CMACS
Computational Modeling and Analysis for Complex Systems

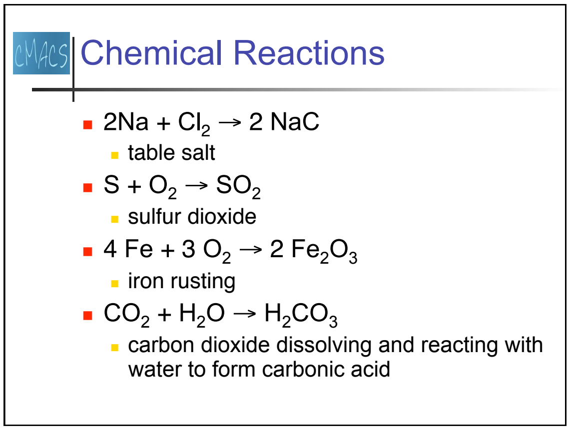
Chemical Kinetics

What is chemical kinetics

- The study of the rates at which chemical reactions take place
- Factors to consider
    - **Concentration**
    - Temperature
    - **Presence of catalysts**

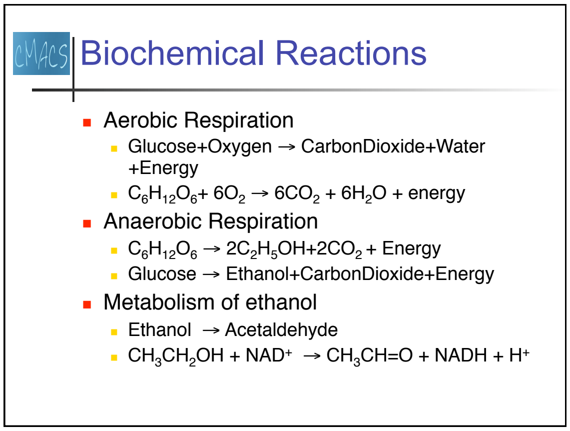
Reaction rates

The ***rate*** of a chemical reaction is a measure of how the concentration (or pressure) of the involved substances changes with time.



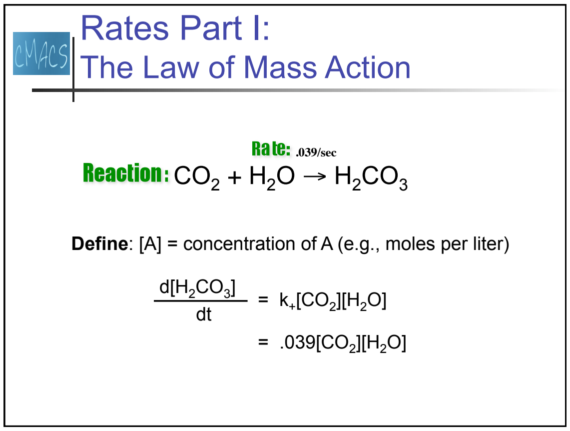
Chemical Reactions

- $2Na + Cl_2 \rightarrow 2\ NaC$
  - table salt
- $S + O_2 \rightarrow SO_2$
  - sulfur dioxide
- $4\ Fe + 3\ O_2 \rightarrow 2\ Fe_2O_3$
  - iron rusting
- $CO_2 + H_2O \rightarrow H_2CO_3$
  - carbon dioxide dissolving and reacting with water to form carbonic acid



Biochemical Reactions

- Aerobic Respiration
  - Glucose+Oxygen → CarbonDioxide+Water +Energy
  - $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$ + energy
- Anaerobic Respiration
  - $C_6H_{12}O_6 \rightarrow 2C_2H_5OH + 2CO_2$ + Energy
  - Glucose → Ethanol+CarbonDioxide+Energy
- Metabolism of ethanol
  - Ethanol → Acetaldehyde
  - $CH_3CH_2OH + NAD^+ \rightarrow CH_3CH{=}O + NADH + H^+$



Rates Part I: The Law of Mass Action

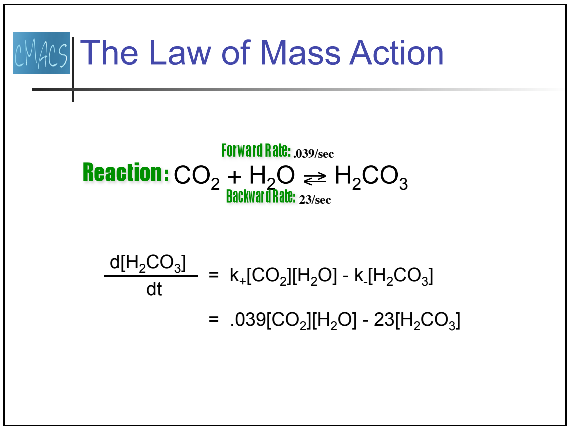
Rate: .039/sec

Reaction: $CO_2 + H_2O \rightarrow H_2CO_3$

Define: [A] = concentration of A (e.g., moles per liter)

$$\frac{d[H_2CO_3]}{dt} = k_+[CO_2][H_2O]$$

$$= .039[CO_2][H_2O]$$

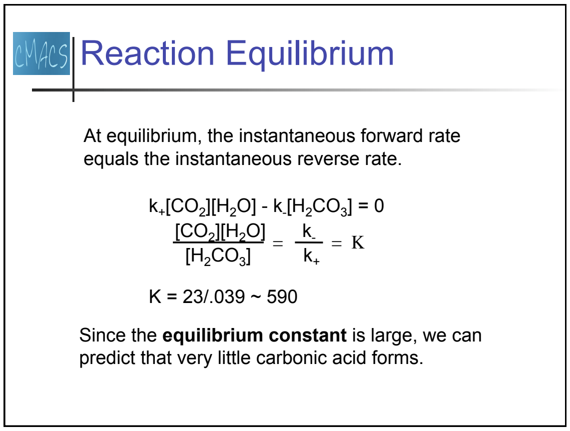


The Law of Mass Action

Reaction: $CO_2 + H_2O \underset{\text{Backward Rate: 23/sec}}{\overset{\text{Forward Rate: .039/sec}}{\rightleftharpoons}} H_2CO_3$

$$\frac{d[H_2CO_3]}{dt} = k_+[CO_2][H_2O] - k_-[H_2CO_3]$$

$$= .039[CO_2][H_2O] - 23[H_2CO_3]$$



Reaction Equilibrium

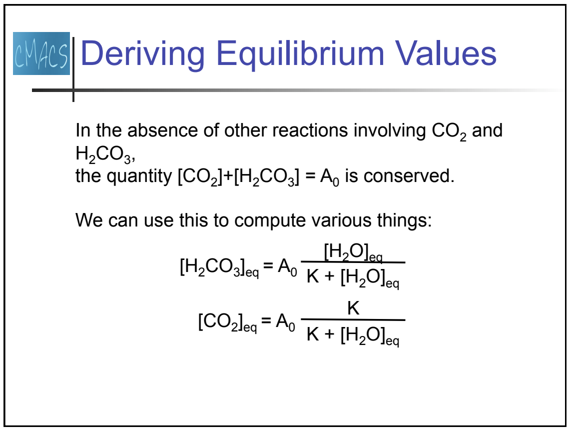
At equilibrium, the instantaneous forward rate equals the instantaneous reverse rate.

$$k_+[CO_2][H_2O] - k_-[H_2CO_3] = 0$$

$$\frac{[CO_2][H_2O]}{[H_2CO_3]} = \frac{k_-}{k_+} = K$$

$K = 23/.039 \sim 590$

Since the **equilibrium constant** is large, we can predict that very little carbonic acid forms.



Deriving Equilibrium Values

In the absence of other reactions involving CO_2 and H_2CO_3,
the quantity $[CO_2]+[H_2CO_3] = A_0$ is conserved.

We can use this to compute various things:

$$[H_2CO_3]_{eq} = A_0 \frac{[H_2O]_{eq}}{K + [H_2O]_{eq}}$$

$$[CO_2]_{eq} = A_0 \frac{K}{K + [H_2O]_{eq}}$$

Forming Dimers

M is a monomer
D is a dimer

$$M + M \underset{k_-}{\overset{k_+}{\rightleftarrows}} D$$

$$\frac{d[M]}{dt} = 2k_-[D] - 2k_+[M][M]$$

Forming Dimers - Exercise

$$\frac{d[M]}{dt} = 2k_-[D] - 2k_+[M]^2$$

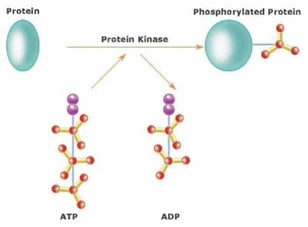
$$\frac{d[D]}{dt} = -k_-[D] + k_+[M]^2$$

$$\frac{d[D]}{dt} = -1/2\frac{d[M]}{dt}$$

[M] + 2[D] is conserved

Organic Chemical Reactions

Phosphorylation



Example of enzymatic action

Enzyme Kinetics

- A kinase is an enzyme
- Enzymes are catalysts that make reactions faster
  - Catalytic power
  - Specificity
  - Regulation
- Can increase speeds up to 1 million times

Enzyme Kinetics

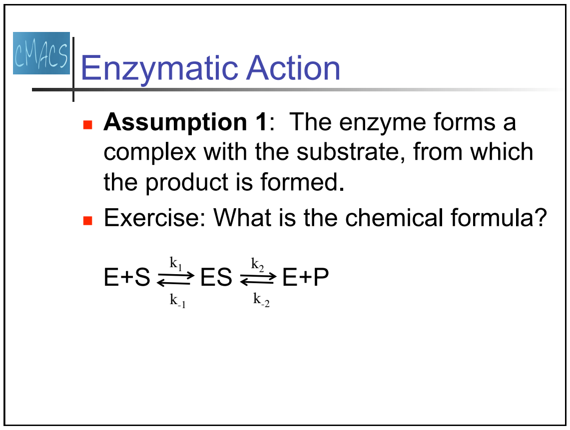
- Enzymes don’t follow the law of mass action directly
- By the law of mass action, the rate of
  S+E->P+E
  would increase linearly with increasing [S]
- In enzymatic reactions, the rate increases less than linearly with the increase in S and reaches a maximum

Rate Laws: Enzymatic Action

Instead of

$S+E \rightleftarrows P+E$

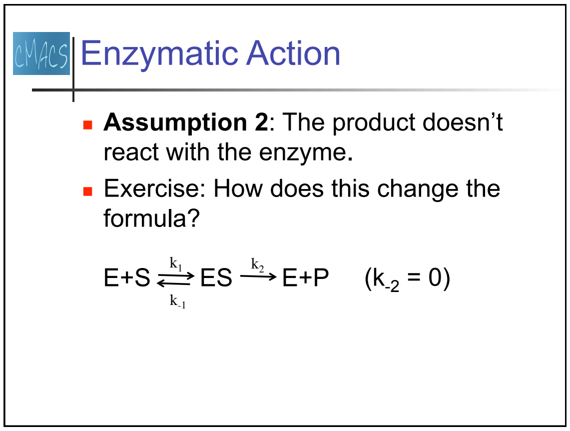
the reaction creates a complex SE from the substrate and enzyme, followed by dissociation of the complex into the product and the enzyme.



Enzymatic Action

- **Assumption 1**: The enzyme forms a complex with the substrate, from which the product is formed.
- Exercise: What is the chemical formula?

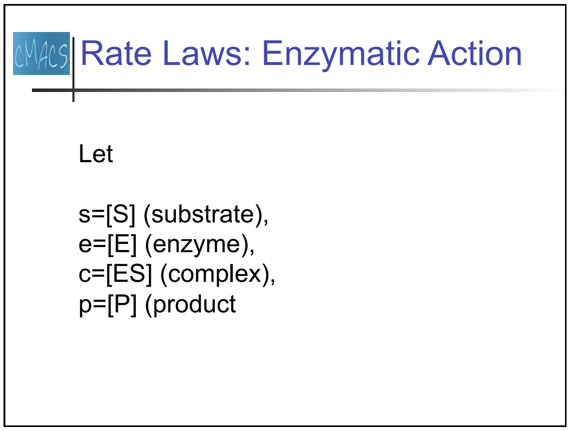
$$E+S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} E+P$$



Enzymatic Action

- **Assumption 2**: The product doesn't react with the enzyme.
- Exercise: How does this change the formula?

$$E+S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow{k_2} E+P \quad (k_{-2} = 0)$$



Rate Laws: Enzymatic Action

Let

s=[S] (substrate),
e=[E] (enzyme),
c=[ES] (complex),
p=[P] (product

Exercises

- Rate of change of substrate:

  $$\frac{ds}{dt} = -k_1se + k_{-1}c$$

- Rate of change of complex:

  $$\frac{dc}{dt} = k_1se - k_{-1}c - k_2c$$

- Rate of change of enzyme:

  $$\frac{de}{dt} = -k_1se + k_2c + k_{-1}c$$

- Rate of change of product:

  $$\frac{dp}{dt} = k_2c$$

Equilibrium Approximation

- $p = 1/2\ k_2\ c^2 + p_0$
- Conserved quantity:

  $$\frac{dc}{dt} + \frac{de}{dt} = 0, \text{ so } c + e = e_0$$

Equilibrium Approximation

- **Assumption 3:**

  $$S+E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C$$

  reaches instantaneous equilibrium:

  $$k_1se = k_{-1}c$$

- From $e+c=e_0$ ($e = e_0 - c$):

  $$k_1se_0 - k_1sc = k_{-1}c$$

  $$k_1se_0 = k_{-1}c + k_1sc$$

  $$c = \frac{k_1se_0}{k_{-1} + k_1s} = \frac{e_0s}{K_1 + s}$$

  where $K_1 = \frac{k_{-1}}{k_1}$

Equilibrium Approximation

- Rate of formation of product:

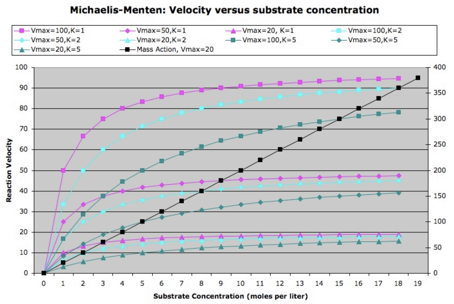
$$V = \frac{dp}{dt} = k_2c = \frac{k_2e_0s}{K_1 + s} = \frac{V_{max}s}{K_1 + s}$$

- Versus Law of Mass Action:

$$S + E \rightarrow P + E$$

$$V = \frac{dp}{dt} = k_2se_0 = V_{max}s$$

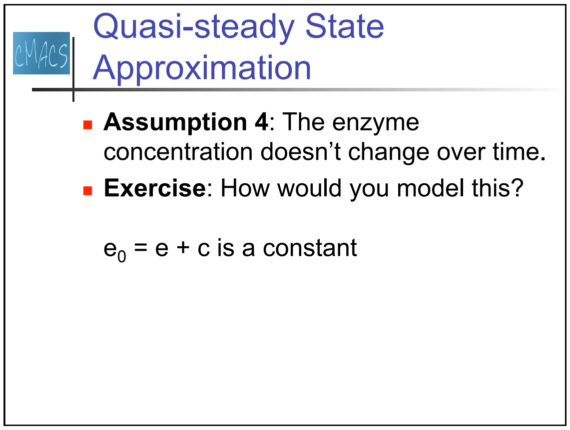
Equilibrium Approximation versus Mass Action



Quasi-steady State Approximation

- **Assumption 3**: The concentration of the complex changes much more slowly than the concentrations of the substrate and the product
- **Exercise**: How would you model this?

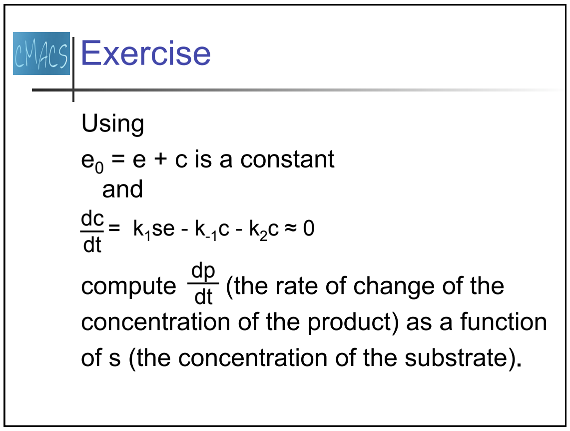
$$\frac{dc}{dt} = k_1se - k_{-1}c - k_2c \approx 0$$



Quasi-steady State Approximation

- **Assumption 4**: The enzyme concentration doesn't change over time.
- **Exercise**: How would you model this?

$e_0 = e + c$ is a constant



Exercise

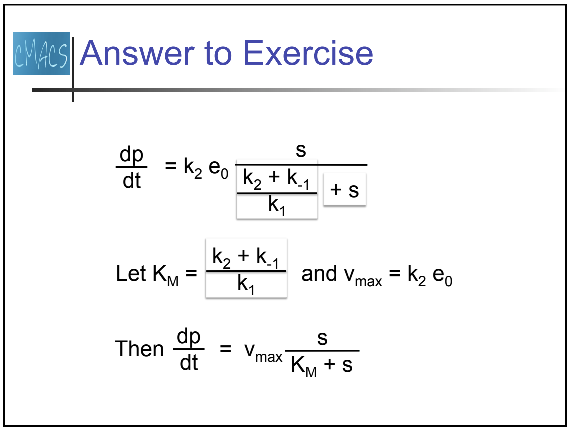
Using

$e_0 = e + c$ is a constant

and

$$\frac{dc}{dt} = k_1 se - k_{-1}c - k_2 c \approx 0$$

compute $\frac{dp}{dt}$ (the rate of change of the concentration of the product) as a function of s (the concentration of the substrate).

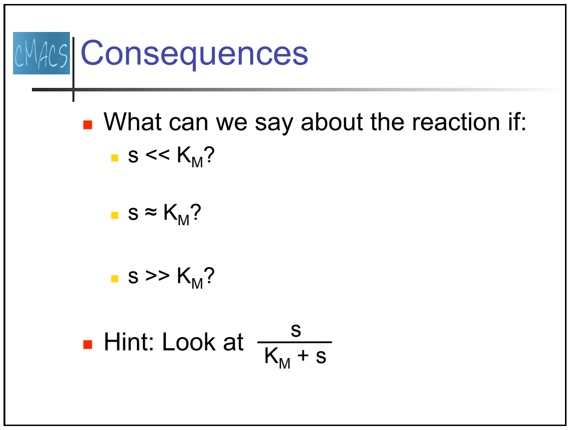


Answer to Exercise

$$\frac{dp}{dt} = k_2 e_0 \frac{s}{\boxed{\frac{k_2 + k_{-1}}{k_1}} + s}$$

Let $K_M = \boxed{\frac{k_2 + k_{-1}}{k_1}}$ and $v_{max} = k_2 e_0$

Then $\frac{dp}{dt} = v_{max} \frac{s}{K_M + s}$



Consequences

- What can we say about the reaction if:
  - $s << K_M$?
  - $s \approx K_M$?
  - $s >> K_M$?
- Hint: Look at $\frac{s}{K_M + s}$