Biophysics I (BPHS 3090)

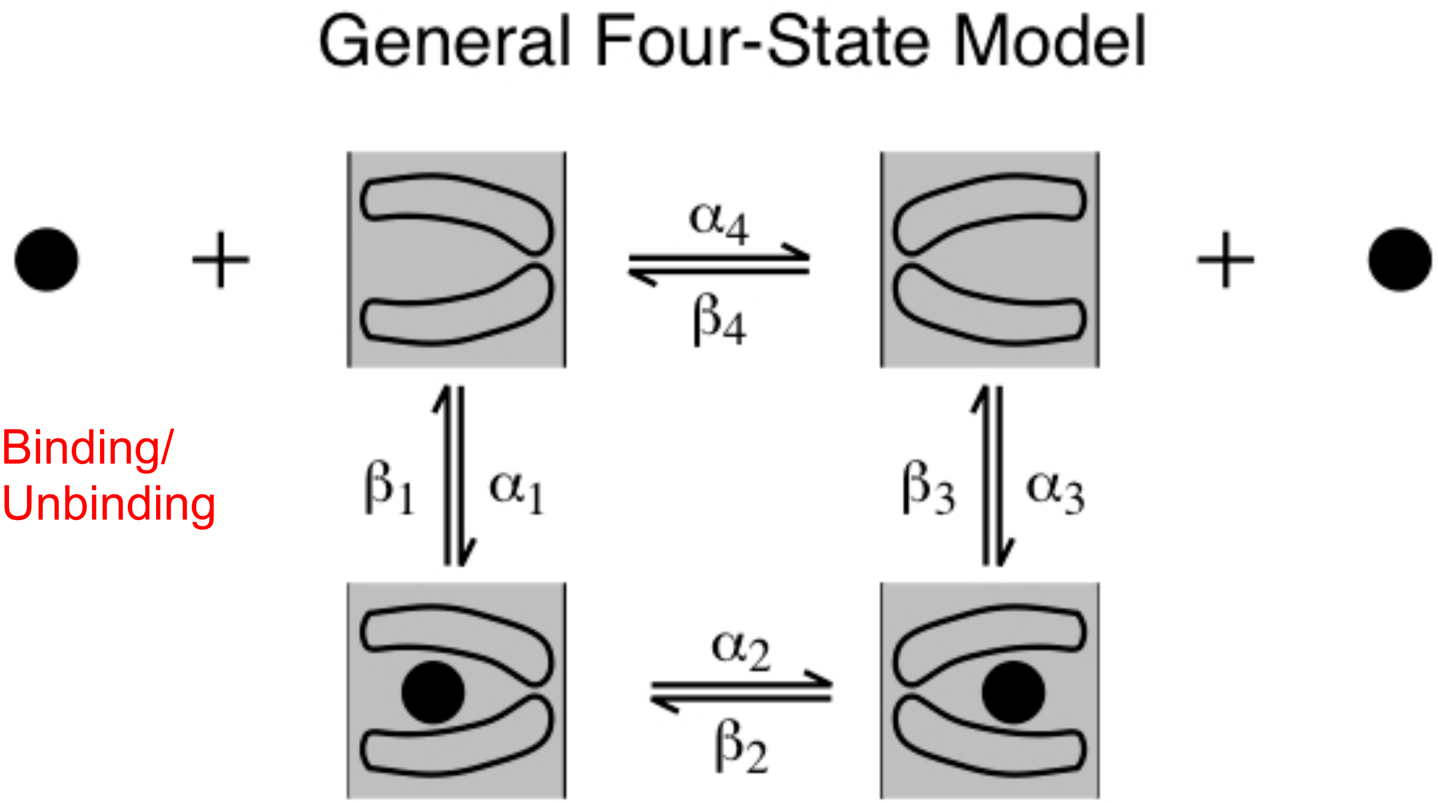
Instructors: Prof. Christopher Bergevin (cberge@yorku.ca)

Website: http://www.yorku.ca/cberge/3090W2015.html

York University
Winter 2015
Lecture 8

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

General Four-State Model

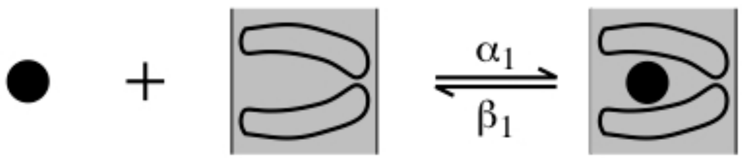


Binding/
Unbinding

Translocation

Chemical Kinetics & 'Carriers'

Binding

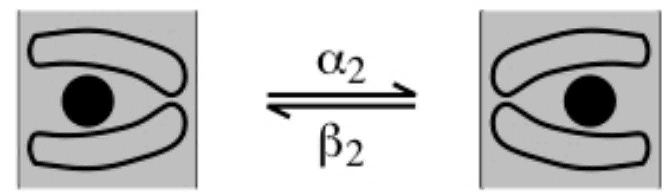


$$S^i + E^i \underset{\beta_1}{\overset{\alpha_1}{\rightleftharpoons}} ES^i$$

$$\frac{dC_{ES}^i}{dt} = \alpha_1 C_S^i C_E^i - \beta_1 C_{ES}^i$$

$$\frac{dC_S^i}{dt} = \frac{dC_E^i}{dt} = \beta_1 C_{ES}^i - \alpha_1 C_S^i C_E^i$$

Translocation



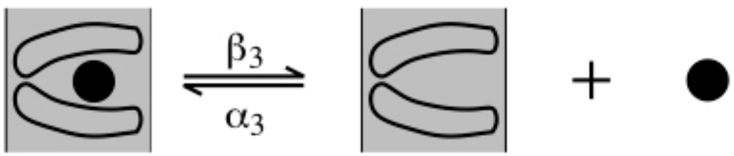
$$ES^i \underset{\beta_2}{\overset{\alpha_2}{\rightleftharpoons}} ES^o$$

$$\frac{dC_{ES}^o}{dt} = \alpha_2 C_{ES}^i - \beta_2 C_{ES}^o$$

$$\frac{dC_{ES}^i}{dt} = \beta_2 C_{ES}^o - \alpha_2 C_{ES}^i$$

Chemical Kinetics & ‘Carriers’

Unbinding

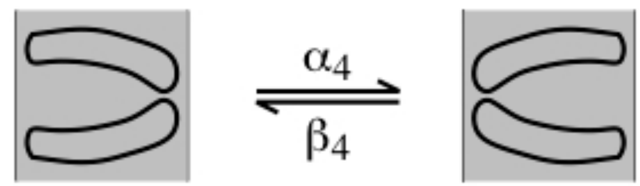


$$ES^o \underset{\alpha_3}{\overset{\beta_3}{\rightleftharpoons}} E^o + S^o$$

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

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

Translocation



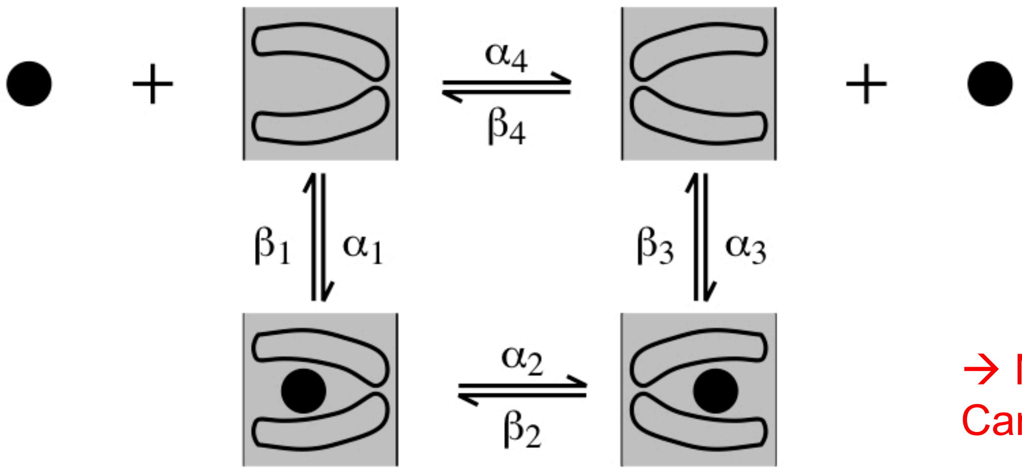
$$E^i \underset{\beta_4}{\overset{\alpha_4}{\rightleftharpoons}} E^o$$

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

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

Chemical Kinetics & 'Carriers'

General Four-State Model



→ Numerous free parameters. Can we simplify?

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

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

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

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

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

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

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

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

Simple, Symmetric Four-State Model

Translocation

Binding/Unbinding
(at equilibrium)

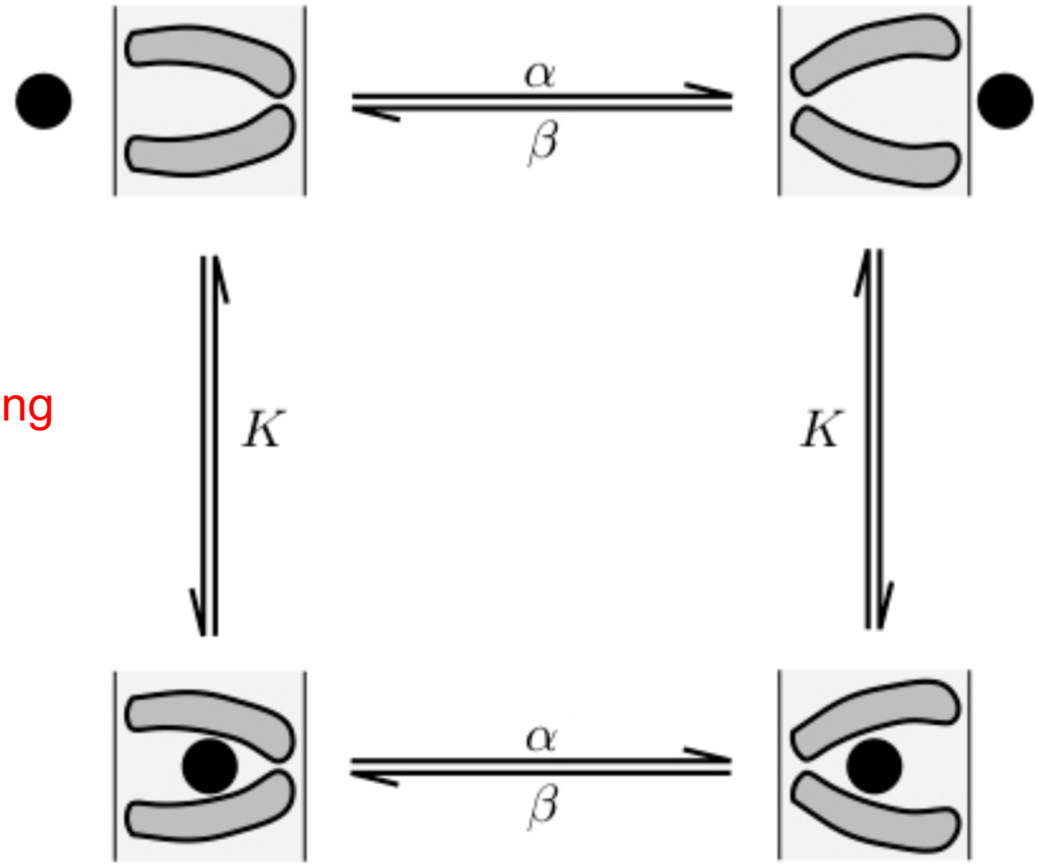


Figure 6.20

Assumption: Steady-state
(i.e., carrier densities are independent of time)

Simple, Symmetric Four-State Model

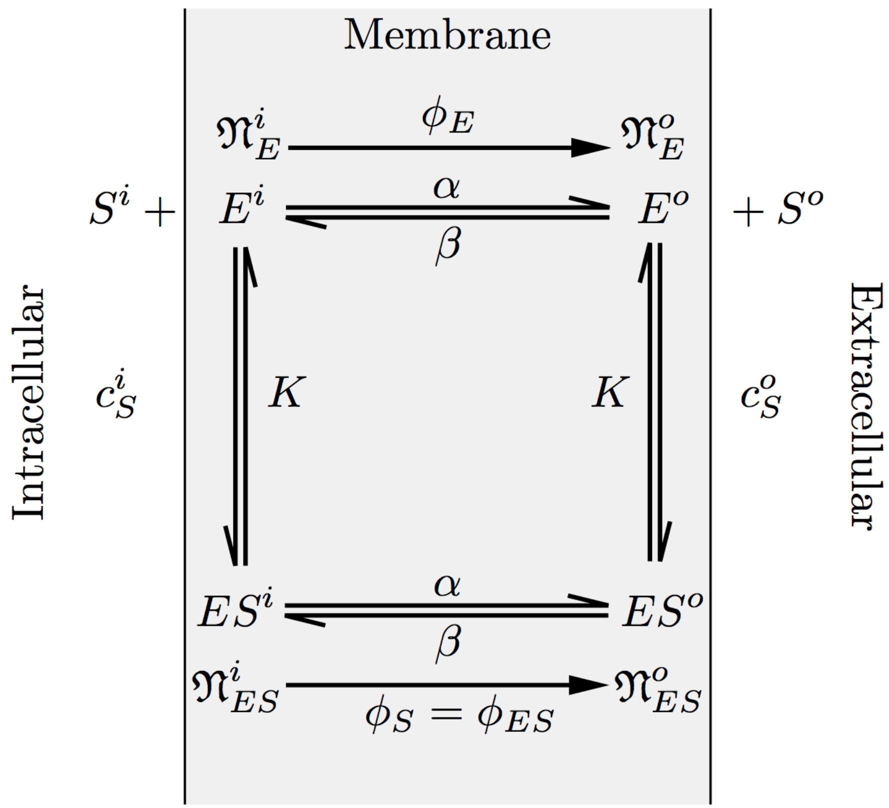


Figure 6.21

1. Conservation of enzyme:

$$\mathfrak{N}_E^i + \mathfrak{N}_E^o + \mathfrak{N}_{ES}^i + \mathfrak{N}_{ES}^o = \mathfrak{N}_{ET}$$

2. Binding is fast (always in steady state):

$$K = \frac{c_S^i \mathfrak{N}_E^i}{\mathfrak{N}_{ES}^i} = \frac{c_S^o \mathfrak{N}_E^o}{\mathfrak{N}_{ES}^o}$$

3. Translocation characterized by fluxes:

$$\phi_{ES} = \alpha \mathfrak{N}_{ES}^i - \beta \mathfrak{N}_{ES}^o$$

$$\phi_E = \alpha \mathfrak{N}_E^i - \beta \mathfrak{N}_E^o$$

4. Net flux of enzyme is zero:

$$\phi_E + \phi_{ES} = 0$$

→ Steady-state

(i.e., carrier densities are independent of time)

Simple, Symmetric Four-State Model

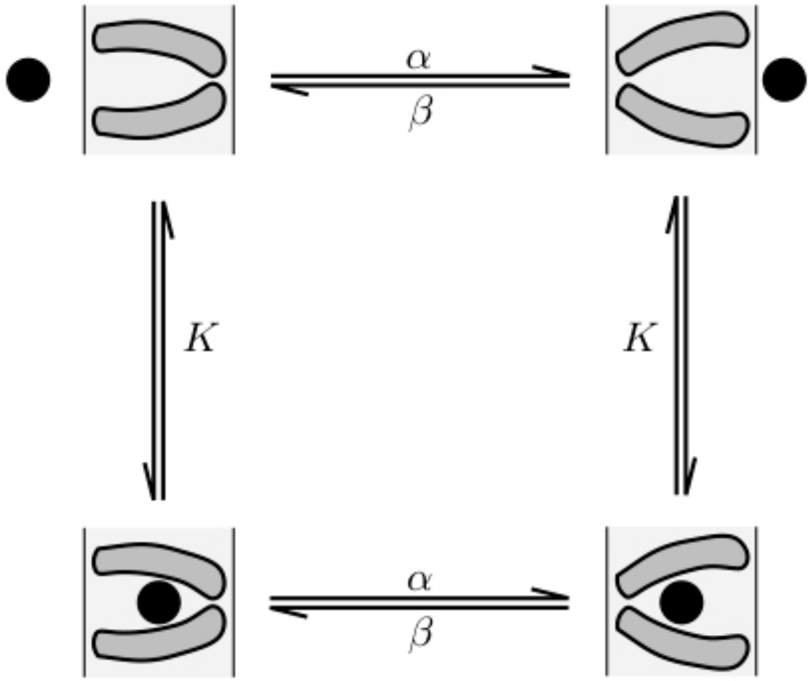


Figure 6.20

$$\mathfrak{N}^i_E + \mathfrak{N}^o_E + \mathfrak{N}^i_{ES} + \mathfrak{N}^o_{ES} = \mathfrak{N}_{ET}$$

$$K = \frac{c^i_S \mathfrak{N}^i_E}{\mathfrak{N}^i_{ES}} = \frac{c^o_S \mathfrak{N}^o_E}{\mathfrak{N}^o_{ES}}$$

$$\phi_{ES} = \alpha \mathfrak{N}^i_{ES} - \beta \mathfrak{N}^o_{ES}$$

$$\phi_E = \alpha \mathfrak{N}^i_E - \beta \mathfrak{N}^o_E$$

$$\phi_E + \phi_{ES} = 0$$

Combing equations...

$$\mathfrak{N}^i_{ES} = \left(\frac{\beta}{\alpha + \beta} \right) \left(\frac{c^i_S}{c^i_S + K} \right) \mathfrak{N}_{ET}$$

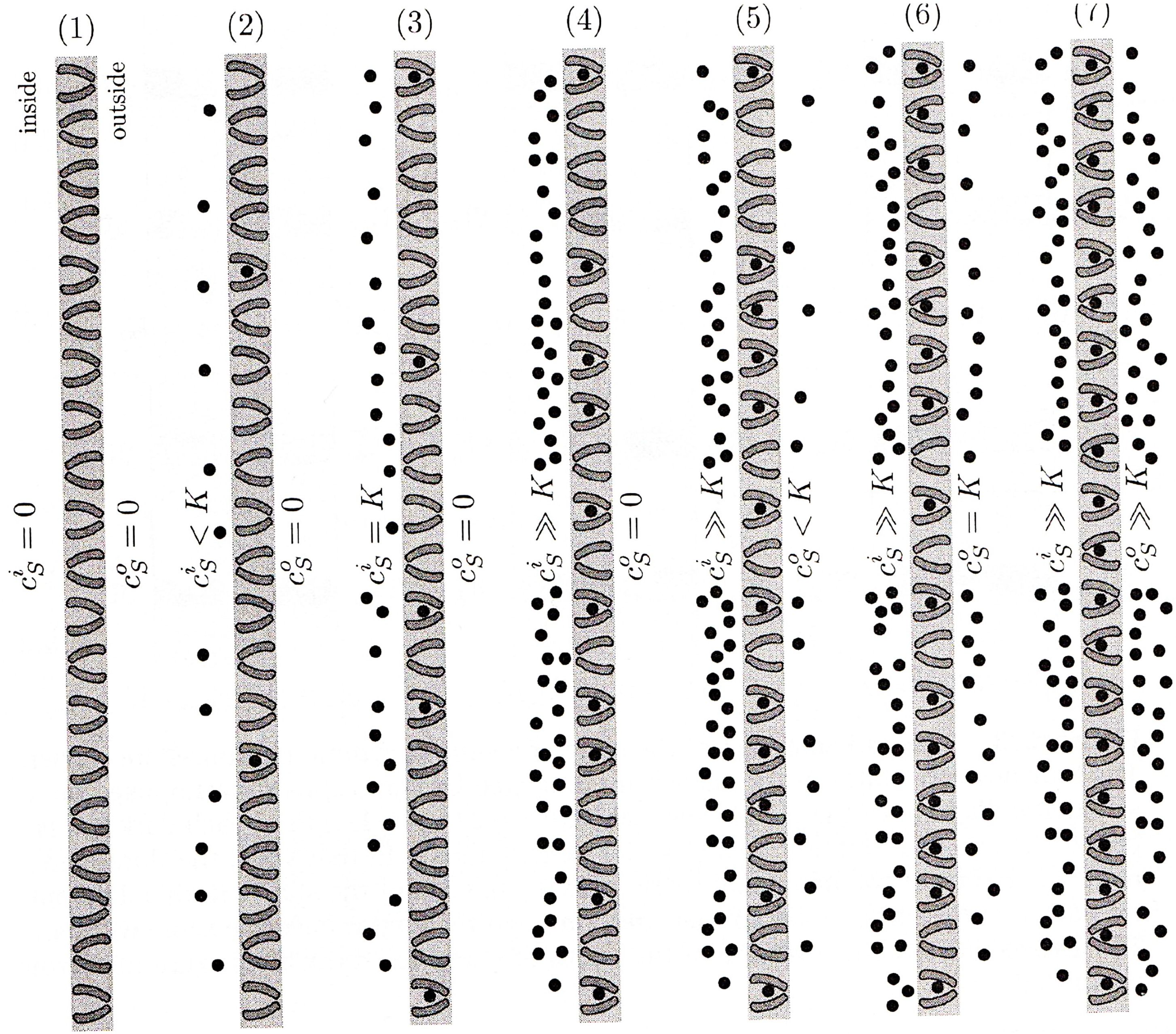
$$\mathfrak{N}^i_E = \left(\frac{\beta}{\alpha + \beta} \right) \left(\frac{K}{c^i_S + K} \right) \mathfrak{N}_{ET}$$

$$\mathfrak{N}^o_{ES} = \left(\frac{\alpha}{\alpha + \beta} \right) \left(\frac{c^o_S}{c^o_S + K} \right) \mathfrak{N}_{ET}$$

$$\mathfrak{N}^o_E = \left(\frac{\alpha}{\alpha + \beta} \right) \left(\frac{K}{c^o_S + K} \right) \mathfrak{N}_{ET}$$

Solving for the solute flux yields:

$$\phi_S = \left(\frac{\alpha \beta}{\alpha + \beta} \right) \mathfrak{N}_{ET} \left(\frac{c^i_S}{c^i_S + K} - \frac{c^o_S}{c^o_S + K} \right)$$



$$K = \frac{c_S^i \mathfrak{N}_E^i}{\mathfrak{N}_{ES}^i} = \frac{c_S^o \mathfrak{N}_E^o}{\mathfrak{N}_{ES}^o}$$

$$\phi_S = \left(\frac{\alpha\beta}{\alpha+\beta}\right) \mathfrak{N}_{ET} \left(\frac{c_S^i}{c_S^i + K} - \frac{c_S^o}{c_S^o + K}\right)$$

Figure 6.22

→ Steady-state

(i.e., carrier densities are independent of time)

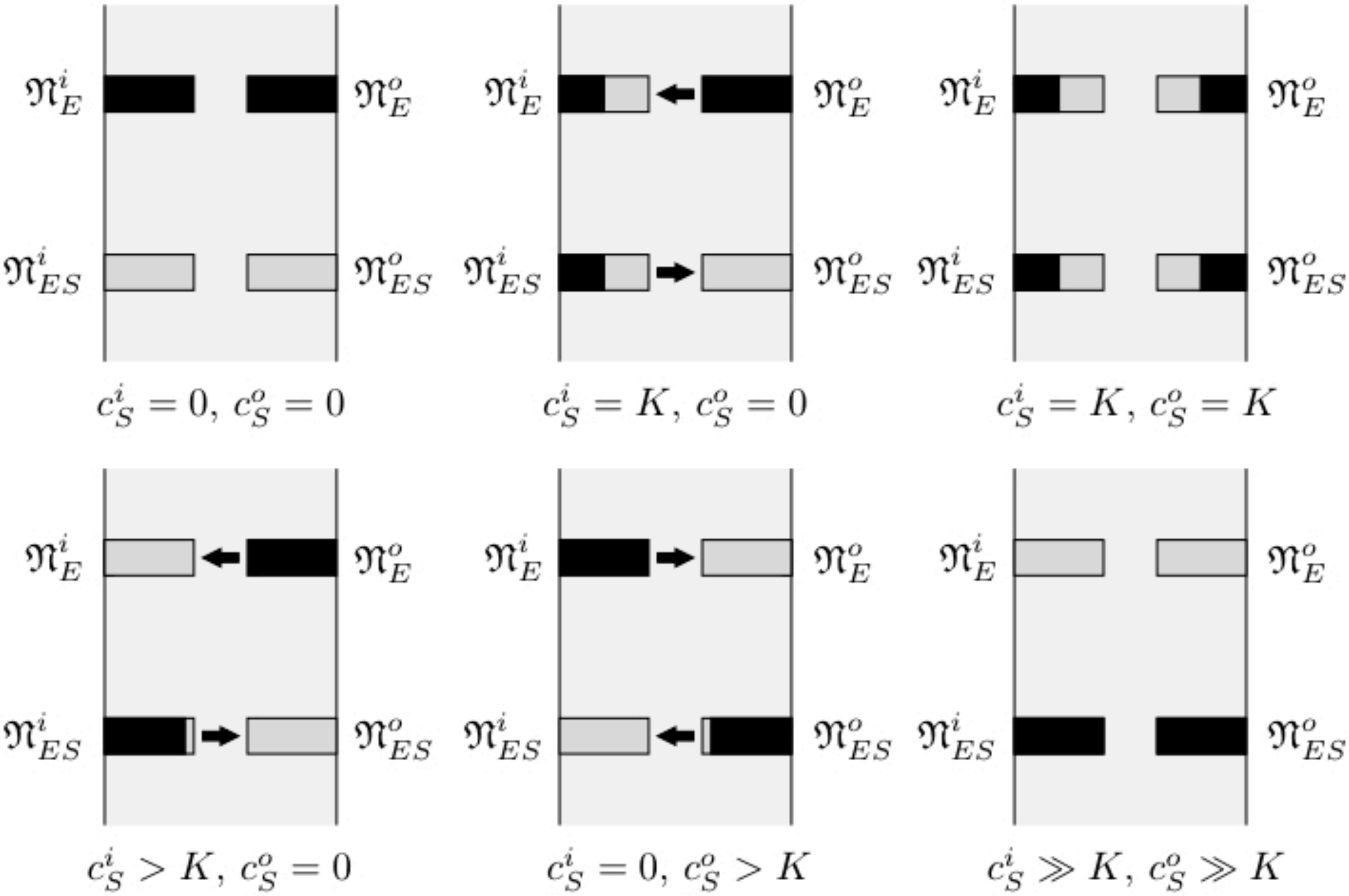


Figure 6.23

$$K = \frac{c_S^i \mathfrak{N}_E^i}{\mathfrak{N}_{ES}^i} = \frac{c_S^o \mathfrak{N}_E^o}{\mathfrak{N}_{ES}^o} \qquad \phi_S = \left(\frac{\alpha\beta}{\alpha+\beta}\right) \mathfrak{N}_{ET} \left(\frac{c_S^i}{c_S^i + K} - \frac{c_S^o}{c_S^o + K}\right)$$