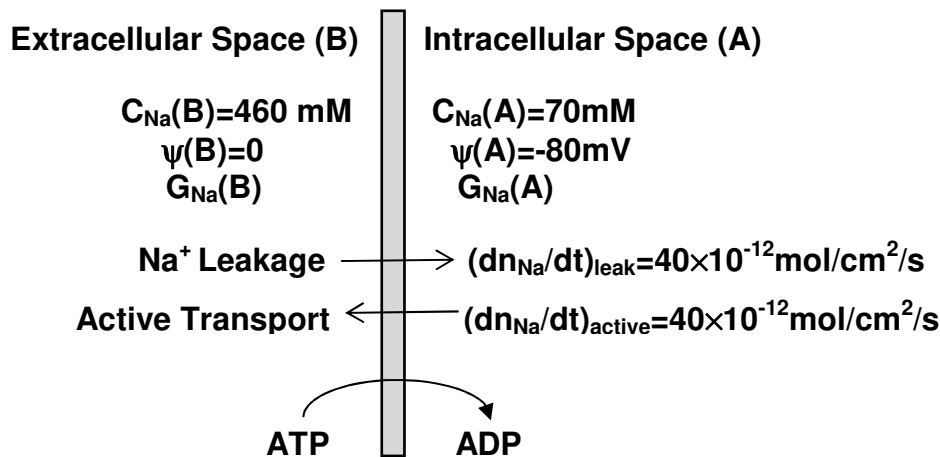


## PART II

### CHAPTER 3.

#### Problem 3-1: Gibbs Free Energy With Active Transport

The intracellular and extracellular concentrations of  $\text{Na}^+$  surrounding a cell membrane are maintained at 70 and 460 mM, respectively, by active transport mechanisms that counteract a  $\text{Na}^+$  leakage into the cell of 40 picomoles/s per  $\text{cm}^2$  of membrane surface. The transmembrane potential inside of the cell is  $-80 \text{ mV}$  relative to the outside of the cell.



- (a) Evaluate the difference in the electrochemical potential of sodium ion ( $\Delta\mu_{\text{Na}}$ ) between the intracellular and the extracellular fluid assuming ideal solution behavior. Use the parameter values  $z_i = +1$ ,  $F = 96485.3 \text{ coul/mol}$ ,  $T = 310 \text{ K}$ .
- (b) Starting with Gibbs Free Energy difference:  $\Delta G_{\text{Na}} = G_{\text{Na}}(\text{B}) - G_{\text{Na}}(\text{A})$  and  $\mu_{\text{Na}} \equiv (\partial G_{\text{Na}} / \partial n_{\text{Na}})_{T,P}$ , use the chain rule to derive

$$\frac{d(\Delta G_{\text{Na}})}{dt} \left( \frac{\text{J}}{\text{s}} \right) = \left[ \mu_{\text{Na}}^{\text{c}}(\text{B}) - \mu_{\text{Na}}^{\text{c}}(\text{A}) \right] \left( \frac{\text{J}}{\text{mol}} \right) \frac{dn_{\text{Na}}}{dt} \left( \frac{\text{mol}}{\text{s}} \right)$$

where  $dn_{\text{Na}}/dt$  is the molar rate of active transport.

- (c) Evaluate the rate of increase in Gibbs Free Energy per membrane surface,  $(1/S)d(\Delta G_{\text{Na}})/dt$ , that is provided by active transport to counteract the sodium ion leakage.
- (d) Let  $\Delta G_{\text{ATP}}$  be the Gibbs free energy released by the  $\text{ATP} \rightarrow \text{ADP}$  reaction to counteract the  $\text{Na}^+$  leakage into the cell. Explain why  $\Delta G_{\text{Na}} + \Delta G_{\text{ATP}}$  must be less than zero. Based on this inequality, estimate the minimum rate at which ATP molecules must be converted to ADP per unit area of membrane in order to maintain sodium ion homeostasis. Note that for

ATP → ADP at 37 °C and 1 atm,  $\Delta G_{\text{ATP}} = -50 \text{ kJ/mol ATP}$ .

### Problem 3-2: Protein Denaturation Temperature

As an approximation, we can assume that proteins exist either in the native (or physiologically functioning) state and the denatured state. The standard molar  $\Delta H$  and  $\Delta S$  of the denaturation of a certain protein is  $+540 \text{ kJ mol}^{-1}$  and  $+1.60 \text{ kJ K}^{-1} \text{ mol}^{-1}$ , respectively.

- Comment on the signs and magnitudes of these quantities.
- Calculate the temperature at which denaturation becomes spontaneous.

### Problem 3-3: Debye-Huckel Theory of Activity Coefficients

Evaluate the activity coefficient at 25°C of a physiological saline solution with  $C_{\text{NaCl}} = 0.154 \text{ M}$  using the modified Debye-Huckel theory:

$$\log(\gamma_{\pm}) = -0.509 z_+ |z_-| \frac{\sqrt{I}}{1 + \sqrt{I}} \quad ; \quad I \equiv \frac{1}{2} \sum_i z_i^2 C_i$$

where  $I$  is ionic strength and  $C_i$  (moles/gm water) is the concentration of the  $i^{\text{th}}$  ion. Assume that NaCl is completely ionized.

### Problem 3-4: Chemical Potential Change With Temperature

Starting with the Gibbs equation for an open system:  $dG = VdP - SdT + \sum_{i=1}^I \mu_i dm_i$ , derive the expression for chemical potential derivative with respect to temperature:  $(\partial \mu_i / \partial T)_{P, m_i} = -\hat{S}_i$ .

### Problem 3-5: Thermodynamics of an Ideal Gas

- From the ideal gas law, show that

$$\hat{V}_i \equiv \left( \frac{\partial V}{\partial m_i} \right)_{T, P, m_j} = \frac{\mathcal{R}T}{P}$$

- From the chemical potential for an ideal gas, show that

$$\left( \frac{\partial \mu_i}{\partial P} \right)_{T, m_i} = \frac{\mathcal{R}T}{P}$$

### Problem 3-6: Water Phase Changes

Compare the difference between  $\Delta H$  and  $\Delta E$  for the following physical changes that occur at constant pressure.

- 1 mole of ice  $\rightarrow$  1 mole of water at 273°K and 1 atm. The molar volumes of ice and water at 273°K are 0.0196 L mol<sup>-1</sup> and 0.0180 L mol<sup>-1</sup> respectively.
- 1 mole of water  $\rightarrow$  1 mole of steam at 373°K and 1 atm. The molar volumes of water and steam at 373°K are 0.0188 L mol<sup>-1</sup> and 30.61 L mol<sup>-1</sup> respectively.
- For both of the above phase changes, is work being done on the system by the surroundings, or is work being done by the surroundings on the system?

### Problem 3-7: Stearic Acid Calorimetry

A closed, rigid calorimeter with an internal volume of 1.00 liters initially contains 2.00g of solid stearic acid (C<sub>18</sub>H<sub>36</sub>O<sub>2</sub>) and pure oxygen gas at T=20.0°C and P=101.3kPa. After igniting the mixture, complete combustion of the stearic acid occurs to form gaseous CO<sub>2</sub> and liquid H<sub>2</sub>O. By removing 2060 kJ of heat from the calorimeter as combustion proceeds, the temperature remains at 20.0°C. At the temperature and pressures of this process, solid stearic acid has a mass density of 0.847 kg/L, liquid water has a mass density of 1.00 kg/L, and a gas phase has a molar density given by the ideal gas law. The molecular weight of stearic acid is 284g/mol and water is 18.0 g/mol.

- Write the stoichiometric equation for the complete combustion of stearic acid.
- Compute the moles  $n_{\text{gas},1}$  and volume  $V_{\text{gas},1}$  of O<sub>2</sub> gas initially present in the calorimeter
- Show that there is sufficient O<sub>2</sub> for complete combustion to occur.
- Compute the moles  $n_{\text{gas},2}$  and volume  $V_{\text{gas},2}$  of O<sub>2</sub>+CO<sub>2</sub> gas finally present in the calorimeter.
- Using the first law of thermodynamics, find the internal energy change of the contents of the calorimeter,  $\Delta E$ .
- Using the definition of enthalpy, find the enthalpy change  $\Delta H$ .

### Problem 3-8: Work During Isothermal Expansion

An adventurous diver explores the depths of Lake Erie. A quantity of 0.89 moles of air (assumed to be an ideal gas) is initially at a pressure of 105 atm at 295 K within the diver's pressurized air supply. Just before the air is delivered to the diver's lungs, a regulator drops the pressure 1 atm, allowing the gas to expand to a much larger volume. Calculate the work per mole air done if the expansion is carried out isothermally and reversibly. Is this work done on the air by the surroundings, or by the air on the surroundings? Comment on the amount of work done under non-reversible conditions.

### Problem 3-9: Integration of the Gibbs-Duhem Equation for Internal Energy

Consider a process in which the moles  $m_i$  of each substance in a system changes by the same factor  $f$ , while the temperature, pressure and volume are unchanged. Applying this change of state to the Gibbs-Duhem Equation, show that  $E=TS+\sum\mu_i m_i$ .

### Problem 3-10: Ideal Gas Law From the Chemical Potential

Derive the ideal gas law from the constitutive equation for the chemical potential:

$$\tilde{\mu}_i(T, p_i) = \mu^\circ(T) + \mathcal{R}T \ln p_i \quad ; \quad p_i \equiv y_i P$$

- (a) Find the derivative  $(\partial\tilde{\mu}_i/\partial P)_{T, m_i}$  in terms of  $\mathcal{R}$ ,  $T$  and  $P$ . Here, the subscript  $m_i$  means that the number of moles of all components are held constant.
- (b) Using Amagat's law of additive volumes for an ideal gas,  $V_i = \sum_i y_i V$ , show that the results of part (a) lead to  $PV=m\mathcal{R}T$ . Note that  $m$  is the total number of moles of gas,  $V$  is the total gas volume and  $V_i$  is the volume of component  $i$ .

### Problem 3-11: Margules Activity Coefficient Model

One form of the Margules model of the activity coefficients for a binary mixture of volatile liquids 1 and 2 is given by:

$$\ln \gamma_i = A_i(1 - x_i)^2 \quad (i = 1, 2)$$

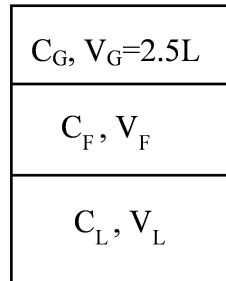
where  $A_1$  and  $A_2$  depend on temperature. Determine the relationship between these two parameters such that the composition dependence of  $\gamma_1$  and  $\gamma_2$  is consistent with the Gibbs-Duhem equation.

## CHAPTER 4.

### Problem 4-1: Gas Distribution Among Tissues

A dental patient inhales a mixture of 10 mole percent nitrous oxide ( $N_2O$ ) in air as an analgesic. The patient's inhaled and exhaled tidal volume are both  $V_T=500$  ml and breathing rate is  $BR=18/\text{min}$ . The patient tissues weigh  $W_B=70$  kg, 25% of which is the fat weight  $W_F$  and the remainder  $W_L$  is lean. The lungs have a functional residual capacity (lung volume at the start of inhalation) of  $V_R=2.5$  L.

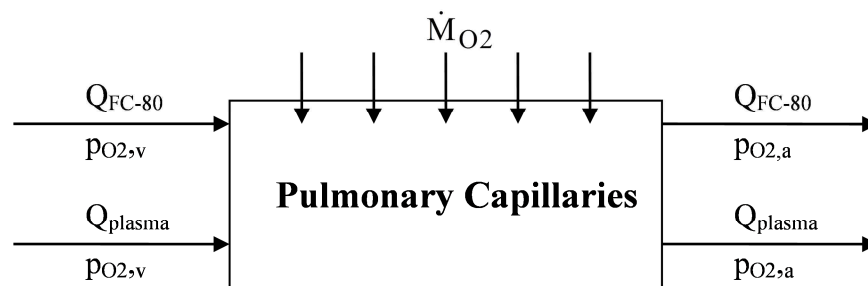
Because  $N_2O$  is metabolized very slowly, it will build up and reach equilibrium in the patient's fat and lean tissues. This can be represented by a 3-compartment model of lung gas, fat, and lean tissue in which their  $N_2O$  equilibrium concentrations are represented by  $C_i$  ( $i=G,F,L$ ).



- (a) What is the  $N_2O$  molar concentration in the lung? Assume an ideal gas under body temperature and pressure conditions.
- (b) Given the equilibrium partition coefficients,  $\lambda^{L,G}=0.466$  and  $\lambda^{F,L}=3.2$ , determine the  $N_2O$  molar concentrations in lean and fat tissue.
- (c) If the density of fat is  $\rho_F=0.91$  and the density of lean tissue is  $\rho_L=1.10$ , determine the number moles of  $N_2O$  in each of the G,F and L compartments.

### Problem 4-2: Oxygen Uptake in Artificial Blood

Perfluorobutyltetrahydrofuran (FC-80) is a fluorinated liquid that is insoluble with water. The Bunsen solubility of oxygen in FC-80 is  $(\alpha_{O_2})_{FC-80}=4.71 \times 10^{-6}$  ml(STP)/(ml-Pa) at  $37^\circ\text{C}$ , which is much greater than that of  $O_2$  in plasma,  $(\alpha_{O_2})_{\text{plasma}}=2.11 \times 10^{-7}$  ml(STP)/(ml-Pa). As a synthetic replacement for blood, we propose to use  $10 \mu\text{m}$  diameter droplets of FC-80 suspended in plasma at a volume fraction of  $H=0.45$ .



- Write the steady-state  $O_2$  mole balance on the synthetic blood flowing through the pulmonary capillaries at a volumetric flow  $Q$  (ml/min). The result should be an equation for total  $O_2$  uptake rate  $\dot{M}_{O_2}$  (mol/min) in terms of  $Q$ ,  $H$ , and the venous (entering) and arterial (exiting)  $O_2$  concentrations,  $C_{O_2,v}$  and  $C_{O_2,a}$ , of the plasma and FC-80 phases.
- Convert the molar  $O_2$  uptake rate to volumetric  $O_2$  uptake,  $\dot{V}_{O_2}$  (ml STP / min) =  $\dot{M}_{O_2} / c_G^\circ$ . In addition, convert the molar  $O_2$  concentration to content  $\hat{C}_{O_2}$  (ml STP / ml) =  $C_{O_2} / c_G^\circ$  and then to partial pressure  $p_{O_2}$  (Pa) =  $\hat{C}_{O_2} / \alpha_{O_2}$  (Assume interfacial equilibrium so that the  $O_2$  partial pressures are the same in the FC-80 and plasma phases).
- The maximum uptake rate  $(\dot{V}_{O_2})_{\max}$  would occur when arterial  $O_2$  is equal to inhaled  $O_2$  concentration  $p_{O_2,\text{inhaled}}$  and all the  $O_2$  was extracted from arterial blood by the time it recirculates to the pulmonary capillary input. Simplify the balance equation under these conditions.
- Compute  $(\dot{V}_{O_2})_{\max}$  when a patient with a cardiac output of 5000 ml/min is inhaling room air. How does compare to the  $O_2$  demand by whole body metabolism under resting conditions?

### Problem 4-3: Pulmonary Oxygen Balance

A person at rest inhales air at a tidal volume of 500ml, temperature of 23°C and a total pressure of 101.3 kPa. Gas is exhaled at a tidal volume of 510 ml, body temperature of 37°C and pressure of 101.3 kPa. As measured with a respiratory mass spectrometer that does not detect water vapor, inhaled air contains a mole fraction  $y_{O_2,\text{dry}}=0.21$  of  $O_2$ , whereas exhaled gas contains a mole fraction  $y_{O_2,\text{dry}}=0.18$  of  $O_2$ . According to a humidity monitor, the relative humidity of inspired air is 50% and expired air is essentially saturated with water vapor.

- Determine the partial pressures of water vapor in inspired air,  $p_{w,\text{in}}$  and expired air,  $p_{w,\text{out}}$ .
- Compute the mole fractions of  $O_2$  in inhaled (wet) air,  $y_{O_2,\text{in}}$ , and exhaled (wet) gas,  $y_{O_2,\text{out}}$ .
- Find the minute volumes of inhaled air,  $\dot{V}_{\text{in}}$ , and exhaled gas,  $\dot{V}_{\text{out}}$ , in ml(STP)/min.
- Calculate the  $O_2$  uptake rate  $\dot{V}_{O_2}$  in ml(STP)/min.

### Problem 4-4: Cancer Detection by Electrical Potential

The measurement of transmembrane potential *in vivo* has been proposed as a method to distinguish tumor tissue from normal tissue during surgery. Experiments in tumor tissue have found that cancer cells have an alkaline intracellular pH=7.6, whereas the extracellular fluid has an acidic pH=6.7. In normal tissue, intracellular and extracellular fluids are both alkaline, at a pH=7.4 and pH=7.2, respectively.

- Using the Nernst equation, calculate the transmembrane potential for the tumor tissue and for normal tissue assuming that the potential is due only to the concentration of hydrogen ions.
- Based on the comparative values of these transmembrane potential differences, is it

worthwhile to develop a “nano-voltmeter” for identifying malignant tissue?

**Problem 4-5: Colloid Osmotic Pressure Difference**

Two compartments, A and B, are separated by a membrane that is permeable to both sodium and chloride ions but impermeable to hemoglobin. Compartment A contains a sodium chloride solution and also contains 0.04 moles per liter of hemoglobin with a charge of +5. Compartment B contains a 0.15 molar sodium chloride solution and does not contain hemoglobin.

A	B
0.04M Hb <sub>4</sub>	0.15M NaCl
T <sup>A</sup> = 310°K	T <sup>B</sup> = 310°K

- (a) Determine the electrical potential difference between the two compartments..
- (b) Assuming ideal solution behavior, compute the colloid osmotic pressure difference between the two compartments.

**Problem 4-6: Extracellular Double Layer**

Suppose the outer surface of a cell membrane located at y=0 bears a negative charge that creates a potential  $\psi_0 - \psi_\infty = +10\text{mV}$  relative to the bulk phase of the extracellular fluid where  $y \rightarrow \infty$ . Assuming the extracellular solution can be approximated by a sodium chloride solution of concentration  $C_\infty = 0.15\text{M}$ , use the Gouy-Chapman double layer model to determine:

- (a) the fixed charge  $\Sigma_0$  at the membrane surface; and
- (b) the  $\text{Na}^+$  concentration partition coefficient,  $C_{\text{Na}} = C_{\text{Na}}(0)/C_\infty$ , between the surface and the bulk solution.

**Problem 4-7: Insulin Loading onto Carrier Particles**

A spherical polymeric drug carrier is designed to deliver human insulin with a molecular weight of 5808 Da directly to blood. Consider a batch of  $10^9$  spherical carrier particles of  $10 \mu\text{m}$  diameter that are initially devoid of insulin. We load insulin into these particles by mixing with 5 mL of an aqueous insulin solution until equilibrium is reached. If the aqueous solution initially contains 50 mg of insulin per ml of solution, determine the final concentration of insulin in the particles. The Nernst equilibrium coefficient of insulin (I) between the polymer (P) and aqueous solution (W) is  $\eta_i^{P,W} = x_i^P / x_i^W = 15$ . The overall molar densities of polymer and aqueous solution are constant at  $c^P = 20 \text{ mol/L}$  and  $c^W = 50 \text{ mol/L}$ , respectively. The polymer volume  $V^P$  and the aqueous solution volume  $V^W$  are constants.

- (a) Obtain the relationship of the initial moles of insulin  $m_I$  in solution to the equilibrium concentrations of insulin in solution  $C_I^W$  and in the polymer  $C_I^P$ .
- (b) Compute the volume of polymer  $V^P$  and the initial moles of insulin  $m_I$ .
- (c) Evaluate the partition coefficient,  $\lambda_I^{P,W} = C_I^P/C_I^W$
- (d) Evaluate the equilibrium insulin concentrations  $C_I^W$  and  $C_I^P$ .

**Problem 4-8: Osmotic Pressure of Physiological Saline**

What is the osmotic pressure of a solution of 0.9 grams of NaCl per 100 ml at body temperature? Can this physiological saline solution (PSS) be used to rehydrate patients by intravenous infusion? Explain.

**Problem 4-9: Gibbs-Donnan Equilibrium for a 1-2 Electrolyte**

Consider a system with two compartments (A,B) separated by a membrane permeable to ions but not to protein molecules. Compartment A contains an aqueous solution of the strong 1-2 electrolyte ( $\text{CaCl}_2 \rightarrow \text{Ca}^{2+} + 2\text{Cl}^-$ ) and a protein P at a concentration  $C_p = 0.01\text{M}$ . The protein has a net electrical charge  $z_p = +10$ . Compartment B contains a 0.2 M aqueous solution of  $\text{CaCl}_2$ . This system is in electrochemical equilibrium at a temperature  $T = 25^\circ\text{C}$ .

- (a) From electrochemical equilibrium (Eq. 4.3-26), relate the concentrations of the  $\text{Ca}^{2+}$  and  $\text{Cl}^-$  ions in the two compartments.
- (b) Neglecting the electrical charge contribution of hydrogen and hydroxyl ions, write the charge-balance equations in each compartment.
- (c) From results of (a) and (b), determine the concentrations of  $\text{Ca}^{2+}$  and  $\text{Cl}^-$  in compartment A. (Hint: a cubic equation must be solved)
- (b) Using these results, determine the potential difference across the membrane.

**Problem 4-10: Derivation of Double Layer Equations**

According to Eq. 4.4-17, the ODE for the double layer model is given by:

$$\frac{d^2\psi}{dy^2} = \frac{1}{2}(e^{+\psi} - e^{-\psi})$$

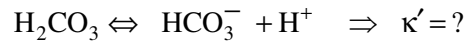
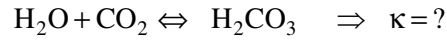
- (a) Verify that Eq. 4.4-17 when is satisfied when  $d\psi/dy$  is given by Eq. 4.4-18
- (b) Show that the final solution for  $\psi$  given by Eq. 4.4-22 reduces to Eq. 4.4-26a for small values of the surface potential  $\psi_0$ . Note that  $e^b \approx 1+b$  when  $b \ll 1$  and  $\ln(1+a) \approx a$  when  $a \ll 1$ .



## CHAPTER 5.

### Problem 5-1: Bicarbonate-CO<sub>2</sub> Equilibrium:

- (a) Express the equilibrium constants for the carbonic acid reactions in terms of the concentrations of the reactants and products.



- (b) Combining the two equilibrium equations and defining  $\text{pK}' \equiv -\log \kappa'$ , show that

$$\text{pH} = \text{pK}' - \log \text{KC}_{\text{H}_2\text{O}} + \log \left( \frac{\text{C}_{\text{HCO}_3^-}}{\text{C}_{\text{CO}_2}} \right)$$

- (c) Based on equilibrium measurements,  $\text{C}_{\text{H}_2\text{CO}_3}/\text{C}_{\text{CO}_2} = 0.0032$  and  $\text{pK}' = 3.6$ . Show that

$$\text{pH} = 6.1 + \log \left( \frac{\text{C}_{\text{HCO}_3^-}}{\text{C}_{\text{CO}_2}} \right)$$

### Problem 5-2: Isoelectric Point of Aspartic Acid

Aspartic acid has two carboxyl groups and one amide group that can each undergo an acid dissociation (see Table A.3-6 in the book). When solving this problem, let  $\text{A}^{2-}$  represent the fully dissociated form of the acid in which both carboxyl groups are in their negatively charged form  $\text{COO}^-$  and the amide group is in its uncharged form  $\text{NH}_2$ . Other forms of the acid can be represented by adding  $\text{H}^+$  groups to  $\text{A}^{2-}$ . For example, the zwitterion will can be represented by  $\text{H}_2\text{A}$ .

- (a) Write the sequence of dissociation equations for  $\text{H}_3\text{A}^+$ ,  $\text{H}_2\text{A}$  and  $\text{HA}^-$  that progressively occur when an aspartic acid solution initially at a very low pH is titrated with a strong base until it reaches a very high pH.
- (b) Write the equation relating the concentrations of charged aspartic acid species at the isoelectric point.
- (c) Let  $\kappa_1$ ,  $\kappa_2$  and  $\kappa_3$  represent the equilibrium constants for the dissociation of  $\text{H}_3\text{A}^+$ ,  $\text{H}_2\text{A}$  and  $\text{HA}^-$ , respectively. Write the formulas for these dissociation constants in terms of species concentrations.
- (d) From the results of (b) and (c), derive an equation for  $\text{C}_{\text{H}^+}$  at the isoelectric point in terms of the  $\kappa_1$ ,  $\kappa_2$  and  $\kappa_3$ .
- (e) Using the values of  $\text{pK}_1 \equiv -\log \kappa_1 = 1.88$ ,  $\text{pK}_2 = 3.65$  and  $\text{pK}_3 = 9.6$ , solve this equation for  $\text{C}_{\text{H}^+}$

numerically and obtain the value of pH at the isoelectric point.

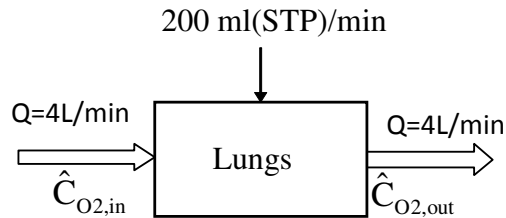
**Problem 5-3: Ligand-Receptor Binding Equilibria**

Derive the ligand-receptor equilibrium expressions in terms of total binding site concentration  $T_R$ , ligand concentration  $C_L$  and the appropriate equilibrium constants for:

- (a) divalent binding of ligand L to receptor R (*i.e.*,  $2L + R \rightleftharpoons LRL$ )
- (b) allosteric binding of ligand L to receptors  $R_1$  and  $R_2$  (*i.e.*,  $L + R_1 \rightleftharpoons LR_1$  ;  $L + R_1 \rightleftharpoons LR_1$ )  
when  $LR_1$  is interconvertible to  $LR_2$  (*i.e.*,  $LR_1 \rightleftharpoons LR_2$ ), but  $R_1$  is not interconvertible to  $R_2$ .

**Problem 5-4: Hyperbaric Oxygen Treatment**

A patient is being treated for gangrene in a hyperbaric chamber in which the partial pressure of oxygen is  $p_{O_2} = 600\text{kPa}$ . The patient’s metabolic demand is  $\dot{V}_{O_2} = 200 \text{ ml(STP)/min}$ , cardiac output is  $Q=4 \text{ L/min}$ , and blood contains  $\rho_{Hb} = 12\text{g/dL blood}$ .



- (a) Assuming steady-state  $O_2$  transport of blood, formulate the oxygen mole balance around the lungs. Then convert this to an equation for venous and arterial  $O_2$  contents,  $\hat{C}_{O_2,in}$  and  $\hat{C}_{O_2,out}$ , in terms of  $Q$  and  $\dot{V}_{O_2}$ .
- (b) Compute the numerical difference in oxygen content between the arterial (output) and venous (input) blood of the lungs. Also compute  $\hat{C}_{O_2,max}^b$ , the maximum content of  $O_2$  in the patient’s blood.
- (c) Assuming that arterial blood is essentially in equilibrium with inhaled gas from the chamber, determine the  $O_2$  partial pressure and the dissolved  $O_2$  content. Also compute the bound  $O_2$  content in arterial blood using the Hill equation neglecting the effects of blood pH and  $CO_2$  (*i.e.* use Eq. 5.5-16 for this computation). What percentage of the total  $O_2$  content is accounted for by physically dissolved oxygen? How does this compare with breathing air at 1 atm?
- (d) Use the result of parts (a) and (c) to compute the estimate the  $O_2$  partial pressure  $p_{O_2,in}$  assuming in venous blood. How does  $p_{O_2,in}$  in this case compare with the usual  $p_{O_2,in} = 5.3\text{kPa}$ ?

### Problem 5-5: Approximation of the CO<sub>2</sub> Dissociation Curve

Carbon dioxide content in blood as a function of p<sub>CO<sub>2</sub></sub>, S<sub>O<sub>2</sub></sub> and pH is given by Eq. 5.5-30 in the book.

$$\hat{C}_{\text{CO}_2} = \left\{ 1 - \frac{0.0299\rho_{\text{Hb4}}[\text{g/dL}]}{(2.244 - 0.422S_{\text{O}_2})(8.740 - \text{pH})} \right\} \alpha_{\text{CO}_2}^{\text{plas}} (1 + 10^{\text{pH} - \text{pK}_{\text{CO}_2}}) p_{\text{CO}_2} \quad (1)$$

As blood moves along a capillary, changes in p<sub>CO<sub>2</sub></sub> and S<sub>O<sub>2</sub></sub> drive changes in pH. If pH is assumed to be constant, however,  $\hat{C}_{\text{CO}_2}$  can be determined directly from this equation. In this problem we will see how this approach compares to the “exact method” applied in example 5.5-5.

- (a) For small changes in p<sub>CO<sub>2</sub></sub> and S<sub>O<sub>2</sub></sub> from to a pair of reference values, p<sub>CO<sub>2,ref</sub></sub> and S<sub>O<sub>2,ref</sub></sub>, linearize Eq. (1) by expanding in a Taylor series to obtain a final equation of the form:

$$\hat{C}_{\text{CO}_2} = \hat{C}_{\text{CO}_2,\text{ref}} + B_1(S_{\text{O}_2} - S_{\text{O}_2,\text{ref}}) + B_2(p_{\text{CO}_2} - p_{\text{CO}_2,\text{ref}}) \quad (2)$$

Here, B<sub>1</sub> and B<sub>2</sub> depend on the reference values, p<sub>CO<sub>2,ref</sub></sub> and S<sub>O<sub>2,ref</sub></sub>, as well as blood properties ρ<sub>Hb4</sub>, pH, pK<sub>CO<sub>2</sub></sub> and α<sub>CO<sub>2</sub></sub><sup>plas</sup>.

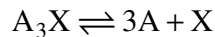
- (b) Using pH (which we are constraining to be constant) and ρ<sub>Hb4</sub> as adjustable parameters, perform a non-linear fit to Comroe’s data (see table below). You should simultaneously regress the data reported at S<sub>O<sub>2</sub></sub> = 0.975 and S<sub>O<sub>2</sub></sub> = 0.700 in order to minimize the summed absolute error between the  $\hat{C}_{\text{CO}_2}$  predictions of Eq. (1) and the entire data set.

	CO <sub>2</sub> Content, $\hat{C}_{\text{CO}_2}$ [ml(STP) / dL]								
S <sub>O<sub>2</sub></sub> =0.700	46.3	47.7	49.0	50.3	51.7	53.0	54.3	55.7	57.0
S <sub>O<sub>2</sub></sub> =0.975	43.1	44.4	45.7	47.1	48.4	49.7	51.1	52.4	53.7
p <sub>CO<sub>2</sub></sub> [kPa]	0	1.33	2.67	4.00	5.33	6.66	8.00	9.33	10.66

- (c) Make a plot comparing the  $\hat{C}_{\text{CO}_2}$  predictions to the data. How does this compare to the results of the “exact method” in figure 5.5-4 in which changes in pH are accounted for.

### Problem 5-6: Dissociation Equilibrium and Standard Free Energy

When added to one liter of an aqueous solution containing 150 mmoles of NaCl, 50 mmoles of compound A<sub>3</sub>X reversibly dissociates into to A and X.

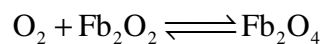
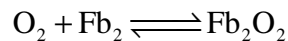


This dissociation reaction reaches equilibrium with an equilibrium constant, K<sub>c</sub>= 25 mM at 310°K and K<sub>c</sub>=50mM at 320°K.

- (a) Compute the standard free energy  $\Delta G^*$  of this reaction.  
 (b) Assuming no volume change upon mixing, calculate the concentration of A, X and  $A_3X$  in the solution at equilibrium when  $T=310^\circ\text{K}$  and  $T=320^\circ\text{K}$ .

**Problem 5-7: Equilibrium Constant for Two Step Protein Binding**

Consider a hypothetical protein, Fobin, that contains two Fb groups, each containing a chromium metal that binds to a single molecule of oxygen. The reaction mechanism is expressed as:



- (a) Develop relationships for the equilibrium constants,  $\kappa_{c1}$  and  $\kappa_{c2}$  for the first and second reaction steps, respectively, in terms of  $\text{O}_2$  partial pressure and molar concentrations of the three Fobin species.  
 (b) Develop a relationship for the fractional saturation of Fobin solely in terms of  $\text{O}_2$  partial pressure.

**Problem 5-8: Dissociation of a Weak Electrolyte**

Acetic acid ( $\text{CH}_3\text{COOH}$ ) is a weak electrolyte that partially ionizes in water according to

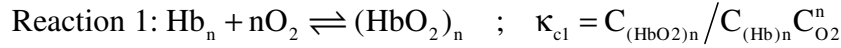


where HAc is  $\text{CH}_3\text{COOH}$  and  $\text{Ac}^-$  is  $\text{CH}_3\text{COO}^-$ . The equilibrium constant for this dissociation reaction at  $25^\circ\text{C}$  is  $K_{\text{HAc}}=1.75 \times 10^{-5}$ . A solution is prepared by dissolving 0.01 mole of solid acetic acid in 1.0 liter of water so that the HAc concentration before it has a chance to dissociate is  $C_0=0.01\text{M}$ . Determine the pH of the solution and the fraction of the original HAc molecules that ionize in the solution.

Hint: The equilibrium constants for the dissociation of acetic acid and of water ( $K_{\text{HOH}} = 10^{-14}$ ) provide two equations for the species concentrations: hydrogen cation ( $C_{\text{H}}$ ), hydroxide anion ( $C_{\text{OH}}$ ), acetate anion ( $C_{\text{Ac}}$ ) and undissociated acetic acid ( $C_{\text{HAc}}$ ). The electroneutrality principle requiring that positive and negative charges be balanced provides another equation. Conservation of carbon, present only in HAc and Ac, provides a fourth equation for the four unknown concentrations.

### Problem 5-9: Carbon Monoxide Poisoning

Exposure of a person to carbon dioxide gas (CO) can be life-threatening. This occurs because of the strong binding affinity of CO, causing the displacement of oxygen (O<sub>2</sub>) from oxyhemoglobin (HbO<sub>2</sub>). We will model this process using the following Hill-type binding kinetics:



Assume that binding equilibrium is reached in the transit of blood through the pulmonary capillaries. In that case, the concentrations of O<sub>2</sub>, CO, (Hb)<sub>n</sub>, (HbO<sub>2</sub>)<sub>n</sub> and (HbCO)<sub>n</sub> are related by the equilibrium constants  $\kappa_{c1}$  and  $\kappa_{c2}$ .

- Derive the saturation fraction  $S_{\text{O}_2}(C_{\text{O}_2}^n, C_{\text{CO}}^n)$  of (HbO<sub>2</sub>)<sub>n</sub> in arterial blood relative to the total Hb concentration when a person breathes air containing CO.
- Obtain the relative saturation,  $\chi \equiv S_{\text{O}_2}(\text{with CO}) / S_{\text{O}_2}(\text{without CO})$ .
- Write the equation for  $\chi$  in terms of the arterial partial pressures,  $p_{\text{O}_2}$  and  $p_{\text{CO}_2}$ , in place of the molar concentrations,  $C_{\text{O}_2}$  and  $C_{\text{CO}}$ . Also introduce the modified equilibrium constants,  $\kappa_{p1} \equiv c_G^o \alpha_{\text{O}_2} \kappa_{c1}^{1/n}$  and  $\kappa_{p2} \equiv c_G^o \alpha_{\text{CO}} \kappa_{c2}^{1/n}$  in place of  $\kappa_{c1}$  and  $\kappa_{c2}$ .
- Consider a healthy person at rest who inhales air containing CO at a volume fraction of 0.01 over many breaths. Compute  $\chi$  using the values of the Hill parameters and arterial partial pressure for O<sub>2</sub> given in chapter 5. Assume that  $\kappa_{p2}$  is 20 times  $\kappa_{p1}$ , but the  $n$  values for O<sub>2</sub> and CO are the same.

### Problem 5-10: Derivation of the Adair Model

Derive Adair's model of oxygen saturation (Eq. 5.5-13) which is defined as:

$$S_{\text{O}_2} = \frac{\text{Moles of O}_2 \text{ Bound to Heme Groups}}{\text{Moles of Heme Groups with and without O}_2}$$