Biophysics I (BPHS 4080)

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Website: http://www.yorku.ca/cberge/4080W2018.html

York University
Winter 2018
Lecture 7

Reference/Acknowledgement:
- TF Weiss (Cellular Biophysics)
- D Freeman

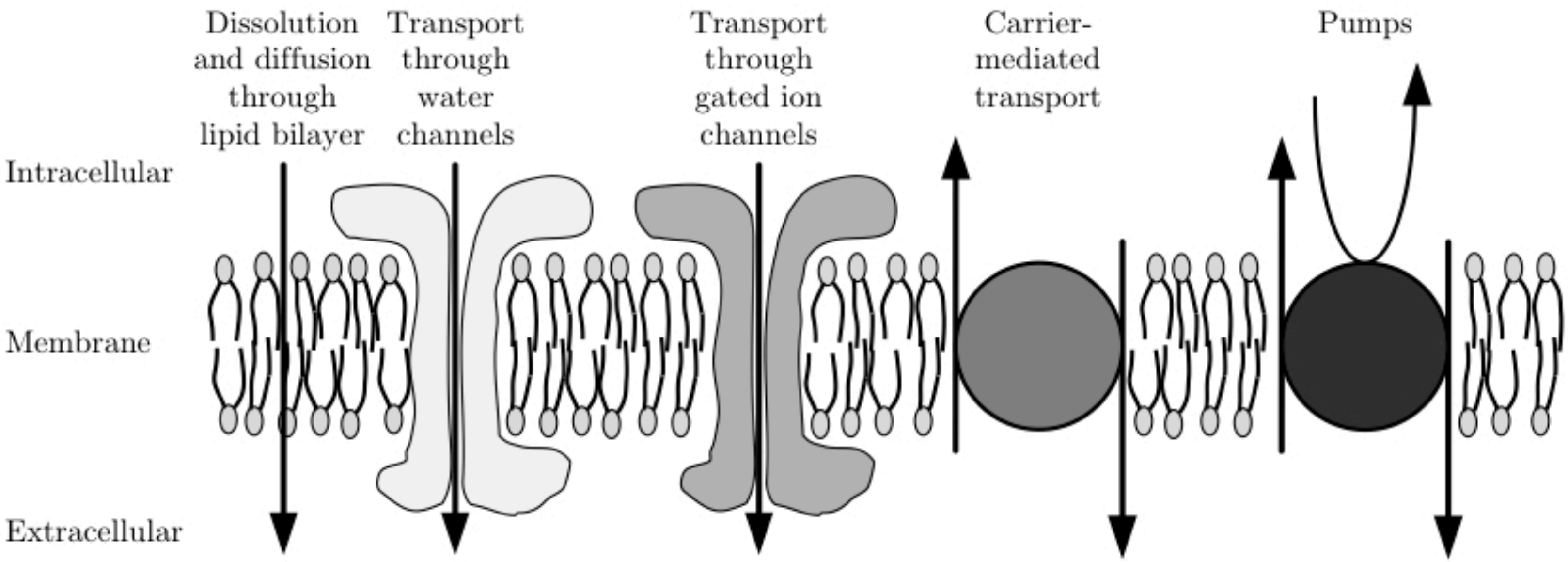

Dissolution and diffusion through lipid bilayer
Transport through water channels
Transport through gated ion channels
Carrier-mediated transport
Pumps
Intracellular
Membrane
Extracellular

Figure 2.19

Passive Transport: More than diffusion?

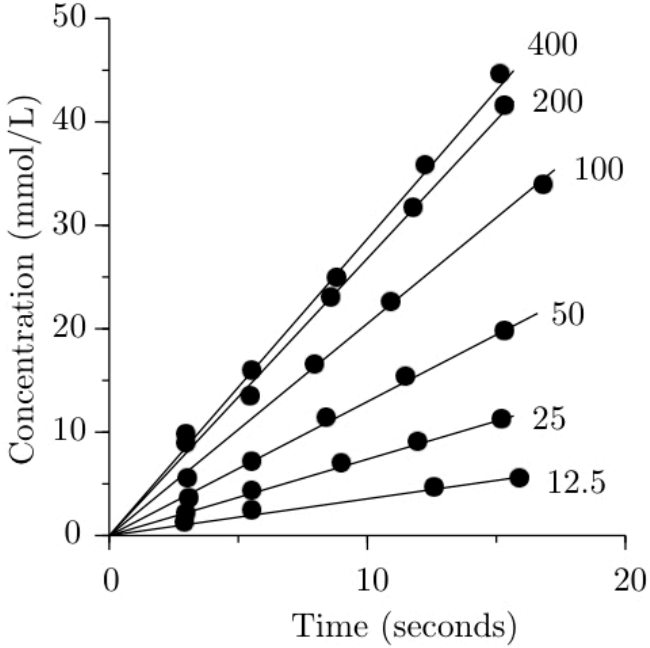


Figure 6.1

- Saturation occurs

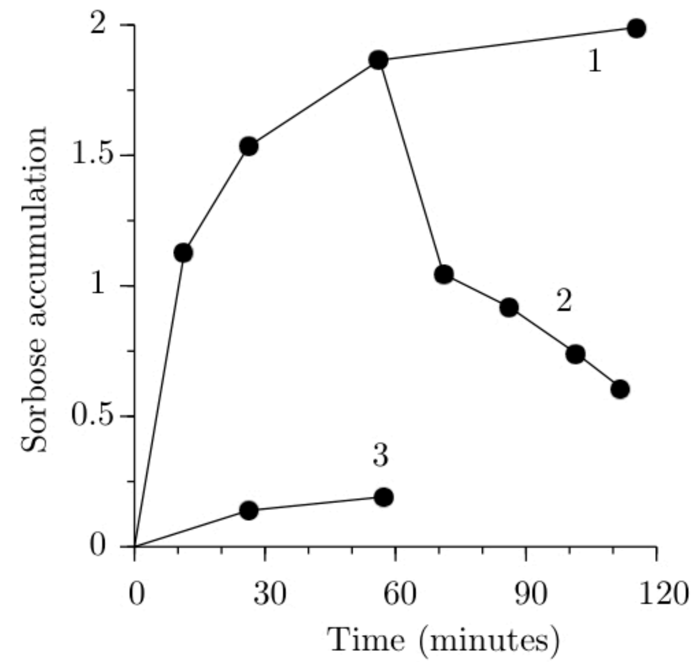


Figure 6.3

- Adding in other sugars affects things in a selective way

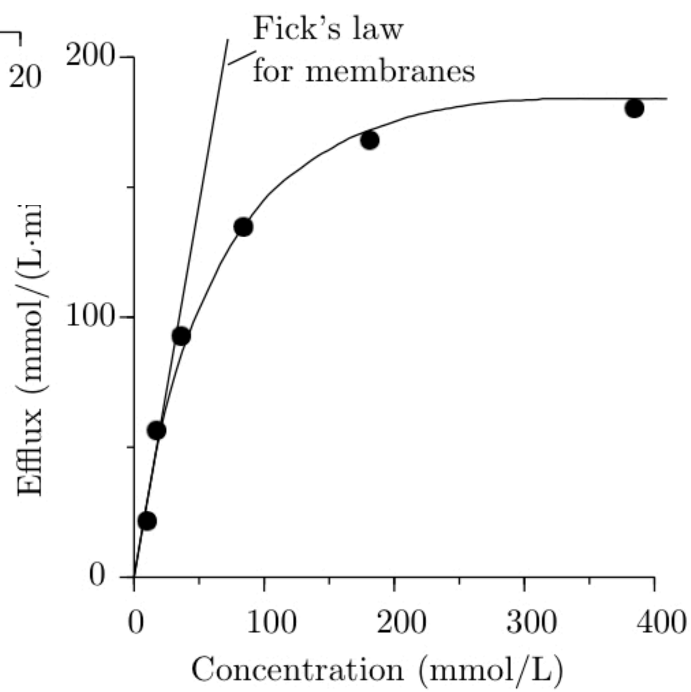


Figure 6.2

Passive Transport: More than diffusion?

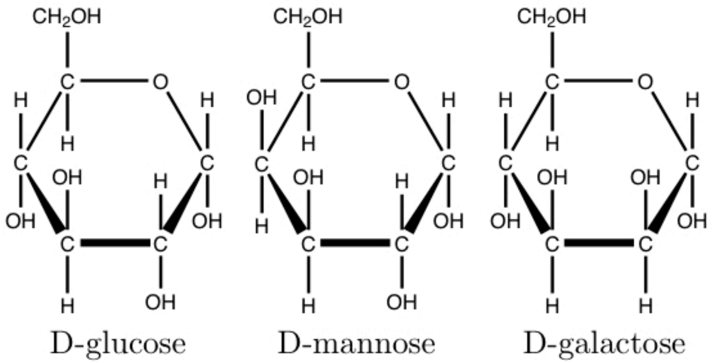


Figure 1.7

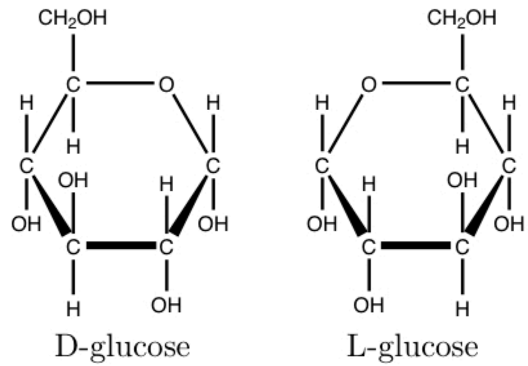


Figure 1.8

→ Structure of different solutes can have a big effect

Notion of a "carrier"

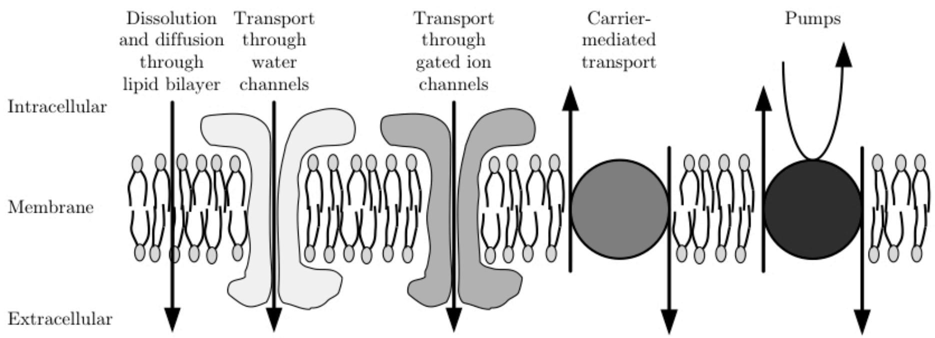
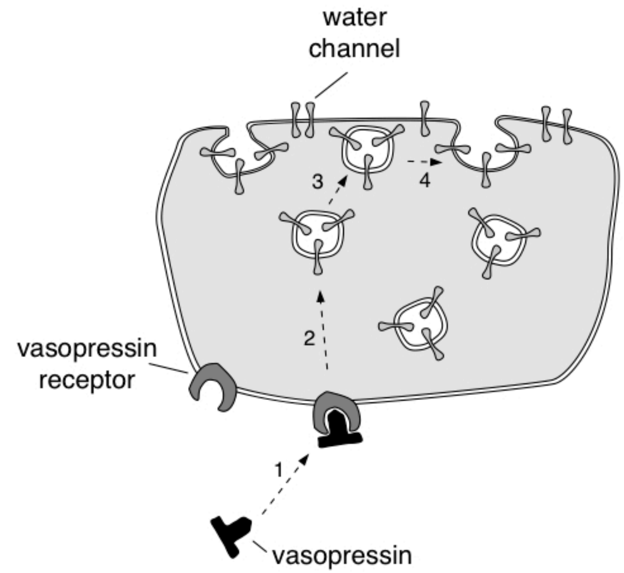


Figure 2.19



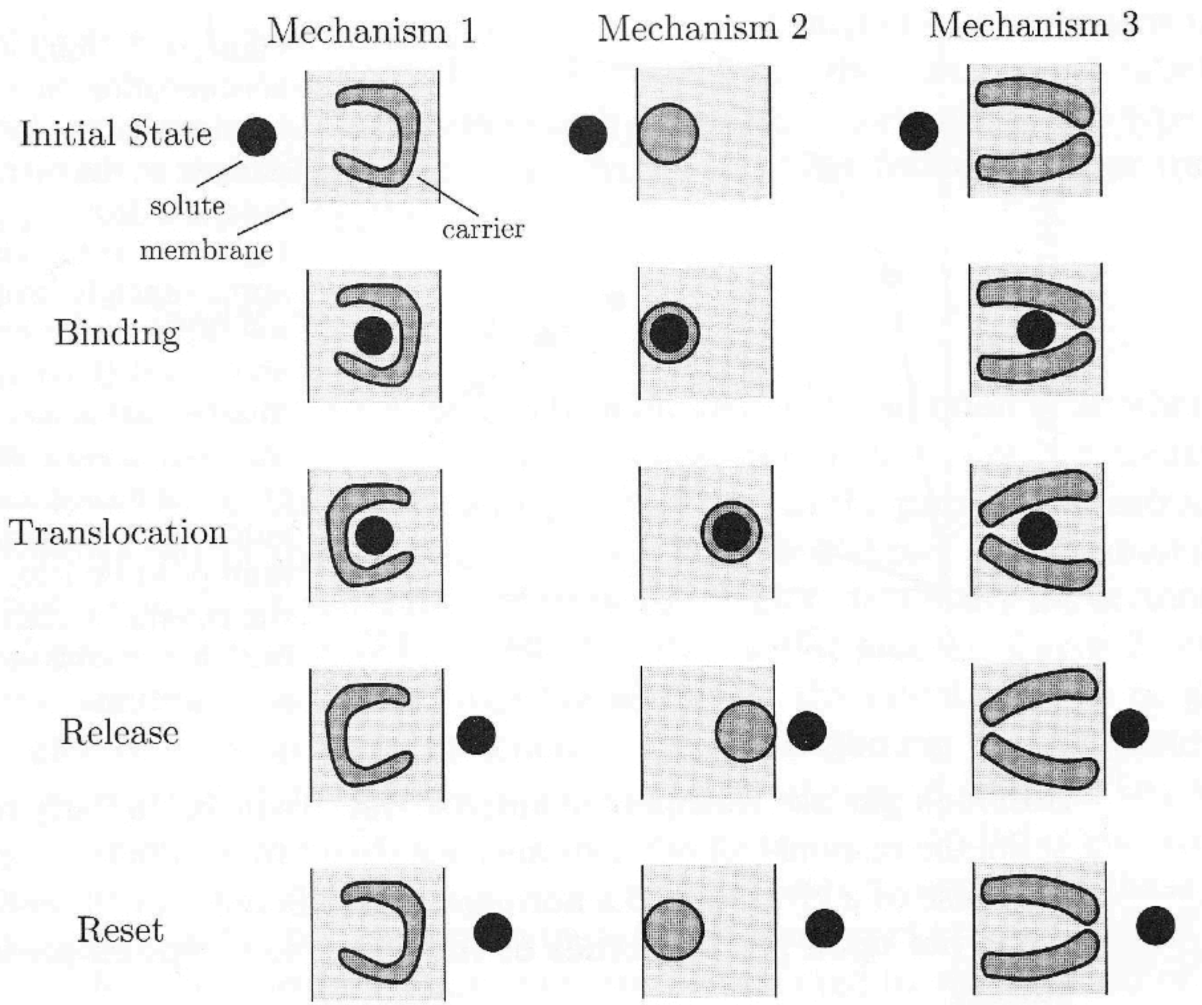
Carrier-Mediated Transport: glucose transporter as example

Distinguishing characteristics of glucose transport:

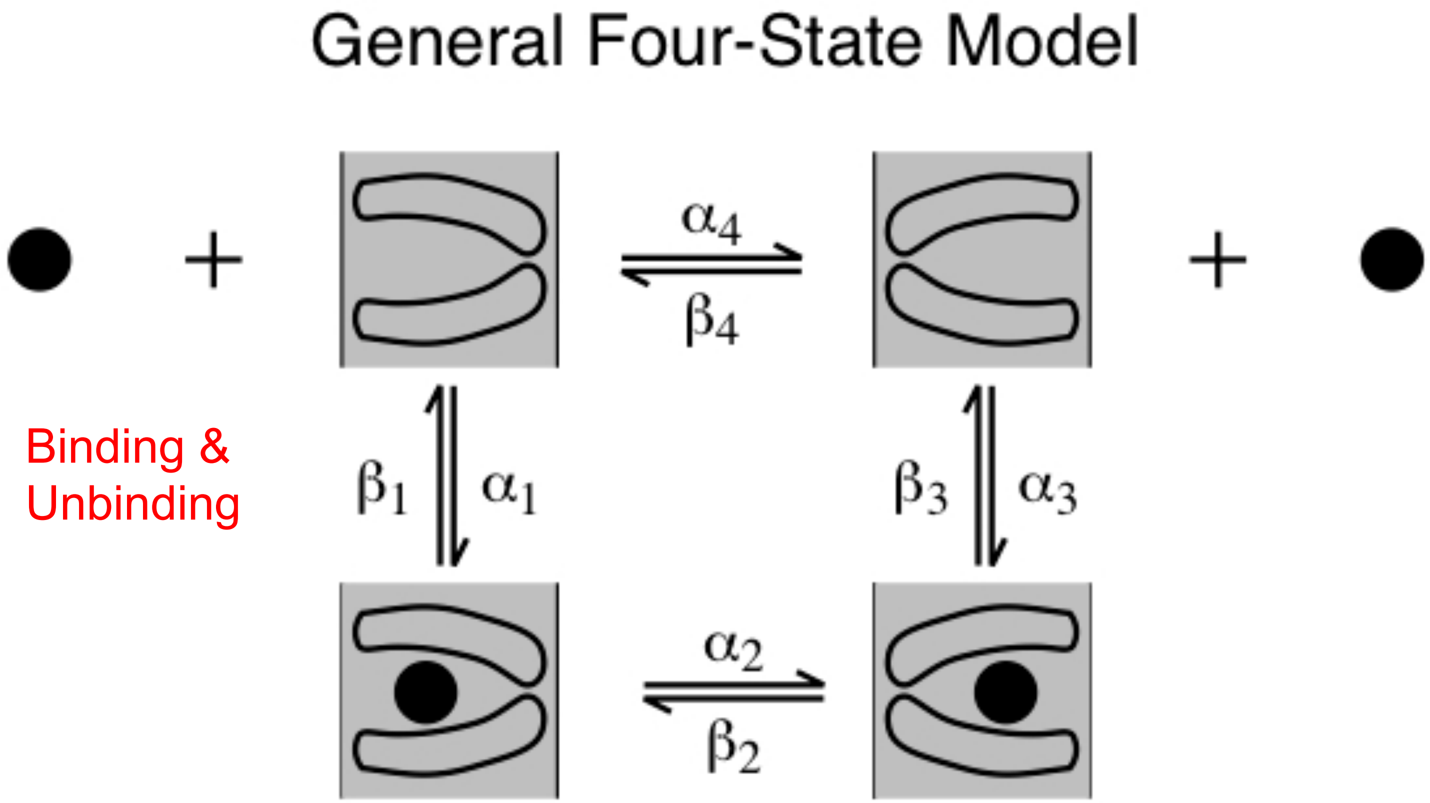
- facilitated -- i.e., faster than dissolve and diffuse
- structure specific -- different rates for even closely related sugars
- passive -- given a single solute, flow is down concentration gradient
- transport saturates -- solute-solute interactions
- transport can be inhibited -- solute-other interactions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

similar to water channels (Hg, vasopressin)

Possible ‘Carrier’ Mechanisms



General Four-State Carrier Model



Binding & Unbinding

Translocation

Chemical Kinetics (v1)

First-order, reversible reaction

$$R \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} P$$

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

Equilibrium:

$$\frac{dc_R(t)}{dt} = \frac{dc_P(t)}{dt} = 0 \quad \rightarrow \quad \beta c_P(\infty) = \alpha c_R(\infty)$$

$$\frac{c_P(\infty)}{c_R(\infty)} = \frac{\alpha}{\beta} = K_a \quad \left(\begin{array}{c}\text{association, equilibrium, affinity,}\\ \text{stability, binding, formation constant}\end{array}\right)$$

Kinetics: assume total amount of reactant and product is conserved

$$c_R(t) + c_P(t) = C$$

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

$$\frac{dc_R(t)}{dt} + (\alpha + \beta)c_R(t) = \beta C$$

Chemical Kinetics (v1)

First-order, reversible reaction

$$R \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} P$$

First-order linear differential equation with constant coefficients

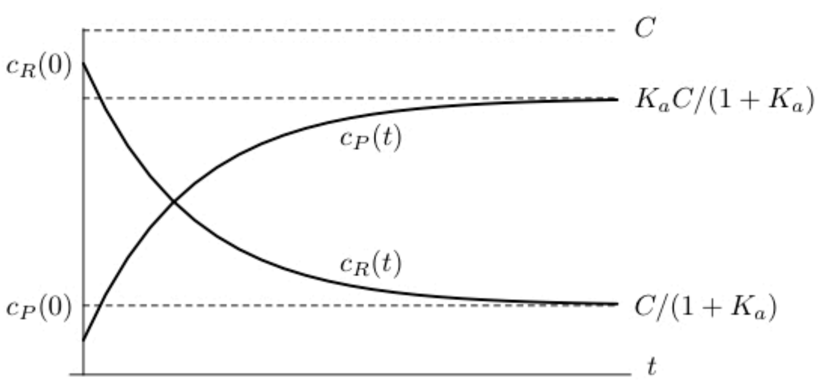
$$c_R(t) = c_R(\infty) - \Big(c_R(\infty) - c_R(0)\Big)\, e^{-t/\tau}, \text{ for } t > 0$$

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

$$c_P(t) = C - c_R(t)$$

First-order, reversible reaction

$$R \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} P$$



$\tau = \frac{1}{\alpha+\beta}$

Chemical Kinetics (v2)

Second-order reversible (binding) reaction

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

$$\begin{aligned} \frac{dc_{ES}(t)}{dt} &= \alpha c_S(t) c_E(t) - \beta c_{ES}(t), \\ \frac{dc_S(t)}{dt} = \frac{dc_E(t)}{dt} &= \beta c_{ES}(t) - \alpha c_S(t) c_E(t), \end{aligned}$$

→ Law of mass action

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: $c_E(t) + c_{ES}(t) = C_{ET}$

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

$$C_{ET} = c_E(\infty) + c_{ES}(\infty)$$

$$C_{ET} = \frac{K c_{ES}(\infty)}{c_S(\infty)} + c_{ES}(\infty) = \left(\frac{K}{c_S(\infty)} + 1 \right) c_{ES}(\infty)$$

$$c_{ES}(\infty) = \left(\frac{c_S(\infty)}{K + c_S(\infty)} \right) C_{ET}$$

→ Michaelis-Menten kinetics

Chemical Kinetics (v2)

Second-order reversible (binding) reaction

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

$$C_{ET} = c_E(\infty) + c_{ES}(\infty)$$

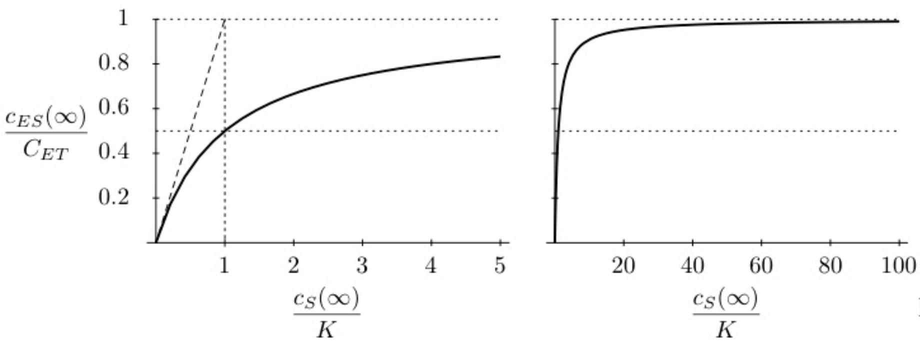
$$C_{ET} = \frac{K c_{ES}(\infty)}{c_S(\infty)} + c_{ES}(\infty) = \left(\frac{K}{c_S(\infty)} + 1\right) c_{ES}(\infty)$$

$$c_{ES}(\infty) = \left(\frac{c_S(\infty)}{K + c_S(\infty)}\right) C_{ET}$$

Second-order reversible (binding) reaction

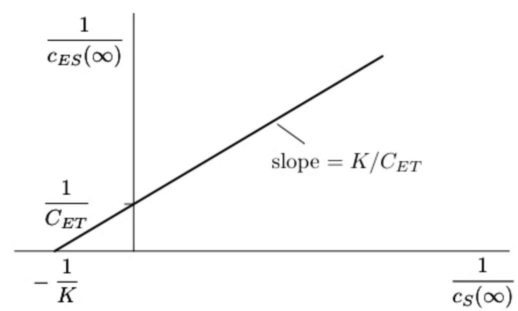
$$S + E \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} ES$$

Rectangular hyperbola: Michaelis-Menten Relation



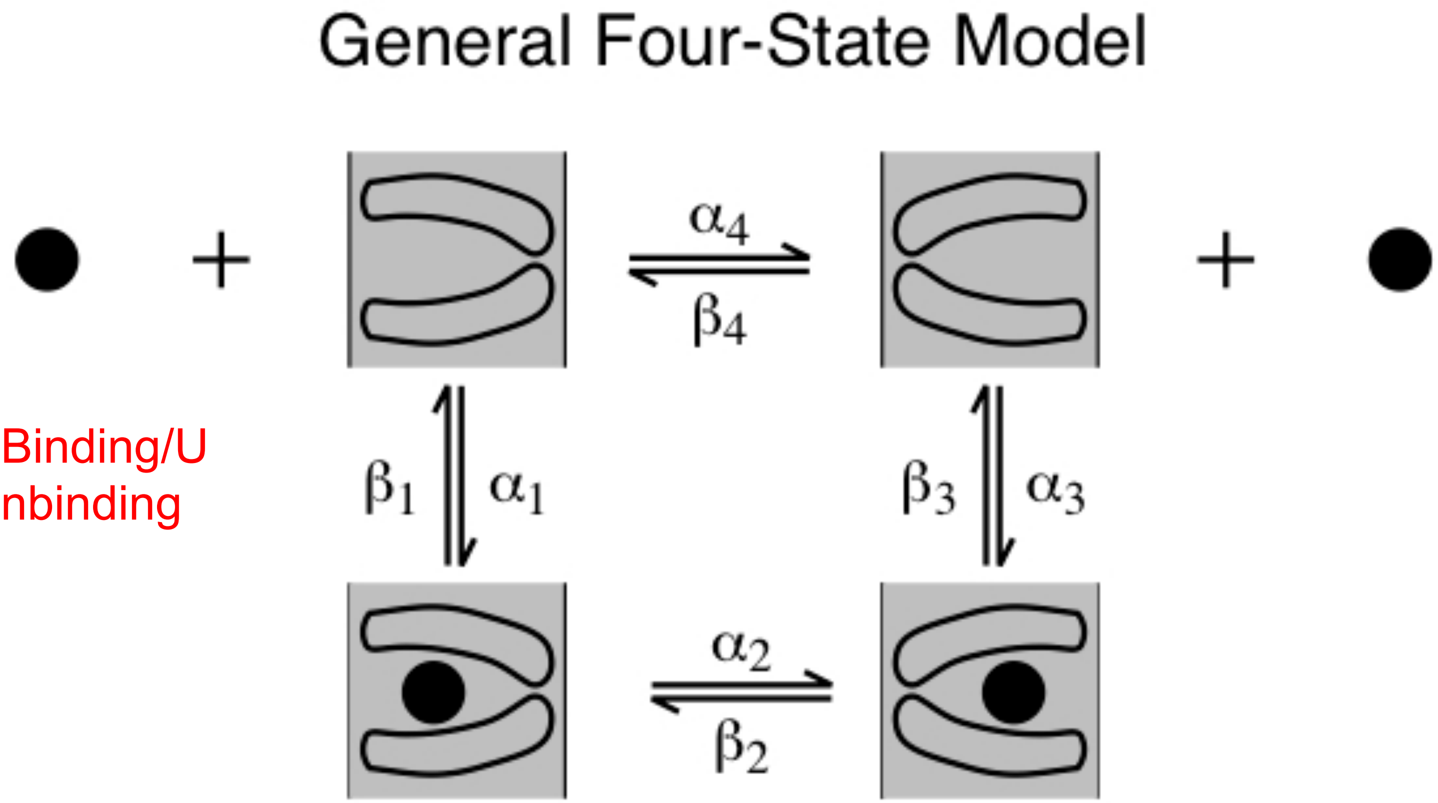
Doubly-reciprocal coordinates: Lineweaver-Burk plot

$$\frac{1}{c_{ES}(\infty)} = \left(1 + \frac{K}{c_S(\infty)}\right)\frac{1}{C_{ET}} = \left(\frac{K}{C_{ET}}\right)\frac{1}{c_S(\infty)} + \frac{1}{C_{ET}}$$



→ Linear way to plot nonlinear relationship!

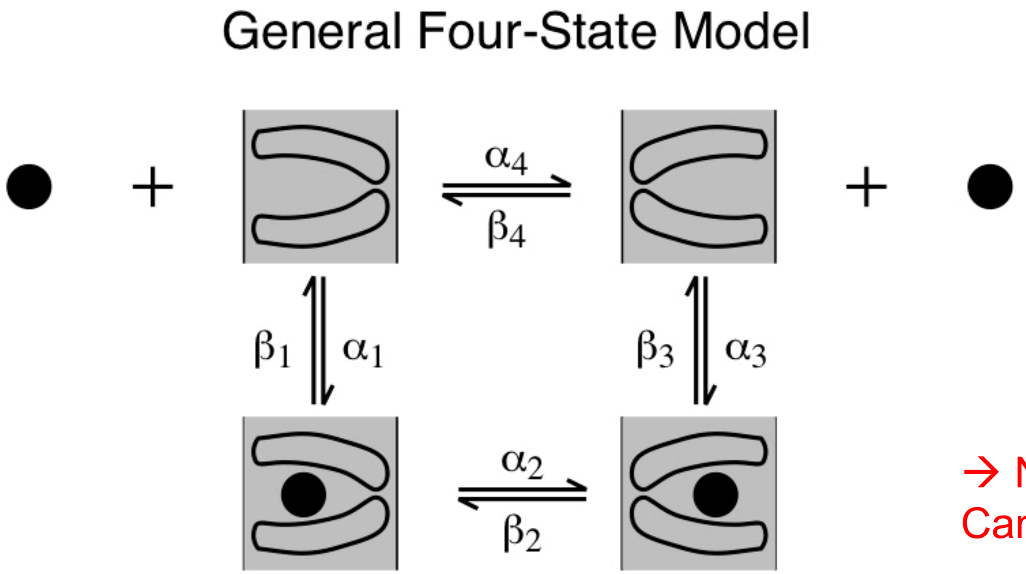
General Four-State Carrier Model



Binding/Unbinding

Translocation

Chemical Kinetics & 'Carriers'



→ Numerous free parameters.
Can we simplify?

$$\frac{dC^i_{ES}}{dt} = \alpha_1 C^i_S C^i_E - \beta_1 C^i_{ES}$$

$$\frac{dC^i_S}{dt} = \frac{dC^i_E}{dt} = \beta_1 C^i_{ES} - \alpha_1 C^i_S C^i_E$$

$$\frac{dC^o_{ES}}{dt} = \alpha_3 C^o_S C^o_E - \beta_3 C^o_{ES}$$

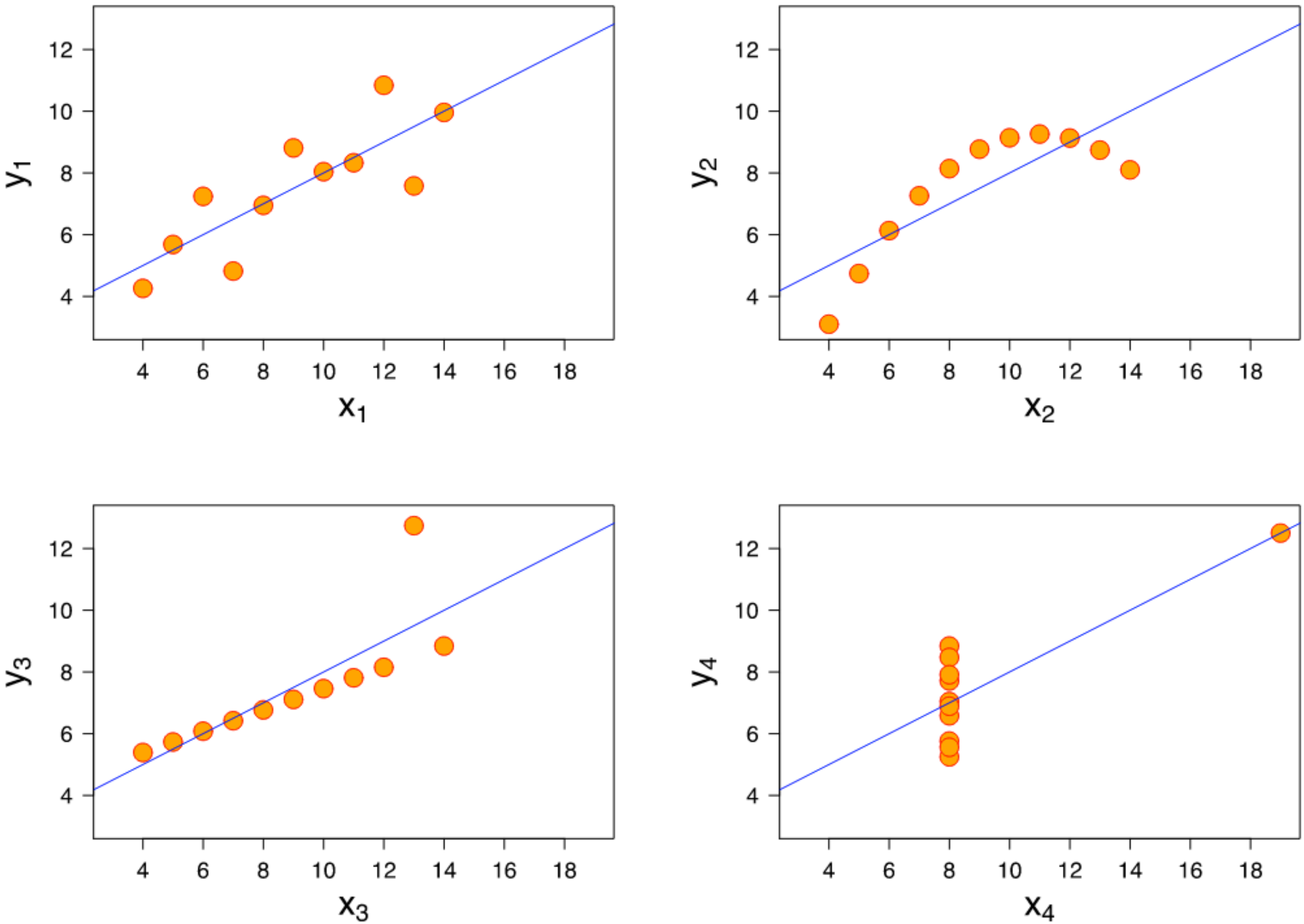
$$\frac{dC^o_S}{dt} = \frac{dC^o_E}{dt} = \beta_3 C^o_{ES} - \alpha_3 C^o_S C^o_E$$

$$\frac{dC^o_{ES}}{dt} = \alpha_2 C^i_{ES} - \beta_2 C^o_{ES}$$

$$\frac{dC^i_{ES}}{dt} = \beta_2 C^o_{ES} - \alpha_2 C^i_{ES}$$

$$\frac{dC^o_E}{dt} = \alpha_4 C^i_E - \beta_4 C^o_E$$

$$\frac{dC^i_E}{dt} = \beta_4 C^o_E - \alpha_4 C^i_E$$


y1
x1
y2
x2
y3
x3
y4
x4
4
6
8
10
12
14
16
18