Problems II
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Problem 1. Kinetic law of mass action.

a) Consider the reaction network:

\[ A \overset{k_1}{\rightarrow} X, \quad X \overset{k_2}{\rightarrow} Y, \quad X + Y \overset{k_3}{\rightarrow} B, \]

where the concentrations of A and B are buffered (i.e. [A] and [B] are fixed model parameters). Construct a differential equation model for the dynamics of [X] and [Y]. Determine the steady-state concentrations of X and Y as functions of [A] and the rate constants. Verify that the steady-state concentration of Y is independent of [A].

b) Consider the reaction scheme

\[ A + B \overset{k_1}{\rightarrow} C + D, \quad D \overset{k_2}{\rightarrow} B, \quad C \overset{k_3}{\rightarrow} E + F. \]

Write down the mass action kinetic equations for [A], [B], [C], [D] Using a conservation equation, determine the steady-state concentrations (some of which are zero).

c) Repeat b) when there is the additional reaction \( k_0 \rightarrow A \), that is, A is produced at a rate \( k_0 \).

Problem 2. Master equation for an ensemble of ion channels. Consider the master equation for the two-state ion channel model:

\[
\frac{d}{dt} P(n,t) = \alpha (N - n + 1) P(n - 1, t) + \beta (n + 1) P(n + 1, t) - \left[ \alpha (N - n) + \beta n \right] P(n, t). \quad (II.2)
\]

(a) By multiplying both sides by \( n \) and summing over \( n \), derive the following kinetic equation for the mean \( \bar{n} = \sum_{n=0}^{N} n P(n,t) \):

\[
\frac{d\bar{n}}{dt} = \alpha (N - \bar{n}) - \beta \bar{n}.
\]

(b) Derive a corresponding equation for the variance \( \sigma^2 = \langle n^2 \rangle - \langle n \rangle^2 \). That is, multiply both sides of the master equation by \( n^2 \) and sum over \( n \) to determine an equation for the second moment, and then use part (a). Show that the variance decays exponentially at a rate \( 2(\alpha + \beta) \) to the steady-state value

\[
\sigma^2 = \frac{\alpha \beta}{(\alpha + \beta)^2},
\]

and hence deduce that fluctuations become negligible in the large \( N \) limit.

c) Compare the results obtained from the master equation with the analysis based on the linear noise approximation.
(d) Construct the master equation for an ensemble of $N$ identical, independent channels each of which has two subunits. That is, determine an equation for the evolution of the probability distribution $P_{n_0,n_2}(t)$ that there are $n_j$ ion channels with $j$ open subunits such that $N = n_0 + n_1 + n_2$.

**Problem 3. Bistability in an autocatalytic reaction.** Consider the following autocatalytic reaction scheme for a protein that can exist in two states $X$ and $Y$:

$$X \overset{k_1}{\underset{k_2}{\rightleftharpoons}} Y, \quad X + 2Y \overset{k_3}{\rightarrow} 3Y.$$  

Let $[X]$ and $[Y]$ denote the concentrations of the molecule in each of the two states such that $[X] + [Y] = Y_{\text{tot}}$ fixed. The kinetic equation for $[Y]$ is

$$\frac{d[Y]}{dt} = -k_2[Y] + k_1[X] + k_3[Y]^2[X],$$

where $V$ is cell volume.

a) Let $y = [Y]/Y_{\text{tot}}$. Show that after an appropriate rescaling of time, the corresponding kinetic equation for $y$ is

$$\frac{dy}{dt} = y(\mu(1 - y)y - 1) + \lambda(1 - y),$$

where $\mu = k_3 Y_{\text{tot}}^2/k_2$, $\lambda = k_1/k_2$. Determine the existence and stability of the fixed points for $y$. Plot the bifurcation diagram with $\mu$ treated as a bifurcation parameter and $\lambda = 0.03$. Hence, show that the system is bistable over a range of values of $\mu$.

b) Suppose that there are $N_0$ molecules, that is, $N_0 = VY_{\text{tot}}$, where $V$ is cell volume. Construct the birth-death master equation for the probability $P_n(t)$ that there are $N(t) = n$ molecules in state $Y$ at time $t$.

c) Show that the steady-state distribution is

$$P^*_n = \frac{C_{N_0} N_0!}{n!(N_0 - n)!} \prod_{m=0}^{n-1} \left[ \lambda + \frac{\mu}{N_0^2 m(m - 1)} \right].$$

Plot $P^*_n(n)$ as a function of $n$ (treated as a continuous variable over the range $[0, 400]$) for $N_0 = 400$, $\mu = 4.5$ and $\mu = 6$ with $\lambda = 0.03$. Comment on the location of the peaks in terms of fixed points of the deterministic system.

d) Derive the corresponding Fokker-Planck equation using a system-size expansion of the master equation in powers of $1/N_0$, and determine the steady-state solution. Calculate the steady-state solution and compare with the exact solution of part (c) for $N_0 = 40$ and $N_0 = 400$.

**Problem 4. Spatial polymerization of a filament.** Suppose that a polymer filament is placed in a cylinder with uniform cross-section $A$. Suppose that the monomers within the tube can undergo diffusion along the axis of the tube, which is taken to be the $x$-axis. Let $x_{\pm}(t)$ denote the
positions of the ± ends of the filament within the tube. The apparent velocities of these ends due
to polymerization/depolymerization are
\[
\frac{dx_+}{dt} = v_+ = t[k_{on}^a(x_+, t) - k_{off}^+]
\]
\[
\frac{dx_-}{dt} = v_- = -t[k_{on}^a(x_-, t) - k_{off}^-].
\]
The ends of the filament act as sources or sinks for monomer, so that the monomer concentration
\(a(x, t)\) along the axis satisfies the inhomogeneous diffusion equation
\[
\frac{\partial a}{\partial t} = D \frac{\partial^2 a}{\partial x^2} - \gamma [\delta(x - x_+)v_+ - \delta(x - x_-)v_-], \quad \gamma = \frac{1}{A_t}.
\]

(a) Derive the diffusion equation by considering conservation of monomer passing through an in-
finitesimal volume \(A\Delta x\) centered about either end of the filament. Explain the minus sign in the
definition of \(v_-\).

(b) Suppose that the tube is infinitely long and
\[a(x, t) \to \alpha, \quad x \to \pm \infty.\]
Look for a traveling wave solution in which the filament maintains a fixed length \(L\) and \(v_\pm = v\),
where \(v\) is the speed of the wave. That is, set \(x_+ = vt, v_- = vt - L\) and go to a moving frame
\(z = x - vt\) with \(a(x, t) = A(z)\) such that
\[-v \frac{dA}{dz} = D \frac{d^2A}{dz^2} + v\gamma[\delta(z + L) - \delta(z)].\]
Explicitly solve this equation by matching the solution at the points \(z = -L, 0\). In particular, show
that
\[A(-L) = \alpha, \quad A(0) = \alpha - 1 + e^{-\gamma v L / D}.
\]

(c) Substituting for \(A\) in the expressions for \(v_\pm\) and setting \(v_+ = v_- = v\), determine \(v\) and \(L\). Show
that a physical solution only exists if
\[\alpha > \frac{k_{off}^+ + k_{off}^-}{k_{on}^+ + k_{on}^-}.
\]

Problem 5. Polymerization ratchet. Consider a Brownian particle moving in the ratchet
potential
\[\mathcal{F}(x) = Fx - n \Delta G, \quad na < x < (n + 1)a.\]
Following the analysis of Lecture 13, we obtain the equation
\[
\frac{d}{dx} \left( e^{\mathcal{V}(x)/k_B T} p_0(x) \right) = -\frac{j_0}{D_0} e^{\mathcal{V}(x)/k_B T}.
\]
for the stationary distribution $\hat{p}_0(x) = \sum_{n=-\infty}^{\infty} p_0(x + na)$.

(a) Integrate the above equation from $0^+$ to $x$, $0 < x < a$, and impose the matching condition
\[
\lim_{x \to a^+} \hat{p}_0(x)e^{F(x)} = \lim_{x \to a^-} \hat{p}_0(x)e^{F(x)}
\]

together with periodicity $\hat{p}_0(a^+) = \hat{p}_0(0^+)$. Hence show that
\[
\hat{p}_0(x) = \frac{\hat{J}_0 k_B T}{FD_0} \left[ Ae^{-Fx/k_BT} - 1 \right],
\]

with
\[
A = \frac{e^{\Delta G/k_BT}}{e^{(\Delta G - Fa)/k_BT}} - 1.
\]

(b) Explain the matching condition used in part (a).

(c) Determine the constant flux $\hat{J}_0$ using the normalization condition $1 = \int_0^a \hat{p}_0(x)dx$. Hence show that the speed of growth $v = \hat{J}_0 a$ is given by
\[
v = D_0 \frac{F^2 a}{(k_BT)^2} \left[ A \left( 1 - e^{-Fa/k_BT} \right) - \frac{Fa}{k_BT} \right]^{-1},
\]

(d) Show that in the regime $\Delta G \gg Fa$ and $k_B T \gg Fa$,
\[
v \approx 2D_0/a.
\]