.
- The <u>stoichiometric coefficient</u> is the difference between the stoichiometric amounts of a given species on the product side and the stoichiometric amount of the same species on the reactant side.

Stoichiometric Coefficients

$$2A \rightarrow B$$

Stoichiometric coefficient of A is -2.

Stoichiometric coefficient of B is 1.

Stoichiometric Coefficients

- Given only the stoichiometric coefficients of species, it is not possible to recreate the original reaction equation.

Reaction Yields

$$C_6H_{12}O_6 \rightarrow 2C_2H_5OH + 2CO_2$$

- If a yeast culture is started with 10g of glucose, what is the maximum amount of ethanol that can be produced if all the glucose is consume?
- The molar mass of glucose is 180; therefore, the number of moles of glucose in 10g is 10/180=0.055 moles.
- From the stoichiometry, 0.111 moles of ethanol will be formed.
- If the molar mass of ethanol is 46, then 5.2g of ethanol are formed.

Elementary Rate Kinetics

- Chemical reactions that involve no reaction intermediates are called elementary reactions.
- Such reactions often have simple kinetic properties, and empirical studies have shown that the rate of reaction is often proportional to the product of the molar concentration of the reactants raised to some power.

The Law of Mass Action

- The law states that the reaction rate is proportional to the probability of a collision of the reactants.

- This probability is in turn proportional to the concentration of the reactants to the power of the molecularity, that is the number in which they enter the specific reaction.

- The basic quantities in modeling are the concentration S of a substance **S**, and the rate v of a reaction (i.e., the change of concentration S per time t).

The Law of Mass Action

- For a simple reaction such as

$$\mathbf{S_1 + S_2 \rightleftharpoons 2P}$$

the reaction rate reads

$$v = v_+ - v_- = (k_+ S_1 \cdot S_2) - (k_- P^2)$$

the rate of forward reaction

the rate of backward reaction

rate constants

[The molecularity of S_1 and S_2 is 1, and of P is 2.]

The Law of Mass Action

- The general mass action rate law for a reaction transforming m substrates with concentrations S_i (i=1,..,m) into n products with concentrations P_j (j=1,..,n) reads

$$v = v_+ - v_- = k_+ \prod_{i=1}^{m} (S_i)^{q_i} - k_- \prod_{j=1}^{n} (P_j)^{q_j}$$

where q_i and q_j are the respective molecularities.

Chemical Equilibrium

- All reactions in a closed system, that is a system which is isolated from the surroundings, will tend to <u>thermodynamic equilibrium</u>.

- At equilibrium, the forward and backward rates will be equal, and the net rate zero:

$$v_+ - v_- = 0$$

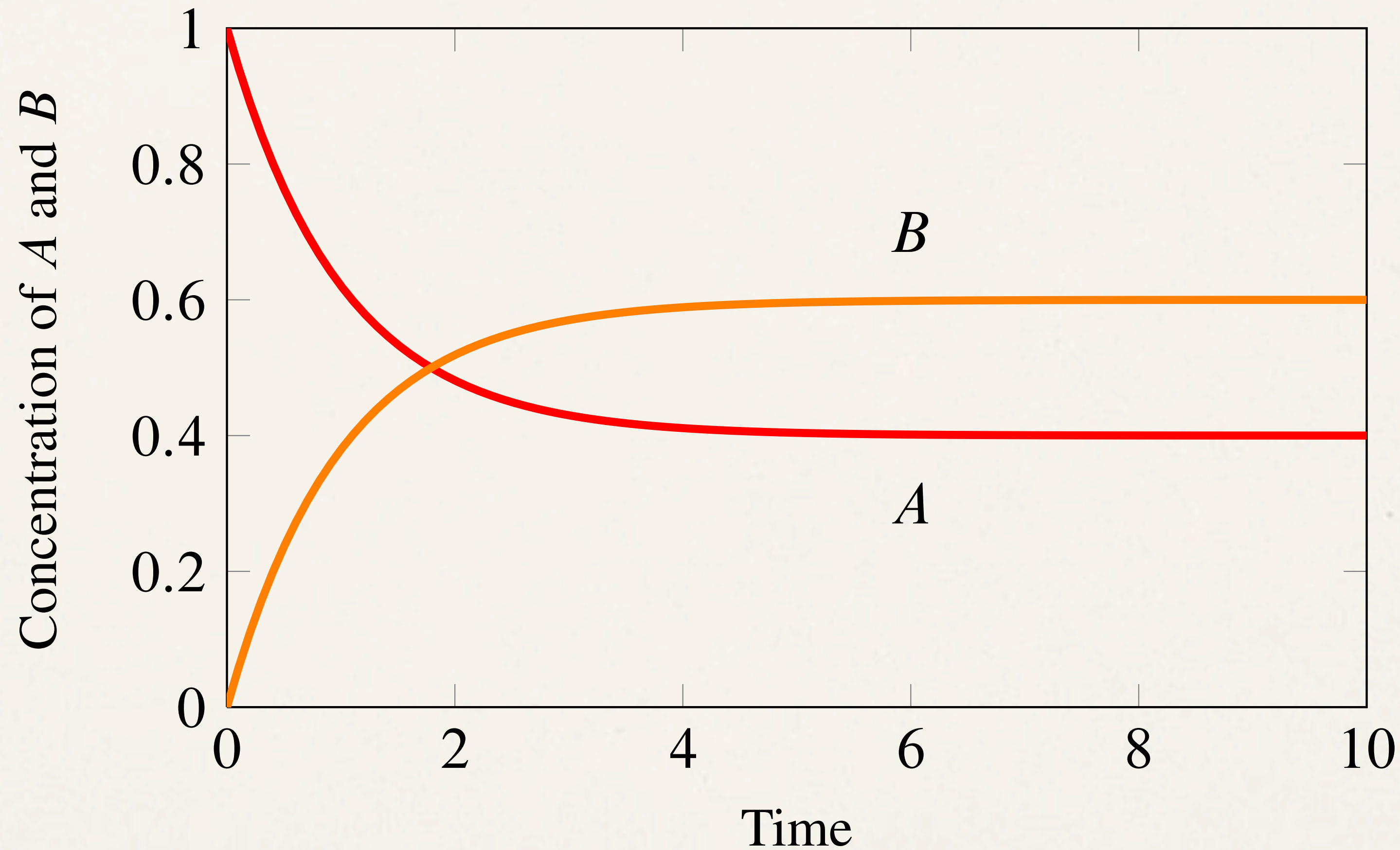
Chemical Equilibrium

- The equilibrium constant K_{eq} characterizes the ratio of substrate and product concentrations in equilibrium, i.e., the state with equal forward and backward rate:

$$K_{eq} = \frac{k_+}{k_-} = \frac{\prod_{j=1}^{n} (P_{j,eq})^{q_j}}{\prod_{i=1}^{m} (S_{i,eq})^{q_i}}$$

Chemical Equilibrium

$$A \leftrightharpoons B \qquad \frac{dA}{dt} = k_2 B - k_1 A$$



Approach to equilibrium: k_1=0.6, k_2=0.4, A(0)=1, B(0)=0.

Chemical Equilibrium

- The equilibrium constant for the reaction

$$\mathbf{S_1 + S_2 \rightleftharpoons 2P}$$

is

$$K_{eq} = \frac{P_{eq}^2}{S_{1,eq} \cdot S_{2,eq}}$$

- The dynamics of the reaction away from equilibrium are described by the ODEs:

$$\frac{\mathrm{d}S_1}{\mathrm{d}t} = \frac{\mathrm{d}S_2}{\mathrm{d}t} = -v \qquad \text{and} \qquad \frac{\mathrm{d}P}{\mathrm{d}t} = 2v$$

Chemical Equilibrium

- For the reaction

$$\mathbf{S_1 + S_2 \rightleftharpoons 2P}$$

the equilibrium constant is also known as the association constant

$$K_a = \frac{P_{eq}^2}{S_{1,eq} \cdot S_{2,eq}}$$

Chemical Equilibrium

- For the reaction

$$\mathbf{2P \rightleftharpoons S_1 + S_2}$$

the equilibrium constant is also known as the <u>dissociation constant</u>

$$K_d = \frac{S_{1,eq} \cdot S_{2,eq}}{P_{eq}^2}$$

Acknowledgments

- *"Enzyme Kinetics for Systems Biology,"* by H.M. Sauro, 2012.