Bio-Systems Modeling and Control

Lecture 17

Rate of Chemical Reaction – the Law of Mass Action

References:

- J.D. Murray “Mathematical Biology”, Second corrected Edition, Springer 1993
- Edward K. Yeargers, Ronald W. Shonkwiler & James V. Herod “An Introduction to the Mathematics of Biology” (With Computer Algebra Models), Birkhauser 1996.

References: (cont'd)

- James Keener & James Sneyd "Mathematical Physiology", Springer - Verlag 1998
- Robert B. Northrop

"Endogenous and Exogenous Regulation and Control of Physiological Systems"

Chapman & Hall / CRC 2000.

Rate Equations of Chemical Reactions

- Rate equations convey information about the speed of specific reactions, and about equilibrium conditions.
- Reactions may be reversible (bi-directional) or irreversible (uni-directional).
- As reactants are consumed their concentrations decay, and simultaneously the concentrations of products build up.

Irreversible Reactions

- Example: A + B → X
- There is one molecule of each of the reactants A and B, chemically combining to make one molecule of a product X.
- By Conservation of Mass the rate of disappearance of the reactants equal the rate of appearance of the product.

Conservation of Mass applied to an irreversible chemical reaction

$$\frac{d[X]}{dt} = -\frac{d[A]}{dt} = -\frac{d[B]}{dt} \Rightarrow$$

$$\Rightarrow [X](t) - [X](0) =$$

$$= -[A](t) + [A](0) = -[B](t) + [B](0)$$

- [A] is the concentration of A etc.
- If any one of the concentrations is known, then we know all other concentrations.
- Must know first how fast the reaction is.

The Law of Mass Action

- Model is due to Lotka (yes, same Lotka whom we met regarding predator-prey models).
- This “law” is not really a “physical-law-with-no-exceptions”. It is a useful model.
- There are many situations in which it is not valid.
- Law says: “ The rate at which chemical reactants combine is proportional to the product of their concentrations”

Law of Mass Action applied to irreversible process

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

$$\frac{d[X]}{dt} = k[A][B]$$

Factor of proportionality (Rate Constant) k depends on the geometrical shapes and sizes of the reactant molecules, and on the temperature of the mixture.

Law of Mass Action Explained

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

$$\frac{d[X]}{dt} = k[A][B]$$

Reaction rate depends on the # of collisions per time unit between the two reactants, and the probability that a collision is sufficiently energetic to overcome the free energy of activation of the reaction. # of collisions is proportional to [A][B].

Long Known Exceptions to the Law of Mass Action

- Model may not be valid if concentrations are very high.
- If concentrations are very low, it may not be appropriate to represent concentration as a continuous variable.
- Many more exceptions to the rule have been discovered recently as technological advances now allow scientists to actually record and observe the progression of many chemical reactions.

What is “concentration”?

- If reaction occurs in a closed reaction vessel (Ex: beaker with a fixed amount of water) → Concentration is “# of molecules divided by the fixed volume of the medium”.
- Open reaction vessels (ex: the heart) are more complicated → concentrations determined by the inflowing volume of reactants.

More about concentrations in a irreversible reaction

- It's ok for the product (or products) to be fully or partially un-dissolved, or to precipitate out of the solution (a reason why a reaction may be irreversible).
- Still, even for an insoluble product, its concentration is the # of molecules per volume of medium.
- Reactants must remain dissolved.

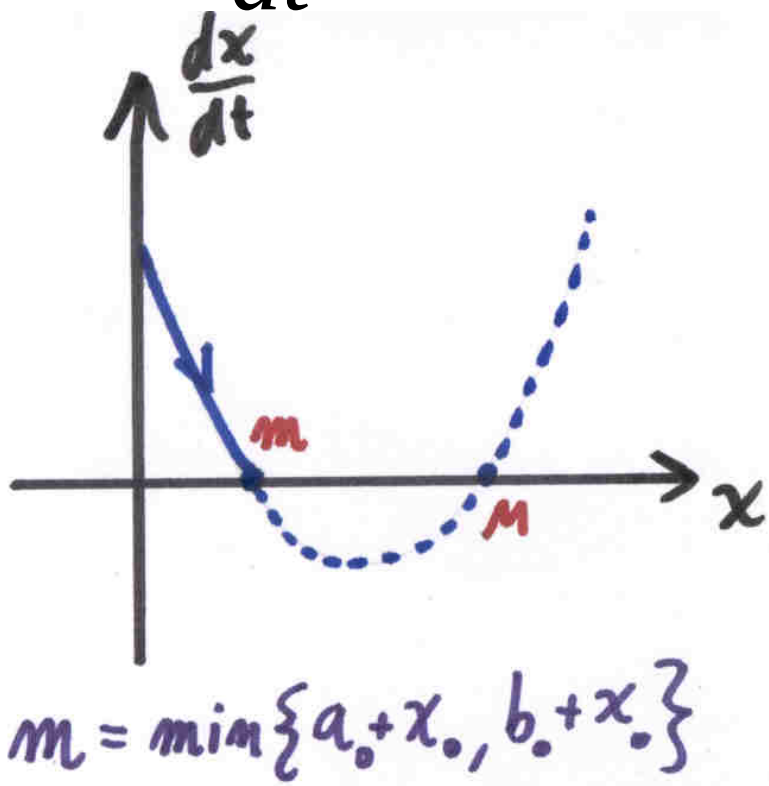
Mathematical analysis of simple irreversible reaction in a closed vessel: (Let [A]=a,[B]=b,[X]=x)

$$\frac{dx}{dt} = kab = k(a_0 + x_0 - x)(b_0 + x_0 - x)$$

- Recall: $x - x_0 = -a + a_0 = -b + b_0$ (conservation of mass)
- As we said, knowing x implies that we know a and b. The three are dependent variables.

Phase-Plane solution

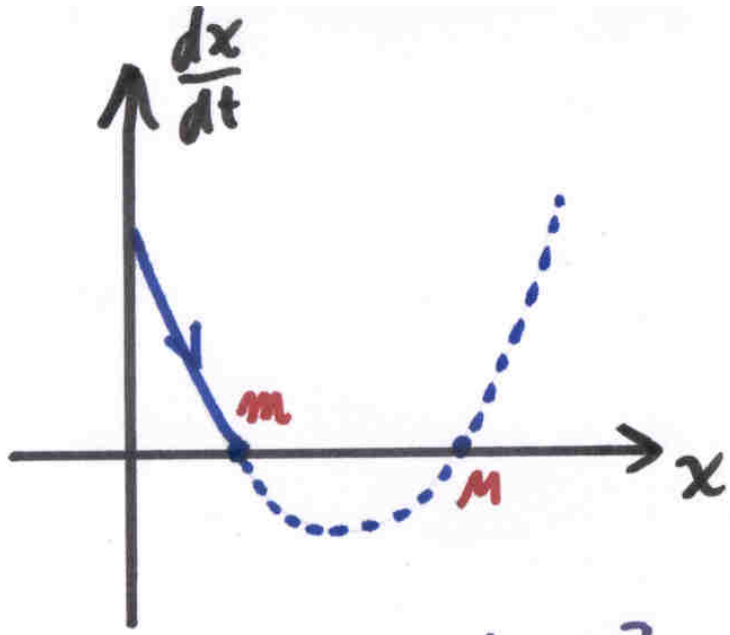
$$\frac{dx}{dt} = kab = k(a_0 + x_0 - x)(b_0 + x_0 - x)$$



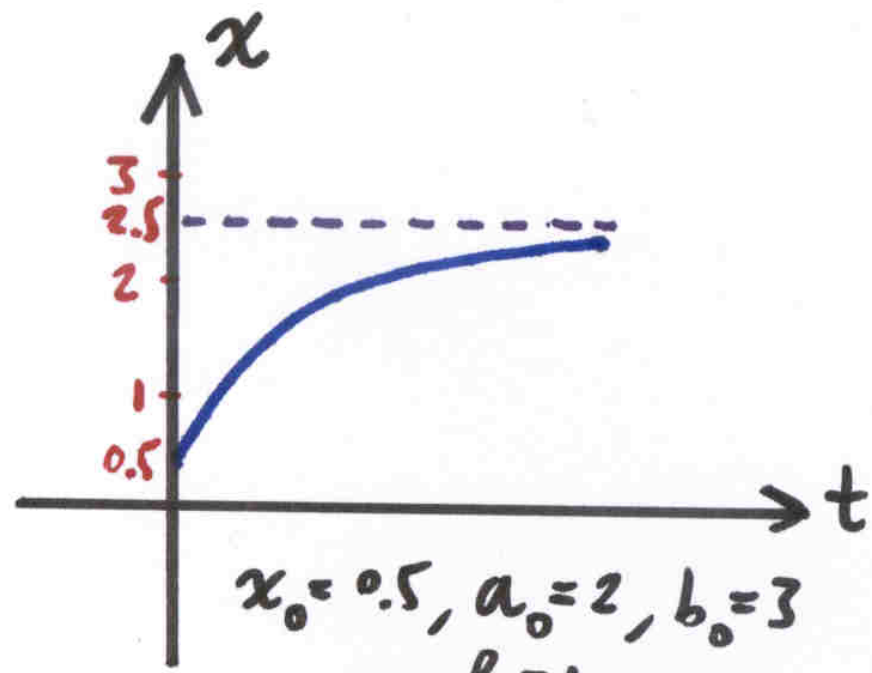
If $a_0 > b_0$ then
$M = a_0 + x_0, m = b_0 + x_0$

And vice versa

Irreversible reactions are limited by the first reactant to be exhausted



$$m = \min\{a_0 + x_0, b_0 + x_0\}$$



$x_0 = 0.5,\ a_0 = 2,\ b_0 = 3$

$k = 1$

Numerical example

Reversible Reactions

- $A+B \rightleftharpoons X+Y$ (example to a reaction involving one molecule of each reactant and one molecule of each of the products X and Y).
- We shall denote by k_+ the forward rate constant, and by k_- the reverse rate constant.
- If a reverse reaction is much slower than the forward reaction ($k_- << k_+$), the whole reaction behaves approximately like an irreversible reaction.

Kinetics of Reversible Reactions

$$\frac{dx}{dt} = \frac{dy}{dt} = -\frac{da}{dt} = -\frac{db}{dt}$$

$$\frac{dx}{dt} = k_{+}ab - k_{-}xy$$

- Under normal circumstances, forward and reverse reactions are independent of each other, and therefore effects on the net rate are additive.
- [A]=a, [B]=b, [X]=x, [Y]=y

Analysis of Reversible Reactions Kinetics

$$\frac{dx}{dt} = k_+ ab - k_- xy =$$

$$= k_+ (a_0 + x_0 - x)(b_0 + x_0 - x) - k_- x(y_0 - x_0 + x) =$$

$$= (k_+ - k_-)x^2 - [k_+ (a_0 + b_0 + 2x_0) + k_- (y_0 - x_0)]x +$$

$$+ k_+ (a_0 + b_0)(b_0 + x_0) =$$

$$= (k_+ - k_-)(x - \alpha)(x - \beta)$$

There are two equilibria: $x_e = \alpha$ and $x_e = \beta$ if rate constants are not equal.

So actually, reversible and irreversible reactions behave very similarly:

$$\frac{dx}{dt} = k_+ ab - k_- xy =$$

$$= (k_+ - k_-)x^2 - [k_+(a_0 + b_0 + 2x_0) + k_-(y_0 - x_0)]x +$$

$$+ k_+(a_0 + b_0)(b_0 + x_0) =$$

$$= (k_+ - k_-)(x - \alpha)(x - \beta)$$

Let $\alpha<\beta$. Then $x(t)$ converges to $x=\alpha$.

The larger $(\beta-\alpha)(k_+-k_-)$ the faster the convergence.

If forward and reverse rate constants are equal ($k_+=k_-=k$) :

$$\frac{dx}{dt} = k(ab - xy) =$$

$$= -k(a_0 + b_0 + x_0 + y_0)x +$$

$$+ k(a_0 + b_0)(b_0 + x_0) =$$

$$= k(x - A)$$

$$A = \frac{(a_0 + b_0)(b_0 + x_0)}{a_0 + b_0 + x_0 + y_0}$$

The only equilibrium point

Steady-state Concentrations

$$\frac{dx}{dt} = 0 = k_{+} a_e b_e - k_{-} x_e y_e$$

We sometimes refer to a constant $K_{eq}=k_{-}/k_{+}$ as the <u>equilibrium constant</u>. It plays a role in determining relative concentrations at steady state.

How to extend to more complex reactions?

- If we have a chemical reaction that is characterized by its stoichiometric coefficients, does the use of the Law of Mass Action follow the upcoming procedure?
- It turns out that things are not so simple…

Wrong Theory Extension to the case:

$$n_A A + n_B B \rightleftharpoons n_X X + n_Y Y$$

$$\boxed{\frac{dx}{dt} = k_+ a^{n_A} b^{n_B} - k_- x^{n_X} y^{n_Y}}$$

Should the stoichiometric chemical reaction balance coefficients (n_A, n_B etc) appear (respectively) as powers to the respective concentrations? (more atoms colliding?!)

Wrong Theory Extension to the case:

$$n_A A + n_B B \rightleftharpoons n_X X + n_Y Y$$

$$\frac{dx}{dt} = k_+ a^{n_A} b^{n_B} - k_- x^{n_X} y^{n_Y}$$

- By conservation of mass, it is still a scalar differential equation.
- What is the relationship among a,b,x and y? → Need to extend these relationships as well.

Conservation of Mass Relationships

$$n_A A + n_B B \rightleftharpoons n_X X + n_Y Y$$

$$n_X \frac{dx}{dt} = n_Y \frac{dy}{dt} = -n_A \frac{da}{dt} = -n_B \frac{db}{dt}$$

- To illustrate the idea let: 2A+B→X.
- If a is the concentration of A (i.e. # molecules per volume), then in the above reaction A is depleted twice faster than B, as each reaction consumes two molecules of A and only one of B.

Conservation of Mass Solution

$$n_A A + n_B B \rightleftharpoons n_X X + n_Y Y$$

$$n_X \frac{dx}{dt} = n_Y \frac{dy}{dt} = -n_A \frac{da}{dt} = -n_B \frac{db}{dt}$$

$$n_X (x - x_0) = n_Y (y - y_0) = -n_A (a - a_0) = -n_B (b - b_0)$$

- Can we now use these extended relationships to convert a,b and y into x expressions in the dx/dt equation?
- For instance: $a=a_0+(n_X/n_A)(x_0-x)$.

Wrong scalar rate equation:

$$n_A A + n_B B \rightleftharpoons n_X X + n_Y Y$$

$$n_X(x - x_0) = n_Y(y - y_0) = -n_A(a - a_0) = -n_B(b - b_0)$$

$$\frac{dx}{dt} = k_+ a^{n_A} b^{n_B} - k_- x^{n_X} y^{n_Y} =$$

$$= k_+ [a_0 + \frac{n_X}{n_A}(x_0 - x)]^{n_A} [b_0 + \frac{n_X}{n_B}(x_0 - x)]^{n_B}$$

$$- k_- x^{n_X} [y_0 + \frac{n_X}{n_Y}(x - x_0)]^{n_Y}$$

The trouble is…

- The extensions to the Law of Mass Action (using the stoichiometric coefficients) were disputed experimentally.
- It is just a theory that has no basis.
- In recent years it has become easier to observe empirically the progression of a chemical reaction, and assess its timing characteristics.

The Order of a Reaction

- The order of an experimental rate equation describes how the rate depends on the power of the concentration terms.
- The following examples are drawn from:
- www.chem.ox.ac.uk/vrchemistry/rates/new html/

Example 1: The decomposition of N_2O_5

$$2N_2O_5 \rightarrow 4NO_2 + O_2$$

$$-\frac{d[N_2O_5]}{dt} = k[N_2O_5]$$

- What is the order of the reaction?
- Answer: First order (and not second order).
- It has nothing to do with the stoichiometric coefficients

Example 2: Reduction of NO with H_2

$$2NO + 2H_2 \rightarrow N_2 + 2H_2O$$

$$-\frac{d[NO]}{dt} = k[NO]^2[H_2]$$

- What is the order of the reaction?
- Answer: 3rd Order overall, 2nd Order w.r.t NO and 1st Order w.r.t H_2
- These are the empirical facts.

Example 3: Reaction of Chlorine with Chloroform to yield Carbon Tetrachloride and Hydrogen Chloride

$$CHCl_3 + Cl_2 \rightarrow CCl_4 + HCl$$

$$\frac{d[HCl]}{dt} = k[CHCl_3][Cl_2]^{1/2}$$

- What is the order of the reaction?
- Answer: 1.5 overall, 1st Order w.r.t $CHCl_3$ and 0.5 Order w.r.t Cl_2
- Orders of reactions may be non-integer.

The reason that the coefficients in the balanced equation and in the rate law generally do not agree is that the actual chemical reaction mechanism usually is not a simultaneous collision of as many molecules as the coefficients indicate. Instead, the overall mechanism is built up from a series of smaller steps.

Here is what really happens

- Four- and five-body simultaneous collisions are very improbable events.
- A reaction in which four or five molecules interact is much more likely to occur in a series of steps, in which two reactant molecules first collide and form an intermediate substance, this substance collides with the next reactant molecule, and so on.

Here is what really happens

- The observed rate law is a summary of all of these steps, and may depend on reactant concentrations in a complicated way.
- The form of the experimental rate law is the first step on the way toward unscrambling the actual mechanism of reaction, but it does not give us the entire story.

Here is what really happens

- Only for simple, one-step reactions will the order of the rate law necessarily agree with the coefficients of the balanced equation.
- This occurs almost exclusively with first-order decompositions and with those relatively rare second-order collisions that are uncomplicated by further reactions.

What about equilibrium conditions?

$$H_2 + I_2 \rightarrow 2HI$$

$$\frac{d[HI]}{dt} = k[H_2][I_2]$$

$$K_{eq} = \frac{[HI]^2}{[H_2][I_2]}$$

$$I_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 2I$$

$$H_2 + 2I \xrightarrow{k_3} 2HI$$

- What has just been said applies to rate expressions, but not to equilibrium-constant expressions.
- The exponential coefficients in the equilibrium-constant expression *do* match the coefficients in the balanced chemical equation.

Multi-Step Reactions

$$H_2 + I_2 \rightarrow 2HI$$

$$\frac{d[HI]}{dt} = k[H_2][I_2]$$

$$K_{eq} = \frac{[HI]^2}{[H_2][I_2]}$$

$$I_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 2I$$

$$H_2 + 2I \xrightarrow{k_3} 2HI$$

- Actually there is a reversible dissociation of I_2 into 2I reaching a rapid equilibrium.
- The next step is slow and this is the one determining the rate of the reaction.