PART IV

CHAPTER 9.

Problem 9-1: Parallel Convection and Diffusion

Consider the transport of a solute s by parallel diffusion and convection at a molar velocity u* in the x direction. Transport occurs through a slab of thickness L with surfaces located at x=0 and x=L at constant concentrations C_{s0} and C_{sL}, respectively

(a) Beginning with the flux equation

$$N_s = u^* C_s - \mathcal{D}_s \frac{dC_s}{dx}$$

show the steps in deriving the solution given Eq. 9.3-6:

$$\dot{N}_s = Q\left(\frac{C_{s0}\, e^{Pe} - C_{sL}}{e^{Pe} - 1}\right)$$

State all assumptions.

(b) Find the limit of $\dot{N}_s$ at small Peclet numbers, $Pe = u^* L/\mathcal{D}_s \to 0$.

(c) Find the limit of $\dot{N}_s$ at $Pe \to \infty$.

Problem 9-2: Similarity Solution to a Transient Diffusion Problem

Show the detailed steps of the analytical solution to the transient diffusion problem.

(a) Express the governing equation (Eq. 9.5-1) and its boundary conditions (Eq. 9.5-2a-c) in terms of the dimensionless variables:

$$C(y,t) \equiv \frac{C_s(y,t) - C_{s\infty}}{\alpha} \quad ; \quad y \equiv \frac{y}{\beta} \quad ; \quad t \equiv \frac{t}{\gamma};$$

where α, β, and γ are arbitrary scale factors.

(b) Set the two dimensionless parameter groups that appear in results to part (a) equal to unity. Show that the equation and its boundary conditions reduce to

$$\frac{\partial C}{\partial t} = \frac{\partial^2 C}{\partial y^2}$$

$$C(y,0) = C(\infty,t) = 0$$

$$C(0,t) = 1$$

Also show how the dimensionless variables defined in part (a) are now related to their dimensional counterparts with β as the only undefined scaling parameter.

(c) Define a new dimensionless independent variable, $\eta = y/\sqrt{t}$. Now, transform the dimensionless problem from the original independent variables (t,y) to the new independent variable η to show that:

$$\frac{d^2C}{d\eta^2} + \frac{\eta}{2}\frac{dC}{d\eta} = 0 \quad (\eta > 0)$$

What are the transformed boundary conditions?

(d) Show by two integrations that the solution to the ordinary differential equation (with integration constants A and B) is

$$C = A\int_0^{\eta} \exp\left(-\xi^2/4\right)d\xi + B$$

To obtain the final dimensionless solution, apply the two boundary conditions to evaluate A and B noting that

$$\int_0^{\infty} \exp\left(-\xi^2/4\right)d\xi = \sqrt{\pi}$$

(e) Express the solution in dimensional form $C_s(y,t)$. Notice that the undetermined scaling parameter β does not appear in the solution.

Problem 9-3: Diffusion From a Small Drug Source

Consider an implanted source of drug that is released into surrounding tissue at a prescribed rate $\dot{R}(t)$. To study long-range effects, we model this process by a singular source in an infinite body of tissue. Assuming an isotropic medium, drug diffusion can be expressed in spherical coordinates:

$$\frac{\partial C_d}{\partial t} = \frac{\mathcal{D}_d}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C_d}{\partial r}\right) \qquad (r>0)$$

with the conditions

$$\dot{R}(t) = \lim_{r\to 0}\left(-\pi r^2 \mathcal{D}_d \frac{\partial C_d}{\partial r}\right), \qquad \lim_{r\to\infty} C_d = 0, \quad C_d(0,r) = 0$$

where C_d goes to zero faster than r goes to infinity.

(a) The differential concentration equation for this model is linear but has variable coefficients. It is simpler to solve a differential equation with constant coefficients. Transform this model, both the differential equation and its conditions, using a new dependent variable,

$\phi(r,t) = rC_d(r,t)$.

(b) Apply the Laplace transform $\tilde{\phi}(r,s) = \mathcal{L}\{\phi(r,\tau)\}$, $\tilde{R}(s) = \mathcal{L}\{\dot{R}(t)\}$ and find the solution in the Laplace domain (see table C4-2).

(c) Obtain the solutions for $C_d(r,t)$ when $\dot{R}(t) = R_d$, a constant.

Problem 9-4: Spherical Drug Delivery Model Development

9-4 *:* A spherical drug delivery device with a radius 'a', surface area S and volume V is implanted in a tumor. The device is covered with a thin membrane. Within the device, drug is bound to very small polymer particles that are suspended in an aqueous gel. Bound drug gradually dissociates from the polymer to produce free drug at a molar rate per unit volume of gel, $\alpha_d \exp(-t/\tau)$. Diffusion is so rapid in the gel that the free drug concentration in the device, $C_d(t)$, is essentially uniform. Diffusion in tumor tissue is a much slower process so that its drug concentration, $C_t(r,t)$, depends on both radial position r and time. Drug is taken up by tumor cells and capillary blood at a first-order rate per unit volume. Drug diffuses across the membrane from the device into the tumor with a molar flux permeability and equilibrium partition coefficient λ.

(a) Develop a model that describes the drug concentration dynamics for the device, $dC_d/dt = ...$ State any additional assumptions.

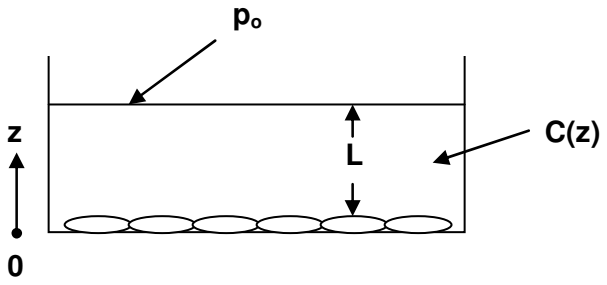
(b) Develop a partial differential equation that describes the drug concentration dynamics in the tumor tissue, $\partial C_d/\partial t = ...$ State any additional assumptions. How would you transform the drug concentration equation in the tumor domain such that it has constant coefficients?

(c) What are appropriate initial and boundary conditions to solve this model with coupled equations ? (Note: Since the solution in the device and the external solution are separated by a membrane, the drug is not in interfacial equilibrium between the two solutions).

(d) Explain what numerical method could be used to solve this problem, which involves both ordinary and partial differential equations.

Problem 9-5: Oxygenation of a Cell Monolayer

A monolayer of endothelial cells is being maintained on the bottom of a Petri dish. The cells are covered with a nutrient solution of height L whose surface is in contact with atmospheric air at an oxygen partial pressure is p_o. The surface of the solution-cell interface per unit volume of the cell layer is ϕ. Oxygen diffuses from the atmosphere through the nutrient layer and into the cells where it is metabolized at constant molar rate R per total cell volume.



(a) Write the equation that describes the oxygen concentration distribution in the nutrient solution C(z) under steady state conditions.
(b) What are the boundary conditions at z=0 and z-L ?
(c) Solve for the concentration distribution.
(d) Determine the oxygen flux at the interface of the nutrient solution with air. Explain why this is the case.

Problem 9-6: Polarographic Electrode With Finite Reaction Rate

In example 9.2-1, we assumed that the O_2 reduction by a polarographic cathode immerged in a large volume of fluid is so fast that O_2 concentration is zero at the electrode surface. Here, we extend this analysis to account for first-order reaction kinetics at the surface of a spherical cathode of radius r=a.

$$R_{O2}[\text{mol/s-m}^2]=-k_r C_{O2}(a)$$

where k_r[m/s] is a surface rate coefficient. Far from the electrode surface, the concentration $C_{O2}(\infty)\equiv C_\infty$ is at a value that is undisturbed by the presence of the electrode.

(a) For this steady-state diffusion problem, what are the governing molar concentration equation and its boundary condition at r=a? Assume a constant diffusion coefficient $\mathcal{D}_{O_2}$.
(b) Convert O_2 concentrations in the results of part (a) to the equivalent O_2 partial pressures using the relation $p_{O2}(r) = C_{O2}(r)/c_G^o\alpha_{O2}$
(c) Solve for $p_{O2}(r)$ in the domain ∞>r>a.
(d) From this analytical solution, obtain $\dot{N}_{O_2}(a)$, the molar O_2 transport rate at r=a.
(e) Formulate the sensitivity of the electrode in terms of c_G^o, a, α_{O2}, $\mathcal{D}_{O_2}$ and k_r.

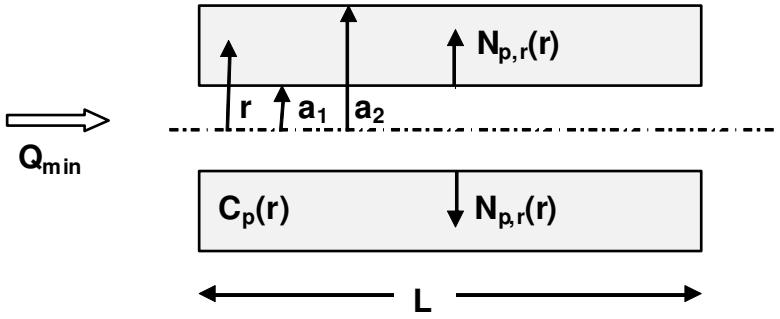
$$i/p_\infty = -4\mathcal{F}\dot{N}_{O2}(a)/p_\infty = ?$$

where $p_\infty = C_\infty/c_G^o\alpha_{O2}$, and $\dot{N}_{O2}(a)$ is the molar oxygen transport rate at the electrode surface. Under what condition does the sensitivity reduce to Eq. 9.2-13?

Problem 9-7: Growth Factor Transport in a Vascular Graft

In fabricating a vascular graft, vascular smooth muscle cells are uniformly seeded throughout a collagen-based hydrogel scaffold in the shape of a cylindrical shell with a length L=10 cm, inner radius a_1=2.25 mm and outer radius a_2=3 mm. A flow of nutrient solution containing PDGF, a molecule which is necessary for cell proliferation, is supplied to the inside surface of the hydrogel shell. For simplicity, we consider the cell-hydrogel mixture to be a homogenous phase. Also, we assume that: 1) the nutrient flow is so rapid that PDGF concentration is maintained at $C_0=10^{-12}$ mol/L everywhere in the nutrient solution including its entry point; and 2) PDGF is depleted in the cell-hydrogel phase at a uniform and constant rate of $R_P=-1 \times 10^{-15}$ mol/s/L. The concentration partition coefficient of PDGF between the nutrient medium and the cell-hydrogel

phase is λ=0.8. The diffusion coefficient of PDGF through the cell-hydrogel phase is $\mathcal{D}_P$=2.25x10^{-6} cm^2/sec. To provide stability, the outer surface of the scaffold is coated with a hard plastic that is impermeable to PDGF.



(a) Formulate the differential equation for the PDGF concentration $C_P(r)$ in the graft $a_2>r>a_1$ based on steady-state radial diffusion with reaction in a material of constant density.
(b) What are the boundary conditions at the inner hydrogel surface $r=a_1$ and the outer hydrogel surface $r=a_2$?
(c) Using results from (a) and (b), develop an algebraic expression for $C_P(r)$.
(d) Using the result of part (c), develop a formula for the radial PDGF flux $N_{r,P}(r)$.
(e) Formulate the minimum volumetric flow rate Q_{min} of culture medium to meet the PDGF requirement for all of the cells. Compute the numerical value for this flow.

Problem 9-8: Derivation of Mole Balance Equations

Derive the mole balance equation for species i during rectilinear transport through a flat slab of constant molar density (Eq. 9.1-12b). Begin with the species mass balance (Eq. 9.1-5) and the equation for the molar flux of a material of constant molar density (Eq. 7.1-5).

Problem 9-9: Derivation of Mean Convective Concentration

Derive Eqs. 9.3.8 for the constant molar flux and 9.3-9 for a representative convective concentration $\tilde{C}_i$ beginning with Eq. 9.3-6 for the molar transport rate by parallel convection and diffusion.

Problem 9-10: Nutrient Diffusion in a Single Cell With First Order Kinetics

Consider a variation of the steady-state, diffusion-reaction model presented in section 9.4.1.

(a) Start with the dimensionless concentration Eq. 9.4-6. Linearize this equation assuming that the concentration is very small relative to the Michaelis constant, $C << K$.
(b) Transform this linearized equation by introducing a change of independent variables: $C(r)=f(r)/r$.
(c) Also letting $C(r)=f(r)/r$, transform the boundary conditions, Eqs. 9.4-7a,b,

(d) Solve the transformed model using hyperbolic functions, sinh and cosh, to find $f(r)$.
(e) Formulate the ratio of central concentration $C(0)$ to the surface concentration $C(1)$.
(f) Plot $C(0)/C(1)$ for values of Da between 0 and 1000 at a value of K=10. Explain your results.

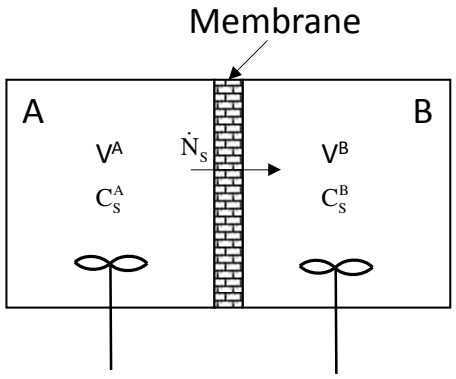
CHAPTER 10.

Problem 10-1: Effect of Cell Membrane Curvature on Membrane Permeation

At some time during dialysis, the intracellular urea concentration of 20mM lags the extracellular concentration of urea that is 10 mM. A nearly spherical cell with an outer diameter of 15.0 μm has a membrane with a thickness of 10 nm and urea permeability of 7.70 nm/sec. Assuming equal solubility of urea in intracellular and extracellular fluid, compute the urea transport rate out of the cell when the membrane (a) is accounted for and (b) is assumed to have an infinitesimal thickness.

Problem 10-2: Membrane Permeability Measurement

To determine permeability P_s of dextran through a non-porous membrane, a diffusion cell was constructed in which a membrane was held in place between two well-mixed chambers (A, B). The chambers were then filled with phosphate-buffered saline (PBS) solution. At t=0, fluorescently labelled 3 kDa dextran was added to chamber A such that its concentration was C_o. Chamber B was sampled continuously to monitor the increasing dextran concentration C_S^B as a function of time. The volume of the chambers were $V^A=V^B=5$ ml and the surface area of the membrane was $S_m=2$ cm^2. In analyzing transport in this apparatus, assume that material transport is so small that the solution volumes in the chambers remain constant and the concentration of solute in chamber A remains constant. Also, assume that the chambers are well-mixed throughout so there are no film resistances at the membrane surfaces.



t (hr)	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2	2.5	3	3.5	4	4.5	5	5.5	6
C_S^B (μM)	3.0	5.1	6.7	8.8	10.5	12.5	14.6	16.3	17.9	20.0	25.4	30.3	34.1	41.5	46.5	52.3	58.1	63.5

(a) Perform a material balance in B to show the dynamics of dextran concentrations in both chambers. Obtain an ODE equation that describes C_S^B vs. t with P_s, V^A and V^B as parameters.

(b) Integrate the above equation to obtain C_S^B as a function of time.

(c) In a particular experiment, C_S^A was set to 1 mM at t=0 and the following data (C_S^B vs t) were obtained. Estimate P_s using a least-squares regression.

Problem 10-3: Transport Through a Composite Membrane

A membrane blood oxygenator separates pure oxygen at atmospheric pressure $p_{O_2}^A = 101.3\,\text{kPa}$ on one side of a planar membrane of surface area S_m from blood on the other side. At a point in the device where the oxygen partial pressure in the blood is $p_{O_2}^A = 6\,\text{kPa}$, compute the local flux $\dot{V}_{O_2}/S_m$ [ml(STP)/(min-cm^2)] of oxygen for the following membranes:

a) Teflon: 1 mil thick.
b) Silicone Rubber: 12 mil thick .
c) Composite Sandwich: 1 mil teflon and 12 mil silicone rubber. Specify any assumptions.

Problem 10-4: Red Cell Shrinking in Hypertonic Solution

Suppose a small amount of solid urea is added to a suspension of red cells in buffered saline solution. Before adding the urea, the saline solution is isotonic so that the cells are in their normal biconcave configuration. Once the urea is added, however, the suspending medium suddenly becomes hypertonic at a concentration of 100 mM. Using Eqs. 10.2-1 and 10.2-2, determine the initial rate of cell volume change, the initial urea flux due to convection and the initial urea flux due to diffusion. Note that the red cell membrane is normally in an unstressed state.

The Kedem-Katchalsky parameters for transport of urea through the red cell membrane are: L_c=4.38 μm/s, L_p=0.00092 μm/kPa/s and σ=0.62. Geometric parameters for the red cell can be found in example 4.3-3.

Problem 10-5: Voltage Clamp Model

The steady-state electro-diffusion model may be improved by relaxing the Goldman assumption. In this model, a channel passes only potassium ion and has a negligibly small fixed protein charge (*i.e.* σ_p=0).

(a) Transform the model (Eqs. 10.3-2 through 10.3-5) into two dimensionless ODEs and four boundary conditions in terms of the following variables:

$$C = \frac{\bar{C}_i^c}{\varpi_i C_i^A}, \quad \psi = \frac{\psi}{\psi_m}, \quad y = \frac{y}{h_m}$$

with dimensionless parameters defined as:

$$J \equiv h_m \bar{J}_i^c \big/ \varpi_i C_i^A \bar{D}_i, \quad \psi_m \equiv \mathcal{F}\psi_m / \mathcal{R}T, \quad C^A \equiv \mathcal{F}\varpi_i h_m^2 C_i^A \big/ \varepsilon_o \psi_m, \quad \alpha \equiv C_i^B / C_i^A$$

(b) Take the y derivative of the dimensionless flux equation in order to eliminate J and then solve the two second order ODE's for $C(y)$ and $\psi(y)$ using physiologically reasonable parameter values (relative to the extracellular fluid at y=0) of ψ_m=-3, C^A=-30) for the case that α=0. Make a plot of $\psi(y)$ and superimpose the electrochemical distribution corresponding to the Goldman assumption.

(c) Numerically solve the two second-order ODE's for $C(y)$ and $\psi(y)$ that involve the parameters ψ_m, C^A and α. Let α=0, ψ_m=-3, C^A=-30, which are physiologically reasonable parameter values relative to the extracellular fluid at y=0. Compare a plot of $\psi(y)$ to the potential distribution when the Goldman assumption is made.

(d) Compute J and compare it to the value obtained with the Goldman assumption (*i.e.,* Eq. 10.3-12).

Problem 10-6: Alveolar-Capillary Permeability

Compute the specific permeability $\hat{P}_s^G$ of the alveolar-capillary membrane (approximated as water) for s=O_2 and s=CO_2, as modeled in example 9.2-2. Compare these values to those in table 10.1-1 for teflon and silicone rubber membranes that are sometimes used in blood oxygenators.

Problem 10-7: Membrane Transport by Diffusion and Convection

Derive Eq. 10.2-9 for transmembrane transport by simultaneous diffusion and convection when the molar flux is constant

(a) Begin with Eq. 10.2-5, which describes $\bar{C}_s(y)$. Integrate between y=0 and y=h_m to find the equation relating the macroscopic concentrations, $\bar{C}_s(0)$ and $\bar{C}_s(h_m)$ at the membrane surfaces.

(b) Simplify the result of (a) by introducing a membrane Peclet number $Pe_m \equiv \beta_s Q_F h_m \big/ \varepsilon_m \bar{\mathcal{D}}_s S_m$ and then for solve for $\dot{N}_s$. Using Eqs. 7.4-42 that relate $\bar{C}_s(0)$ and $\bar{C}_s(h_m)$ to the concentrations in the external continuous media, C_s^A and C_s^B, show that

$$\dot{N}_s = \varpi_s \beta_s Q_F \left(\frac{e^{Pe_m} C_s^A - C_s^B}{e^{Pe_m} - 1} \right)$$

(c) When convection is absent, purely diffusive transport rate through a membrane $\left[\dot{N}_s\right]_{diff}$ can be inferred from the diffusion flux, Eq. 7.4-45. Subtract this diffusive component from

the result of part (b) to determine the transport rate due to convection alone:

$$\left[\dot{N}_s\right]_{conv} = \varpi_s \beta_s Q_F \left[C_s^A - \left(C_s^A - C_s^B\right)\left(\frac{1}{Pe_m} - \frac{1}{e^{Pe_m}-1} \right) \right].$$

(d) Combine the diffusive and convective contributions

$$\dot{N}_s = \left[\dot{N}_s\right]_{conv} + \left[\dot{N}_s\right]_{diff}$$

to verify Eq. 10.2-9 .

Problem 10.8: Membrane Resting Potential

A thin uncharged membrane separates two well-mixed compartments (A and B) of aqueous solutions containing 2-2 electrolytes (*e.g.* $CaSO_4$, $MgSO_4$, etc.). Each electrolyte *i* is completely dissociated into its corresponding cations *ci* and anions *ai*. These ions each have a different concentration, C_{ci}^B and C_{ai}^B, in the two compartments and a different permeability, P_{ci} and P_{ai}, through the membrane. Assume steady-state and unidirectional transport.

(a) Starting with Eq. 10.3-17 in which the dimensionless electrical potential difference is ψ_m, show that

$$\sum_i P_i z_i^2 \left[\frac{C_i^A - C_i^B \exp\left(\mathcal{F} z_i \Delta\psi / \mathcal{R}T\right)}{1 - \exp\left(\mathcal{F} z_i \Delta\psi / \mathcal{R}T\right)} \right] = 0$$

where $\Delta\psi = \psi^A - \psi^B$ is the electrical potential difference between the compartments.

(b) Express the equation of part (a) in terms of the ion permeabilities, the ion concentrations and a single exponential, $\exp\left(-2\mathcal{F}\Delta\psi / \mathcal{R}T\right)$.

(c) Solve the result of part (b) for $\exp\left(-2\mathcal{F}\Delta\psi / \mathcal{R}T\right)$ and then for $\Delta\psi$.

(d) Compare your result to the analogous equation for 1-1 electrolytes given in textbook. Judging from this result, how is the potential difference across a membrane affected by the magnitude of the charge of permeable ions.

CHAPTER 11.

Problem 11-1: An Alternative Uniport Model

Derive the uniport flux equation when the equilibrium binding coefficients for solute-transport binding have different values ($\kappa_1 \neq \kappa_2$), and the translocation constants do not depend on direction ($P_1=P_{-1}$ and $P_2=P_{-2}$).

(a) Combine Eqs. 11.1-8a,b with Eq. 11.1-6 to formulate the ratio C_{ST}^B / C_{ST}^A.

(b) Combine Eqs. 11.1-8a,b with Eq. 11.1-7 to formulate the ratio C_{ST}^A / T_T.

(c) Combine the results of parts (a) and (b) with Eq. 11.1-4 to obtain the net flux N_S in terms of C_S^A, C_S^B and T_T.

(d) Show that this result reduces to Eq. 11.1-11 when the binding equilibrium constants are equal on the two sides of a membrane.

Problem 11-2: Completion of the Static Head Graph for Antiport

Sketch the static head graph for antiport (Fig. 11.2-2) in all four quadrants of the x-y plane. Label the direction of the S_1 and S_2 fluxes (either >0 or <0) in each of the eight regions between the static head lines. In which regions will secondary active transport of S_1 occur and in which regions will secondary transport of S_2 occur?

Problem 11-3: Numerical Illustration of Cotransport

Species S_1 and S_2 undergo cotransport across a cell membrane according to the competitive binding model shown in figure 11.2-1. The equilibrium parameters are known to be κ_1=3.0mM and κ_2=1.0mM. The concentration of S_1 on the two sides of the membrane are $C_{S_1}^A = 20\text{mM}$ and $C_{S_1}^B = 2.0\text{mM}$. The concentration of S_2 on the A side of the membrane is $C_{S_2}^A = 25\text{mM}$.

(a) Using these values, plot the zero flux lines on a graph of $\left(C_{S_1}^A - C_{S_1}^B\right)$ versus $\left(C_{S_2}^A - C_{S_2}^B\right)$ as in figure 11.2-2. Label the region where secondary active transport occurs.

(b) On the graph from part (a), mark the points corresponding to static head conditions of this system. What are the constraints on the value of $C_{S_2}^B$ for active transport to occur? What range of $C_{S_2}^B$ values will not produce active transport?

(c) With trial values of $C_{S_2}^B = 10, 0, 5$ that each fall within one of the three conditions found in part (b), find the numerical signs of the S_1 and S_2 fluxes. Do the flux directions relative to their driving forces correspond to the expected behavior?

Problem 11-4: An Alternative Inhibited Cotransport Model

Derive a model of the inhibited cotransport of S and S* when the inhibitor I is on the outside surface (B) of the cell rather than on the instead surface (B). Note that Eqs. 11.3-1 and 11.3-2 still apply:

$$\kappa = \frac{C_S^A C_T^A}{C_{ST}^A} = \frac{C_{S^*}^A C_T^A}{C_{S^*T}^A} = \frac{C_S^B C_T^B}{C_{ST}^B} = \frac{C_{S^*}^B C_T^B}{C_{S^*T}^B}$$

$$P_1\left(C_{ST}^A - C_{ST}^B\right) + P_1\left(C_{S^*T}^A - C_{S^*T}^B\right) = P_2\left(C_T^B - C_T^A\right)$$

(a) Modify the equations for the inhibitor-transporter equilibrium constant κ_I (11.3-19) and the total transporter concentration T_R (Eq. 11.3-20).

(b) Using these four equations, show that

$$C_T^B = \frac{T_T\kappa - C_T^A\left(\kappa + \underset{\sim}{C}_S^A\right)}{\left(\kappa + \underset{\sim}{C}_S^B + C_I\kappa/\kappa_I\right)} \quad \text{and} \quad C_T^A\left(P_1\underset{\sim}{C}_S^A + P_2\kappa\right) = C_T^B\left(P_1\underset{\sim}{C}_S^B + P_2\kappa\right)$$

Then, for the free transporter at the two membrane surfaces obtain:

$$C_T^A = \frac{\kappa T_T\left(P_1\underset{\sim}{C}_S^B + P_2\kappa\right)}{\left(P_1\underset{\sim}{C}_S^A + P_2\kappa\right)\left(\kappa + \underset{\sim}{C}_S^B + C_I\kappa/\kappa_I\right) + \left(P_1\underset{\sim}{C}_S^B + P_2\kappa\right)\left(\kappa + \underset{\sim}{C}_S^A\right)}$$

$$C_T^B = \frac{\kappa T_T\left(P_1\underset{\sim}{C}_S^A + P_2\kappa\right)}{\left(P_1\underset{\sim}{C}_S^A + P_2\kappa\right)\left(\kappa + \underset{\sim}{C}_S^B + C_I\kappa/\kappa_I\right) + \left(P_1\underset{\sim}{C}_S^B + P_2\kappa\right)\left(\kappa + \underset{\sim}{C}_S^A\right)}$$

where $\underset{\sim}{C}_S^A \equiv C_S^A + C_{S^*}^A$ and $\underset{\sim}{C}_S^B \equiv C_S^B + C_{S^*}^B$ represent the summed concentrations of labeled and unlabeled solute molecules on the two membrane surfaces.

(c) With the net flux of tagged ligand S* through the membrane given by

$$N_{S^*} = P_1\left(C_{S^*T}^A - C_{S^*T}^B\right)$$

derive the final model equation (analogous to Eq. 11.3-21).

Problem 11-5: Charge Effects During Antiport

Analyze the effect of electrical charge on the competitive antiport of ligands S_1 and S_2 by a transporter T in the presence of an electric field. Consider the case in which the S_1, S_2 and T have the same charge number z_X. In the absence of an electric field, assume that the translocation

rate constant for S_1, S_2 and T has the same value (P_o) and this value is independent of transport direction.

(a) In the presence of an electric potential difference $\Delta\psi$, show that the translocation constants of the three charged species remain equal and have a unique value (P_+) for forward transport and a different value (P_-) for reverse transport.

(b) The model for the S_1 flux during antiport (Eq. 11.2-6) was based on translocation rate constants that were equal for the three species and had the same value in both transport directions. Derive the S_1 flux when the translocation constant is different in the two transport directions: P_+ for all species when transport is from surface A to surface B and P_- in the opposite direction. After modifying the model equation(s), show that

$$C^B_{S_1T} = C^A_{S_1T}\,\frac{P_+}{P_-}\,\frac{\left(1+\kappa_1/C^A_{S_1}+\kappa_1 C^A_{S_2}/\kappa_2 C^A_{S_1}\right)}{\left(1+\kappa_1/C^B_{S_1}+\kappa_1 C^B_{S_2}/\kappa_2 C^B_{S_1}\right)}$$

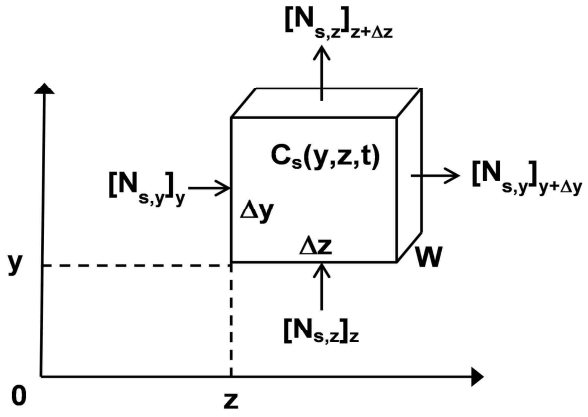
Then, use the equation $N_{S_1} \equiv P_+ C^A_{S_1T} - P_- C^B_{S_1T}$ to show that

$$N_{S_1} = \frac{T_T}{1/P_+ + 1/P_-}\left[\left(1+\kappa_1/C^A_{S_1}+\kappa_1 C^A_{S_2}/\kappa_2 C^A_{S_1}\right)^{-1} - \left(1+\kappa_1/C^B_{S_1}+\kappa_1 C^B_{S_2}/\kappa_2 C^B_{S_1}\right)^{-1}\right]$$

(c) Determine the relative S_1 flux $N^{\Delta\psi}_{S_1}/N^{o}_{S_1}$, where $N^{\Delta\psi}_{S_1}$ is the flux when a transmembrane potential $\Delta\psi$ acts across a cell membrane, and $N^{o}_{S_1}$ is the flux when there is no transmembrane potential. How does the sign of the charge affect the relative flux?

CHAPTER 12.

Problem 12-1: Multidimensional Transport Equations



Applying the shell balance method to the control volume ($\Delta V = W\Delta y\Delta z$) shown above, derive Eq. 12.1-7 for two-dimensional transport in the absence of chemical reaction.

Problem 12-2: Effect of Flow Orientation on Mass Transfer

In designing an oxygenator with hollow fibers, an engineer is considering whether blood flow outside of the fibers should be in a cross-flow or parallel flow configuration. The device will contain hollow fibers that are 5cm long and have an outer diameter of 0.03 cm. The blood flow, either parallel to or perpendicular to the outside of a fiber, will be set at a velocity of 10 cm/sec. Starting with appropriate correlations relating the Sherwood number to the Reynolds and Schmidt numbers, determine the ratio of the mass transfer coefficients in blood for these two flow configurations. Which configuration will maximize the O_2 transport rate into blood.

Problem 12-3: O_2 Supply to a Vascular Graft

In fabricating an endothelialized vascular graft, cells are initially seeded onto the inner surface of a cylindrical tube made of a fluoropolymer with a constant and uniform density. The tube has a length L=10 cm and an inside diameter d=3 mm. After seeding, the cells are cultured to form a complete surface layer while fresh medium flows through the tube at a velocity u. The medium entering the tube has been equilibrated with pure oxygen such that its oxygen partial pressure is 100kPa. The oxygen consumption rate per unit area of tube surface covered by cells is $k_r^c C_{O_2}^c$. Here $C_{O_2}^c$ is the molar O_2 concentration at the cell surface and k_r^c=0.3cm/hr is a reaction rate constant, the kinematic viscosity of the medium is $7\times10^{-7}m^2/s$ and the O_2 diffusion coefficient is $3.3\times10^{-9}m^2/s$.

The objective of this problem is to determine u values that meet the following requirements: 1) to keep the cells alive, O_2 partial pressure at the cell surface cannot go below $p^c_{O_2}$=60kPa; 2) in order to minimize damage to the cells, the medium must be in laminar flow; 3) O_2 partial pressure in the medium is to be maintained as close to $p^b_{O_2}$=100 kPa as possible along the entire tube length. Assume that the medium has a kinematic viscosity of $\upsilon=6.98\times10^{-7}m^2/s$ and an oxygen diffusion coefficient of $\mathcal{D}_{O_2} = 3.3\times10^{-9} m^2/s$.

(a) Recognizing that O_2 transport to the cell surface and consumption by the cells are equal, determine the minimum value of the mass transfer coefficient k_{O_2} in the medium that will meet requirement 1).
(b) Determine the range of u values that can achieve this minimum k_{O_2} when the O_2 concentration profile is not fully developed. Use entry 1a of table 12.2-1 for this computation and also the requirement that the flow be laminar.
(c) Repeat part (b) for an O_2 concentration profile that is fully developed (Entry 1b of table 12.2-1)
(d) Which of the results for u found in parts (b) and (c) are more likely to fufill requirement 3)? Restate this restriction in terms of the flow rate Q of the medium expressed in ml/min.

Problem 12-4 Artificial Liver: Part I. Mass Transfer Coefficient

An extracorporeal artificial liver device is designed to treat patients with acute liver failure. It consists of a parallel array of n_f=3,000 thin-walled hollow fibers of radius a_f=100μm surrounded by a cylindrical shell packed with porcine liver parenchymal cells (hepatocytes).

To minimize immunological reactions with hepatocytes, a patient's blood is continuously separated into a cell-free plasma stream and a suspension stream enriched in erythrocytes, leukocytes and platelets. The cell-free plasma flowing at Q=400ml/min is uniformly distributed among the insides of the fibers. Urea and creatinine transported across the fiber walls from the cell-free plasma are detoxified by the hepatocytes. Oxygen also transported across the fiber walls is necessary to maintain viability of the hepatocytes (The transport parameters have values of $\upsilon=8\times10^{-7}m^2/s$, α_{O2}=0.021ml/(dL-kPa) and $\mathcal{D}_{O_2} = 3.0\times10^{-9} m^2/s$).

(a) Confirm that the plasma inside of the fibers is in laminar flow.
(b) Determine the minimum fiber length to establish a fully-developed O_2 concentration profile within each fiber (table 12.1-1; entry 1).
(c) Compute the value of the individual mass transfer coefficient k_{O2} for O_2 on the inside of the fibers when the fiber lengths are greater than this minimum.

12-5 Artificial Liver: Part II. Required Fiber Surface

Consider the artificial liver device described in part I of this problem. Additional geometric parameters are: the cross-sectional area of the cylindrical shell containing the fibers (A), the fiber

length (L), and the fraction of the shell occupied by hepatocytes (ε). The hepatocytes are metabolizing O_2 at a constant (maximum) rate V_m[moles/time/volume hepatocytes], which is so fast that the O_2 concentration in the hepatocyte region is close to zero.

(a) Formulate A in terms of n_f, a_f and ε.
(b) Beginning with Eq. 2.4-25, perform a steady state oxygen balance in the device to obtain an ordinary differential equation for the oxygen partial pressure in a hollow fiber p_{O2} as a function of distance z from the plasma inlet at z=0. Assume that O_2 transport across the fiber wall is limited by the individual mass transfer coefficient k_{O2} through the flowing plasma.
(c) If p_o is the O_2 partial pressure at a fiber inlet, integrate this ODE to obtain an algebraic expression for the O_2 distribution.
(d) Using this result, formulate the maximum length of the device such that all cells will be supplied with O_2 at a rate that satisfies its metabolic demand.
(e) For a particular bioartificial liver device, $V_m=10^{-7}$ mol/m^3/hr, ε=0.5 and the entering plasma has been pre-oxgenated to reach a p_o=70kPa. The values of Q, a_f, n_f and k_{O2} are the same as in part I of this problem. Compute the maximum length of this device. Does this result seem reasonable?

Problem 12-6: Continuous Ambulatory Peritoneal Dialysis (CAPD)

During a session of CAPD, typically carried out at home, a dialysate consisting of a physiologic electrolyte solution with an osmotic agent such as dextrose is gravity fed through an indwelling catheter into the peritoneal cavity that surrounds the lungs. After several hours the dialysate is drained by gravity into an empty container. While it remains in the body, the dialysate accumulates toxins and some protein by passive diffusion from blood that perfuses the peritoneal surfaces. This results in an osmotic filtration of water from the blood. After a few hours, the dialysate is drained into an empty container.

A frequently used model of this process consists of two well-mixed compartments: a body compartment of volume $V^B(t)$ and a dialysate compartment of volume $V^D(t)$, separated by a semi-permeable peritoneal membrane. For simplicity, assume that osmotic filtration across the membrane as well as metabolic urea production during the CAPD session can be neglected.

(a) Formulate mole balances for urea concentration in the dialysate $C_u^D(t)$ and the blood $C_u^B(t)$.
(b) Solve the differential equations of part (a) to find an equation for C_u^D/C_{uo}^B as a function of time when dialysate is initially free of urea and the initial urea concentration in the body compartment is C_{uo}^B.
(c) Obtain a least-squares estimate of the model parameters by fitting the results from part (b) to the following data (Lysaght MJ, Farrell PC. J Membrane Sci. 44:5-33, 1989):

C_u^D/C_{uo}^B	0.03	0.19	0.33	0.57	0.68	0.74	0.87	0.89	0.91	0.96	0.96	0.98	0.985	0.975
t(min)	10	25	50	95	150	190	255	280	310	370	400	430	460	490