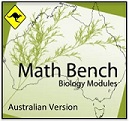
# Cell Processes:



# Diffusion Part 1: Fick’s First Law

**URL**: <http://mathbench.umd.edu/modules-au/cell-processes_diffusion/page01.htm>

## Measuring Movement

## Learning Outcomes

After completing this module you should be able to:

* Explain the linear relationship between the rate of movement of a substance and its concentration gradient (Fick’s First Law).
* Measure the rate of movement of a substance from one area to another as a function of the concentration gradient and the diffusion coefficient of that substance in the medium.

## Directed vs. Undirected Movement

In this module, we’re going to talk about movement of materials over very short distances. First however, we need to describe two different types of movement. Living in the macroscopic world as we do, it is natural to think only of "**directed" movement**. When we move somewhere, we usually move with a purpose! We are used to standing in line or driving along a road. Or we might think of blood being pumped through a circulatory system, or air being sucked in and pushed out of our lungs. Even though the paths followed by blood and air are complicated, they are still examples of materials flowing in some organized, directed way.

However, this sort of organised movement (especially within a cell or body) is a relatively recent evolutionary development. True vertebrates, insects, and plants all have it and use it, but early life forms didn’t. Single-celled organisms like bacteria don’t have circulatory systems, and after completing this entire module, you'll see why. Single-celled organisms were the earliest forms of life and still represent the lion’s share of modern biodiversity. We're going to focus our module on the type of movement that these biological pioneers relied and still rely upon.

So, early life forms didn’t actively suck in, circulate, or spit out material. How then did they accomplish getting necessary gases such as oxygen to all parts of their "bodies"? The answer is that **small particles, like gas molecules and ions, move around and bounce off of each other constantly, in an undirected way**. You can think of the movement of each individual particle as being essentially random – like balls bouncing around in a pinball machine, or people milling around at a party.

In fact, one of the most prominent modern physicists, Richard Feynman, said that if all scientific knowledge was destroyed and humans could pass on only one sentence to the next generation, it should begin with:

“All things are made of atoms – little particles that move around in random motion”

From your chemistry studies you might recognise this as Brownian motion. So, when we think about movement, we now know that there are two main types of movement -- **directed** and **undirected** -- and our focus in this module is on undirected movement

**Measuring Movement Using Flux**

Since we are interested in a specific process (movement), we need a good way to measure that process. As scientists, we love to measure things. In fact, if we can't measure something, we're probably not very interested in it. As it turns out, there are all sorts of ways to measure movement but we are going to focus on the quantity known as flux.

Flux is an unusual concept for many people because its ordinary (conversational) meaning is rather different from its scientific meaning. For most people (meaning the two people we just asked!) Flux means changes in conditions, similar to “ebb and flow” or “fluctuations”. Mathematically, however, Flux means **“the net rate at which particles move through a certain area”.**

In other words, flux is the ***net*** movement of particles across a specified area in a specified period of time. The particles may be ions or molecules, or they may be larger, like insects, rabbits or cars. The units of time can be anything from milliseconds to millennia. Here are some examples of flux:

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| The number of cars that pass through a toll booth every day. | The net number of rabbits that cross a fence every hour. | The net number of salt ions that pass out of a cell membrane every minute |

**Flux is not the same thing as velocity or speed**, which are measured in the units of distance per time, rather than number per time. Individual oxygen molecules may be moving very fast, but since they are going in a variety of directions (they are undirected), there may be no net movement of oxygen from one place to another.

Likewise, **flux is also not the same thing as density or concentration**, which are measured as particles per volume. A cell may be chock-full of oxygen, but if none of the oxygen molecules are going anywhere, there is no flux. Or there may be only a little oxygen, but what is there is quickly leaking out, so in that case, flux is high.

Finally, **movement itself is not enough.** If (like some cats I know) you continually go in and out of the same door, we wouldn’t say there was high flux through the door. Instead, flux is a measure of *net* movement, where ‘net’ is only taking into account the remaining ‘gain’ after all positives and negatives have been accounted for or *cancelled out*.

So what is flux? First we need the *flow rate* which is the number of particles moving in a specified time (mol s-1). Flux is the flow rate divided by the area through which the substance is moving. The units of flux are mol m-2 s-1 or mol cm-2 s-1.

Flux = flow rate/area and

Flow rate = flux\*area

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| In one minute 0.001 moles of water move into a cell and 0.0008 moles move out of the cell. One mole of water weights 18 g, and the volume of the cell is 13 µm3. What is the flow rate of water molecules into the cell?  * All you need to know is the net rate of movement. The rest of the information is unnecessary. * Net movement into the cell = movement in - movement out.  Answer: Flow rate = (movement in - movement out) / time  = (0.001 moles - 0.0008 moles) / 1 minute = 0.0002 moles/min |

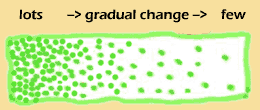
## GRADIENTS AND DIFFUSION

So diffusion occurs through the process of random movement. We will see that, based on these random individual movements, particles demonstrate flux or net movement in a predictable direction. However this raises a tricky question: **if movement is random, how can flux (net movement in a particular direction) occur?** The key to understanding this apparent contradiction is the concentration gradient -- namely, a difference in concentration of particles between two areas.

In this next section, we are going to introduce the idea of how random movement and gradients interact to produce a predictable level of flux.

## Watching diffusion happen

Fundamentally, the word "gradient" in this context is taken to mean the change in the concentration of particles over two points. Consider the diagram below, where the number of particles changes from “lots” to “few”.



**Now imagine all these particles randomly bouncing around. In fact, small particles like atoms are in constant motion and this is what causes diffusion.** How? Well, at the left, where there are lots of particles, none of them will travel very far without bumping into another particle. So, they will keep bouncing around, back and forth, up and down, and not get very far. On the other hand, on the right, where are few particles, they can move a long distance without any bounces. In particular, once a particle is heading for an empty area, it keeps going -- there's nothing there to stop its progress.

More succinctly, we say that:

* **When the concentration is high, mean displacement (average distance moved) is small**
* **When the concentration is low, mean displacement is high**

The applet below will help you visualise diffusion. Before you start the applet you should realise that the particles in the box are not distributed randomly and not spread out evenly. Instead, they are clustered at the centre of the box. We say there is a **steep gradient** between the centre and the sides of the box. Now start the simulation. Notice that although each particle is moving randomly, **the net effect is that the clumped particles get spread out evenly.** In the other words, there is a flux of particles from the centre to the edges at least until the particles are spread out evenly. After that, there is no net movement - no flux.

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| The online version of this module has an interactive applet which allows you to practice principles of diffusion. To find this applet go to: <http://mathbench.umd.edu/modules-au/cell-processes_diffusion/page05.htm> |  |

Applet courtesy of N. Betancourt

You can also click to turn off the trace function so that you can watch the particles moving about randomly.

If you run the simulation several times with different numbers of particles, then you will see that the particles always move from a state of high order (all particles in the centre of the screen) to a state of less order or disorder (all particles distributed rather evenly throughout the screen).

You can also see that diffusion only occurs when there is a gradient. After the gradient is gone, then the continual movement no longer results in a net change in distribution. In other words, **without a gradient there is no flux.**

(If you don't see the applet, you can download java at <http://java.com/en/download/index.jsp>. )

## Visualising the gradient

We saw in the last page that diffusion tends to spread things out, making them less "ordered". A central concept of order then is the “gradient”, a fancy way of saying the difference in particle density between two areas. If there is only a slight difference, then the distribution changes only slightly. But if all the molecules are concentrated on one side, then the distribution changes a lot over time. .

Another way to say this is that the **NET movement of particles is PROPORTIONAL to the difference between the particle density of two sides** – or, proportional to the “steepness” of the gradient.

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| Which gradient is steeper?  |  |  | | --- | --- | |  |  | | (a) | (b) |   ***Answer: (a)***  ***So, steeper gradient means faster diffusion*** |

**Fick’s First Law**

So now you know this Incredibly Important Concept:

#### ****Flux is directly proportional to the gradient****

This concept is known as Fick's First Law. In this section, I will introduce a mathematical version of this law and explore some of the things that we can learn by expressing this law mathematically.

**The gradient in Fick’s First Law**

Here are our two main points again. If you understand these two sentences, you will have half of diffusion sorted out:

* **Diffusion is the net flux of particles down a concentration gradient due to random movement, and**
* **Flux is directly proportional to the gradient (Fick’s First Law).**

Let’s make it look more technical. It's easiest to think of a gradient in one dimension (so there is a left and right side). The picture below shows a gradient from left (high) to right (low). While it is convenient to represent the gradient in one dimension to keep things simple, remember that we are really talking about concentrations of substances in a volume i.e. in three dimensions, and these substances move through a cross-sectional area.

**How can we measure this gradient?** The easiest thing to do would be to find out the difference between the concentrations on the left and on the right, and the distance between the left and the right. The gradient is the difference between concentrations divided by the distance between the ends:

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| What is the left to right gradient? (Use figure above)  * On the left, there are 17 particles in a 1 cm slice, the concentration is 17 particles per cm. On the right, there are only 4 particles in a 1cm slice, the concentration is 4 particles per cm. * The change in concentration is thus 13 particles per cm * The distance between the two slices is 10 cm.  Answer: The gradient is 13 particles per cm over 10 cm, or 1.3 particles per cm squared. |

**You could also measure the concentrations closer and closer together** to get more exact information. For example you could measure the gradient every centimetre.

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| What is the left to right gradient? (Use figure above)  * On the left are 3 particles in a 1 mm slice. On the right, there are only 2 particles in a 1 mm slice. * The distance between the two slices is 10 mm.  Answer: Concentration changes by 1 particle per mm over 10 mm, or 0.1 particles per mm squared. |

You could also measure the gradient every millimetre, or every micrometre. Here is where calculus comes in handy. Calculus allows you to calculate gradients over infinitely many intervals that are each infinitesimally short. Instead of taking the difference between concentrations on the left and right side of some distance, we take the difference between concentrations that are infinitesimally close together, and call it dC. Instead of using some large distance like 1 centimetre or 1 millimetre, we use an infinitesimally small distance, dx. **So the gradient is dC/dx (which, you may recall, is a "derivative" in calculus).** dC/dx tells you how much the concentration changes as you move.

**The gradient is measured in units of M m-1 or M cm -1.**

We can't directly measure the concentration of particles in infinitely many infinitesimally small slices!! But on the graph, we can interpret the gradient as the slope of the line -- which tells us how concentration changes when distance changes very slightly.

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## We have introduced the calculus notation for gradient not to confuse you, but because the ****flux equation is almost always written using the notation dC/dx for the gradient**.** In fact, you can think of dC/dx simply as a single symbol or quantity that represents the "gradient".

## A familiar equation for Fick's first law

**Fick's Law again:** Flux is directly proportional to the gradient.

So now we know that the gradient is represented by dC/dx, but what does “directly proportional” mean? Put simply, it means this:

**small gradient → small diffusion,**

**BIG gradient → BIG diffusion.**

When we have a small gradient, there is not much diffusion going on, but when the gradient is BIG, then diffusion can be substantial. But how can we represent this mathematically? Well, **if two quantities are directly proportional, they are related to each other through an equation like y = mx**. Hmmm.... this equation should sound familiar -- it is the equation for a line which goes through the origin (0,0).

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| **Continuous version** | **Discrete version** |
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So, FINALLY, a mathematical equivalent to Fick's Law in both a continuous (calculus) and discrete version. Notice that they both have the same basic form that is directly analogous to the basic equation for a straight line that intersects the origin (y=mx).

When Fick’s Law is represented on a graph, the flux (like “y”) is plotted along the vertical axis and the gradient (like “x”) is plotted along the horizontal axis. **The Flux depends (and is therefore called the dependent variable) on two quantities:** 1) the steepness of the gradient (in red) and 2) a proportionality coefficient based on the particular substance being measured (called the **Diffusion coefficient**, "D" - more on that later).

One last note ... **Why is there a negative sign in front of the diffusion coefficient???** This is because diffusion always goes DOWN the concentration gradient -- its direction is opposite to the concentration gradient. That’s why the diffusion coefficient has a negative sign. **Movement always occurs in a direction OPPOSITE to that of the gradient.**

**Review so far**

**The Rate of FLOW of particles (dn/dt, i.e. the number of particles moving in a specified time) through an area is the FLUX. The symbol for flux is J. The units of Flux are mol m-2 s-1.**

**Flux (J) = 1 dn**

**A dt**

**The number of particles n in a certain volume V is the Concentration C (C =n/V) so we can also express the Flux equation in terms of the change in concentration with time. The units of dC/dt are mol cm-3 s-1.**

**Flux (J) = V dC**

**A dt**

**Fick’s First Law states that Flux is proportional to the CONCENTRATION GRADIENT, and the proportionality constant D is the DIFFUSION COEFFICIENT.**

**Flux (J) = -D dc**

**dx**

What does the diffusion coefficient, D, really represent biologically? One way to figure that out is to look at the units of D to see what it is really describing. The units of D are length2/time (m2 s-1), and usually reported as cm2/sec (cm2 s-1). The diffusion coefficient (D) describes how long it takes a particular substance (like oxygen or proteins, etc.) to move through a particular medium (like water or molasses).

## Drawing a graph of Fick’s First Law

We know that the equations describing Fick's First Law are analagous to the general equation for a straight line with a negative slope that intersects the origin (y = -mx), and so you should already have a pretty good idea of what the graph of this relationship will look like (the continuous version is below, but the discrete version would look exactly the same!).

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In this case, the dependent variable is flux, and the independent variable is the gradient (dC/dx). Remember, dC/dx only looks scary. In reality it just a notation for "the gradient".

**But what is the biological meaning of the slope of the relationship in Fick’s First Law?** Or, put another way, how is the driving force (the gradient) translated into a response (flux)? As we mentioned earlier, the proportionality constant in the equation gets its own name, D (called the diffusion coefficient**). The actual value of D is not given by Fick’s Law but is something that needs to be measured, and it is different for each unique situation (a particular molecule in a particular medium at a particular temperature).** For example, the diffusion coefficient of oxygen in water is a consistent value at room temperature, but if you heat up the water, D goes up – the oxygen diffuses faster when the temperature is higher or if you substitute molasses for water, D goes down – oxygen has a hard time diffusing through molasses (and so would you!). If a larger molecule (say, a protein) is diffusing through water, D will go down again, since big molecules move less and therefore diffuse more slowly than small ones.

So what happens to the flux vs gradient graph if the diffusion coefficient changes? According to Fick's First Law, these quantities are directly proportional to each other (remember the function is like y = mx) and -D is the slope. If you are interested in the diffusion of glucose instead of oxygen, you get a different diffusion coefficient D, and so the line has a different slope. In other words, **when D is high, the same gradient causes more diffusion and when D is low, the same gradient causes less diffusion**.

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## How does flux depend on distance?

Now let's think about Fick's First Law in a different way. Before we were interested in the gradient as the independent variable (what happens to the flux when the gradient gets steeper?). Now we're going to switch gears and think about how flux changes as the distance changes. **In other words, we will choose to work with the distance as the independent variable** (isn't this fun? we can make the independent variable almost anything we want!). To do this, we'll need to use the discrete version of Fick's First Law:

The discrete version →



This time, Δx is the independent variable, and we assume that all the other quantities that appear on the right hand side of the equation are not going to change while we are interpreting the equation. The relationship is now an example of "inverse variation", otherwise known as what happens when you divide by the independent variable, or try to graph something like y = a/x.

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If the distance Δx is very small, then the flux is huge. As the distance increases, flux falls off quickly. With a big value of Δx, flux is almost zero (although it never quite reaches zero).

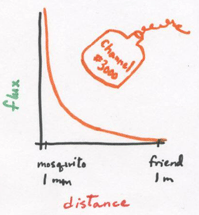
So, what does this mean biologically?

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| An E. coli cell average about 2 µm in length, while a S. cerevisiae (baker's yeast) cell measures about 9 µm. Assuming the same gradient and D occurs in each cell, how would you compare the flux?  * Flux in the E. coli would be: -D \* ΔC/2 * Flux in the S. cerevisiae would be:-D \* ΔC/9 * What is the ratio of two fluxes?  Answer: -D \* (ΔC/2) / (-D \* ΔC/9) = 9/2, so flux in E. coli is 4.5 times greater than in S. cerevisiae |

## A fragrant example

What this means is that **as distance increases, flux falls precipitously!**

We'll give an example. Let’s say you walk into a room wearing your latest favorite perfume / aftershave. The gradient between you and the rest of the room is steep, because no one else in the room is wearing your fragrance. A mosquito buzzing right next to your ear gets a noseful almost immediately – diffusion (flux) occurs very quickly over this short distance. However, diffusion to even a few centimetres away occurs much more slowly. More importantly **diffusion to the object of your desire, a person standing a metre or more away, occurs at a glacial pace (assuming you and the other person are standing still and not moving closer to each other).**



Luckily, you don't have to wait around for diffusion to occur. What actually happens, the reason why a person all the way across the room can smell you within seconds, is that **there are also air currents, carrying the perfume**.

## General Transport Equations and Fick's First Law

Before we move from Fick’s First Law to his (creatively named) Second Law, it is worth noting that **Fick's Law is really just one of several “transport equations” that all have a common form.** In these equations, J stands for transport (because it represents something like particles, or charge, or heat being transported from some location to another). So you can see that the same equation that we have been learning about is applicable in almost the exact same form in several different fields!

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| **Diffusion** | where D is the diffusion coefficient, C is the concentration of particles and x is the distance. |
| **For charge** | where *V* is voltage, so the flux of ions (*J*) is directly proportional to the difference in voltage (the voltage potential), and σ (also called electrical conductivity) is a coefficient that relates to the properties of the medium the charge is traveling through. |
| **For Energy (heat)** | where T is temperature (Kelvin), so that heat transfer (J) is directly proportional to the difference in temperatures. k is called the coefficient of thermal conductivity. |

## Summary

* Flux is the movement of particles per time (through a given area).
* In diffusion, individual particles are moving at random, and **net movement is a result of more particles moving from high to low concentrations** than are moving from low to high, thus, (Fick’s First Law)



* Fick’s First Law shares the same form as several other transport equations.
* D (the diffusion coefficient) has units of m2 s-1 or cm2 s-1, and is NOT equal to the speed at which an individual particle moves.

## Learning Outcomes

You should now be able to:

* Explain the linear relationship between the rate of movement of a substance and its concentration gradient (Fick’s First Law).
* Measure the rate of movement of a substance from one area to another as a function of the concentration gradient and the diffusion coefficient for that substance in the medium.