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BIOLOGICAL DIFFUSION PROCESSES

Allen R. Killpatrick
University of Redlands

Norman J. Chonacky
Southern Connecticut State College

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Physical Science Module for Bioscience Students

BIOLOGICAL DIFFUSION PROCESSES

by

Allen R. Killpatrick
Johnson College
University of Redlands
Redlands, California  92373

and

Norman J. Chonacky
Southern Connecticut State College
New Haven, Connecticut  06515

(NOTE: Suggestions and/or solutions are omitted.)

Project Address:  PSMBS, 213 Ferguson Hall, University of Nebraska,
Lincoln, NE  68588.
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BIOLOGICAL DIFFUSION PROCESSES

Introduction

What happens in the lung is that air meets blood. Figure 1 shows the lung's architecture. Focus your attention upon the smallest scale structures which are the termini of the air passages. These are the alveolar air sacs or, simply, alveoli.

![Diagram of lung architecture](image)

Figure 1: The relationship of the alveoli to the entire lung.

The inhalation/exhalation actions of the lung, alternately, flood these alveoli with atmospheric air and expel its oxygen-poor/carbon dioxide-rich replacement. Figure (2a) depicts, in a somewhat simplified manner, these
alveoli with their appended venous blood suppliers, the pulmonary arteries. Figure (2b) shows the structure of the blood distribution system over a small, typical portion of the alveolar surface in much more detail. Here lies an extensive system of capillaries. The blood comes in from above and left, then flows through the expansive capillary bed, toward the right and out.

Figures 2(a): Alveoli with pulmonary arteries.
2(b): Magnified section of alveolar surface showing capillary bed.

What happens at these alveolar surfaces is that the venous blood and the alveolar air meet at the capillary bed surfaces, separated there by only
one or two microns of membrane. It is through this thin membrane, which maintains both the integrity of the air passages on one side and the integrity of the blood system on the other, that oxygen and carbon dioxide gases move in opposite directions. The process of this movement of matter is called diffusion, and is the subject of this module.
EXPLORATIONS IN THINKING

Do you believe in pheremones? Have you ever had the sensation that someone was in the room, even before noise or vision indicated that presence?

Have you ever been in a room when a bottle of ammonia was uncorked there? Isn't it remarkable? Even in still air, the pungency quickly reaches even the most distant corner of that room.
EXPLORATIONS IN DOING

1. Using a bottle of ammonia and a group of three to six people in a quiet draft-free room, try the following experiment. Station the individuals at approximately equal spacings, from the bottle location out to the farthest removed point of the room. Then uncork the bottle and start a seconds-timer. Record the elapsed time (from the bottle uncorking) at which each person on station first perceives the ammonia smell. Note: Those near the bottle may have to "creep" slowly away as the smell grows stronger. They must do so without undo disruption of the still air, however.

2. Use a section of (plastic) dialysis tubing filled with very concentrated NaCl solution to measure the rate (diffusive flow) at which NaCl is lost through this membrane into fresh water outside.

   How? Hold this filled and sealed tubing in a stream of flowing fresh water which, as nearly as possible, completely bathes the tube. This may take quite a while, so you might stick the tubing in a beaker of fresh water constantly refreshed by overflowing fresh water. Periodically weigh the tube to determine the salt loss. Plot the mass of the "bag" contents versus time. How many moles of NaCl are being lost per second after 30 minutes have elapsed?

3. Drop a few crystals of methylene blue (or a few drops of food coloring) in cold water and simultaneously drop a few in hot water. Observe and write a brief description of what ensues.
INVENTION

Prerequisites:

1. Write a brief definition for and give an explanatory description of material flow rate (moles/sec) of a solute in a solution.

2. Recognize the notation for an exponential function of time, and be able to evaluate it and/or sketch a graph of it.

3. Utilize the continuity equation for relating various material currents and densities in a solution to one another.

4. Write a definition for concentration gradient and be able to evaluate it from data for concentration versus distance, given those data in a table or graph.

Objectives:

1. Recognize the physical conditions which give rise to a diffusion process in a given physical system.

2. Estimate the rate and/or amount of diffusive flow (material current) for a system where either: (a) the mean free path, velocity, or other parameters of the random walk of the diffusing substituent are known; and/or (b) the temperature and solute concentrations of the system are given.

3. Given the concentration profile of a solution (i.e., concentration versus position in the solution) at various times, evaluate the various quantities in the resultant diffusive flow processes.

4. Recognize which diffusion situations represent exponential approach to equilibrium conditions, and in that circumstance evaluate both the
characteristic time of such a process and the concentration of the equilibrium state.

5. Utilize various characteristics of a diffusion process to describe its role in the functioning of a given biological system.

6. Describe the difference between osmosis and diffusion; recognize the circumstances in which each is a significant factor in the material flow processes of a given system.

7. Give approximate values of the diffusion coefficient, as requested, of one of a variety of common biochemical substituent (e.g., sucrose) in solution.
A. Diffusion across a membrane; Fick's Law.

In the Exploration Activity #2, you can observe that a cellophane tube containing a high salt solution gradually loses mass when bathed continually in fresh water. In fact, if you were to examine (e.g., taste!) the bath water, there would be traces of salt in it. The situation is depicted below in Figure (3).

Figure A3: Dialysis of concentrated salt solution by means of fresh running water.

It might be helpful to have some typical data from such an experiment, in addition to your

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>0</th>
<th>260</th>
<th>1000</th>
<th>1750</th>
<th>2300</th>
<th>2800</th>
<th>3300</th>
<th>5000</th>
</tr>
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<tbody>
<tr>
<td>Mass of tubing contents (gm) including solute and water</td>
<td>4.77</td>
<td>5.02</td>
<td>4.85</td>
<td>4.62</td>
<td>4.49</td>
<td>4.41</td>
<td>4.33</td>
<td>4.31</td>
</tr>
<tr>
<td>Mass of contents minus equilibrium mass (gm)</td>
<td>0.52</td>
<td>0.77</td>
<td>0.60</td>
<td>0.37</td>
<td>0.24</td>
<td>0.17</td>
<td>0.08</td>
<td>0.06</td>
</tr>
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Table A1: Mass of solution in tubing "bag" versus elapsed time of flushing with fresh water.
The tubing appears to be "leaky" to salt. How can you be sure? The "taste test" is specious. In this situation it is unlikely that you would be able to actually taste the minute concentrations of salt that are rapidly diluted by the flowing fresh water. You might try logical inferences.

You might think of salt molecules moving around in the water. The cellophane membrane is quite thin, and is made of a polymeric mesh randomly arranged, perhaps is likely to have some "holes" straight through this small thickness. That way, the moving salt molecules inside could wander out. The data indicate that the tube's mass goes down with time. What do you expect happens to the mass of the contents if an NaCl molecule wanders out? If one NaCl leaves, then there should be less mass inside. But doesn't it leave a space? Water is a small molecule too, and may wander in to fill that space; perhaps two water molecules fit into one NaCl space! Hmmm.

There is a lesson here which provides a keynote for our approach to explaining diffusion. Ultimately you would probably like to know what is happening on the molecular level. However, the problems of explaining living systems always present themselves in macroscopic terms. Therefore it is encumbent upon us to always first examine the macroscopic data and formulate explanations which are first consistently faithful to them, even while we are proceeding to the more general and more satisfying microscopic (i.e., molecular) explanations of the phenomenon.

Let's try another approach by logical inference. The available data indicate that the mass of the tubing contents diminishes with time. The tube, except for the very beginning which we shall discuss later, maintains a constant volume. Therefore the density of the contents must be decreasing. Now it is already known that NaCl solutions are more dense than pure water. Thus we can conclude that the contents' density becomes more like that of
water; salt must be exiting. And from this we further conclude that the tubing membrane must be porous to salt.

How porous? The mass loss data indicate that after establishing some maximal value, the salt inside flows outward with a gradual but ever decreasing rate. One possible explanation is that the membrane porosity decreases with time. A somewhat different point of view emerges if you realize that the salt flow decreases as the salt concentration inside $C_i$ (moles/cm$^3$) approaches that of the outside $C_o$, in this case zero. This point of view, that the membrane stays the same, but that the flow is an effect of the solute concentration difference, is seminal in our treatment of material transport here. We express this point of view by writing the descriptive equation which assumes that the solute current $I$ (moles/sec) is directly proportional to the difference between the solute concentration inside $C_i$ (moles/cm$^3$) and the concentration outside $C_o$ the membrane tube surface of total area $A$.

$$I = pA(C_i - C_o)$$

This relationship is called Fick's Law for diffusive membrane transport. The proportionality constant $p$ is called the permeability of the membrane. (It has a value which depends upon the solute size and solvent; for small molecules such as NaCl and cellophane of the type used in the Exploration Activity #2, so-called dialysis tubing, a typical value would be $p \approx 10^{-3}$ cm/sec).

Notice that the factor of total membrane area $A$ has been separated from the permeability factor in writing this equation. This reflects the
fact, undemonstrated here but nonetheless plausible, that the transport process is a surface phenomena and that this is reflected in an experimentally displayed direct proportion between solute flow rate $I$ and total membrane surface area $A$.

$$I \propto A$$

This distinction is the first in a series in which we move toward a progressively more microscopic explanation of diffusive flow.

One comment ought to be made about this treatment of solute flow through the membrane which presumes that the membrane stays the same, viz. is a passive participant in the transport process. This point of view is adequate to explain only one class of components of material flows which occur across biological membranes. Another point of view is required to explain another class of material flows which occur simultaneously with these passive transport processes, and which often dominate in biological membrane systems. In the latter class, chemical reactions occur at the membrane surface which are selective to certain solute species, energy is utilized, and flow components occur which can be in the direction opposite to that described in equation (1a). As a class these are known as active transport processes. Although vitally important, these are not diffusive flows, and we mention them here only for the sake of perspective.

Returning to passive transport, it is well to remark that equation (1a) does not describe all possible situations. For example, fresh water from a river mixes salt water in estuaries not primarily by diffusive flow, but by volume flow in which large portions of high salt and low salt solutions flow and intermix in moving streams. Volume flow proceeds by the collective motion of large numbers of molecules in a single locale, whereas diffusive
flow proceeds by the random motion of individual molecules. A more complete description of these characterizations of passive transport flows is reserved for later. We should point out here only that our purpose in presenting diffusion by using membrane tubing and nature's purpose for using membranes in the architecture of living systems are in fact one and the same. Membranes restrict volume flows. These would disrupt the solute separation which we wish to demonstrate the flow between, and which nature uses to concentrate biochemicals for the operation of living systems.

In proceeding toward a more microscopic explanation of what occurs in a diffusive flow, you might benefit from seeing a model (viz. a picture) of what the porous membrane might look like if it functions in the manner indicated by the data. A schematic diagram of one possibility appears in Figure (4) below.

---

Figure A4: Schematic diagram of a cross-section of a portion of a typical dialysis membrane having randomly distributed pores.
The use of a membrane to experiment with diffusion simplifies the measurement of diffusive flow and its dependence upon the concentration gradient between two regions. Two bodies of solutions having known (different) concentrations can be prepared with the membrane inserted between. This membrane, then, clearly defines the region of the concentration gradient which is responsible for the diffusive flow. The value of this concentration gradient can be calculated from the measured membrane thickness $\Delta X$ and the known solute concentration difference $\Delta C = C_i - C_o$.

But the most general theories of diffusion, and in particular the microscopic explanations we seek, are formulated in terms of bulk solutions rather than in terms of membrane/solution systems. Thus, in order to relate our experiments with membranes to a general theory, we must establish the connections between membrane and bulk diffusion.

Roughly speaking, we try to imagine that diffusion takes place within a pore in the same manner that it does in bulk solution. (As you will see, this is not always true.) In this view, the membrane only serves to reduce the area through which the diffusive flow may occur, and the key quantity becomes the pore fraction ($A_{\text{pore}}/A$). Moreover, it is clear that in some situations the individual pore size ($r_{\text{pore}}$) also is significant in determining the diffusive behavior of solutes through the membrane. Indeed, one vital function of membranes is that they have the ability to discriminantly pass molecules according to their size (relative to the pore size). If, for example, red blood cells or even their much smaller component hemoglobin molecules had been included in the dialysis tubing of your diffusion experiment, during salt outflow these larger molecules would have remained inside. The need to know, then, the pore fraction and pore size of the membrane in order to relate the diffusion through it to diffusion through a bulk solution presents an additional experimental complication since these cannot be measured directly.
Fortunately, the presence of pores through which water can pass faster than salt is a complication which can also work for us as well. Notice that when the dialysis tubing is first filled with high salt solution and tied, some air is inevitably trapped. When you first stick it into the fresh water bath, its size and mass grows, and the membrane becomes tight. There is an influx of a volume of pure water through the pores due to a pressure decrement inside, which is called the osmotic pressure of the NaCl solution. You see the tubing swell and the volume of that trapped air bubble compressed as the hydrostatic pressure inside the tubing increases. When that hydrostatic pressure increment just equals the osmotic pressure decrement of the interior salt solution, the net pressure difference across the membrane is zero; volume flow of water ceases, and the succeeding solute flow is purely diffusive. This system, after this initial influx of pure water, thus affords the example of purely diffusive solute flow which we desire.

During that time in which the osmotic pressure is causing volume flow through the pores, the current velocity inward retards the diffusive solute flow which must now take place "upstream". This is an example of coupled flows. In general you must always regard the possibility of both types of passive transport in every situation. In certain biological cases such as the flow of blood plasma across the glomerular membrane in the kidney nephron, volume flow is the only type which occurs. It is maintained principally by a hydrostatic pressure difference provided by the heart. Again, although an important component of biological material transport, we shall reserve discussion of volume flow for elsewhere and here discuss only the diffusive flow component.
Exercise A1

Consider a dialysis tubing bag, as described above and used in Exploration Activity #2 (see Figure 3). Suppose its dimensions are given by:

- length = 2.4 cm.
- diameter = 1.6 cm
- surface area = 16 cm$^2$
- volume = 4.8 cm$^3$ (i.e., ml.)
- wall thickness = 2 x $10^{-3}$ cm
- original mass = 4.77 grams

1. Suppose that after 1000 seconds the mass of the bag-plus-contents now is 4.85 grams. Evaluate the solute flow current and the solute flow current density at this point in time.

2. Calculate the initial concentration gradient across the membrane assuming that the concentration at each surface if fixed by the respective body of solution there on that side. N.B. the flowing fresh water should be assumed to dilute the exiting salt completely.

3. Graphing Table 1, calculate the mass current I through the tubing at each point of elapsed time which appears as a table entry, using the slope of that graph at each such point. Compare the value obtained here for $t = 1000$ seconds with that obtained from (#1) above. In which do you have more confidence?

Solutions and/or suggestions on next page.
So things are more complicated with membranes than they appear at first glance. Nonetheless we shall try to join the simple membrane experimental results to a somewhat more abstract, but conceptually simpler and more general, theoretical description of what takes place when two solutions, having different concentrations, meet one another. Keep in mind that the membrane data suggest that the solute flow rate $I$ through the membrane is directly proportional to the difference in solute concentration $\Delta C$ (moles/cm$^3$) between the solution on one side and the solution on the other. This is the defining characteristic of diffusive flow.

Proceeding toward a more general account of diffusion, you are asked to believe that the diffusive solute flow rate depends upon only that portion of the total membrane area which consists of the pores, call it $A_{pore}$.

$$I \propto A_{pore}$$

This is only an ideal. To the extent that it is found to be true, the diffusive behavior of the molecules in the pores of such membranes approximates that which occurs in an equivalent volume of bulk solution, without the membrane. Motivated by this ideal we define the density of the diffusion current through the membrane as a quantity which is independent of $A_{pore}$.

$$J = \frac{I}{A_{pore}} \text{ (moles/sec.cm$^2$)}$$

Further, you are asked to believe that which is less obvious but nonetheless generally true, that the solute diffusion flow rate is inversely proportional to the membrane thickness $\Delta x$.

$$I \propto \frac{1}{\Delta x}$$

Again, this fact has less to do with membrane specifically as with the general
bulk properties of diffusive flow. Generally the more abrupt is
the change in solute concentration, the greater is the diffusive flow.

What a membrane of thickness $\Delta x$ normally does is to provide the
limiting barrier to diffusive flow in a system. The solute can quickly
diffuse through the volumes comprising each of the two bodies
of solution. Thereby each maintains its uniform concentration value $C_0$
or $C_i$ throughout. However, the relatively small pore area is a bottleneck.
The total flow rate through these pores is normally quite low due to their
small fractional (of $A_{total}$) area. Thus the surfaces of the two solution
bodies which adjoin the membrane, each having area $A_{total}$, are able to
supply/receive the system's small diffusion current with only a miniscule
local concentration difference to support them.

Combining these ideas allow us to restate Fick's Law in a way in which
the bulk character is more transparent.

$$J = D \frac{\Delta C}{\Delta x}$$  \hspace{1cm} (A1b.)

The proportionality constant $D$ (cm$^2$/sec) is called the diffusion constant
and has a value which, for small molecules and/or large pores (molecular
diameter $< 5\%$ of the pore diameter) is independent of the membrane and
dependent only on the solute/solvent combination (a truly microscopic
detail!). Typically these values for NaCl in water at room temperature
are of order of magnitude $D \approx 10^{-5}$ cm$^2$/sec.

How successful a bulk theory is this? It is successful to the extent that the value $D$ does not depend upon the details of the pores
such as their size and shape; or failing that, to the extent that we can
provide another theory to predict the departures of $D$ from the "large pore"
limiting values. In short, if one measures $D$ for a certain molecule using
large pore membranes, or bulk solution (without membranes), and then again for other cases of smaller pores with the results $D_{\text{eff}} < D$ in each case, then a theory to predict the hindrance factor

$$D_{\text{eff}} = (D) \text{ (hindrance factor)}$$

is desirable. And even if this is not possible, one may still measure hindrance factors for different porosity membranes and use them to describe the expected diffusive flow for various situations. Some success at formulating a reasonable theory has in fact been achieved, but is beyond the scope of our discussion.

Once we realize that the hindrance factors for different molecules have different values for a given membrane, then we can appreciate the possibilities for using membranes to selectively separate molecules from a common mixture according to their relative sizes. In fact this is an appreciation which nature has already had for a long time, as we shall see.
**Exercise A2**

1. The diffusion constant for NaCl in water near room temperature is approximately $D = 10^{-5}$ cm$^2$/sec. Evaluate the diffusion current which you expect to flow, according to Fick's Law, across 1 cm$^2$ of dialysis membrane having 2 micron thickness and total pore area equal to 10% of the actual, full surface area. The conditions for this flow are that the membrane divides a 1M NaCl from a 2M NaCl solution.

2. Using the data given in Table 1, apply Fick's Law to the system at different points in time and thereby deduce several individual values for the "effective" diffusion constant of the entire membrane surface. How close do they agree with one another? Then make a new table which compares each concentration difference $\Delta C$ with the corresponding solute current $I$. Does this relationship graph as a straight line? Use the graph and the membrane data from Exercise A1 to determine an "average value" for the diffusion constant $D$.

3. In problem #2 here, you have necessarily disregarded the proposition that the "free flow" of solute occurs only through the pore regions since the pore fraction of the total area was not known. Using the previously given (problem #1 here) value for the NaCl diffusion constant (bulk solution value), calculate a value for the fraction of the total surface area which one can suppose belongs to the pores (i.e., the pore fraction).

4. Repeat problem #3 using your own data from Exploration Activity #2, provided that you have derived sufficient data from that exercise.

5. In each kidney nephron (see Figure A5.) there is a place (Bowman's capsule) where the incoming blood (in the glomerulus) passes very
close to the terminal end (origin) of that nephron's renal tubule. (These tubules ultimately converge into the bladder.) The basement membrane, separating the blood in the glomerulus from the glomerular filtrate in the tubule origin in these capsules, is very large in surface area (1.5-4.5 m²) and very thin (0.4-0.6 microns). (The figures given are for the human kidney.) The only way in which the renal fluid (e.g., water, salts, urea, etc.) enters these tubular origins is from the glomeruli through the basement membranes.

The basement membrane is of such a structure (i.e., porous) that it passes all major ions, glucose, amino acids, and urea freely, along with water. Yet it excludes completely erythrocytes and blood plasma proteins. The blood plasma (minus the proteins) is simply pushed across (i.e., filtered) through this membrane in a volume flow by means of a pressure difference (between the arteries and the renal tubules) maintained by the heart. Assuming that the largest amino acid has approximately a 50 nm diameter, estimate the diameter of the smallest molecule which this membrane should be capable of completely excluding.

Suppose for a moment that there were no pressure difference across the basement membrane, but instead that the renal fluid circulated rapidly inside the tubules to carry away the diffusing material and thereby keep the concentration of solutes on the inner side of the membrane near zero. Knowing that the blood contains (about) 150 mM NaCl and assuming a diffusion constant for NaCl of 10⁻⁵ cm²/sec, find out what pore fraction of the basement membrane would be necessary in order to maintain the functional NaCl current of J = 0.25 millimoles/cm³ flowing into the tubules by diffusion alone.

Solutions and/or suggestions are on the next page.
Fig. A5: Schematic drawing of the nephron, the principal functional unit of the kidney. Much of the arterial blood entering the glomerulus is filtered through the basement membrane into the renal tubules. Reabsorption of the filtrate takes place between the tubules and the capillary bed surrounding it.
B. The time course of diffusion; equilibrium.

The dialysis tubing containing NaCl solution flushed with fresh water (Exploration Activity #2) was presented as an example of diffusive flow. The salt, we argued, flowed out in a diffusion current whose relationship to the surface area and thickness of the tubing and to the concentration difference between the inner and outer solutions is described by Fick's Law.

The solute current, however, decreased with time. This is expected. Since the salt outflow results in a depletion of salt from the inside which remained at fixed volume, consequently the inside salt concentration necessarily fell. Then because the outside salt concentration remained fixed at some small value (continually flushed with fresh water), this lowering of salt concentration inside reduced the inside/outside concentration difference and hence, by Fick's Law, the diffusion current as well.

We wish to examine, now, the time course of these events as well as the final (equilibrium) state. To do this most concisely we would have to use the reasoning of the mathematical calculus. Here, in the interests of less sophistication, we shall avoid using that language but arrive at similar results, albeit in a more cumbersome, lengthy way.

We know three facts:

1. The initial concentration inside the tubing of volume V is some known value \( C_{10} \) and the concentration outside is fixed at \( C_0 = 0 \).
2. The time rate of change of the (mole) number of molecules inside \( (\Delta N_1/\Delta t) \) is related to the solute current into the tubing \( (I_{1n}) \) and the solute current out of the tubing \( (I_{1out}) \) by means of the continuity equation

\[
\Delta N_1/\Delta t = I_{1n} - I_{1out} \quad \text{(B2.)}
\]
3. The net solute current $I$ out of the tubing is stipulated by Fick's Law (equation 1)

$$I = D_{\text{NaCl}} A_{\text{pore}} \frac{C_i - C_o}{\Delta x} = pA \left( C_i - C_o \right)$$

(Ala.) and (Alb.)

First we utilize the connection between number of molecules $N_i$ and concentration $C_i$ (i.e., $\Delta C_i = \Delta N_i / V$ where $V$ is the total volume of the inside of the tubing). Then noting that $I = I_{\text{out}} - I_{\text{in}}$, you find that

$$\frac{\Delta C_i}{\Delta t} = \frac{I_{\text{in}} - I_{\text{out}}}{V} = -I/V$$

Since the flushing process keeps $C_o = 0$, then $(C_i - C_o) = C_i$ and

$$\frac{\Delta C_i}{\Delta t} = -\left( \frac{D_{\text{NaCl}} A_{\text{pore}}}{V \Delta x} \right) C_i = -\left( \frac{pA}{V} \right) C_i$$

(B3a.)

For simplicity you can set $(D_{\text{NaCl}} A_{\text{pore}}/V x) = pA/V = K(\text{sec}^{-1})$; then the result is

$$\frac{\Delta C_i}{\Delta t} = -K C_i$$

(B3b.)

What does equation (3) mean and what does it tell us regarding the consequent time course of the changing concentration $C_i$?

First, the left-hand side of equation (3) reads "change in inside salt concentration per unit time." The entire equation (3) indicates that this rate of change in concentration (in other words the rapidity of the salt outpouring from inside) should be greater when the inside concentration itself is greater and vice-versa. Notice from the data that the salt outpouring is greatest near the beginning of the flushing process, before any salt has been depleted from the inside (and hence inside salt concentration is greatest).
Moreover, the larger the value of \( K \) (which is fixed by porosity of the membrane to the solute substituent chosen) so more rapid should be the salt outflow at any given inside salt concentration compared with what it would be with the same salt concentration but in a tubing with smaller \( K \) (less porous). If, for example, the pore area \( A \) were larger, or thickness \( \Delta x \) were smaller, or inside volume \( V \) were smaller, (i.e., larger \( K \)) then the diffusion current would be larger. So too if the diffusing species (here NaCl) were different and had a higher diffusion constant (that is, diffused more readily through the given membrane), then the diffusion current would likewise be larger.

Second, note the negative sign in equation (3). Since \( K \) and \( C_i \) must have positive values by virtue of their definition, the minus sign means that when \( C_0 = 0 \) the salt always decreases in concentration inside the tubing, toward the value \( C_i = 0 \). Moreover, looking back at the derivation of equation (3a) above, you can note that had the outside concentration \( C_0 \) not been equal to zero, and in fact if \( C_0 > C_i \), then the minus sign of equation (3) would require that the concentration of salt inside must increase, toward \( C_0 \). This fact of diffusion, namely that the diffusive flows always occur from regions of higher to regions of lower concentration is an essential characteristic of the diffusion process. The molecular reason for this behavior will be discussed in Section C of this module. Its consequence can be simply paraphrased however. Diffusive flows always are such as to equalize molecular concentrations of every substituent species throughout regions where those molecular species are able to move.

The last question, about the time course for \( C_i \) indicated by equation (3), can be answered by means of a calculation which you can do (see appendix), and are so requested to do in the following exercise. The results of this calculation, however, are summarized here:
Equation (3b) together with fact (1), from above, require that the salt concentration inside $C_i$ vary with the passage of time according to the rule

$$C_i = C_{i0} e^{-Kt}$$

where $C_{i0}$ is the salt concentration when the elapsed time $t = 0$, that is, at the beginning of the flushing process, and $K$ is the same quantity as appears in equation (3). It should be noted that the value $1/K$ (sec) is a time, and that this is the so-called "time constant" or "relaxation time" of the exponential function. It is valuable to realize that the system equilibrium value ($C_i = 0$ for the above function) is practically reached (within 1%) after a few multiples of this time constant have elapsed.
Exercise B3

1. The molecular weight of sodium chloride (NaCl) is about 58 gm/mole. What is the concentration $C$ (moles/cm$^3$) of NaCl in a 10 ml solution which has a mass of 11.74 grams? (Assume that the volume occupied by this much NaCl is a negligible fraction of the solution volume.)

2. Consider a dialysis tubing section having 33 cm$^2$ of total surface area surrounding a 10 ml volume of 1 M NaCl. The solution has a mass of 10.58 gm. For a period of $10^4$ seconds there is an almost steady outflowing diffusive current of $10^{-7}$ moles/sec. Calculate the value of the concentration of the NaCl which remains inside this tubing at the end of this period of time. Has the concentration of NaCl decreased much from its original value during this period of time? By what fraction has the concentration decreased?

3. Fick's Law describes the value of the diffusion current $I$ to expect from the tubing in the previous problem in terms of the concentration difference $C_i - C_o$, membrane permeability $p$, and membrane surface area $A$, namely

\[ I = pA (C_i - C_o) \]

Evaluate the permeability which this membrane must have in order to pass the $10^{-7}$ mole/sec current at the initial instant (see above, #2) when the inside concentration is $C_i = 1.00 \times 10^{-3}$ mole/cm$^3$ and the outside concentration is $C_o = 0$. If during a certain period of time, the inside concentration falls to 0.90 moles/cm$^3$ and the outside concentration remains at 0, what value of diffusion current does Fick's Law predict for that instant at the end of this period?
Compare the fractional reduction in diffusion current with the fractional reduction in $C_i$ during the described time interval.

4. For the same system as in problems #2 and #3 above, calculate the successive values of the inner (tubing) salt concentration at the ends of successive time intervals, each of duration $10^4$ seconds. For the purposes of this calculation assume that the diffusion current has a (different) uniform value during each entire $10^4$ second interval, even though the decreasing inside salt concentration requires that the diffusion current actually must decrease somewhat during this time span. (The error in doing this can be kept small provided that the chosen uniform value does not differ "too much" from any of the varying actual values of current during a given interval. This is discussed in the appendix.) The value of current you should use for each interval should be that value which is appropriate to the exact beginning of each particular time interval as determined by equation (A1). Present your results by completing the table below.
Table B2: Pattern of concentrations at successive time intervals of $10^4$ seconds due to diffusion.

<table>
<thead>
<tr>
<th>Time (sec.)</th>
<th>Solute concentration $C_i (10^{-3} \text{ moles/cm}^3)$</th>
<th>Assumed constant current $(10^{-7} \text{ moles/sec})$</th>
<th>Loss of concentration $\Delta C_i (10^{-3} \text{ moles/cm}^3)$ due to diffusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
<td>0.10</td>
</tr>
<tr>
<td>1</td>
<td>0.90</td>
<td>0.90</td>
<td>0.09</td>
</tr>
<tr>
<td>2</td>
<td>0.81</td>
<td>0.81</td>
<td>0.08</td>
</tr>
</tbody>
</table>
5. Draw a graph of the data calculated in problem #4 above, presenting the results of your calculations as salt concentration inside versus total elapsed time. On the same graphical axes draw a graph of the equation (4) as it applies to this case; namely

\[
C_i = (10^{-3} \text{ moles/cm}^3) e^{-(10^{-5}/\text{sec})t}
\]

where \(C_i\) is the (predicted) internal salt concentration (i.e., within the tubing) and \(t\) is the total elapsed time.

6. Equation 3b is definitive for the diffusion process which is described by the three facts at the beginning of this section. Verify that the time behavior of \(C_i\) described by equation 4 is consistent with the stipulation of equation 3b, namely that the slope of the \(C_i\) versus \(t\) graph (i.e., \(\Delta C_i/\Delta t\)) must equal \(-K\) times the particular value of \(C_i\) (i.e., \(-KC_i\)), where both the value and the slope are determined, for any particular instant of time \(t\), from the aforementioned graph. Do this using an actual graph, where you pick some arbitrary (simple) value for \(C_{i0}\) and for \(K\), for the purpose of doing this graphing.

Solutions and/or suggestions on the next page.
C. Diffusion Pictured as Molecular Motion

We will now describe a way of looking at the diffusion process as the result of the random motion of the molecules of the diffusing material. We will describe the random motion processes and connect their results with Fick's Law, with the value of the diffusion constant, and with the values of the microscopic quantities, free path, and velocity. The particular model which we use restricts the motion to one dimension for the sake of simplicity. But the more general, three-dimensional case is more complicated without revealing any new features and so it will not be treated here. We first, here, discuss some results which any molecular motion theory must predict.

Recall the Exploration Activities which you did, specifically the uncorked bottle of ammonia. The times it took for the smell to travel different distances are related to those distances in the following way.

\[ \text{time} \propto (\text{distance})^2 \]

It takes four times as long for the diffusing molecules to travel six meters as compared to the travel time for three meters from the source. The molecular explanation must make this prediction.

In the analysis of the diffusion data, the relationship between the constituted concentration gradient and the resultant observed diffusion is summarized by Fick's Law which states that the material flow rate (i.e. diffusion current) is proportional to the concentration gradient. In other words, the ratio of the difference in concentrations between two regions and the rate of transfer of material between those regions is a constant number, a value fixed by the type of diffusing materials and perhaps the temperature but not changing during the progress of the diffusion. The molecular explanation must feature this behavior.
The usefulness of the molecular picture will be measured in part by the extent to which you can make connections between the values of quantities used in that molecular description and the values of quantities which are readily measurable in the laboratory. Thus, such quantities as concentration, concentration gradient, diffusion current, and diffusion constant should be readily identifiable parts of the molecular explanation.

If we wish to conceive of diffusion as the result of random molecular motions, then a good place to start our (one dimensional) explanation is with the "drunkard's" walk (also known as the random walk). In this scenario we view the progress of a drunkard from some starting position (call it the origin \( O \) on the line) if his/her movements consist of uniform-sized steps taken, at random, backward or forward. We wish to examine the likelihood that \( N \) such successive steps of length \( \lambda \) will result in the drunkard's being a distance \( X_m = m\lambda \) away from the origin (i.e. starting place). If we denote by \( n_+ \) the number of steps forward out of a total of \( N \), and \( n_- = N - n_+ \) those taken backward, then our result \( X_m \) can be expressed as

\[
X_m = m\lambda = (n_+ - n_-)\lambda = (2n_+ - N)\lambda
\]

where \( m = 2n_+ - N \) has a range

\([-N \leq m \leq +N]\)

and has either all even (if \( N = \text{even} \)) or all odd (if \( N = \text{odd} \)) values separated by two units.

This problem is closely related to the "coin-flipping" problem in which one asks: "How many heads \( (n_+) \) turn up each time you flip a series of \( N \)?". Because it is clear that it is possible for every (odd or even) outcome
within the allowed range of "m" to occur, but that each outcome happens with a different likelihood in general, then we can only describe these outcomes as the pattern of possible results. This pattern may be established by actually trying random walks and tabulating a collection of results. Or we may logically deduce each possible outcome and tabulate a hypothetical collection of results from all possible drunkard's walks (or N-fold coin flips). We call either such collection a statistical ensemble.

The equivalence of the derivations of the statistical ensemble just described requires that we must limit the predictive power of the theory to a description of probabilities of various outcomes. This limitation of the description will not seriously compromise our use of the drunkard's walk as the basis for our molecular motion model of diffusion however. This is because we wish only to describe the resultant movement of thousands upon thousands of molecules, each of which moves (more or less) independently of the others. Thus each molecule's particular fate is like one drunkard's walk, one element of the statistical ensemble. And the pattern of the entire ensemble alone is what we observe at our level of experience in the world. It is only that, therefore, which we seek to explain.

The pattern of results of the drunkard's walk is summarized for the particular case of four steps (i.e. N = 4) by the following graph of Figure 8.
This graph was obtained by enumerating all the various possible different ways the 4-step drunkard's walk could progress (e.g. one step forward, two backward, and then one step forward; etc.). Notice that there is more than one way, in general, to arrive at any given final position. For \( m = -2 \), there are four separate distinct combinations of back and forward steps which deliver the drunkard there. This graph, then, is a summary of such reasoned considerations.

The relationship of this graph to the actual drunkard's walk (or the motion of real molecules) is colored somewhat differently. There are a total of \( 1 + 4 + 6 + 4 + 1 = 16 \) separate walks reported there. If you were to make a graph of this kind of reporting the results of 16 actual 4-step drunkard's walks, the chances are large that the pattern would not exactly match Figure 8. If, however, you reported 160 walks then the pattern would be much more probably very close to Figure 8. (If you were careful to divide the 160-study results by 10 and the 1600-study results by 100, then in fact not just the pattern, but also the values of your report would agree with Figure 8. Such a tactic is called "normalizing" the data.)

Now the relationship of the graph to the real world should be clear. As the number of cases of random walks is enlarged, the distribution pattern that emerges approaches that of the ensemble. For our case of wanting to relate the random walks of billions of molecules to the ensemble pattern, there is no doubt but that the ensemble behavior represents a reliable description of what actually occurs. Incidentally, these statistical ensembles are of interest for a variety of applications in science and mathematics. Their significance is such that they have been given a special name. The Figure 8 graph is one case of a binomial distribution.
The same mathematical logic which leads to the graph (Figure 8) can be used to construct an equation for the general case of an N-step random walk ensemble. The number of ways in which an N-step random walk can lead to the particular result \( m \) is given by

\[
M(m; N) = \frac{N!}{\binom{N+m}{2} \binom{N-m}{2}}
\]  

(C.11a)

N.B. The notation \( 6! = 6 \cdot 5 \cdot 4 \cdot 3 \cdot 2 \cdot 1 \); thus \( N! = N \cdot (N-1) \cdot (N-2) \cdot \ldots \cdot 3 \cdot 2 \cdot 1 \).

Frequently, these distributions are normalized so that the sum of \( M(m; N) \) for all allowed values of \( m \) (for a given \( N \)) equals unity. In this case the individual ensemble values will constitute the probability that that particular end point will occur each time such a random walk is executed. Since the number of distinct combinations in an N-step random walk is \( 2^N \), one has the (normalized) probability distribution

\[
P(m; N) = \frac{1}{2^N} \frac{N!}{\binom{N+m}{2} \binom{N-m}{2}}
\]  

(C.11b)

What can the random walk ensemble tell us about the progress of ammonia molecules through the room when a bottle is uncorked? Each molecule moves at a virtually constant velocity until it collides with oxygen, nitrogen, or another ammonia molecule, whereupon it caroms away and is off at another (in general different) constant velocity (e.g. until its next collision). Our simplifications to one-dimension are that the distances travelled between collisions are all to be considered equal (this value is called the free path \( \lambda \)) and the velocities of all the molecules (this value is called the molecular velocity \( v \)) are considered to be identical, save for a plus/minus ambivalence which indicates the direction of travel. If these values
are set at, respectively, the observed mean free path length and the calculated R.M.S. average thermal speed of an actual collection of molecules, then these approximations give reasonably decent predictions of actual diffusion behavior.

Now we must examine a set of random walk distributions from a sequence of increasingly long random walks if we are to make any predictions about what we expect to be the time development of the moving molecules. We do this (see Table 3) for only the very smallest numbers of steps in order to get some idea of what sort of development to expect for a realistic case of thousands of steps. (N.B. an ammonia molecule in an atmosphere of air at normal temperature and pressure has a mean free path of $\lambda = 6.5 \times 10^{-8}$ m and R.M.S. thermal speed $\bar{v} = 670$ m/sec which means that it makes an average of $10^{10}$ collisions, that is separate steps, each second!)
| (N) | | Final Positions |
|-----|---|---|---|---|---|---|---|---|---|---|
|     | No. of steps | 0   | 2   | 4   | 6   | 8   | 10  | 12  | 14  | 16  | 18  | 20  |
| 2   | 50,000       | 25,000 |     |     |     |     |     |     |     |     |     |     |
| 4   | 37,500       | 25,000 | 6,250 |     |     |     |     |     |     |     |     |     |
| 6   | 31,250       | 23,438 | 9,375 | 1,562 |     |     |     |     |     |     |     |     |
| 8   | 27,344       | 21,875 | 10,938 | 3,125 | 391 |     |     |     |     |     |     |     |
| 10  | 24,609       | 20,508 | 11,719 | 4,394 | 976 | 97  |     |     |     |     |     |     |
| 12  | 22,558       | 19,336 | 12,085 | 5,371 | 1,611 | 293 | 24  |     |     |     |     |     |
| 14  | 20,947       | 18,329 | 12,219 | 6,110 | 2,222 | 555 | 85  | 6   |     |     |     |     |
| 16  | 19,638       | 17,456 | 12,219 | 6,665 | 2,777 | 854 | 183 | 24  | 2   |     |     |     |
| 18  | 18,547       | 16,692 | 12,140 | 7,082 | 3,268 | 1,167 | 311 | 58  | 7   | <1  |     |     |
| 20  | 17,620       | 16,018 | 12,013 | 7,393 | 3,696 | 1,478 | 462 | 109 | 18  | 2   | <1  |     |

Table C3: No. of 100,000 random walking molecules ending up at various positions to the right of the origin.
Now what can we say about the ammonia experiment? First, keep in mind that the development with time is analyzed by going downward on the table. Elapsed time is directly proportional to the number of steps taken (i.e. N). Clearly, the "leading" molecules (i.e. highest m) advance in direct proportion to time. However, the number in that leading edge (out of 100,000 starting) diminishes dramatically as time elapses. (e.g. After 2 steps, 6250 molecules are in the leading edge, while after 18 steps less than one molecule remains. Whereas, at the center of the molecular distribution, i.e. m = 0, 37,500 and 18,547 are the respective numbers for 2 and 18 steps. The latter is a much smaller fractional decrease.) Accordingly, a more appropriate way to use the distribution to predict the progress of the molecular motions would be to examine the average progress of all the molecules.

One way to evaluate the average progress from the ensemble would be to average the different final positions of the molecules by adding up all their possible final positions (m = 0, 2, 4, 6, 8, ..., N; there are (N/2 + 1) of these for each ensemble), and then dividing by the number of values added (i.e. N/2 + 1). But this method which treats all final positions equally obviously neglects the fact that more molecules end up at lesser m values than those at higher m values (see Table 3). A fairer average would include some recognition of this variability; obviously those final positions where more molecules end up ought to be weighted more heavily in the average than those which have fewer arriving molecules after N steps. The following formula is such a weighted sum of final positions, where each molecule counts as one unit of importance. We have divided by 50,000 because out of the original 100,000 molecules (see Table 3) we are evaluating only those which have ended up to the right (i.e. positive "m" values) of where they started. On the average this is one-half of the total.
\[
m = \frac{(2)n_2 + (4)n_4 + (6)n_6 + \ldots + Nn_N}{50,000}
\]

Doing this we obtain the following progress "reports" (columns 1 and 2 in Table 4) for the average molecule out of a set of 100,000 for several different total numbers of steps.

<table>
<thead>
<tr>
<th>N</th>
<th>Average Progress (unit steps)</th>
<th>(Avg. Prog.)^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>1.50</td>
<td>2.56</td>
</tr>
<tr>
<td>8</td>
<td>2.19</td>
<td>4.8</td>
</tr>
<tr>
<td>12</td>
<td>2.71</td>
<td>7.3</td>
</tr>
<tr>
<td>16</td>
<td>3.14</td>
<td>9.9</td>
</tr>
</tbody>
</table>

Table C4: Average distances moved to the right in random walks of various durations.

Notice that the progress (column 2) is not proportional to the total number of steps, but increases more slowly. Thus, although the total number of steps down the table increases as 1, 2, 3, and 4 (multiples of 4), this four-fold increase in N from top to bottom is matched by only a two-fold increase in the average progress in the walk process. The squares of the progress, by comparison, increase in roughly the same ratio as the step numbers themselves. Thus we conclude that

\[
(\text{average progress})^2 \propto (\text{total no. of steps})
\]

or

\[
(\text{average progress}) \propto \sqrt{\text{elapsed time}}
\]

In this last statement we acknowledge that our model predicts that elapsed time and total step number are directly proportional to one another. This is indeed found to be the case and should compare favorably with your ammonia
data of the Exploration Activity. Also for comparison, some data obtained by students in such an exercise is included below.

**EXERCISE C5**

1. Carry out the evaluation of equation (12a) for the cases \( N = 4, 8, 12, \) and 16, and thereby verify the values for average progress listed in Table (4).

2. The values given in Table (3) are incomplete to the extent that negative values of \( m \) are not listed. However, simple symmetry requires that the number of molecules ending up at \(-m\) and \(+m\) should be the same; hence the molecular numbers (i.e. entries in this table) \( n_{+m} = n_{-m} \) for all values of \( m \).

This fact is to be used in the following evaluations.

Equation (12a) is somewhat unorthodox way of evaluating molecular progress in a random walk. More convention is the so-called n.m.s. (root-mean-square) progress which is defined by

\[
\overline{m^2} = \frac{(2)^2 n_2 + (-2)^2 n_{-2} + \ldots + (N)^2 n_N + (-N)^2 n_{-N}}{100,000}
\]

\[
m = +N
\]

\[
m^2 n_{m}^2
\]

\[
\overline{m^2} = \frac{m = -N}{m = +N} \equiv \sigma_N^2
\]

\[
m = -N
\]

(Note that \( \sigma_N \) has been introduced as simplified notation).
Use equation (12b.) to evaluate the average progress for the same cases as in the previous problem and compare them with the former. Show that \( \overline{m^2} = N \).

Solutions and/or suggestions appear on the following page.
An examination of Table (3) verifies that, as time develops, the molecules originally localized at some point \((m = 0)\) move generally outward to regions removed from the origin. The question arises as to whether we can predict what will be the rate of the movement outward past any point along the line of movement. Fick's Law (Equations 1) indicates that the movement of actual molecules past any such point is directly proportional to the gradient in the concentration at that point. To visualize what to expect in this regard for the situation of our randomly walking molecules, it helps to examine a graph of the molecular positions after a given number of steps. Figure (C8) has presented these data for \(N = 4\). The pattern is somewhat more apparent in the results for \(N = 16\) given below (Figure 9).

![Graph of molecular positions](image)

**Figure C9:** Ensemble of the 16-step and 18-step Random Walks for 100,000 molecules.

Since the concentration of molecules is proportional to their number at any point, Figure (9) is also a graph of concentrations at the instant of time corresponding to 16 steps. (The values of the concentration is defined as the number of molecules per unit length, and here is given by
The concentration gradient is, then, the slope of this (concentration) graph at any point. Clearly, the slope varies. Near \( m = 0 \) and \( |m| > 10 \) it is lower than in the intervening region \((4 > |m| < 10)\). We wish to correlate the outward movement (from \( m = 0 \)) of these molecules between this instant of time and the next (say \( N = 18 \) steps), with the value of this gradient at each point.

Information about the movement outward of the molecules is more subtly contained in these graphs than is the gradient information. Clearly, 18-step molecules lie more at the extreme positions and less at the center positions than do the 16-step molecules. (Compare the crosses with the open circles in Figure 9.) A way to evaluate the number that have moved past some point, \( m = 6 \) for example, in a unit of time is to count all those molecules beyond \((m > 6)\) at the instant \( N = 16 \) steps, and then again recount \((m > 6)\) at the instant \( N = 18 \) steps. The difference between these numbers is the number of molecules \( \Delta n \) moving beyond \( m = 6 \). (The value of current is \( I = \Delta n/(2 \text{ unit time steps}) \) since this movement occurs over a two step time period.) We then wish to evaluate the ratio of current to gradient. The latter value is given in this situation by

\[
\frac{\Delta (\text{concentration})}{\Delta m} = \frac{(n_6/2 \text{ unit lengths})-(n_8/2 \text{ unit lengths})}{2 \text{ unit lengths}}
\]

We have done these calculations for the point \( n = 6 \), and for a number of others below. Notice that, consistent with Fick's Law, the predicted values of molecular diffusion current are proportional to the corresponding values of the particle gradient to within 5%.
### Table C5:
Values of the Random Walk "Diffusion Constant" Evaluated from Currents and Concentration Gradients between Steps N = 16 and N = 18.

<table>
<thead>
<tr>
<th>Point Along Line (m)</th>
<th>Current Value ( \Delta n(&gt;m)/\Delta t )</th>
<th>Gradient Value ( (\Delta n_m +2/\Delta m - \Delta n_m/\Delta m)/\Delta m )</th>
<th>Ratio: Current Gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>485</td>
<td>975</td>
<td>0.498</td>
</tr>
<tr>
<td>4</td>
<td>693</td>
<td>1375</td>
<td>0.504</td>
</tr>
<tr>
<td>8</td>
<td>240</td>
<td>487</td>
<td>0.492</td>
</tr>
</tbody>
</table>

**EXERCISE C6**

1. Carry out the evaluations reported in Table (5) using the data of Table (C3) for the random walk results. What are the units of the "diffusion constant" (i.e., the ratio current/gradient) in terms of unit time steps and unit length steps. Compare these units with those listed for the diffusion constants discussed in sections A and B of this module.

2. Carry out the evaluation of the predicted "molecular diffusion constant" for the time interval \( N = 18 \rightarrow N = 20 \) steps, at the position \( m = 6 \) steps from the origin. Compare this value with those reported in the Table (5), last column.

*Solutions and/or suggestions on the following page.*
It is now our final task to make the connections between those quantities involved in our random walk model and those employed in the description of actual diffusion. Thus we must link "step size" ($\lambda$) and collision frequency ($1/t_{\text{coll.}}$) with the diffusion constant ($D$). We have, of course, just evaluated $D$ for the special case ($\lambda = 1, 1/t_{\text{coll.}} = 1$). Finding the general relationship is somewhat difficult to do exactly without using sophisticated mathematics. We will make a heuristic derivation of the result which is:

$$D = \frac{\lambda^2}{2t_{\text{coll.}}}.$$

Our reasoning will be as follows in doing this evaluation. The larger the number of steps $N$ in a random walk, so the more widely distributed is its ensemble (which summarizes all possible walks of that number of steps). This was shown in Figure C9 for two cases of $N = 16$ and $N = 18$ steps. In order to prove the general relationship of equation (13), we must discuss, not a specific number of steps, but rather an arbitrary number, say $N$. We shall be interested in examining the rate of transfer (i.e. diffusive flow) of (randomly walking) particles outward past a given point, and relating that number to the corresponding concentration gradient. In Figure (10) are pictured the resultant distributions for two cases, one of $N = N_0$ steps and the other of $N = 2N_0$ steps.
Figure C10: Particle ensemble for two random walks differing by a factor of 2 in step number.
This kind of graph could be made by using equations (C11) for any chosen value \( N_0 \). The important thing for later use is that we have chosen (arbitrarily) the step number be doubled for the second (lower) graph as compared to the first graph (upper).

Now just as we argued we could predict the "average" distance of travel in \( N \)-steps (see equations (12)), we can, further, relate that average distance of travel to the number of particles which have not yet travelled that distance after \( N \)-steps. It is crucial to realize that these calculations (i.e. average distance and number of particles in a given part of the distribution) are equivalent. This is because it happens that for the particular distribution of outcomes (i.e. binomial) resulting from 2 drunkard's walk of \( N \) steps, the same number of outcomes is included within an average travel distance \( \sigma = m^2 \) always, regardless of the number of steps \( N \). It must be taken as an article of faith that within an interval equal to the average travel distance \( \sigma = m^2 \) (obtained from an evaluation of equation (12b.)) on either side of the departure \( (m = 0) \) point, lie (approximately) \( 2/3 \) of the randomly walking particles after a (given) number of \( N \) steps. Further recall that it has also been shown that the average travel distance (again, as calculated by (12b.)) lies at that step number \( \sigma_N = m^2 = \sqrt{N} \).

If we wish to express the average travel distance in terms of actual distance \( \overline{x} \) instead of an equivalent number of steps \( \overline{m} \), then we may do so by using the specified actual step size \( \lambda \) (this is the average distance between collisions of the molecules we are attempting to describe). One has

\[
\overline{x} = \sigma_N \lambda = \sqrt{N} \lambda
\]

(C.14)

If we wish to express the elapsed time (duration \( t \) of the walk of \( N \)-steps) in terms of the average time between molecular collisions \( t_{coll} \), then
\[ t = N \tau_{\text{coll}}. \] 

(C.15)

In the problem which we are constructing here, there are two random walk ensembles \( N = N_0 \) and \( N = 2N_0 \), so that we have, from equation (15)

\[ t = N_0 \tau_{\text{coll}}. \]

\[ t' = 2N_0 \tau_{\text{coll}}. \]

In case #1 the distribution has

\[ \overline{x} = \sqrt[N_0]{\lambda} \]

and in case #2 the distribution has

\[ \overline{x'} = \sqrt[2N_0]{\lambda} \]

Before we "prove" the actual connection stated in equation (13) we must point out one other fact. The particle distribution equation (11a.), which has been graphed in Figures (8) and (9), represents the number of particles as heights of "bars" (or "points") on the graph. We can conceive of a real physical system only in terms of a continuous rather than such a discrete distribution of particles. Therefore it is better to think of the number of particles depicted "at each definite point" as, rather, being "spread" out over a full interval between such adjacent definite points. In this case the number of particles per length interval (i.e. the actual density of real particles) correlates with the height of the "spread out" graph, and the area underneath any given section of the graph (say between \( x_1 \) and
$x_2$ correlates with the actual number of particles between those positions along the line.

Your appreciation of the foregoing analysis is not essential to the understanding of the meaning of what follows, but may be helpful. The important result is that one may make a graph which summarized (for all cases of $N$) the relative number of particles which have not yet travelled a given distance from the origin after $N$-steps. In the language of the previous paragraph, this graph is of the area (versus $m$) under that portion of the (ensemble) distribution graph which lies between the origin and some general point $m$ located a distance $m - x/\lambda$ from the origin. This graph, expressing the relative (i.e. fractional) numbers not having progressed beyond some value $m$ (after $N$-steps) is given in Figure (11). The values $x$ for any particular system may thus be calculated using $x = m\lambda$.

Figure C11: Fractional numbers not having travelled $m$ after $N$ steps in a random walk.
Referring back to Figure (10), we may now make our evaluation. We can compute the concentration (i.e. density) of particles along the line after N-steps of a random walk from \( x = 0 \), expressing this in terms of the step size \( \lambda \). We then, somewhat arbitrarily, choose two equal adjacent intervals \( (0 \leq x \leq x_1 = \sqrt{N_0 \lambda}) \) and \( (x_1 \leq x \leq x_2 = 2x_1) \), calculating these respective concentrations:

\[
C_1 = \frac{0.68 n}{\sqrt{N_0 \lambda}}; \quad C_2 = \frac{0.27 n}{\sqrt{N_0 \lambda}}
\]

where \( n \) = the total number of particles which are randomly walking. This latter factor will drop out of our expression for the diffusion constant. Refer to Figure (10) for the proper visualization of these quantities, and to Figure (11) for the particle numbers between the interval limits.

Then, we wish to evaluate the diffusive flow of the particles from the first to the second of these regions.

The concentration gradient responsible for this is:

\[
\text{gradient} = \frac{\Delta C}{\Delta x} = \frac{C_2 - C_1}{\sigma_N} = \frac{0.4n/\sqrt{N_0 \lambda}}{\sqrt{N_0 \lambda}} = \frac{0.4n}{N_0 \lambda^2}
\]

Now the current can be evaluated if we compare the number of particles in the first interval \( (0 \leq x \leq \sqrt{N_0 \lambda}) \) after \( N_0 \) steps, with the corresponding number, in that same region, after \( 2N_0 \) steps. The elapsed time \( \Delta t \) between these situations is calculable from the individual times \( t \) and \( t' \) for \( N_0 \) and \( 2N_0 \) steps, respectively. Thus

\[
t = N_0 \ t_{\text{coll}}.
\]

\[
t' = 2N_0 \ t_{\text{coll}}.
\]

\[
\Delta t = t' - t = N_0 \ t_{\text{coll}}.
\]
The diffusion current is given in terms of the **difference** in particle numbers $N$ within the first interval between $t$ and $t'$ by the expression

$$\text{current} = \frac{\Delta N}{\Delta t}$$

The "trick" now is to determine what fraction of the particles are still within the region $0 \leq x \leq \sqrt{N_0 \lambda}$ by the time $(t')$ at which the **average** distance has increased to

$$x' = \sqrt{2N_0 \lambda}$$

Clearly, there are **less**; the question is: "How much less?". Figure (11) can answer the question, provided we can obtain the proper abscissa value for the point $x/\lambda = \sqrt{N_0}$ in terms of the new value of $\sigma' = \sqrt{2N_0}$.

Since

$$\frac{x}{\lambda} = \sqrt{\frac{N_0}{\lambda}} = \frac{\sqrt{2N_0}}{\sqrt{2}} = \frac{\sigma'}{\sqrt{2}}$$

one must have the point of the distribution corresponding to $x = \sqrt{N_0 \lambda}$ now at a position closer to the origin (than $\sigma$) by a factor of $1/\sqrt{2}$. See Figure (10). Then use the Figure (11) graph to calculate

$$\Delta N = 0.68n - 0.52n$$

The current during $\Delta t$ is

$$\text{current} = \frac{0.16n}{N_0 \Delta t} \text{coll.} \quad (C.17)$$

The diffusion constant is defined by Fick's Law (equations (A1.)) to be equal to the ratio

$$D = \frac{\text{current}}{\text{gradient}}$$
Using equations (16) and (17) one has

\[ D = \frac{0.16n/N}{0.4n/N} \left( \frac{\lambda^2}{t_{\text{coll}}} \right) = \frac{1}{2.5} \left( \frac{\lambda^2}{t_{\text{coll}}} \right) \]

Comparing this with equation (13), one sees that our approximate evaluation leads to the proper dependence of D upon \( \lambda \) and \( t_{\text{coll}} \), with the discrepancy only in the value of the numerical factor (1/2 versus 1/2.5). This completes the "proof" of equation (13) which can be used to connect the molecular motion model with the actual diffusion experimental data.

**EXERCISE C7**

1. In the discussion subsequent to Figure (10) it was stated that 2/3 of all randomly walking particles lie within \( \pm \sqrt{N} \) of the origin after N steps. This is strictly true only for large N. Try to check this for the particular cases N = 10, 14, 20.

2. In Figure (11) are depicted the results of fractions of particles remaining within \( \pm n \) step lengths of origin after N random steps. Verify this relationship for the case N = 20 by making a graph of this type on your own.

3. Use the graph you make in #2 above to verify the expressions used for the concentrations \( C_1 \) and \( C_2 \) used in arriving at equation (16).

4. Use the same graph as above to verify the evaluation of N in Equation (17).
APPLICATIONS

A. Illustrative Problem Solving

The problems in this section can be solved with selection of one or more of the following equations:

**Fick's Law**

\[ I = pA(C_i - C_0) \]  \hspace{1cm} (A.1a)

**Fick's Law**

\[ J = D\left(\frac{\Delta C}{\Delta x}\right) \]  \hspace{1cm} (A.1b)

**Continuity Equation**

(single compartment)

\[ \frac{\Delta N_1}{\Delta t} = I_{in} - I_{out} \]  \hspace{1cm} (B.2)

**Continuity Equation**

(two compartments)

\[ N_{TOT} = C_1V_1 + C_2V_2 \]  \hspace{1cm} (B.6)

**Flow/Concentration Relationships**

(one compartment)

\[ \frac{\Delta C_i}{\Delta t} = -\frac{(pA)}{V}C_i \]
\[ = -K_i C_i \]  \hspace{1cm} (B.3a)

**Flow/Concentration Relationships**

(two compartments)

\[ \frac{\Delta C_1}{\Delta t} = -K_1(C_1 - C_2) \]  \hspace{1cm} (B.5)

\[ \frac{\Delta C_2}{\Delta t} = +K_2(C_1 - C_2) \]  \hspace{1cm} (B.5)

**Flow/Concentration Relationships**

(difference between two compartments)

\[ \frac{\Delta C}{\Delta t} = -KC \]  \hspace{1cm} (B.8)

**Exponential Approach to Equilibrium**

(one compartment)

\[ C_i = C_{i0}e^{-Kt} \]  \hspace{1cm} (B.4)

**Exponential Approach to Equilibrium**

(two compartments)

\[ C_1 = C_\infty + (C_{10} - C_\infty)e^{-Kt} \]  \hspace{1cm} (B.10)

\[ C_2 = C_\infty + (C_{20} - C_\infty)e^{-Kt} \]  \hspace{1cm} (B.10)

**Exponential Approach to Equilibrium**

(difference between two compartments)

\[ C = C_0e^{-Kt} \]  \hspace{1cm} (B.9)

**Equilibrium Concentration**

\[ C = \frac{C_{10}V_1 + C_{20}V_2}{V_1 + V_2} \]  \hspace{1cm} (B.7)

**Random Walk (Binomial)**

Probabilities for Progress from the Origin in \(N\)-steps

\[ P(m;N) = \frac{1}{2^N} \frac{N!}{(N+m)!((N-m)!)} \]  \hspace{1cm} (C.11b)
Average Distance Moved in \( N \)-steps of Random Walk
\[
\bar{x} = \sqrt{N} \lambda \quad \text{(C.14)}
\]

Diffusion Constant in Terms of Microscopic Quantities
\[
D = \frac{\lambda^2}{2 \tau_{\text{coll}}} \quad \text{(C.13b)}
\]

It will be useful for you to have values for the diffusion coefficients of certain biologically important molecules when dissolved in water. These are contained in Table (6).

<table>
<thead>
<tr>
<th>Solute</th>
<th>( D \times 10^6 \text{(cm}^2/\text{sec)} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>(approx.) 15</td>
</tr>
<tr>
<td>Urea</td>
<td>13.8</td>
</tr>
<tr>
<td>Molecular oxygen (O(_2))</td>
<td>11.5</td>
</tr>
<tr>
<td>Sucrose</td>
<td>5.21</td>
</tr>
<tr>
<td>beta-Dextrin</td>
<td>3.22</td>
</tr>
<tr>
<td>Ribonuclease</td>
<td>1.18</td>
</tr>
</tbody>
</table>

Table 6: Diffusion coefficients for various solutes in aqueous solution (After Benedek and Villars, Physics with Illustrative Examples from Medicine and Biology, II, pg. 2-87; Addison and Wesley, 1974)

Of course, to solve the problems, you must first establish the proper correspondences between the factors in these equations and the physical quantities described in the problems. The problems are graduated in level of difficulty. Those first problems require that you make only simple correspondences, while those last problems require considerable additional reasoning skills.
1. A membrane of the type described in Exploration Activity #2 has a permeability of \( p = 7.0 \times 10^{-4} \) cm/sec for sodium chloride dissolved in water. It is formed into a sphere like that pictured below.

![Diagram of a spherical membrane](image)

This membrane has a thickness of \( 2.7 \times 10^{-3} \) cm and encloses a full volume of 1.0 M (one molar) NaCl solution. If this spherical membrane is immersed in a beaker of pure water (i.e. no NaCl), what is the value of the sodium chloride current established by virtue of the membrane's permeability to NaCl? If the beaker instead contains 1.5 M NaCl solution, what is the value of the NaCl current? What direction of current flow is expected in each case?

2. Suppose the solution inside of the spherical membrane described above is 0.1 M NaCl (this is approximately physiological salinity) and the outside concentration is zero. What is the value of the diffusion current? What is the value of the diffusion current if the spherical radius is, instead, \( r = 10^{-3} \) cm (the approximate size of a tissue cell)? What is the diffusion current density in each of these two situations?
3. Evaluate the concentration gradient of NaCl in each of the two cases stipulated in problem #2 above. Evaluate an "effective" diffusion constant for NaCl through this membrane in each case also. How do these values of diffusion constant compare?

4. Suppose that actual tissue cell membrane were of the same material as that described above except that its thickness were 75 angstroms (typical thickness of biological cell membrane). Which quantities important to description of the resulting diffusion remain the same as in problems #1-#3? Which are now different? Evaluate the diffusion current density in this second case.

5. Compare the value for the "effective" diffusion constant for the normal cellophane membrane, considering in problems #1-#3 above, with the value of diffusion constant for NaCl in (bulk) aqueous solution (c.f. Table 6.). What if the situation with respect to salt solutions were that described in problem #2 with \( r = 1.5 \) cm except that the membrane material were suddenly removed. That is, the sphere of \( 0.4 \) M NaCl were left intact and the region of the (former) membrane was filled with a "shell" of solution whose NaCl concentration changes smoothly from zero at its outer surface to \( 0.1 \) M NaCl at its inner surface. What now would be the value of the diffusion current density in this new situation? What is the effect of the membrane?

6. A type of artificially prepared (i.e. man-made) membrane which shares some of the properties of biological membranes is a bilayer of lipids which are depicted below as a section cut through the plane of the membrane, as well as in a view directly from above the membrane surface. (Figure 12).
Notice that the complex lipid molecules have been simplified, in drawing, to cylinders. These molecules are "ambiphilic", that is they have one end which is polar and is thus energetically disposed to contact water while they have their other end which is apolar and is thus energetically disposed to be away from water and in contact with other apolar species.

Such molecular arrangement, as pictured in Figure 12 can be produced by using dilute solutions of lipids in which the lipid molecules accumulate on the surface in this alignment with their apolar ends sticking up in air and their polar ends stuck into the water. This constitutes one-half of the total final membrane (bilayer) which is thus produced by introducing another such solution to the apolar side, in place of the air, and consequent mating of a second such monolayer whose apolar surface matches itself to the apolar surface of the first monolayer to form a bilayer as shown in Figure 12.
Figure 12: Schematic drawing of a lipid bilayer showing the membrane from two points of view: (a) in cross-section; (b) normal to the surface. Dimensions are all typical and approximate; the proportions of length to breadth are purposely distorted.
Now suppose that the spaces between these closely packed cylinders were "filled" with aqueous solution connecting one surface solution body with the other. The diffusion of "small" (compared with intermolecular space sizes) solutes between the solution bodies separated by such a membrane could then be pictured as taking place in the same manner as in bulk solution except that the "effective" are for diffusion would be limited to these spaces between the molecules.

Using this type of a "model" for the cellophane membrane (but remember that its thickness = 2.7 x 10^-3 cm), can you account for the difference between the "effective" diffusion constant for NaCl obtained from the observed membrane permeability data and the bulk diffusion coefficient value which is appropriate to NaCl in water (without the presence of a restricting membrane)?

7. You are to calculate an estimated value for the permeability of lung membrane to oxygen. In this process, the oxygen is first dissolved from lung air (in the aveoli) into a water layer covering the aveolar membrane. The solubility of O_2 in water (or blood) is about 0.02 milliters of O_2 (at STP) per 1 milliliter of water (or blood) per one atmosphere of (partial) pressure of O_2 of the air in contact with the water. The resting body maintains an oxygen content in the aveolar air averaging about 18% of the total volume of air there, and requires that 14.5 liter of O_2 each hour pass from the aveolar air into the blood through the aveolar membrane.

What additional information do you require to obtain your estimate of aveolar membrane permeability to O_2?
8. Here are some additional data on human lungs. Some of the values are not necessarily physiologically correct, but are reasonable simplifications which avoid discussion of the hemoglobin role.

Total aveolar membrane area = 100 m$^2$
Average membrane thickness = $4 \times 10^{-5}$ cm
Blood flow rate through lungs (resting) = 5 liter/min
Time required for lung transit (resting) = 20 seconds
Average $O_2$ concentration is lung blood during transit = 50%

Use all the data which you require to obtain an actual estimate of permeability for aveolar tissue. Use this permeability value to obtain an "effective" diffusion coefficient for $O_2$ through the membrane. Use the "effective" diffusion coefficient to obtain an estimate for the apparent fraction of lung tissue having space for "bulk" $O_2$ diffusion. How does this fraction compare to that which you expect from close-packed cylinders in the rectangular array depicted in Figure (12)?

9. In Figure 13, an artificial kidney (hemodialyzer) is pictured. In Figure 14, a schematic diagram of the functional element, where the diffusion of urea (etc.) from the body blood takes place, is drawn. In one such device, the dialysis membrane has:

- thickness = $5 \times 10^{-3}$ cm
- $\rho$ (urea) = $5 \times 10^{-4}$ cm/sec
- membrane surface = 2 m$^2$

The body fluid volume is about 40 liters and for a certain patient contains 100 grams of urea. How long would it take this device, which always maintains zero concentration of urea in the dialysate by pumping, to reduce that urea burden to 10 grams?
Figure 13: Typical Artificial Kidney Hemodialyzer.
Figure 14: Schematic representation of the process of hemodialysis: (From C. Colton, Ph.D. thesis, M.I.T., Cambridge, Mass., 1969)
10. Suppose that there are two membranes sandwiched together to form a single membrane in the manner of Figure (15). Let $p_1$ and $p_2$ be their (respective) permeabilities for some substance.

(a) How would you go about defining an overall permeability for the single (two layered) composite membrane in terms of an experimental arrangement in which solutions of two (controlled) concentrations $C_1$ and $C_2$ were placed, one on either side of the membrane?

(b) How is the diffusion current through #1 related to the current through #2 in the situation where all diffusing particles leaving solution #1 end up in #2 (or vice versa)?

(c) What equations relate the given concentrations $C_1$ and $C_2$ to the particular concentration $C_{12}$ which is that at the (intermediate) layer where membrane #1 joins membrane #2?

(d) Find an expression for the permeability $p$ of the composite membrane in terms of the permeabilities $p_1$ and $p_2$ of the component membranes.
11. In an experiment with an uncorked ammonia bottle, it was found that the times for the smell to travel various distances were given as in the table (7) below.

<table>
<thead>
<tr>
<th>distance</th>
<th>1 m</th>
<th>2 m</th>
<th>3 m</th>
<th>4 m</th>
</tr>
</thead>
<tbody>
<tr>
<td>time</td>
<td>30</td>
<td>45</td>
<td>60</td>
<td>90</td>
</tr>
</tbody>
</table>

Table 7: Distance of "smellers" from ammonia versus time of first smell.

Use these data to evaluate a diffusion coefficient $D$ for the ammonia molecule in this situation by assuming that the diffusion proceeds by a simple, one-dimensional random walk process from the bottle to each observer.
B. Applications for the Laboratory.

5% agar solution forms a matrix for water through which dye molecules can diffuse. This matrix can be prepared by "cooking" the agar solution for ten minutes or so and subsequently cooling it. The resulting jell "holds" the water, thus preventing convection yet allowing dye diffusion.

Prepare such jell mixtures in some Petri dishes and then punch out small plugs (for example with a cork borer or a scalpel) into which you introduce an aqueous solution of dye. (See Figure 16.) Using this system, you can monitor the progressive diffusion of the dye (outward) through the agar/water matrix by visual observation of the apparent diameter of the dyed portion of the system. At first this will be a number \( d_0 \) equal to the diameter of the excised hole. Later this will be a larger number \( d > d_0 \) which marks the "leading" edge of the dye. (There will be some ambiguity as the diffusion proceeds because the dye "edge" becomes spread and consequently less well defined.)

A Table (3) appears below which lists some common dyes, many of which are used by microbiologists for stains. They have a range of molecular weights (i.e. sizes), therefore they diffuse at different rates.
Figure 16: Agar jell used for conducting dye diffusion experiments.

<table>
<thead>
<tr>
<th>CHEMICAL</th>
<th>MW</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 M Neutral Red</td>
<td>238</td>
</tr>
<tr>
<td>0.1 M Potassium Dichromate</td>
<td>294</td>
</tr>
<tr>
<td>0.1 M Malachite Green</td>
<td>364</td>
</tr>
<tr>
<td>0.1 M Methylene Blue</td>
<td>374</td>
</tr>
<tr>
<td>0.1 M Gentian Violet</td>
<td>484</td>
</tr>
<tr>
<td>0.1 M Eosin Y</td>
<td>691</td>
</tr>
<tr>
<td>0.1 M Congo Red</td>
<td>695</td>
</tr>
</tbody>
</table>

Table 8: Water soluble dyes of various molecular weights and commonly found in laboratories.
1. Is the system of agar/water jell with a cylinder cut out of it one in which the diffusion taking place is describable by Fick's Law (equations Al.)? These equations are one-dimensional; thus the diffusion is pictured as occurring between planes (drawn through the solution) in each of which the concentration of the diffusing substance is uniform. Your systems have cylindrical geometry so that the surfaces of uniform concentration would be expected to be cylindrical, not planar.

Now as we have seen, one of the underlying (molecular) characteristics which leads to this behavior is that the diffusing molecules proceed to move as if in a random walk. This predicts that the (average) progress of the diffusing molecules should be

\[ \text{progress} = \sqrt{N} \lambda \]

where \( N \) is the number of random steps and \( \lambda \) is the mean step length. Clearly, since the total elapsed time \( t \) for diffusion is

\[ t = N t_{\text{collision}} \]

where \( t_{\text{collision}} \) is the mean time between intermolecular collisions, then

\[ \text{progress} = \sqrt{t} \left( \frac{\lambda}{\sqrt{t_{\text{coll}}}} \right) \]

(19a.)

is a relationship which should hold if the diffusion is proceeding according to Fick's Law in one dimension.

Test the applicability of Fick's Law by testing the relationship of the proportionality statement (19a) above. Do this by using one of the dyes and comparing (e.g. on a log-log graph) the data of (progress) versus (elapsed time) with that expected if the square root (19.) relationship were valid. Make this test a sequence in which you use
ever larger sizes for the insertion (i.e. reservoir) hole. Larger holes should produce more nearly planar geometries. Do your data show this trend?

2. Using one (standard) convenient-sized insertion hole of your choice, run a series of tests on measuring the comparative diffusion rates for dyes of various molecular weights.

If the previously described one-dimensional random walk molecular motion description is valid, then equation (19a) holds

\[
\text{progress} = \left( \frac{\lambda}{\sqrt{t_{\text{coll}}}} \right) \sqrt{t}
\]  \hspace{1cm} (19a.)

Thus one expects that

\[
\left( \text{progress} \right)^2 = \left( \frac{\lambda^2}{t_{\text{coll}}} \right) t
\]  \hspace{1cm} (19b.)

and a graph of square of the diffusion distance occurring in an elapsed time \( t \) should be a straight line with a slope value which is different, in general, for different molecules.

Now

\[
D = \frac{1}{2} \left( \frac{\lambda^2}{t_{\text{coll}}} \right)
\]  \hspace{1cm} (C13b.)

according to the random walk theory. Thus \( D = \frac{1}{2} \) slope of the graph of equation (19b) (provided it turns out to be a straight line).

Using the procedure for data analysis suggested by the above discussion, obtain values of \( D \) from progress/time data for your dye series. Is there a simple relationship between \( D \) and the molecular weight (M.W.) of the various dye molecules. Try a log-log graph of \( D \) versus M.W. to test this.
APPENDIX
Evaluation of the Time Progress of Diffusion from One Compartment of Fixed Volume

The discrepancy between the results of the "stepwise" calculation from Exercise B3. problem (#4) and the results of the evaluation of equation (B.4) at successive instants of total elapsed time (separated by $10^4$ seconds) can be reduced by redoing the calculation with a modification of the procedure which brings the assumptions of the calculation more into line with reality, equation (B.4). To see how that calculation is compromised, consider the following elaboration of one calculation "step".

At the onset of the flushing process, elapsed time $t=0$, you have a salt concentration inside given as $C_i = 10^{-3}$ mole/cm$^3$. The amount of salt outflow during the next $10^4$ seconds can be estimated (as you have already done) by assuming that this inside concentration remains constant, even as the salt flows out. This is a contradiction, of course, but perhaps not so serious. We can examine the seriousness of this compromising assumption by reviewing that calculation. Thus the salt outflow (assuming constant inside concentration)

$$\frac{\Delta C_i}{\Delta t} = -K C_i$$

$$\Delta C_i = -(K C_i) \Delta t$$

$$= -(10^{-5}/\text{sec})(10^{-3} \text{ moles/cm}^3) \times 10^4 \text{ sec.}$$

$$\Delta C_i = -10^{-4} \text{ moles/cm}^3$$

Thus the concentration is expected to decrease (N.B. negative sign) by $10^{-4}$ moles/cm$^3$ during this $10^4$ sec. of elapsed time, provided that the rate of flow is fixed at that value predicted by Fick's Law but strictly appropriate only to the actual concentration at the first instant of this $10^4$ second interval.
You may be better able to visualize the results of this assumption by examining Figure (11) where the calculation is compared to what actually occurs.

Figure 11: Graph indicating the time dependent behavior of inside salt concentration (a) assumed and (b) calculated in the stepwise calculation, as well as that (c) actually occurring.

The assumption that the inside salt concentration holds steady at its initial value during each time interval is necessary so that we may make the multiplication

$$\Delta C_i = -K(C_i) \Delta t$$

which is the application of Fick's Law. If $C_i$ is not a constant, then the term $C_i$ on the right-hand side cannot be assigned a definite value. If the initial value of $C_i$ for that time interval is assigned, then the outflow, $\Delta C_i$, may be calculated; however it is too large. This is because in reality the outflowing salt depresses $C_i$ from its initial value during each time interval.
The assumed values of constant concentration are depicted in Figure (1) for each of the first four time intervals by the horizontal lines. The resulting calculated depression (ΔC) of inside salt concentration is pictured in each interval as the sloping (solid) straight line.

In reality, the declining inside salt concentration actually experienced during each interval will result in steadily smaller outflow (during that interval) than the initial value. Thus the inside salt concentration is depressed less rapidly in reality (dashed line) over the course of each interval than that calculated. It is only at the end of each calculation interval that this fact of declining inside salt concentration is acknowledged, and the value of \( C_i \) for the next interval outflow calculation is assigned by subtracting the previously calculated value of ΔC.

Finally, the seriousness of discrepancy (between solid and dashed lines) thus introduced depends upon the length of time duration which is chosen for the purposes of the calculation. The shorter this time interval, the less the calculation is compromised (before \( C_i \) is revised at the end of that interval) and the less is the departure of calculated from actual salt concentrations. This can be illustrated for the first \( 10^4 \) seconds of flushing time by comparing the following. The first column is a one step calculation which uses \( 10^4 \) second time intervals. The second column is a two step calculation which uses two \( 5 \times 10^3 \) second time intervals to cover the same total elapsed time.
Given $K = 10^{-5}$/sec and starting with $C_i = 10^{-3}$ moles/cm$^3$

$\Delta t = 10^4$ sec

one step

From Fick's Law

$\Delta C_i = k C_i \Delta t$

$\Delta C_i = -(10^{-5})(10^{-3})(10^4)$ moles/cm$^3$

$= -10^{-4}$ moles/cm$^3$

From the definition

$\Delta C_i = (C_i)_{\text{after}} - (C_i)_{\text{before}}$

or

$(C_i)_{\text{after}} = (C_i)_{\text{before}} + \Delta C_i$

Again from Fick's Law

$\Delta C_i = -(10^{-5})(9.5\times10^{-4})(5\times10^3)$

$= -(4.75\times10^{-5})$ moles/cm$^3$

Again from the definition

$C_i = 10^{-3} + (-0.100\times10^{-3})$

$C_i = (0.900\times10^{-3})$ moles/cm$^3$

Compare these values of calculated salt concentration at $t=10^4$ seconds.

The two step value of $C_i = (0.902\times10^{-3})$ moles/cm$^3$ is closer to the actual value (dashed line on the graph) than the one step value of $C_i = (0.900\times10^{-3})$ moles/cm$^3$ at the end of $10^4$ seconds of elapsed time.
What we learn from this are:

(1) The step-wise calculation is generally close to reality provided the concentration change $\Delta C_i$ calculated for any step is not a large fraction of the initial (for that step) concentration value $C_i$.

(2) The shorter the time step $\Delta t$, the closer the agreement between calculation and reality.

(3) For a real system whose diffusion current is described by Fick's Law:

$$\frac{\Delta C_i}{\Delta t} = -K C_i$$

and whose initial ($t=0$) concentration is $C_{i0}$, the actual concentration $C_i$ versus time $t$ is properly described by the equation

$$C_i = C_{i0} e^{-Kt} \quad \text{(B4.)}$$

The method by which (B4) can be deduced is by evaluating the limit of the step-wise calculation results as the step size is made very small.
EXERCISE

1). Extend the stepwise calculation of the preceding example (K = 10^{-5}/sec; C_{i0} = 10^{-3} moles/cm^3) for two additional time periods (i.e. up to t = 3\times10^4 seconds) in two different ways:
   (a) by two steps of \Delta t = 10^4 seconds each
   (b) by four steps of \Delta t = 5\times10^3 second each

2). Evaluate equation (B.4), the actual pattern of concentration change, for the 0.5\times10^4 second intervals over the period t=0 \rightarrow t=3\times10^4 seconds. Compare these values with those calculated in problem #1 above.

3). Find the limiting salt concentration inside the bag by using progressively larger values of t in equation (4) and looking for a limiting value.

________________________________________________________________________

Solutions and/or suggestions on next page.