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Quantitative Physiology: Cells and Tissues

Homework Assignment #4

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Due: Thursday October 5, 2006

Exercise 1. Assume that transport of a solute S is governed by the simple, symmetric, four-state carrier model. After transport has reached steady-state, the densities of carriers in each of the four states are found to be

$$\mathfrak{N}_E^i = 10 \text{ carriers}/\mu\text{m}^2, \quad \mathfrak{N}_E^o = 20 \text{ carriers}/\mu\text{m}^2,$$

$$\mathfrak{N}_{ES}^i = 5 \text{ carriers}/\mu\text{m}^2, \quad \mathfrak{N}_{ES}^o = 10 \text{ carriers}/\mu\text{m}^2.$$

Each part of this question focuses on a statement. For each part, indicate if the statement is TRUE or FALSE and explain how you know it is true or false. If more information is needed to determine whether the statement is true or false, indicate MORE INFORMATION and explain what additional information is needed.

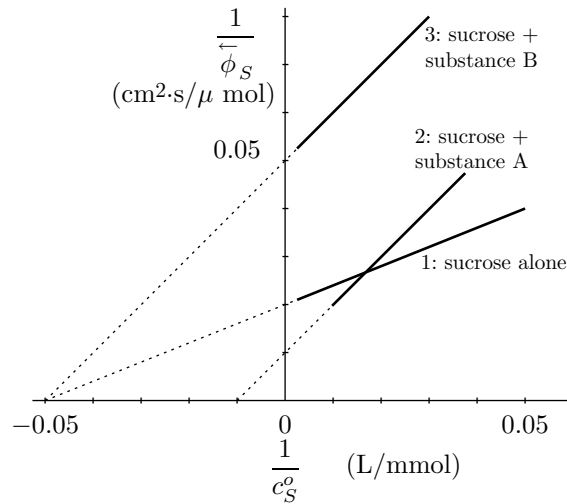
- a) The extracellular concentration of solute is greater than the intracellular concentration of solute.
- b) The forward translocation rate α is greater than the reverse translocation rate β .
- c) The net flux of solute is inward.

Exercise 2. Consider the simple, symmetric, four-state carrier model. For each of the following conditions, find \mathfrak{N}_E^i , \mathfrak{N}_E^o , \mathfrak{N}_{ES}^i , \mathfrak{N}_{ES}^o , and ϕ_S . Explain the physical significance of each of your answers.

- a) $\alpha = 0$.
- b) $\beta = 0$.
- c) $K = 0$.

Exercise 3. Consider the simple, symmetric, four-state carrier model when $c_S^i = c_S^o = 0$. Sketch the carrier density in each of its four states as a function of α/β . Give a physical interpretation of your results.

Exercise 4. The following plot shows the relation between the initial flux of sucrose across a cell membrane when the bath contains (1) sucrose with concentration c_S^o , (2) sucrose with concentration c_S^o plus 10 mmol/L of substance A, and (3) sucrose with concentration c_S^o plus 10 mmol/L of substance B.



- When the bath contains low concentrations of sucrose (i.e. 1 mmol/L), which condition (1, 2, or 3) results in the greatest influx of sucrose? Explain.
- When the bath contains high concentrations of sucrose (i.e. 200 mmol/L), which condition (1, 2, or 3) results in the greatest influx of sucrose? Explain.
- Does substance A act as a competitive inhibitor? Explain.
- Does substance B act as a non-competitive inhibitor? Explain.

Problem 1. Sharp Wan loads a cell with a radioactive sugar to a concentration c_S^i and measures the efflux of sugar $\bar{\phi}_S$ as a function of c_S^i with the results shown in Figure 1. The extracellular concen-

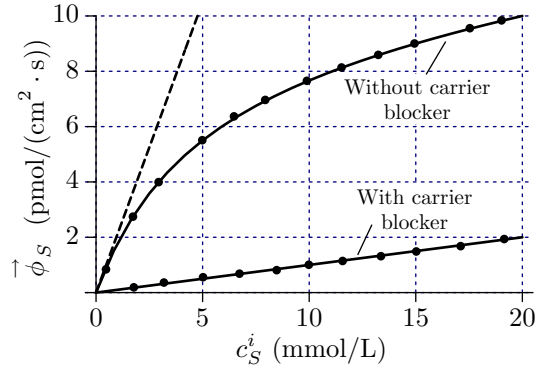


Figure 1: Sugar efflux as function of sugar concentration in the presence and absence of a carrier blocker. The dashed line shows the initial slope of the dependence of the efflux on concentration without the presence of the carrier blocker.

tration of labeled sugar is kept at zero. The cell is known to contain a sugar carrier that has been characterized by a simple, symmetric four state carrier model. However, Sharp Wan notices that the efflux of sugar does not saturate as a function of the intracellular sugar concentration. Therefore, he decides to use a known blocker of the carrier and obtains the results shown in Figure 1. Sharp Wan proposes that in this cell, sugar transport is mediated by both diffusion and by a simple, symmetric four-state carrier.

- Determine the diffusive permeability of the membrane for the sugar P_S .
- Determine both the maximum flux $(\phi_S)_{max}$ and the dissociation constant K_S for the carrier model.

Problem 2. A spherical cell of radius $30 \mu\text{m}$ is loaded with glucose and immersed in a large quantity of isotonic, glucose-free solution. You may assume that the external glucose concentration remains zero, and that the change in cell water volume is negligible. The cell membrane transports glucose by a simple, symmetric, four-state carrier with dissociation constant K and maximum flux ϕ_M . Two different experiments are performed to measure intracellular glucose concentration, $c_G(t)$.

- Experiment#1* — When the initial internal glucose concentration is low, i.e., $c_G(0) \ll K$, it is found that

$$c_G(t) = c_G(0)e^{-t/\tau}$$

where $\tau = 10$ minutes.

- Experiment#2* — When the initial internal glucose concentration is high, i.e., $c_G(0) \gg K$, it is found that the initial rate of change of internal glucose concentration is

$$\left(\frac{dc_G}{dt}\right)_{t=0} = -10^{-8} \text{ mol/cm}^3 \cdot \text{s}$$

Determine the values of K and ϕ_M .

Problem 3. A spherical cell of radius r is loaded with glucose and placed in a large bath of isotonic, glucose-free solution. The cell membrane contains a glucose carrier with dissociation constant K and maximum flux ϕ_m . The internal concentration of glucose at time t is $c_G(t)$ and the initial concentration is C . Assume that the change in intracellular osmolarity is negligible.

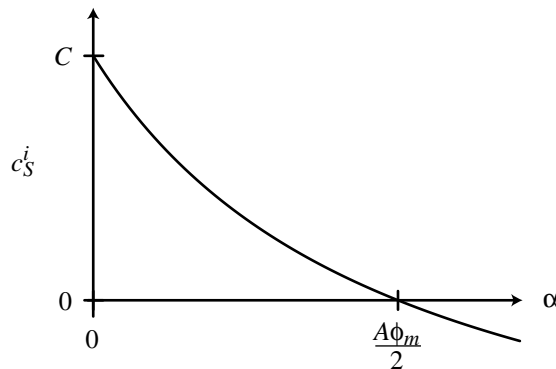
- Find the differential equation satisfied by $c_G(t)$ in terms of r , K , and ϕ_m .
- Solve the differential equation to obtain a relation between $c_G(t)$ and t . You need not obtain c_G as an explicit function of t !
- Find the solution for $K \gg c_G(t)$. Explain the significance of the form of this solution.
- Find the solution for $K \ll c_G(t)$. Explain the significance of the form of this solution.

Problem 4. To understand how metabolic rate might affect glucose concentration in cells, we wish to analyze a simple model. Assume that glucose is transported across the cell membrane by a process that can be represented by a simple, symmetric, four-state carrier model, so that the flux of glucose crossing the membrane is given by

$$\phi_S = \phi_m \left(\frac{c_S^i}{c_S^i + K} - \frac{c_S^o}{c_S^o + K} \right)$$

where K represents the dissociation constant for the binding of glucose to the carrier and ϕ_m represents the maximum flux through the carriers. Assume that the cell is surrounded by fluid that contains glucose and that the extracellular concentration is constant, i.e., $c_S^o = C$. Assume that the cell is metabolizing (consuming) glucose at a constant rate α mol/s. Assume that these conditions persist, and a steady-state condition is reached in which the intracellular concentration of glucose c_S^i is a constant. Assume that the surface area A and volume \mathcal{V} of the cell are constant.

- Determine the steady state relation between the rate of glucose consumption α and the flux of glucose ϕ_S through the cell membrane.
- In the steady state, the concentration of glucose in the cell is constant. Determine an expression for this concentration (c_S^i) in terms of the rate of glucose consumption α and constant parameters of this system.
- The solution to the equation developed in Part b is plotted in the following figure for the special case $K = C$.



- Provide a *physical interpretation* of the result shown for $\alpha = 0$.
- Provide a *physical interpretation* for the results shown for $0 < \alpha < A\phi_m/2$.
- Provide a *physical interpretation* of the result shown for $\alpha > A\phi_m/2$.