Biophysics I (BPHS 3090)

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Website: http://www.yorku.ca/cberge/3090W2015.html
Figure 2.19
Passive Transport: More than diffusion?

- Adding in other sugars affects things in a selective way.
- Saturation occurs.

Figure 6.1: Concentration (mmol/L) vs. Time (seconds)

Figure 6.2: Efflux (mmol/L-m) vs. Concentration (mmol/L)

Figure 6.3: Sorbose accumulation vs. Time (minutes)
Passive Transport: More than diffusion?

Structure of different solutes can have a big effect
Notion of a “carrier”

Carrier-Mediated Transport: glucose transporter as example

Distinguishing characteristics of glucose transport:
- facilitated -- i.e., faster than dissolve and diffuse
- structure specific -- different rates for even closely related sugars
- passive -- given a single solute, flow is down concentration gradient
- transport saturates -- solute-solute interactions
- transport can be inhibited -- solute-other interactions
- pharmacology (cytochalasin B)
- hormonal control (insulin)

similar to water channels (Hg, vasopressin)
Possible ‘Carrier’ Mechanisms

Mechanism 1

Initial State
- Solute
- Membrane

Binding

Translocation

Release

Reset

Mechanism 2

Mechanism 3
General Four-State Carrier Model

[Diagram showing the four-state model with states labeled as follows:

- $\bullet +$ to $\bullet$
- $\beta_1 \leftrightarrow \alpha_1$
- $\beta_4 \leftrightarrow \alpha_4$
- $\beta_3 \leftrightarrow \alpha_3$
- $\beta_2 \leftrightarrow \alpha_2$

Legend:
- Binding/Unbinding
- Translocation]
First-order, reversible reaction

\[ R \xrightleftharpoons[\beta]{\alpha} P \]

\[
\frac{dc_R(t)}{dt} = \beta c_P(t) - \alpha c_R(t) \quad \text{AND} \quad \frac{dc_P(t)}{dt} = \alpha c_R(t) - \beta c_P(t)
\]

Equilibrium:

\[
\frac{dc_R(t)}{dt} = \frac{dc_P(t)}{dt} = 0 \quad \Rightarrow \quad \beta c_P(\infty) = \alpha c_R(\infty)
\]

\[
\frac{c_P(\infty)}{c_R(\infty)} = \frac{\alpha}{\beta} = K_a \quad \text{(association, equilibrium, affinity, stability, binding, formation constant)}
\]

Kinetics: assume total amount of reactant and product is conserved

\[ c_R(t) + c_P(t) = C \]

\[
\frac{dc_R(t)}{dt} = \beta \left( C - c_R(t) \right) - \alpha c_R(t)
\]

\[
\frac{dc_R(t)}{dt} + (\alpha + \beta)c_R(t) = \beta C
\]
First-order, reversible reaction

\[ R \xrightleftharpoons{\alpha}{\beta} P \]

First-order linear differential equation with constant coefficients

\[ c_R(t) = c_R(\infty) - \left( c_R(\infty) - c_R(0) \right) e^{-t/\tau}, \text{ for } t > 0 \]

\[ c_R(\infty) = \frac{-\beta}{\alpha + \beta} C = \frac{1}{1 + K_a} C \quad \text{AND} \quad \tau = \frac{1}{\alpha + \beta} \]

First-order, reversible reaction

\[ R \xrightleftharpoons{\alpha}{\beta} P \]

\[ c_P(t) = C - c_R(t) \]

\[ \tau = \frac{1}{\alpha + \beta} \]
Second-order reversible (binding) reaction

\[ S + E \xrightarrow{\alpha}{\beta} ES \]

\[ \frac{dc_{ES}(t)}{dt} = \alpha c_S(t)c_E(t) - \beta c_{ES}(t), \]
\[ \frac{dc_S(t)}{dt} = -\frac{dc_E(t)}{dt} = \beta c_{ES}(t) - \alpha c_S(t)c_E(t), \]

Equilibrium:

\[ \frac{dc_{ES}(t)}{dt} = \frac{dc_S(t)}{dt} = \frac{dc_E(t)}{dt} = 0 \]

\[ \alpha c_S(\infty)c_E(\infty) - \beta c_{ES}(\infty) = 0 \]

\[ \frac{c_{ES}(\infty)}{c_S(\infty)c_E(\infty)} = \frac{\alpha}{\beta} = K_a \quad \text{(association constant)} \]

\[ \frac{1}{K_a} = \frac{c_S(\infty)c_E(\infty)}{c_{ES}(\infty)} = K \quad \text{(dissociation constant)} \]

Assume enzyme conserved: \[ c_E(t) + c_{ES}(t) = C_E \]

How does \( c_{ES} \) depend on \( c_S \)? Eliminate \( c_E \).

\[ C_E = c_E(\infty) + c_{ES}(\infty) \]

\[ C_E = \frac{Kc_{ES}(\infty)}{c_S(\infty)} + c_{ES}(\infty) = \left( \frac{K}{c_S(\infty)} + 1 \right) c_{ES}(\infty) \]

\[ c_{ES}(\infty) = \left( \frac{c_S(\infty)}{K + c_S(\infty)} \right) C_E \]

\( \rightarrow \) Law of mass action

\( \rightarrow \) Michaelis-Menten kinetics
Chemical Kinetics (v2)

Second-order reversible (binding) reaction

\[ S + E \overset{\alpha}{\underset{\beta}{\rightleftharpoons}} ES \]

Second-order reversible (binding) reaction

\[ S + E \overset{\alpha}{\underset{\beta}{\rightleftharpoons}} ES \]

Rectangular hyperbola: Michaelis-Menten Relation

\[ \frac{c_{ES}(\infty)}{C_{ET}} \]

\[ \frac{c_{S}(\infty)}{K} \]

Doubly-reciprocal coordinates: Lineweaver-Burk plot

\[ \frac{1}{c_{ES}(\infty)} = \left(1 + \frac{K}{c_{S}(\infty)} \right) \frac{1}{C_{ET}} = \left( \frac{K}{C_{ET}} \right) \frac{1}{c_{S}(\infty)} + \frac{1}{C_{ET}} \]

\[ \text{slope} = \frac{K}{C_{ET}} \]

→ Linear way to plot nonlinear relationship!
General Four-State Carrier Model

Binding/Unbinding

Translocation