BIO 5329: PROBLEM SET 1

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Due at the start of class on September 13.

1. Molecular populations (20 points)

Imagine we have a population of molecules which randomly convert between two forms A and B with rates k_1 and k_2: such that the rate of change in each species is

$$\frac{dc_A(t)}{dt} = -k_1 c_A(t) + k_2 c_B(t) \tag{1.1}$$

$$\frac{dc_B(t)}{dt} = k_1 c_A(t) - k_2 c_B(t) \tag{1.2}$$

where $c_A(t)$ and $c_B(t)$ are the concentrations of form A and B at time t. In what follows, we will assume we start with concentrations $c_A(0) = c_{A,0}$ and $c_B(0) = c_{B,0}$.

- **a.** (5 points) Let $c(t) = c_A(t)+c_B(t)$ be the total concentration of molecules, regardless of their form. Find $c(t)$ for $t > 0$.
- **b.** (15 points) Find $c_A(t)$ and $c_B(t)$ for $t > 0$. Hint: use the result from previous question to help you simplify these coupled equations; use a transformation of variables to simplify the resulting integration.

2. Substrate concentrations (20 points)

Suppose we have a catalyst E which converts substrate A into product P with rate k_1 according to the very simple (and completely unrealistic) kinetic scheme

$$E + A \xrightarrow{k_1} E + P. \tag{2.1}$$

Now suppose there is an inhibitor present in solution which slowly poisons the catalyst with rate k_3

$$E + I \xrightarrow{k_3} EI. \tag{2.2}$$

The differential equations that govern this system are

$$c'_A(t) = -k_1 c_E(t) c_A(t) \tag{2.3}$$

$$c'_P(t) = k_1 c_E(t) c_A(t) \tag{2.4}$$

$$c'_E(t) = -k_3 c_E(t) c_I(t) \tag{2.5}$$

$$c'_I(t) = -k_3 c_E(t) c_I(t) \tag{2.6}$$

and the initial concentrations are $c_E(0) = c_{E,0}$, $c_A(0) = c_{A,0}$, $c_P(0) = c_{P,0}$, and $c_I(0) = c_{I,0}$. As it stands, this is a nasty nonlinear problem. However, we will assume that I is in such great excess over the other components that $c'_I(t) \approx 0$.

a. (10 points) What is the concentration of E at time t?

b. (10 points) What is the concentration of A at time t?

3. Membrane electrostatics (20 points)

Suppose you run a molecular simulation of an aqueous membrane in the presence of excess charges on the lipids (e.g., anionic lipids) and neutralizing counterions. After running the simulation, you accumulate statistics along the membrane normal, $0 \leq z \leq Z$, by assuming symmetry along the x and y directions. In particular, you obtain an average charge distribution $\rho(z)$ due to the excess charges (lipids and ions) and an average dielectric constant $\epsilon(z)$

due to water and lipid relaxation. The electrostatic potential $\phi(z)$ is governed by Poisson's equation

$$-\nabla \cdot (\epsilon(z)\nabla\phi(z)) = 4\pi\rho(z) \tag{3.1}$$

In what follows:

- Recall from your physics courses that $\epsilon(z) \geq 1$,
- Assume

$$\left[\epsilon(z)\frac{d}{dz}\phi(z)\right]_{z=0} = 0 \tag{3.2}$$

a. (7 points) Solve for $\phi(z)$; leave your answer as an integral.

b. (6 points) Show that

$$\int_0^z \int_0^{z'} \rho(z'')dz''dz' = \int_0^z (z - z')\rho(z')dz'. \tag{3.3}$$

c. (7 points) Assume $\epsilon(z) = 1$ is constant; in other words, $\rho(z)$ includes the charge density for the solvent and solute. Many molecular simulations are performed under periodic boundary conditions. What condition(s) on the charge distribution $\rho(z)$ must be satisfied to ensure continuity of the potential across the z boundary:

$$\phi(0) = \phi(Z)? \tag{3.4}$$

(Show your work...)

4. Diffusion in the presence of sources and sinks (20 points)

We're going to take a several-week jump ahead in the course and solve a challenging ordinary differential equation related to diffusion in the presence of forces as well as sources and sinks which create and destroy the diffusing species. In particular, we're going to solve Smoluchowski's equation

$$\frac{\partial p(x,t)}{\partial t} = \nabla \cdot \left(D(x)\left(\nabla p(x,t) + p(x,t)\nabla w(x)\right)\right) + s(x,t) \tag{4.1}$$

where $p(x,t)$ is the probability (concentration) of the diffusing species at position x at time t, $D(x)$ is the diffusion constant, $w(x)$ is an potential energy function (e.g., applied field, fluid flow, etc.) acting on the diffusing species, and $s(x,t)$ is a function which describes the addition or removal of species from the system. To simplify things a bit, we'll consider the steady-state problem

$$\frac{\partial p(x,t)}{\partial t} = 0 \tag{4.2}$$

with a constant diffusion coefficient $D(x) = D$, in one dimension such that our equation has the form

$$\frac{d}{dx}\left(\frac{dp(x)}{dx} + p(x)\frac{dw(x)}{dx}\right) + s(x) = 0 \tag{4.3}$$

a. (7 points) Show that Eq. 4.3 can also be written as

$$-\frac{d}{dx}\left(e^{-w(x)}\frac{d}{dx}\left(e^{w(x)}p(x)\right)\right) = s(x). \tag{4.4}$$

b. (7 points) Use the above formulation of the Smoluchowski equation to write the solution $p(x)$ in terms of a double integral of the sink/source term of the form

$$p(x) = \cdots - \int_0^x e^{w(x')} \int_0^{x'} s(x'')dx''dx' \tag{4.5}$$

where the $\cdots$ denotes additional terms you should supply in your solution.

c. (6 points) Using the solution above, find $p(x)$ for $w(x) = x$ and $s(x) = -1$.

5. Fun with complex analysis (20 points)

a. (5 points) Given the function $f(x) = \ln(-x)$, where $x \in \mathbb{R}$ and $x > 0$, write expressions for $\mathrm{Re}\,(f(x))$ and $\mathrm{Im}\,(f(x))$.

b. (5 points) A Fourier series representation of a periodic function $f : [-L, L] \mapsto \mathbb{R}$ has the form

$$f(x) = \sum_{n=-\infty}^{\infty} c_n e^{\imath \pi n x / L} \tag{5.1}$$

where $c_n \in \mathbb{C}$. However the same series can be represented by Fourier sine and cosine series of the form

$$f(x) = \frac{a_0}{2} + \sum_{n=1}^{\infty} a_n \cos\left(\frac{n\pi x}{L}\right) + \sum_{n=1}^{\infty} b_n \sin\left(\frac{n\pi x}{L}\right). \tag{5.2}$$

Relate a_n and b_n to c_n.

c. (5 points) Solve $\cos z = 3$ for $z \in \mathbb{C}$.

d. (5 points) Prove that

$$\imath^\imath = e^{-\frac{\pi}{2} \pm 2n\pi} \tag{5.3}$$

for $n = 0, 1, 2, \ldots$. Hint: use the relationship $z^c = e^{c \ln z}$.