Homework solutions
The Postulates – Chapter 1

Homework Problem T1.1: Looking at Chapter 3, what other terms besides -FL (force × distance = energy) could one add to the energy or chemical potential, to account for a charge Q in an electric potential V_e, or for surface area A with surface tension σ?

Solution: For a charge Q in the presence of an electric potential V_e, the total energy is QV_e, which is added to the energy or free energy, i.e. $E=TS-PV+\mu n+V_eQ+\cdots$, or $G = E- TS+PV=\mu n+V_eQ+\cdots$. As always, there is a pair of variables, Q being the extensive variable and V_e the corresponding intensive variable, such that $\partial E/\partial Q = V_e$ is the slope of E with respect too Q. Since $Q=zn$, where z is the molar charge (Coulombs/mole), and the chemical potential or "molar free energy" is $m=\partial G/\partial n = \partial(\mu n+QV_e)/\partial n = \partial(\mu n+ znV_e)/\partial n = \mu+zV_e$. The total free energy G has units of Joules (or kJ), the chemical potential μ has units of kJ/mole.

Surface energy quantifies the work that must be done to overcome the intermolecular forces which occurs when a surface is created, like expanding a soap bubble. The surface tension σ is defined as the force per unit length of the surface, i.e. $\sigma=F/L$, and is the intensive variable. For a given total surface area A (the extensive variable), the surface energy contributes $A\sigma$ to the energy and free energy, and $a\sigma$ to the chemical potential $\mu=\partial G/\partial n$, where a is the molar surface area. Note that unlike the -PV term, $A\sigma$ has a + sign because σ is a surface tension, not a surface pressure. If we worked with the surface pressure instead (simply the negative of the tension), then there would be a – sign just like in -PV.

Homework problem T1.2: The concentration of Mg^{++} ions near a negatively charged RNA molecule is 5 time greater than in the surrounding solvent, so the RNA has a 'Mg-cloud' around it. Using the Boltzmann factor, how much lower, in kJ/mole, is the chemical potential for the ions near the RNA than in the bulk solution?

Solution: We learned from class that compared with the region near a positively charged RNA, the region near a negatively charged RNA has a higher Mg^{2+} concentration because of the lower standard chemical potential for Mg^{2+}. The concentration is related to the standard chemical potential by

$$c_i(x) = c_{i0}e^{-\mu_{0i}/RT}.$$

where c_{i0} is the integration constant. Therefore, the concentrations near a negatively charged RNA and a positively charged RNA are

$$c_{neg}(x_{neg}) = c_0e^{-\mu_{0,neg}/RT}$$
$$c_{pos}(x_{pos}) = c_0e^{-\mu_{0,pos}/RT}$$

Given in the question that $c_{neg} = 5c_{pos}$ so

$$c_0e^{-\mu_{0,neg}/RT} = 5c_0e^{-\mu_{0,pos}/RT}$$

$$\exp\left(\frac{u_{0,pos} - u_{0,neg}}{RT}\right) = 5$$

so at room temperature T = 298 K solving for the chemical potential difference gives ≈4.0 kJ/mole.

Deriving all the 'classic' transport and equilibrium equations - Chapter 2

Homework problem T2.1: Let $c(x) = c_0 e^{-\left(\frac{x}{2\Delta x}\right)^2}$, i.e. the concentration initially looks like a Gaussian of width Δx and maximum concentration c_0 at x=0. For a protein, D=50 μm^2/s, c_0=1 mM and Δx = 1 mm initially, at what rate is the protein concentration changing at x=0? Is it increasing or decreasing according to the sign you get?

Solution: The rate of the concentration changing at position x is given by the Fick's second law of diffusion

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}$$

where D is the diffusion coefficient. Now $c(x) = c_0 e^{-\left(\frac{x}{2\Delta x}\right)^2}$, let's find the second-order partial derivative of the concentration c

$$\frac{\partial c}{\partial x} = c_0 e^{-\left(\frac{x}{2\Delta x}\right)^2}\left[-2\left(\frac{x}{2\Delta x}\right)\left(\frac{1}{2\Delta x}\right)\right] = c_0 e^{-\left(\frac{x}{2\Delta x}\right)^2}\left[-\left(\frac{x}{2\Delta x^2}\right)\right]$$

$$\frac{\partial^2 c}{\partial x^2} = c_0 e^{-\left(\frac{x}{2\Delta x}\right)^2}\left[-\left(\frac{x}{2\Delta x^2}\right)\right]\left[-\left(\frac{x}{2\Delta x^2}\right)\right] + c_0 e^{-\left(\frac{x}{2\Delta x}\right)^2}\left[-\left(\frac{1}{2\Delta x^2}\right)\right]$$

$$\frac{\partial^2 c}{\partial x^2} = c_0 e^{-\left(\frac{x}{2\Delta x}\right)^2}\left[\left(\frac{x^2}{4\Delta x^4}\right) - \frac{1}{2\Delta x^2}\right]$$

So

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} = Dc_0 e^{-\left(\frac{x}{2\Delta x}\right)^2}\left[\left(\frac{x^2}{4\Delta x^4}\right) - \frac{1}{2\Delta x^2}\right]$$

For a protein, D=50 μm^2/s=5.0·10^{-11}m^2/s, c_0=1 mM=0.001 M and Δx = 1 mm=0.001 m and at x = 0 the concentration changing

$$\frac{\partial c}{\partial t} = Dc_0 * 1\left[0 - \frac{1}{2\Delta x^2}\right] = -5.0\cdot 10^{-11}\mathrm{m^2 s^{-1}}\cdot 0.001\mathrm{M} * \left(\frac{1}{2*(0.001\ \mathrm{m})^2}\right)$$
$$= -2.5 * 10^{-8}\mathrm{M/s}$$

There is a minus sign: the protein concentration is decreasing at x=0 where it is initially highest. The sign switches when $x^2/(4\Delta x^4) = 1/(2\Delta x^2)$, or $x=\sqrt{2}\cdot\Delta x$: further away, the protein concentration increases due to diffusion. So there is a 'magic spot' where the concentration remains constant even though it is changing everywhere else.

Homework problem T2.2: For a DNA of charge -10e per molecule (e is the elementary charge), field of 10 V/cm and diffusion coefficient of 10 μm^2/s, at what velocity does the DNA move

through the solution? Tip: remember, in Chapter 6 of Stat Mech, we talked about Langevin's equation, which relates $D=Uk_BT$ and $\gamma=1/U$ (in per molecule units; $D=URT$ in molar units).

Solution: The Faraday's law for electrophoresis states that the ion drift velocity is proportional to applied field and charge, but inversely proportional to the viscosity of the fluid

$$v_x = zUE_x$$

where the charge z= +10, applied field E=10 V/cm=1000 V/m and the diffusion coefficient D = 10 μm^2/s. From Chapter 6 we have the expression for the diffusion coefficient $D = \frac{k_BT}{\gamma}$ and the friction coefficient $\gamma=1/U$. At room temperature T=298K the Einstein's mobility

$$U = \frac{D}{k_BT} = \frac{10\ \mu m^2 s^{-1}}{1.38 * 10^{-23} JK^{-1} * 298K} = 2.43 * 10^9\ s \cdot kg^{-1}$$

So the velocity

$$v_x = qUE_x = 10 * 1.602 * 10^{-19} C * 2.43 * 10^9\ s \cdot kg^{-1} * 1000 V \cdot m^{-1} = 3.89 * 10^{-6} m \cdot s^{-1}$$

Note, here we worked it out with U per molecule; we could have used $U=D/RT$ instead, then we would have had to convert the charge z to units of Coulombs per mole instead of Coulombs per molecule. The answer would of course be the same.

Homework problem T2.3: Two KCl solutions are connected by a salt bridge, so a current can flow through electrodes connected to the outside of the cell via a Voltmeter. If one cell (let's say the one located at x=0) has 0.1 M KCl, and the other has 10 M KCl in it, what is the voltage difference between the cells? So, it is possible to make a battery even with just one ionic solution, as long as the concentrations are different. How many of these would you have to stack to get 1.5 V? An actual measurement will often show a smaller voltage, unless things are very carefully set up. Give one possible reason for why you might not get the full voltage out.

Solution: The concentration gradient of solute generates an electric potential which can be calculated by the Nernst equation

$$\Delta V = V_e(x) - V_e(0) = -\frac{RT}{z_i} \ln \frac{c_i(x)}{c_i(0)},$$

Here in this question, the concentrations of KCl in two different cells are $c_i(0) = 0.1M$ and $c_i(\mathrm{x}) = 10$ M so at room temperature T=298 K

$$\Delta V = -\frac{RT}{z_i} \ln \frac{c_i(x)}{c_i(0)} = \frac{-8.314\ \mathrm{J \cdot K^{-1} \cdot mol^{-1}} * 298\ \mathrm{K}}{1 * 96485.33\ \mathrm{C \cdot mol^{-1}}} \ln \frac{10M}{0.1M} = -0.118\ \mathrm{V}$$

Le Châtelier's principle tells us that the reaction spontaneously should reduce the concentration difference in the cell by the transfer of ions or the oxidation/reduction reaction on two sides. Either way will cause the electron flow from the low-concentration side to the high-concentration side and make the low-concentration side at the negative voltage. As calculated above, the voltage difference of one cell is 0.118V, so the number of cells we need to stack is

$$n = \frac{1.5\ V}{0.118\ V} = 12.7 \approx 13$$

There are many factors that can make the actual voltage lower than the theoretical value for an ideal system. For example, compared with the reaction rate, the mass transport may be relatively slow. As a consequence, the reactant molecules cannot be supplied or the products cannot be removed from electrode efficiently, resulting in depletion of the reactants or the accumulation of the products at the electrode surface. That will change the local ion concentration thus reduce the actual voltage.

Here are some good recourses of concentration cells and concentration overpotential, check them for interest:

- Concentration cell
  - Wiki: https://en.wikipedia.org/wiki/Concentration_cell
  - Chemistry LibreTexts https://chem.libretexts.org/Bookshelves/Analytical_Chemistry/Supplemental_Modules_(Analytical_Chemistry)/Electrochemistry/Voltaic_Cells/Electrochemical_Cells_under_Nonstandard_Conditions/Concentration_Cell
- Concentration overpotential
  - Wiki: https://en.wikipedia.org/wiki/Overpotential

Homework problem T2.4: In a cell, total protein concentration is ≈20 mM. If a cell is dunked in distilled water, what's the osmotic pressure on its membrane due to the proteins?

Solution: Le Châtelier's principle says that water will go inside the cell (through aquaporins n the membrane) to equalize the concentrations of water inside (less water, more protein) and outside (pure water). The osmotic pressure caused by the concentration difference crossing the membrane at room temperature T=298 K

$$\Delta P = -RT\Delta c = -0.08205\ liter \cdot atm \cdot mol^{-1} \cdot K^{-1} * 298\ K * 0.02\ M \approx -0.5\ atm$$

Of course, you could work this out in Pascal by using R = 8.31 J·mol^{-1}·K^{-1}. So it would be easy to measure a protein concentration in the millimolar range by measuring its osmotic pressure against distilled water. The minus sign indicates that to prevent water from entering the cell, you would have to apply 0.5 atm from within the cell to keep the water out, or pull with a hydrostatic tension of -0.5 atm on the outside.

Homework problem T2.5: Derive the above equation in detail from Postulates 1 and 2, using the same steps as for the Nernst equation. For a molar mass of air m=0.029 kg/mol and assuming a constant T = 298 K, what is the pressure 1 km above sea level? How do you think temperature changes and humidity could affect the equation?

Solution: According to Postulate 1 of transport, we can use (dropping "i" if we are looking onlyh at one gas):

$$\mu_g = \mu(T,P,x) + V_{gravity} = \mu(T,P,x) + mgx$$

$$\frac{d\mu_g}{dx} = RT\frac{\partial \ln(c)}{\partial x} + \frac{\partial V_{gravity}}{\partial x} = RT\frac{\partial \ln(c)}{\partial x} + mg$$

For an ideal gas at constant temperature the partial pressure is proportional to the concentration by the ideal gas equation $PV=nRT$ so the concentration can be replaced by the partial pressure

$$\frac{d\mu_g}{dx} = RT\frac{\partial \ln(P)}{\partial x} + mg$$

Inserting into Postulate 2 we obtain

$$J = -Uc\left(RT\frac{\partial \ln(P)}{\partial x} + mg\right)$$

At equilibrium the net flux is zero. Thus setting equation $J = 0$ and equating the two terms in parentheses,

$$RT\frac{\partial \ln(P)}{\partial x} = -mg \text{ or } RT\, d\ln(P) = -mgdx.$$

Integrating on both sides we obtain the expected equation

$$\ln\frac{P_2}{P_1} = -\frac{mg(x_2 - x_1)}{RT}.$$

1 km above sea level, and using P_1= 1 atm at sea level for reference,

$$\ln\left(\frac{P}{1\text{ atm}}\right) = -\frac{0.029\frac{\text{kg}}{\text{mole}}9.81\frac{m}{\text{s}^2}(1000\text{ m} - 0\text{ m})}{8.31\frac{\text{J}}{\text{mole K}}298\ K} = -0.11$$

we get 0.89 atm solving for the natural logarithm of P. The air's getting a bit thinner, and if you plug in 8.9 km, you understand why many people choose to use an oxygen mass on Mt. Everest. The exact calculation would give a slightly different pressure because we did not take the atmospheric temperature gradient into account - but we could by adding the entropy-temperature term $-sdT$ to our physicochemical potential derivative, instead of just $-mgdx$.

The integrated form of flux and kinetics - Chapter 3

Homework T3.1: In steady-state, flux is 0. Use the Bayesian formula to write the ratio of concentrations in terms of a ratio of conditional probabilities. In equilibrium, $c(0)=c(x)$, so what relationship is there between the conditional probabilities in equilibrium? This is an example of the principle of microscopic reversibility: the probability of getting from 'a' to 'b' must be the same as getting from 'b' to 'a', then the system is in equilibrium.

Solution: In steady-state, set the flux equal to 0

$$J_x = -\frac{D}{L}[c(0)P(x|0) - c(x)P(0|x)] = 0$$

$$c(0)P(x|0) - c(x)P(0|x) = 0$$

$$\frac{c(x)}{c(0)} = \frac{P(x|0)}{P(0|x)}$$

In equilibrium, $c(0)=c(x)$ so

$$\frac{c(x)}{c(0)} = \frac{P(x|0)}{P(0|x)} = 1$$

give us $P(x|0) = P(0|x)$ which states that the probability of one molecule moving from 0 to x is the same as the probability of the converse pathway.

Homework problem T3.2: At higher temperatures (more typical of a reactions with a barrier), the viscosity decreases by a factor of *ca*. 5 for every 100 °C, and χ is typically 1/2, as seen in the Figure above. If the data for the in-class exercise was at 25 °C, what would be the prefactor at 225 °C, and what would be the rate constant k if the maximum in the free energy profile is at $\Delta\mu^\dagger$ = 100 kJ/mole? [**Hint**: the relationship between diffusion coefficient, friction and viscosity is discussed in Chapter 6 of Stat Mech.]

Solution: At room temperature T=298 K, the diffusion coefficient is 10^{-9} m^2/s and the reaction distance is 0.5 Å so

$$prefactor = \frac{\chi D}{x^2} \approx 2 \times 10^{11}$$

The diffusion coefficient is proportional to T/viscosity and at 225 °C the viscosity decreases by a factor of 5^2=25 and absolute temperature has increased by a factor 498/298≈1.67, so the diffusion coefficient at 225 °C has increased by the combined factor to $D \approx 4.1\times10^{-8}$ m^2/s. Thus

$$prefactor = \frac{\chi D}{x^2} \approx 8.3 \times 10^{12} \text{ s}^{-1}$$

If you plug in 100 kJ/mole and 498 K, the rate constant k is given by

$$k_f = \frac{\chi D}{(x^\dagger)^2} e^{-\Delta\mu^\dagger/RT} \approx 270 \text{ s}^{-1}$$

Note that the actual reaction, the moment of crossing the barrier, is almost instantaneous (the inverse of 8.3×10^{12} s^{-1} is about 120 femtoseconds), whereas the macroscopic reaction takes a

fraction of a second because the activation barrier is high, so most collisions of the ion do not result in reaction. This takes us right back to the very first lecture, when we talked about single molecule transitions vs. average bulk rate.

Homework problem T3.3: On the other hand, for a protein folding reaction at room temperature, the characteristic reaction distance is ~1 nm (size of a helix or beta strand that need to diffuse together to fold the protein), and the diffusion coefficient is ~10^{-10} m^2/s. What is the prefactor in that case? We call this the "speed limit" of protein folding, and some small proteins come remarkably close to this value, so protein evolution has optimized the folding reaction of some proteins. In a sentence, why do you think not all protein folding reaction rates would be optimized by evolution to be as fast as possible?

Solution: At room temperature T=298 K, given that the reaction distance x=1 nm=1.0×10^{-9} m, the diffusion coefficient D=10^{-10} m^2/s, and letting the transmission coefficient $\chi = 0.5$ again,

$$prefactor = \frac{\chi D}{x^2} = 5.0 \times 10^7 \text{ s}^{-1}$$

So the prefactor for proteins is quite a bit slower than for ions, the inverse of the above is 20 ns. The fastest folding protein fold in about 500 ns, so their activation barrier also must be quite small.