PART III

CHAPTER 6.

Problem 6-1: Diffusion Flux Constraint

(a) Show that the sum of the molar diffusion fluxes is zero:

$$\sum_{i=1}^{I} \mathbf{J_i} = \sum_{i=1}^{I} C_i(\mathbf{u_i} - \mathbf{u}^*) = 0$$

(b) Show that the sum of the mass diffusion fluxes is zero:

$$\sum_{i=1}^{I} \mathbf{j_i} = \sum_{i=1}^{I} \rho_i(\mathbf{u_i} - \mathbf{u}) = 0$$

Problem 6-2: Chemical Species Flux

Consider the axial transport of air in trachea during inhalation. In an experiment, the axial component of the mass averaged velocity of the mixture was 120 mm/sec. Using isotope analysis (O^{18}), the axial component of oxygen velocity was found to be 119 mm/sec.

(a) Determine the mass averaged and molar averaged axial velocities of the mixture.
(b) Determine the molar diffusional fluxes of oxygen and nitrogen.

Problem 6-3: Multicomponent Diffusion

Alveolar gas is a quaternary mixture of oxygen (component 1), carbon dioxide (component 2), nitrogen (component 3) and water vapor (component 4) at a relative humidity of 100%. The mole fractions of the first three component gases on a dry basis are y_1=0.15, y_2=0.05 and y_3=0.80.

(a) Determine the actual mole fractions of the four components in the alveolar air.
(b) Compute the multicomponent diffusion coefficients $\mathcal{D}'_{ij}$ (i,j=12) for this gas mixture at T=37°C and P=101.3 kPa given the binary diffusion coefficient values:

$$\mathcal{D}_{12} = \mathcal{D}_{21} = 0.166 \text{ cm}^2/\text{sec}$$
$$\mathcal{D}_{13} = \mathcal{D}_{31} = 0.219 \text{ cm}^2/\text{sec}$$
$$\mathcal{D}_{14} = \mathcal{D}_{41} = 0.282 \text{ cm}^2/\text{sec}$$

$$\mathcal{D}_{23} = \mathcal{D}_{32} = 0.177 \text{ cm}^2/\text{sec}$$
$$\mathcal{D}_{24} = \mathcal{D}_{42} = 0.201 \text{ cm}^2/\text{sec}$$
$$\mathcal{D}_{34} = \mathcal{D}_{43} = 0.259 \text{ cm}^2/\text{sec}.$$

(c) Write the multicomponent diffusional flux equations for oxygen and for carbon dioxide. Under what conditions would these diffusion rates be approximated by pseudo binary diffusion equations resembling Fick's Law? Are the diffusion coefficients in these simplified equations, $\mathcal{D}'_{12}$ and $\mathcal{D}'_{21}$ equal as they would be in Fick's Law?

Problem 6-4: Nernst-Planck Equation

Starting from the equations

$$\mathbf{J}_i = -\left(\frac{c_L x_i \mathcal{D}_i}{\mathcal{R}T}\right)\nabla\mu_i$$

and

$$\mu_i(T,P,x_1) = \mu_i^*(T,P) + \mathcal{R}T\ln(\gamma_i x_i) + z_i\mathcal{F}\psi$$

derive the Nernst-Planck equation in the form

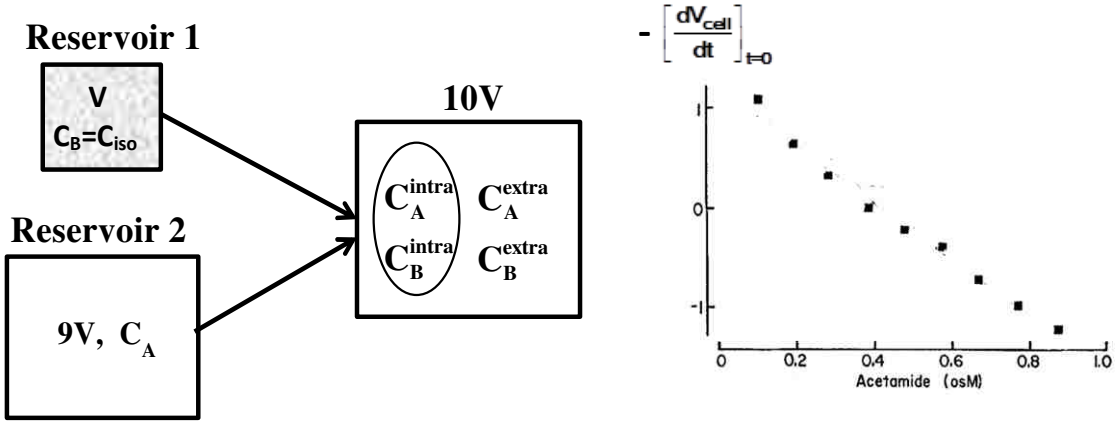
$$\mathbf{J}_i = -\mathcal{D}_i\left[\nabla C_i + \left(\frac{z_i\mathcal{F}}{\mathcal{R}T}\right)C_i\nabla\psi\right]$$

What assumptions are necessary to arrive at this result?

Problem 6-5: Stopped Flow Measurement of the Reflection Coefficient

Owen and colleagues (J. Membrane Biol, 26:287-299, 1976) describe a stopped flow method of evaluating the Staverman reflection coefficient σ_A of a permeable species A through the red cell membrane. The experiment consists of rapidly mixing the contents of a reservoir 1 of volume V with the contents of reservoir 2 of volume 9V. Reservoir 1 contains red cells suspended at a very low volume fraction in a medium containing impermeable species B (mainly NaCl) at an isotonic concentration $C_B = C_{iso}$. Reservoir 2 contains a solution of species A at a concentration C_A, which might be hypotonic (or hypertonic).

In an experiment carried out at any particular C_A, red cell volume $V_{cell}(t)$ is continuously monitored by light scattering after the reservoir contents are mixed. From this volume record, the initial rate of red cell volume shrinkage, $-[dV_{cell}/dt]_{t=0}$, is deduced. The above graph shows the $-[dV_{cell}/dt]_{t=0}$ values obtained from nine separate experiments with permeant A=acetamide present at premixed concentrations C_A between 0.1 to 0.9 osmolar.



After mixing of the two reservoir contents, the velocity of water out of (or into) the cells can be modeled by Starling's equation (Eq. 6.5-32) in the form:

$$u^* = L_P\left[\Delta P - (\sigma_A \Delta\pi_A + \sigma_B \Delta\pi_B)\right]$$

where the 'Δ' refers to the difference between intracellular and extracellular quantities.

(a) What is the value of σ_B, the reflection coefficient of the species B?

(b) What are the values of u* and ΔP when $[dV_{cell}/dt]_{t=0}=0$.

(c) What can we say about the intracellular and extracellular concentrations, C_A^{intra}, C_B^{intra}, C_A^{extra} and C_B^{extra}, when $[dV_{cell}/dt]_{t=0}$?

(d) Using the Van't Hoff equation to express osmotic pressure differences, incorporate the results of parts (a)-(d) to show that when $[dV_{cell}/dt]_{t=0}$, Starling's equation reduces to

$$\sigma_A = \frac{C_{iso}}{C_A}$$

.

(e) Compute σ_A using the information in the graph.

Problem 6-6: Solute Diffusion Fluxes in a Dilute Multicomponent Solution

Assume a very dilute, thermodynamically ideal solution consisting of i=1,2,…(I-1) uncharged solutes with mole fraction $x_i=\varepsilon << 1$ in a solvent i=I with mole fraction, $x_I=1-\varepsilon$. Using a quatrinary solution (*i.e.*, I=4) as an example, show that Eq. 6.3-18 for the solute diffusion fluxes reduces to

$$\mathbf{J}_i = -c\mathcal{D}_{iI}\nabla x_i \quad (i=1,2,...I-1)$$

where $\mathcal{D}_{iI}$ is the binary diffusion coefficient of solute i in the solvent.

Problem 6-7: Free Diffusion of Two Strong Electrolytes

Consider a dilute aqueous solution that contains both NaCl and KCl, which is usually the case in biological systems. The diffusion coefficients of the individual ions in this solution are $\mathcal{D}_{Na}$, $\mathcal{D}_{K}$ and $\mathcal{D}_{Cl}$.

(a) Using a modification of the approach in section 6.4, formulate the local value of the electrical potential gradient $\nabla\psi$ generated by the free diffusion (*i.e.*, open electrical circuit) of NaCl and KCl when their local mole fractions and mole fraction gradients are x_{NaCl}, x_{KCl}, ∇x_{NaCl} and ∇x_{KCl}.
(b) Show that this result is consistent with Eq. 6.4-9 for a solution containing a single 1-1 electrolyte 'ca'.
(c) Formulate the effective diffusion coefficient of NaCl in the solution: $\mathcal{D}_{NaCl} \equiv -\mathbf{J}_{NaCl}/c_L \nabla x_{Na}$. How is this result different from $\mathcal{D}_{NaCl}$ in an aqueous solution of NaCl alone?

Problem 6-8: Relationship Between Molar and Mass Diffusion Fluxes

According to Eq. 6.1-13, two ways of expressing the transport flux of a solute i are in molar units as $\mathbf{N_i}$ or mass units as $\mathbf{n}_i$.

$$\mathbf{N_i} \equiv \mathbf{u}^* C_i + \mathbf{J_i}$$
$$\mathbf{n_i} = \mathbf{u}\rho_i + \mathbf{j_i}$$

Derive the relationship between $\mathbf{j}_i$ and $\mathbf{J}_i$ so that these equations for $\mathbf{N}_i$ and $\mathbf{n}_i$ are equivalent. The final equation should be written in terms of the quantities: $\mathbf{J}_i$, $\mathbf{j}_i$ $\mathbf{u}_i$(species velocity), x_i (mole fraction), c(molar density), M_i (species i molecular weight) and I(number of species in solution).

Problem 6-9: Diffusion Flux of a Trace Solute in a Multicomponent Solution

A stable isotope of xenon, Xe^{188}, is frequently used as a tracer gas in respiratory experiments. Assume dry air containing mole percentages of 1%Xe (component 1), 79%N_2(component 2), and 20%O_2(component 3). At P=101.3 kPa and T=310°K, the binary diffusion coefficients between these components in [cm^2/s] are:

$$\mathcal{D}_{12} = \mathcal{D}_{21} = 0.133\,, \quad \mathcal{D}_{13} = \mathcal{D}_{31} = 0.129\,, \quad \mathcal{D}_{23} = \mathcal{D}_{32} = 0.219$$

Determine the multicomponent molar flux equations for each of the three components.

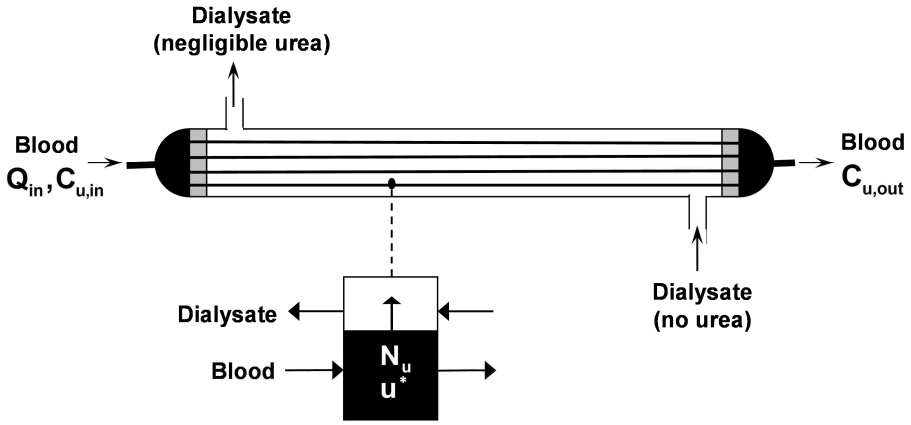
(a) From Eqs. 6.3-14 and 6.3-15, obtain the components of the [B] matrix with oxygen as component, I=3
(b) When the mole fraction and thus the concentration gradients of the three components are

similar (*i.e.* $\nabla C_1 \approx \nabla C_2 \approx \nabla C_3$), how do the coupled terms in the flux equations compare to the principle (Fickian diffusion) terms?

(c) How do the multicomponent diffusion coefficients of the principle terms compare to the binary coefficients of these gases with one another? Explain why is this is the case.

Problem 6-10: Performance of a Hollow Fiber Dialyzer

A Toray B2-100 dialyzer contains 11,000 polymethyl methacrylate hollow fibers with a total surface area of $S_t=1.21m^2$ (Sakai K, J. Biomaterials Applications. 4:71-101, 1989). At the entrance of the device, a blood flow of $Q_{in}=5000$ is uniformly distributed among the insides of the fibers. Dialysate, which flows outside the device, is a physiological salt solution that enters with no urea and leaves with just negligible urea.



The thin walls of a hollow fiber act as a membrane that allows diffusion of urea from blood to dialysate with urea permeability, $P_u=6.51$ μm/s. A higher pressure in the blood relative to the dialysate results in uniform serum filtration through the fiber walls at a total rate of $Q_{wall}=20$ ml/min.

(a) For the conditions of this device, use appropriate simplifying assumptions such that the Starling equation for urea flux across the fiber walls (Eq. 6.5-30) can be reduced to $N_u=P_{u,eff}C_u$ where $P_{u,eff}=u^*+P_u$ is an effective permeability that accounts for convection and diffusion.

(b) Use the relation between u^* and Q_{wall} for the computation of $P_{u,eff}$. What percentage of $P_{u,eff}$ is due to diffusion alone?

(c) Treating the collection of all the fibers as a single tube with surface area S_t, use the spatially distributed model from example 2.4-2 to determine the efficiency of urea removal, $E=(1-C_{u,out}/C_{u,in})$, for a single pass of blood flow through this device. If there are N passes, what is the overall efficiency . Is this adequate for treating a patient?

CHAPTER 7

Problem 7-1: Prediction of a Gas Phase Diffusion Coefficient

Use the Fuller Equation (Eq. 7.2-10) to estimate the diffusion coefficients of acetone-air gas mixture at:

(a) STP conditions
(b) 2 atm and 37^{o}C

Problem 7-2: Prediction of Liquid Phase Diffusion Coefficients

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(a) Use the Wilke-Chang equation (Eq. 7.3-13) to evaluate diffusion coefficients of glucose in water at 37^{o}C at infinite dilution.
(b) Potassium chloride dissociates in water to form Na^{+} cation (c) and Cl^{-} anion (a). Estimate the diffusion coefficient of KCl in water at 25^{o}C using equation 7.3-18.

Problem 7-3: Hydration Shell Radius of an Ion

(a) Develop a relationship to estimate the radius of an ion in a dilute solution by equating the hydrodynamic mobility from the Stokes solution (Eq. 7.3-10) with the electrophoretic mobility (Eq. 7.3-16).
(b) Use the above relationship to compute the radii of hydrated sodium and chloride ions at body temperature at which the viscosity of water is 7×10^{-4} Pa-s.

Problem 7-4 Renkin Model

The hindered diffusion coefficients of a number of solutes have been measured (Beck and Schultz. Science. 1302-1305, 1970) in mica sheets that have been fission etched to produce pores of quite uniform diameters with essentially no tortuosity. Using the data below, estimate the radius of the pores in the membrane. The diffusivities correspond to a temperature of 25^{o}C at which the viscosity of water is $\mu=0.900\times10^{-3}$ kg/(m-s).

Solute	Urea	Glucose	Sucrose	Raffinose	2-Dextrin	β-Dextrin	Ribonuclease
$\mathcal{D}_s^{\infty}[10^{-10}m^2/s]$	13.8	6.73	5.21	4.34	3.44	3.22	1.18
$\bar{\mathcal{D}}_s[10^{-10}cm^2/s]$	12.0	5.05	3.69	2.86	2.03	1.79	0.118

Problem 7-5: Diffusion in a Cell Suspension

To see whether the thinness of a red cell contributes much to O_2 transport, you are to compare the hindered diffusion coefficient of blood for normal red cells (a_1/a_2=1/4) to that of spherical cells (a_1/a_2=1) using the approach of example 7.5-2. In particular, predict $\bar{\mathcal{D}}_{O2}/\bar{\mathcal{D}}^{c}_{O2}$ at both aspect ratios and at various capillary p_{O2} from 5 to 10 kPa. Assume a typical hematocrit of 45%. Make a graph that compares the results you obtained at the two aspect ratios (Note that the parameters on the curves in the left panel of figure 7.4-4 should be "a_1/a_2").

Problem 7-6: **Difference between Molar and Mass Average Velocities**

Based on Eqs. 7.1-4 and 7.1-3, the mass and molar flux equations for the diffusion of component 1 in a mixture of two components are:

$$\mathbf{n}_1 = \rho \mathbf{u} \omega_1 - \rho \mathcal{D}_{12} \nabla \omega_1 \tag{1}$$

$$\mathbf{N}_1 = \rho \mathbf{u} x_1 - \rho \mathcal{D}_{12} \nabla x_1 \tag{2}$$

(a) By starting with the relationship between ω_1 and x_1 (Eq. 6.1-4), show that:

$$\nabla \omega_1 = \frac{M_1 M_2}{M^2} \nabla x_1 \tag{3}$$

where M_1 and M_2 are the molecular weights of the two components, and M is the molecular weight of the solution.

(b) By dividing the mass flux equation for component 1 (Eq. 1) by M_1, show that:

$$\mathbf{N}_1 = c \mathbf{u} x_1 - c \mathcal{D}_{12} \frac{M_2}{M} \nabla x_1 \tag{4}$$

(c) By equating Eq. 2 to Eq. 4, show that the difference between mean and molar average velocity is of the form $\left(\mathbf{u}^* - \mathbf{u}\right) = -c \beta \mathcal{D}_{12} \nabla x_1$ where β depends only on molecular weights. Under what condition will this velocity difference be negligible?

Problem 7-7: Oxygenation of Red Cell Suspension

Example 7.5-2 illustrates a model of O_2 diffusion through a red blood cell suspension. The enhancement of the diffusion coefficient because of oxyhemoglobin formation can be obtained from Eq. 7.5-25:

$$\frac{\left\langle \bar{\mathcal{D}}_{O2} \right\rangle}{\mathcal{D}^{c}_{O2}} - 1 = \frac{1}{p_{O2,2} - p_{O2,1}} \int_{p_{O2,1}}^{p_{O2,2}} I(p_{O2}) dp_{O2}$$

with the integrand defined as:

$$I(p_{O2}) = \frac{\varepsilon_H}{1/[1-\chi_{O2}(p_{O2})] - (1-\varepsilon_H)/[1+\eta_{O2}(\chi_{O2})]}$$

Here, $\chi_{O2}(p_{O2})$ is given by Eq. 7.5-24, and $\eta_{O2}(\chi_{O2})$ is then found from figure 7.5-4 using a value of $a_1/a_2=1/4$ (Note that the parameters on the curves in the left panel of this figure should be "a_1/a_2" not a_2/a_1).

In this problem, you are to estimate the enhancement, $\left\langle \bar{\mathcal{D}}_{O2} \right\rangle / \mathcal{D}^c_{O2} - 1$, across a planar layer of a red cell suspension of hematocrit ε_H=0.50. The surfaces of the layer are exposed to O_2 partial pressures of $p_{O2,1}$=0 kPa and $p_{O2,2}$=10 kPa. You are to evaluate the integral based on the trapezoid rule with ten uniform intervals of $\Delta p_{O2} = (p_{O2,2} - p_{O2,1})/10$.

$$\int_0^{10} I(p_{O2})dp_{O2} \approx \frac{1}{2(10\Delta p_{O2})}\left[I(0\Delta p_{O2}) + 2I(\Delta p_{O2}) + ...2I(9\Delta p_{O2}) + I(10\Delta p_{O2})\right]$$

Why is the resulting enhancement small?

Problem 7-8: Sclera Permeability-Fiber Matrix Model

The sclera is the outer protective layer of the eyeball which also constitutes a diffusion barrier to drug delivery. Using a two-chamber diffusion apparatus, Ambati and coworkers (Retina. 41(5):1181-1185, 2000) measured the permeability of a number of high molecular weight, fluorescent tracers dissolved in physiological salt solution through rabbit sclera incubated at 37°C. The mean±SD thickness of the 8 sclera samples used in the measurements was 416±21μm.

Tracer s	Molecular Radius a_s[nm]	Mean Permeability±sd P_s[nm/s]
Sodium Fluorescein	0.5	845±161
FITC-D (4 kDa)	1.3	252±51
FITC-D (20 kDa)	3.2	67.9±41.8
FITC-D (40 kDa)	4.5	27.9±15.8
FITC-BSA (67 kDa)	3.62	54.9±21.2
Rhodamine D (70 kDa)	6.4	13.5±7.7
FITC-D (70 kDa)	6.4	13.9±8.8
FITC-IgG (150 kDa)	5.23	46.1±21.7
FITC-D (150 kDa)	8.25	13.4±8.8

These investigators related their permeability data to structural information by the following fiber matrix model:

$$P_s = \frac{\varepsilon \mathcal{D}_s^{\infty}}{h} \exp\left[-(1-\varepsilon)\left(\frac{2a_s}{a_f} + \frac{a_s^{\,2}}{a_f^{\,2}} \right) \right] \exp\left[-\sqrt{1-\varepsilon}\left(1 + \frac{a_s}{a_f} \right) \right] \quad \text{(corrected Eq. 7.5-3)}$$

(a) Assuming a viscosity of 4×10^{-4} Pa-s for the physiological solution at 37°C, estimate the diffusion coefficient $\mathcal{D}_s^{\infty}$ in the physiological medium for each of the tracers.

(b) Plot log(P_s) versus a_s for the data on the same graph as log(P_s) predicted by the model for various values of the pore radius a_p and the pore volume fraction ε. What pair of a_p and ε values provide a good fit of the predicted log(P_s) curve to the data using a least-squares fit?

(c) Do the these values of a_p and ε make physical sense? How well does the model follow the data?

Problem 7-9: Sclera Permeability-Pore Model

Repeat problem 7-8, this time modeling the Ambati data (Retina. 41(5):1181-1185, 2000) by the Renkin pore model instead of the fiber matrix model.

(a) Formulate the permeability P_s when the hindered diffusion coefficient $\bar{\mathcal{D}}_s$ is given by the Renkin pore model.

(b) Plot log(P_s) versus a_s from the data on the same graph as log(P_s) predicted by the model for various values of the pore radius a_p and the dimensionless parameter group $\beta \equiv \varpi\varepsilon/\tau_p$. What pair of a_p and β values provide a good fit of the data points to the predicted log(P_s) curve?

(c) Do the these values of a_p and β make physical sense? How well does the pore model follow the data? How does this compare to fit of the fiber matrix model?

Problem 7-10: Temperature Correction of Binary Diffusion Coefficients

(a) At 0°C, the binary diffusion coefficient of oxygen through nitrogen is 1.81×10^{-5} m^2/s. Estimate this diffusion coefficient at body temperature.

(b) At 25°C, the binary diffusion coefficient of a dilute solution of glucose in water is 6.73×10^{-10} m^2/s. Estimate this diffusion coefficient at body temperature.

CHAPTER 8

Problem 8-1: Batch Reaction

Suppose we are studying the acid-catalyzed hydrolysis of sucrose (S) into glucose (G) and fructose (F) in a well-mixed batch (*i.e.*, closed) reactor. This is an elementary reaction that occurs according to the following equation:

$$S + H_2O \rightarrow G + F$$

With 100 grams of sucrose dissolved in 1 liter of very dilute acid aqueous solution, we measured sucrose concentrations after 1000 seconds elapsed. In two separate experiments, sucrose concentrations of 0.245 and 0.130 molar remained when reactor temperature was maintained at 25°C and 35°C, respectively.

(a) What is an appropriate reaction rate expression ($R_{sucrose}$) for this reaction assuming that the concentration of water is far in excess of the sucrose concentration?
(b) Perform a material balance to obtain an ordinary differential equation for the sucrose concentration $C_s(t)$.
(c) If C_{So} is the initial sucrose concentration, integrate the material balance to determine $C_s(t)$.
(d) Determine the values of the reaction rate constant for the acid-catalyzed hydrolysis of sucrose at 25 and 35°C.
(e) Compute the half-times (*i.e.*, time for the sucrose concentration to be reduced to 1/2 of its initial value) of the reaction at 25 and 35°C.
(f) Determine the values of the pre-exponential constant and the activation energy for this reaction.

Problem 8-2: Receptor Binding by Competitive Antagonism.

In the analysis of competitive antagonism, drugs A and B bind reversibly with the same receptor R:

$$A + R \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} X$$

$$B + R \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} Y$$

Let C_A and C_B represent the unbound concentrations of A and of B; C_X and C_Y represent the receptor-bound concentrations of A and of B; T_A and T_B represent the total (constant) concentrations of A and of B in unbound and bound forms. Let C_R represent the concentration of free receptors and T_R represent the total (constant) concentration of receptors in bound and free forms.

(a) Write the intrinsic reaction rates of the two reaction steps, $\bar{r}_1$ and $\bar{r}_2$, in terms of the species concentrations C_A, C_R, C_X, C_B and C_Y for the two reaction steps.
(b) Determine the intensive reaction rates for the bound ligands, R_X and R_Y, in terms of the

species concentrations.

(c) By introducing T_A, T_B and T_R, show that:

$$R_X = k_1 (T_A - C_X)(T_R - C_X - C_Y) - k_{-1} C_X$$
$$R_Y = k_2 (T_B - C_Y)(T_R - C_X - C_Y) - k_{-2} C_Y$$

Under what experimental conditions can these expressions be linear with respect to C_X and C_Y?

Problem 8-3: Pseudo Steady-State Hypothesis for Enzyme Kinetics

According to the pseudo steady-state hypothesis, enzyme-substrate binding is so rapid that occupied enzyme sites quickly adjust to any change in the surrounding substrate concentration.

In the book, the product formation rate R_P for Michaelis-Menten kinetics was derived using the quasi-equilibrium hypothesis. As an alternative, you are to derive R_P using the pseudo steady state hypothesis that the rate of change of occupied enzyme sites $R_{ES} \approx 0$.

(a) Write the intrinsic reaction rates, $\bar{r}_1$ and $\bar{r}_2$, in terms of the species concentrations C_E, C_S and C_{ES} for the two reaction steps given by Eq. 8.5-2a,b.

(b) Determine the intensive reaction rates, R_E, R_S, R_{ES} and R_P, in terms of C_E, C_S and C_{ES}.

(c) Apply the pseudo steady-state assumption to R_{ES} so that R_P and R_S can be expressed only in terms of C_S and the total enzyme concentration T_E. How does the result differ from Eq. 8.5-7?

Problem 8-4: Competitive Enzyme Kinetics

The competitive reactions of substrate (S) and inhibitor (I) that produce a desired product (P) and an undesired product (Q), respectively, have the following kinetics and equilibrium constants:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P \quad ; \quad \kappa_k \equiv \frac{C_{ES}}{C_E C_S} = \frac{k_1}{k_{-1}}$$
$$E + I \underset{i_{-1}}{\overset{i_1}{\rightleftharpoons}} EI \xrightarrow{i_2} E + Q \quad ; \quad \kappa_i \equiv \frac{C_{EI}}{C_E C_I} = \frac{i_1}{i_{-1}}$$

(a) Formulate the intensive reaction rate of desired product formation R_P in terms of the species concentrations C_E and C_{IE} and the total enzyme concentration T_E of occupied and unoccupied sites.

(b) Apply the quasi-equilibrium assumption to the two reversible reaction steps so that R_P is expressed solely in terms of the concentrations C_S, C_I and T_E.

(c) Rearrange R_P in a Lineweaver-Burk form (Eq. 8.5-11a) and sketch a graph of this equation for a family of lines with increasing C_I values.

Problem 8-5: Papain Activity

Papain (E) is a protease that acts on peptide bonds and is used as a meat tenderizer. In an experiment (Stockell and Smith, JBC, 1956), papain activity was evaluated indirectly by measuring the concentration (C_B) of ammonia (B) produced in a hydrolysis reaction of the substrate, benzoyl-L-argininamide (S).

$$S \xrightarrow{E} B$$

The reaction was carried out in a constant volume batch reactor at different initial substrate concentrations (C_{S0}). The results in the following table list the dynamic values of C_B [10^{-4}M] observed for five different C_{S0}.

C_{S0}=0.01M		**0.02 M**		**0.04 M**		**0.06 M**		**0.08 M**	
Time*	**C_B**	**Time**	**C_B**	**Time**	**C_B**	**Time**	**C_B**	**Time**	**C_B**
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7.6	1.5	8.4	2.5	9.1	3.9	9.6	5.6	10.4	7.1
12.1	2.4	12.8	3.8	13.5	6.4	14.2	8.5	14.9	10.3
17.4	3.2	18.1	5.5	18.8	8.4	19.2	11.4	19.9	13.7
22.9	4.2	23.8	7.1	24.3	11.5	25.0	14.3	25.6	17.1
27.6	5.1	28.3	8.6	28.9	13.6	29.6	17.1	30.1	20.0

*Time is in minutes

(a) Assuming that the reactor is well-mixed and that the reaction occurs by Michaelis-Menten kinetics, show that the dynamic changes in product B can be modeled from material balance equations as follows:

$$\frac{dC_B}{dt} = \frac{V_{max}C_{S0} - V_{max}C_B}{(K_M + C_{S0}) - C_B} \quad ; \quad C_B(0) = C_{B0}$$

(b) Plot C_B vs time for the different values C_{S0} in the table. Explain in terms of the model equation why the behavior is linear at each fixed value of C_{S0}.
(c) Find the slopes of the C_B versus t plots.
(d) Estimate V_{max} and K_M by regressing the reciprocal of these slopes to the reciprocal of the model equation.

Problem 8-6: Temperature Dependence of Reaction Rate

It is frequently said that a reaction rate constant will double for every 10^oC increase in temperature. Using the Arrhenius equation, determine:

(a) what activation energy must a reaction have if the reaction rate constant is doubled for a 10^oC change in temperature from 25 to 35^oC;
(b) whether the same activation energy will lead to a fourfold increase in the rate constant when there is a 20^oC increase in temperature from 25 to 45^oC;

(c) the same activation energy leads to a doubling of the reaction rate constant when the starting temperature is 35°C?

Problem 8-7: Kinetics of a Two-Step Enzymatic Reaction

For the enzymatic reaction:

$$A + 3B \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 2C \xrightarrow{k_3} D + 2E$$

(a) Write this reaction in terms of two reaction steps, and formulate the intrinsic reaction rates, $\bar{r}_1$ and $\bar{r}_2$, in terms of the species concentrations C_A, C_B, C_C, C_D and C_E.
(b) Determine the extensive reaction rates, R_A, R_B, R_C, R_D and R_E, in terms of the five species concentrations.
(c) Apply the quasi-equibrium assumption to the first reaction so that the extensive reaction rates are expressed only in terms of C_A and C_B.

Problem 8-8: Monovalent Binding in a Well Mixed Batch Reactor

Equation 8.4-10 describes the dynamics of monovalent binding of a ligand L to a receptor R to form the ligand-receptor complex LR in a batch reactor.

(a) Make this initial value problem dimensionless using the variables: $t \equiv (k_r/\kappa_c)t$, $C_{LR} \equiv C_{LR}/C_{LR}(0)$, $\kappa_c \equiv \kappa_c C_{LR}(0)$, $T_L \equiv T_L/C_{LR}(0)$ and $T_R \equiv T_R/C_{LR}(0)$.
(b) Rewrite the equation and initial conditions for a reactor that is first loaded with a solution containing receptors fully saturated with ligand and no unbound ligand.
(c) Find the analytical solution to the dynamic equation and its initial condition when κ_c=1. Note that

$$\int \frac{d\xi}{(a+b\xi)(a'+b'\xi)} = \frac{1}{ab'-a'b}\ln\left(\frac{a'+b'\xi}{a+b\xi}\right)$$

(c) Make a plot of $C_{LR}(t)$. Explain this result.

Problem 8-9: Elution of Heparin From a Vascular Stent

To regain patency of a blocked artery, a heparin coated stent is surgically inserted along the inner wall of the blood vessel. Elution of the heparin coating into flowing blood is intended to improve biocompatibility of the stent surface.

Consider a stent in the form of a cylindrical shell of length L and radius 'a'. Heparin is eluted intro blood from its inner surface at a flux N_H[mol/(s-m^2]. The heparin undergoes enzymatic reactions with blood components at an overall rate that can be modeled with Michaelis-Menton kinetics:

$$R_H[\text{mol}/(\text{s}-\text{m}^3)] = -\frac{V_m C_H}{K_m + C_H}$$

Here, the maximum rate V_m[mol/s] and the the equilibrium paramter K_m are constants. The heparin concentration C_H[mol/m^3] varies with distance z along the stent.

(a) Start with the PDE model Eq. 2.4-25 for the heparin concentration distribution $C_H(z,t)$ between the upsteam (z=0) and downstream (z=L) ends of the stent when the volumetric blood flow in the artery is constant, Q[m^3/s]. Express the parameters of this model in terms of radius 'a' and a velocity u.

(b) What is the steady-state form of the model equation $C_H(z)$ found in part (a)? Simplify the reaction term for the case that there is a small buildup of heparin concentration along the stent? What is the boundary condition at z=0, if we only consider a single pass of heparin-free blood along stent?

(c) Express this model in terms of the dimensionless variables:

$$C_H = C_H / B, \quad z = z / L$$

Obtain the dimensionless scaling factor B such that the dimensionless equation has the form:

$$\frac{dC_H}{dz} = 1 - \alpha C_H, \quad C_H(0) = ?$$

What grouping of model parameters makes up the dimensionless parameter α?

(d) Solve this problem to find $C_H(z)$.

Problem 8-10: Analytical Solution to Competitive Binding in a Batch Reactor

The model for the competitive binding problem of ligands L1 and L2 to a receptor R is given by Eqs. 8.4-30 and 8.4-31.

(a) Simplify these equations when $F_{L1R}(0) = F_{L2R}(0) = 0$, $\kappa_{c1}=\kappa_{c2}=1$ and $\xi=1$.

(b) Show that the Laplace transform of this model then leads to $F_{L1R} = F_{L2R}$.

(c) Obtain the time domain solution for $F \equiv F_{L1R} + F_{L2R}$.

(d) Make a plot of $F_{L1R}(t)$ and $F_{L2R}(t)$, and explain their dynamic behavior.