Nelson, Problem 4.2, pg 153 (10 pts)

a) From the introductory paragraph to the problem, we understand "the number of distinct one-base mutations" to mean the number of $10^4$-letter long sequences with one (and only one) of the letters being different from what it was in the original. Since there are exactly 3 ways any given letter can be different from the original, the number of distinct one-base mutations is $3 \times 10^4 = 30,000$.

Similarly, to determine "the number of distinct two-base mutations", we need to multiply the number of ways any given set of two letters can be different from the original, that is $3^2 = 9$, by the number of distinct pairs of sequence locations those two letters might come from, which is $\binom{10^4}{2} \approx 5 \cdot 10^7$. (If you don’t understand this last computation, re-read the first three pages (p.110-113) of Section 4.1.2.) The answer is, therefore, $4.5 \cdot 10^7$.

b) We’re told the probability that any given base is copied incorrectly, $p = 1/(3 \cdot 10^4)$. We’re also told that probability of exactly two errors, $P_2$, is the probability of two bases being copied incorrectly, $p^2$, times the probability that the remaining 9998 bases being copied correctly, $(1-p)^{9998}$; times the number of distinct ways to specify which two bases (i.e., positions in the sequence) get copied incorrectly. We’re asked to solve for $P_2$:

$$P_2 = p^2 (1-p)^{9998} \left(\binom{10^4}{2}\right) = (3.3 \cdot 10^{-5})^2 (0.999967)^{9998} \left(\frac{10,000 \cdot 9,999}{2}\right) = 0.4$$

(1)

c) Following the argument given in the second paragraph of the problem statement, the number of newly infected white blood cells receiving a copy of the viral genome with exactly two mutations in one day is the number of new virus particles formed in one day \times the fraction of those that manage to infect a new white blood cell \times the probability that a new copy of the viral genome will have exactly two mutations. (Note: the last term was calculated in part b.) That is, $10^{10} \times 0.01 \times P_2 = 4 \cdot 10^7$.

This is similar to the number of distinct two-base mutations we calculated in part a), which means that, if a viral genome needs two (and only two) specific mutations in order to avoid the action of an anti-viral drug and remain virulent, that specific genome will be created and successfully infect a cell in the body of an asymptomatic HIV patient, in about one day.

d) The number of distinct three-base mutations is

$$3^3 \times \left(\binom{10^4}{3}\right) = 27 \times \frac{10,000 \cdot 9,999 \cdot 9,998}{3 \cdot 2} = 4.5 \cdot 10^{13}$$

The probability of exactly three errors occurring in the production of a new viral genome is

$$P_3 = p^3 (1-p)^{9997} \left(\binom{10^4}{3}\right) = (3.3 \cdot 10^{-5})^3 (0.999967)^{9997} \left(\frac{10,000 \cdot 9,999 \cdot 9,998}{3 \cdot 2}\right) = 0.04$$

(3)

The expected number of three-letter mutant viruses infecting new white blood cells per day is $10^{10} \times 0.01 \times P_3 = 4 \cdot 10^6$, much less than the total number of possible three-base mutations.

e) The total number of possible one-base mutations is small compared to the expected number of mutant viruses infecting new white blood cells in one day. If the virus can evolve to avoid any one antiviral drug by making a single base mutation, then a therapy based on a single antiviral drug will not be effective because the particular one-base mutation that allows the virus to remain virulent in is sure to arise many times in just one day. Using three anti-viral drugs at the same time, on the other hand, means that, to remain virulent, the viral genome would have to acquire three specific single-base mutations at once. But the number of those arising in a day is 7 orders of magnitude smaller than the number of distinct possibilities, so the chance of the right one arising in one day, $\approx 1/10^7$, or even in one thousand days (i.e., three years), $\approx 1/10^4$, is very small.

<table>
<thead>
<tr>
<th>mutation</th>
<th># of distinct possibilities</th>
<th>expected rate of infection (/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>one-base</td>
<td>$3 \cdot 10^4$</td>
<td>$3 \cdot 10^7$</td>
</tr>
<tr>
<td>two-base</td>
<td>$4.5 \cdot 10^7$</td>
<td>$4 \cdot 10^7$</td>
</tr>
<tr>
<td>three-base</td>
<td>$4.5 \cdot 10^{13}$</td>
<td>$4 \cdot 10^6$</td>
</tr>
</tbody>
</table>
4.3 a) Estimate the diffusion coefficient $D$ for an object the size of the vesicle in the figure. 2.19b.

The vesicle has a radius $R = 50 \text{ nm}$. Einstein's relation: $\zeta D = k_B T$ (4.16) stroke's $\zeta = 6\pi \eta R$ (4.14).

Combining these to solve for $D$ gives:

$$D = \frac{k_B T}{6\pi \eta R}$$

For room temperature $\sim 300K$, $k_B T = 4.1 \times 10^{-12} \text{N} \cdot \text{m} \cdot \text{s}$, $\eta \sim 10^{-3} \text{ kg} / \text{m} \cdot \text{s}$.

Then $D = 4.1 \times 10^{-12} \frac{\text{kg} \cdot \text{m}}{\text{s}^2} \cdot \frac{1}{10^{-9} \text{m}} \frac{1}{6\pi \cdot 10^{-3} \text{kg}} \frac{1}{50 \cdot 10^{-9} \text{m}} = 4.4 \times 10^{-12} \text{m}^2 / \text{s}$.

b) What is the diffusive flux $j_{\text{diff}}$ along the axon?

Fick's law (eqn 4.19) gives the diffusive flux $j$:

$$j_{\text{diff}} = -D \frac{dc}{dx} \quad \text{and} \quad \frac{dc}{dx} = -\frac{c_0}{L}$$

$$\Rightarrow j_{\text{diff}} = 4.4 \times 10^{-12} \frac{\text{m}^2}{\text{s}} \cdot \frac{c_0}{1 \text{m}} = \frac{4.4 \times 10^{-12} \text{m}}{\text{s}} \cdot c_0$$

(c) At the joscope, observe vesicles moving $\sim 400 \text{ mm per day}$.

Given a number density $c_0$, flux observed $J_{\text{obs}} \sim \frac{400 \cdot 10^{-3} \text{m} \cdot c_0}{\text{day}} \sim 4.6 \times 10^{-6} \text{m} / \text{s}$.

(d) Ratio $\frac{J_{\text{diff}}}{J_{\text{obs}}} = \frac{4.4 \times 10^{-12} \text{m}}{10^{-6} \text{m}} \sim 10^{-6}$, so flux due to diffusion alone is much too small to
4.6 Find the thickness of the membranes in the experiments from Fig. 4.13

The thickness is \( \frac{BD}{P_s} \) check units: \( [BD] = \frac{L^2}{T} \) \( [P_s] = \frac{L}{T} \)

We can take two points from the graph:

\[ BD = 10^{-8} \text{ cm}^2 \text{ s}^{-1}, \quad P_s = 10^{-2} \text{ cm} \text{ s}^{-1} \]

\( 10^{-10} \) \( 10^{-4} \)

\[ t = \frac{\Delta BD}{\Delta P_s} = \frac{10^{-10} - 10^{-8}}{10^{-4} - 10^{-2}} \sim 10^{-6} \text{ cm} \sim [10 \text{ nm}] \]
Phys 150 HW 4 solutions

Nelson, Problem 4.7, pg 156 (5 pts)

a) Starting with the definition of permeability, $\mathcal{P}$, we can follow the same derivation as outlined in the Example on page 136.

\[
\begin{align*}
    j_s &= -\mathcal{P}_s \Delta c \\
    \frac{1}{A} \frac{dN}{dt} &= -\mathcal{P}_s \Delta c \\
    \frac{V}{A} \frac{d(N/V)}{dt} &= -\mathcal{P}_s \Delta c \\
    \frac{V}{A} \frac{d(\Delta c)}{dt} &= -\mathcal{P}_s \Delta c \\
    \frac{d(\Delta c)}{dt} &= -\frac{AP_s}{V} \Delta c
\end{align*}
\]

The solution to this differential equation is $\Delta c(t) = e^{-t/\tau}$, where $\tau = \frac{V}{AP_s} = (\pi r^2 L)/(2\pi r \mathcal{P}) = r/2\mathcal{P}$.

b) The constraint that blood not flow faster than it takes for all the oxygen to diffuse through the capillary wall means that $v \leq L/\tau = L/(r/2\mathcal{P}) = 2\mathcal{P}L/r$. Using the numbers given in the problem, $v \leq (2 \cdot 3 \mu m \cdot s^{-1} \cdot 10^3 \mu m)/(4 \mu m) = 1700 \mu m \cdot s^{-1}$. The actual speed of $\approx 400 \mu m \cdot s^{-1}$ does indeed satisfy this constraint.
Phys 150 HW 4 solutions

Nelson, Your Turn 4G, pg 143 (6 pts)

a) To establish that the proposed gaussian solution, \( c(x,t) = Be^{-x^2/(2At)} \), when integrated over all space, is not constant in time, remember the normalization condition for a Gaussian distribution (cf. Nelson, page 73.)

\[
\int_{-\infty}^{\infty} e^{-x^2/(2\sigma^2)} dx = \sigma \sqrt{2\pi}.
\]

(1)

Substituting \( \sigma = \sqrt{At} \) and multiplying by \( B \) makes it clear that

\[
\int_{-\infty}^{\infty} c(x,t) dx = \int_{-\infty}^{\infty} Be^{-x^2/(2At)} dx = B\sqrt{2\pi At} \neq \text{constant}.
\]

(2)

Of course, if we introduce a factor of \( 1/\sqrt{t} \) into \( c(x,t) \) (and replace \( A \) with \( 2D \)), then

\[
\int_{-\infty}^{\infty} c(x,t) dx = \int_{-\infty}^{\infty} \frac{\text{const}}{\sqrt{t}} e^{-x^2/(4Dt)} dx = \frac{\text{const}}{\sqrt{t}} \sqrt{4\pi Dt} = \text{const} \sqrt{4\pi D}
\]

(3)

which is constant. Setting this equal to the total number of particles, \( N \), yields \( \text{const} = N/\sqrt{4\pi D} \).

b) Substituting into the diffusion equation

\[
\frac{d}{dt} c(x,t) = D \frac{d^2}{dx^2} c(x,t)
\]

(4)

\[
\frac{d}{dt} \frac{N}{\sqrt{4\pi Dt}} e^{-x^2/(4Dt)} = D \frac{d}{dx^2} \frac{N}{\sqrt{4\pi Dt}} e^{-x^2/(4Dt)}
\]

(5)

\[
\frac{N}{\sqrt{4\pi Dt}} \left(-\frac{1}{2} \frac{d}{dt} e^{-x^2/(4Dt)} + \frac{1}{\sqrt{t}} e^{-x^2/(4Dt)} \frac{d}{dt} e^{-x^2/(4Dt)}\right) = \frac{ND}{\sqrt{4\pi Dt}} \left( e^{-x^2/(4Dt)} \frac{d}{dx} \frac{d}{dx} e^{-x^2/(4Dt)} - \frac{2}{4Dt} e^{-x^2/(4Dt)}\right)
\]

(6)

\[
\frac{N}{\sqrt{4\pi Dt}} \left(-\frac{1}{2} \frac{d}{dt} e^{-x^2/(4Dt)} + \frac{1}{\sqrt{t}} e^{-x^2/(4Dt)} \frac{d^2}{dx^2} e^{-x^2/(4Dt)}\right) = \frac{ND}{\sqrt{4\pi Dt}} \left( e^{-x^2/(4Dt)} \frac{d}{dx} \frac{d}{dx} e^{-x^2/(4Dt)} - \frac{2}{4Dt} e^{-x^2/(4Dt)}\right)
\]

(7)

\[
\frac{1}{2} e^{-x^2/(4Dt)} = \frac{D}{\sqrt{t}} \left( \frac{d}{dx} e^{-x^2/(4Dt)} - \frac{2}{4Dt} e^{-x^2/(4Dt)}\right)
\]

(8)

\[
\frac{1}{2} e^{-x^2/(4Dt)} = \frac{D}{\sqrt{t}} \left( \frac{d}{dx} e^{-x^2/(4Dt)} - \frac{2}{4Dt} e^{-x^2/(4Dt)}\right)
\]

(9)

\[
\frac{1}{2} e^{-x^2/(4Dt)} = \frac{D}{\sqrt{t}} \left( \frac{d}{dx} e^{-x^2/(4Dt)} - \frac{2}{4Dt} e^{-x^2/(4Dt)}\right)
\]

(10)

\[
\frac{1}{2} e^{-x^2/(4Dt)} = \frac{D}{\sqrt{t}} \left( \frac{d}{dx} e^{-x^2/(4Dt)} - \frac{2}{4Dt} e^{-x^2/(4Dt)}\right)
\]

(11)

we get a true statement, indicating that \( c(x,t) = \frac{N}{\sqrt{4\pi Dt}} e^{-x^2/(4Dt)} \) is a solution.

c) Find \( \langle x^2 \rangle \) from the definition

\[
\langle x^2 \rangle = \int_{-\infty}^{\infty} x^2 P(x) dx = \int_{-\infty}^{\infty} x^2 \frac{N}{\sqrt{4\pi Dt}} e^{-x^2/(4Dt)} dx
\]

(12)

using the same trick as used on pages 74-75 of Nelson. Recognizing the profile as a normalized Gaussian with \( \langle x \rangle = 0 \) and \( \sigma = \sqrt{2Dt} \), the variance(\( x \)) = \( \langle x^2 \rangle - \langle x \rangle^2 = \langle x^2 \rangle \) is equal to \( \sigma^2 = 2Dt \). (Note that the time-dependence of the normalization factor doesn’t matter here because the integral is only over the spatial co-ordinate.)
Phys 150 HW 4 solutions

Nelson, Problem 4.14, pg 580 (8 pts)
a) The problem is framed in terms of a one-dimensional random walk, but this is just an example of a series of events, each of which can have one of two possible outcomes (a step to the left or a step to the right). The question is ‘What is the probability, \( P_m \), that the first outcome (in the series) happens a total of \( m \) times, if the total number of events is \( N \)?’ given that the probability for the first outcome is \( p \) (and, therefore, the probability for the opposite outcome is \( 1 - p \)). To show that

\[
P_m = p^m (1 - p)^{N-m} \binom{N}{m}
\]

realize first that there are \( N! \) ways you can arrange \( N \) outcomes in a series. This is because, in choosing the first of those outcomes you have \( N \) choices, but for the second you have only \( N - 1 \) choices, and so on. Now, if \( m \) of those outcomes in your series are identical, then it doesn’t matter which one of those \( m \) outcomes appears at any one of the positions in the series that had that type of outcome. So the number \( N! \) is over-counting by a factor of \( m! \). In this random walk example, the other \( N - m \) outcomes are also identical. So the number \( N!/m! \) is still over-counting by a factor of \((N - m)! \). The total number of possible series of \( N \) outcomes that have \( m \) outcomes of one type and \( N - m \) outcomes of the opposite type, is therefore

\[
\frac{N!}{m!(N-m)!} = \binom{N}{m} = \binom{N}{N-m}
\]

Now we want to take this total number of series (characterized by having \( m \) outcomes of one type) and multiply it by the probability of \( m \) outcomes, and only \( m \) outcomes, of that type occur. That would be the probability of having \( m \) outcomes of one type, and \( N - m \) outcomes of the other type. Since each event is independent of every other event, the probabilities for the individual events just multiply. Therefore, the probability of having \( m \) outcomes of one type (e.g. the type that was the first to occur in the series, for our example), and \( N - m \) outcomes of the other type is

\[
P_m = p^m (1 - p)^{N-m}
\]

Accordingly, multiplying equations (2) and (3) together, yields equation (1).

b) Using equation (1), and setting \( N = cV_* \) and \( p = V/V_* \) gives

\[
P_m = \left( \frac{V}{V_*} \right)^m \left( 1 - \frac{V}{V_*} \right)^{cV_* - m} \binom{cV_*}{m}.
\]

In the limit that \( V_* \to \infty \), we can neglect the \( m \) in the middle term’s exponent and approximate the rightmost term as

\[
\binom{cV_*}{m} = \frac{(cV_*)!}{m!(cV_* - m)!} \approx \frac{(cV_*)^m}{m!}.
\]

Equation (4) can therefore be rewritten with the leftmost and rightmost terms combined

\[
P_m = \left( \frac{V}{V_*} \right)^m \left( 1 - \frac{V}{V_*} \right)^{cV_*} \frac{(cV_*)^m}{m!}
\]

\[
= \left( 1 - \frac{V}{V_*} \right)^{cV_*} \frac{(cV_*)^m}{m!}.
\]

Again, in the limit that \( V_* \to \infty \), the middle term can be expanded in a Taylor series:

\[
P_m = \left( 1 - cV_* \left( \frac{V}{V_*} \right) \right) + \frac{(cV_*)(cV_* - 1)}{2!} \left( \frac{V}{V_*} \right)^2 - \frac{(cV_*)(cV_* - 1)(cV_* - 2)}{3!} \left( \frac{V}{V_*} \right)^3 + \cdots \frac{(cV_*)^m}{m!}
\]

and the small numbers being subtracted from the large numbers can be ignored

\[
P_m = \left( 1 - cV_* \left( \frac{V}{V_*} \right) \right) + \frac{(cV_*)(cV_* - 1)}{2!} \left( \frac{V}{V_*} \right)^2 - \frac{(cV_*)(cV_* - 1)(cV_* - 2)}{3!} \left( \frac{V}{V_*} \right)^3 + \cdots \frac{(cV_*)^m}{m!}.
\]
The series expansion then simplifies to
\[ P_m = \left( 1 - CV + \frac{(CV)^2}{2!} - \frac{(CV)^3}{3!} + \cdots \right) \frac{(CV)^m}{m!}. \] (10)

which you should be able to recognize as the Taylor expansion of \( e^x = \sum_{n=0}^{\infty} \frac{x^n}{n!} \), where \( x = -CV \). Thus the probability of finding exactly \( m \) fluorescent molecules in a small volume \( V \), when the comparatively infinite bath the volume is in contact with has a concentration \( C \) of those molecules is
\[ P_m = e^{-CV} \frac{(CV)^m}{m!}. \] (11)

This distribution function, known as the Poisson distribution, is well worth memorizing since it applies to all sorts of situations.

\[ \text{c) To find the mean, value of } m, \text{ we take the sum of } m \times P_m \text{ for all } m. \]
\[ \langle m \rangle = \sum_{m=0}^{\infty} mP_m \] (12)
\[ = 0 + \sum_{m=1}^{\infty} mP_m \] (13)
\[ = \sum_{m=1}^{\infty} e^{-CV} \frac{(CV)^m}{m!} = \sum_{m=1}^{\infty} e^{-CV} \frac{(CV)^m}{m-1!} \] (14)
\[ = \sum_{m=1}^{\infty} e^{-CV} CV \frac{(CV)^{m-1}}{m-1!} = e^{-CV} CV \sum_{m=1}^{\infty} \frac{(CV)^{m-1}}{m-1!} \] (15)
\[ = e^{-CV} CV \sum_{n=0}^{\infty} \frac{(CV)^n}{n!} \] (16)
\[ = e^{-CV} CV e^{CV} = CV \] (17)

To find the variance of \( m \), \( \sigma_m^2 = \langle m^2 \rangle - \langle m \rangle^2 \), we first calculate \( \langle m^2 \rangle \), which is the sum of \( m^2 \times P_m \) for all \( m \).
\[ \langle m^2 \rangle = \sum_{m=0}^{\infty} m^2P_m \] (18)
\[ = \sum_{m=0}^{\infty} (m^2 - m + m)P_m \] (19)
\[ = 0 + \sum_{m=2}^{\infty} (m^2 - m + m)P_m \] (20)
\[ = \sum_{m=2}^{\infty} (m^2 - m)P_m + \sum_{m=2}^{\infty} mP_m + P_1 \] (21)
\[ = \sum_{m=2}^{\infty} (m^2 - m)P_m + \sum_{m=0}^{\infty} mP_m \] (22)
\[ = \sum_{m=2}^{\infty} (m)(m-1)P_m + CV \] (23)
\[ = CV + \sum_{m=2}^{\infty} (m)(m-1)e^{-CV} \frac{(CV)^m}{m!} = CV + \sum_{m=2}^{\infty} e^{-CV} \frac{(CV)^m}{(m-2)!} \] (24)
\[ = CV + e^{-CV}(CV)^2 \sum_{m=2}^{\infty} \frac{(CV)^{m-2}}{(m-2)!} = CV + e^{-CV}(CV)^2 \sum_{n=0}^{\infty} \frac{(CV)^n}{n!} \] (25)
\[ = CV + e^{-CV}(CV)^2 e^{CV} = CV + (CV)^2 \] (26)

Then, we calculate \( \sigma_m^2 = \langle m^2 \rangle - \langle m \rangle^2 = CV + (CV)^2 - (CV)^2 = CV \). So, for the Poisson distribution, \( \langle m \rangle = \sigma_m^2 = CV \).
DNA $l = 50000 \text{ bp}$  
blob $d = 2\mu m$

How big are the blobs for DNA of $5 \cdot 10^6 \text{ bp}$?

The mean square displacement \( \left\langle (x_N)^2 \right\rangle = NL^2 \) for a walk of N steps with step size L.

The RMS displacement (in 3D) is:

\[
\sqrt{\left\langle (r_N)^2 \right\rangle} = \sqrt{\left\langle (x_N)^2 \right\rangle + \left\langle (y_N)^2 \right\rangle + \left\langle (z_N)^2 \right\rangle} = \sqrt{NL^2 + NL^2 + NL^2} = L\sqrt{3N}
\]

A polymer like DNA can be thought of as a random coil with a step size of one polymer unit, the base pair, and N units in the coil.

Then the coil's radius is \( R = \sqrt{\left\langle (r_N)^2 \right\rangle} = L\sqrt{3N} \)

The DNA in both samples will have the same step size, so we can find the new blob size by taking the ratio:

\[
\frac{R_{5.10^6}}{R_{5.10^4}} = \frac{L\sqrt{3 \cdot 10^6}}{L\sqrt{3 \cdot 10^4}} \Rightarrow R_{5.10^6} = 2\mu m \sqrt{10} = 20\mu m
\]

**C4.18**

Release $10^9$ molecules with $D = 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ at $x=0$ in the center of a capillary tube. An $E$-field pulls molecules to the right with drift velocity $1 \text{ mm} \text{ s}^{-1}$.

After 80s, see some molecules are to the left of $x=0$.

In one dimension (since the capillary tube is long and narrow), due to diffusion alone:

\[
X_{\text{RMS}} = \sqrt{\left\langle (x_N)^2 \right\rangle} = \sqrt{2Dt} = \sqrt{2 \cdot 10^{-6} \text{ cm}^2 \text{ s}^{-1} \cdot 80 \text{s}} = \sqrt{(1.6 \cdot 10^{-4} \text{ cm})^2} = 1.3 \cdot 10^{-4} \text{ m}
\]

In the same time, the molecules will travel a distance $X_E = V_E \cdot t = 1 \cdot 10^{-6} \text{ m} \cdot 80 \text{s} = 8 \cdot 10^{-5} \text{ m}$ toward the right due to the electric field.
Nelson, Problem 4.17, pg 582 (4 pts)

a) We’re given the fluorescence intensity immediately after bleaching, \(\psi(x, t = 0)\), and asked to calculate its mean, \(\langle \psi(x, t = 0) \rangle\). To find the mean, we compute the total intensity by integrating \(\psi(x, t = 0)\) over the entire volume, and then divide by the total volume, \(V = XYZ\).

\[
\langle \psi(x, t = 0) \rangle = \frac{\int \psi(x, t = 0) dV}{\int dV} = \frac{1}{XYZ} \int dz \int dy \int (C_0 + C_1 \sin(2\pi x/L)) dx
\]

\[
= \frac{1}{X} \left( C_0 \int dx + C_1 \int \sin(2\pi x/L) dx \right)
\]

\[
= \frac{1}{X} \left( C_0 X - \frac{C_1 L}{2\pi} \cos(2\pi x/L) \right)
\]

\[
= C_0 - \frac{C_1 L}{2\pi X} \cos(2\pi x/L)
\]

Since \(\cos(2\pi x/L) \leq 1\), as long as \(X \gg L\), the rightmost term is small and \(\langle \psi(x, t = 0) \rangle = C_0\)

b) To find the fluorescence intensity at later times, we use the diffusion equation (Eq. 4.20 on page 131)

\[
\frac{dc}{dt} = D \frac{d^2 c}{dx^2}
\]

because it relates how concentration changes over time to how it is distributed in space, and fluorescence intensity is directly proportional to the concentration of fluorophore. First we solve for the time-derivative, by plugging in:

\[
\frac{d\psi(x, t)}{dt} = D \frac{d^2 \psi(x, t)}{dx^2}
\]

\[
\frac{d}{dt} \left( C_0 + \Delta(t) \sin(2\pi x/L) \right) = D \frac{d}{dx} \frac{d}{dt} \left( C_0 + \Delta(t) \sin(2\pi x/L) \right)
\]

\[
\frac{d\Delta(t)}{dt} \sin(2\pi x/L) = D \frac{d}{dx} \Delta(t) \frac{2\pi}{L} \cos(2\pi x/L)
\]

\[
\frac{d\Delta(t)}{dt} \sin(2\pi x/L) = -D \Delta(t) \frac{4\pi^2}{L^2} \sin(2\pi x/L)
\]

\[
\frac{d\Delta(t)}{dt} = -\frac{4\pi^2 D}{L^2} \Delta(t)
\]

The solution to this first-order differential equation is an exponential, \(\Delta(t) = e^{-t/\tau}\), where \(\tau = L^2/(4\pi^2 D)\). So, the fluorescence intensity as a function of position and time becomes

\[
\psi(x, t) = C_0 + e^{-4\pi^2Dt/L^2} \sin(2\pi x/L).
\]

Now, in the limit that our region of interest is small compared to the whole cell, we are effectively sampling only the shortest times, so \(\Delta(t) \approx 1 - 4\pi^2 Dt/L^2\). In other words, the amplitude of the sinusoidal distribution will decrease linearly in time, at first, at a rate \(4\pi^2 D/L^2\).
DNA $l = 50000$ bp  
blob $d = 2 \mu m$

How big are the blobs for DNA of $5 \cdot 10^4$ bp? 

The mean square displacement $\langle (X_N)^2 \rangle = NL^2$ for a walk of $N$ steps with step size $L$.

The RMS displacement (in 3D) is

$$\sqrt{\langle (n)^2 \rangle} = \sqrt{\langle (X_N)^2 \rangle + \langle (Y_N)^2 \rangle + \langle (Z_N)^2 \rangle} = \sqrt{NL^2 + NL^2 + NL^2} = L \sqrt{3N}$$

A polymer like DNA can be thought of as a random coil with a step size of one polymer unit, the base pair, and $N$ units in the coil.

Then the coil's radius is $R = \sqrt{\langle (n)^2 \rangle} = L \sqrt{3N}$

The DNA in both samples will have the same step size, so we can find the new blob size by taking the ratio

$$\frac{R_{5 \cdot 10^4}}{R_{5 \cdot 10^6}} = \frac{L \sqrt{3 \cdot 10^4}}{L \sqrt{3 \cdot 10^6}} \implies R_{5 \cdot 10^6} = 2 \mu m \sqrt{10^2} = 20 \mu m$$

**C4.18** Release $10^4$ molecules with $D = 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ at $x = 0$ in the center of a capillary tube. An $E$-field pulls molecules to the right with drift velocity $1 \mu m \text{ s}^{-1}$.

After 80s, see some molecules are to the left of $x = 0$.

In one dimension (since the capillary tube is long and narrow) due to diffusion alone:

$$x_{\text{RMS}} = \sqrt{\langle (X_N)^2 \rangle} = \sqrt{2Dt}$$

$$= \sqrt{(2 \cdot 10^{-6} \text{ cm}^2 \text{ s}^{-1} \cdot 80 \text{ s})} = (1.6 \cdot 10^{-4} \text{ cm}^2)^{1/2} = 1.3 \cdot 10^{-4} \text{ m}$$

In the same time, the molecules will travel a distance $x_E = V_E \cdot \frac{t}{3} = 1 \cdot 10^{-6} \text{ m} \cdot 80 \text{ s} = 8 \cdot 10^{-5} \text{ m}$ toward the right due to the electric field.