Physical Principles in Biology
Biology 3550
Spring 2025

Lecture 16:

Diffusion Continued: Fick's First and Second Laws

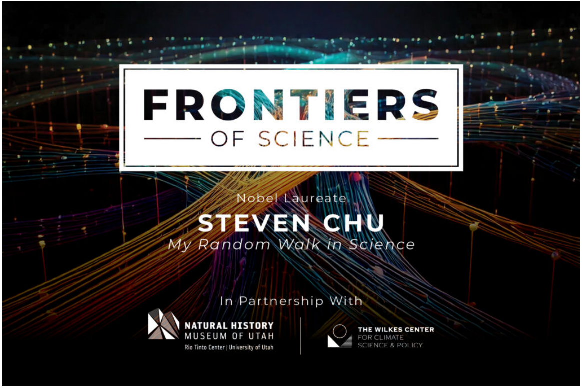
Wednesday, 12 February 2025

University of Utah
goldenberg@biology.utah.edu

Announcements

- Quiz 3:
  - Friday, 21 February
  - 25 min, second half of class.
- Problem set 3:
  - Due 11:59 PM, Wednesday, 26 February.
  - Download problems from Canvas.
  - Upload work to Gradescope and, optionally, Canvas (spreadsheet)!
  - Work must be typed!
- Discussion/Problem-solving Sessions:
  - Mondays, 3:00 P.M. - AEB 306
- Instructor Office hours:
  - Wednesdays, 11:00 AM - ASB 306
  - Other times by appointment

Frontiers of Science Lecture



- Tuesday, 18 February, 6:00 PM
- Natural History Museum of Utah
- RSVP by Wednesday, 12 February:
  https://science.utah.edu/frontiers-of-science-steven-chu/

SRI-CAP Guest Speaker

ANDREW HEMMERT

From

bioMérieux

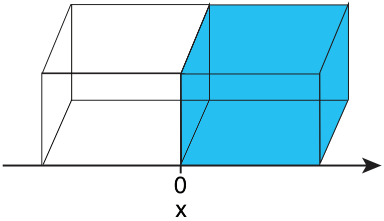
SVP, Molecular RD and Programs

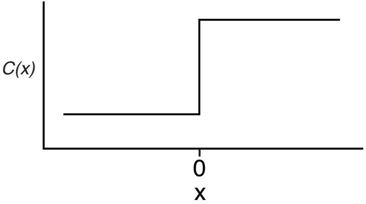
Friday, **Feb. 21**

11:30AM-12:30PM

CSC 206

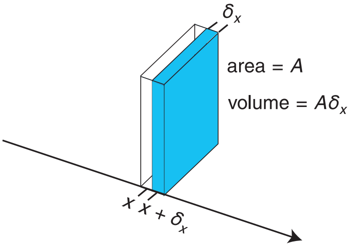
An Idealized Macroscopic Diffusion Experiment





- How will plot of $C(x)$ versus x change with time?

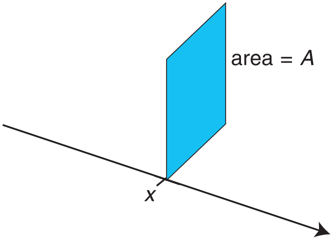
Diffusion Across a Thin Slice of Volume



- Slices are δ_x thick and have cross-sectional area across the x-axis of A
- Volume of each slice is $A\delta_x$
- During time τ, all of the molecules will move (on average) the distance δ_x along the x-axis.
- In a given slice, 1/2 of the molecules will move to the right and half to the left.

Fick's First Law of Diffusion

$$J = -\frac{\delta_x^2}{2\tau}\frac{dC}{dx}$$



- Symbols:
  - $J =$ flux of molecules (or moles) per unit area per unit time:
  - $\delta_x =$ RMS step length along the x-direction.
  - $\tau =$ average duration of random steps.
  - $\frac{dC}{dx}$ = derivative of concentration with x, "concentration gradient."
- If concentration increases with x, flux is in the negative x direction.

The Diffusion Coefficient, D

- Consider the term from Fick's first law: $\frac{\delta_x^2}{2\tau}$

  Both δ_x and τ are parameters describing the random walk of molecules (or larger particles) undergoing diffusion, and are constant for a given type of particle under defined solution conditions.

- Define a new parameter, the diffusion coefficient, D:

$$D = \frac{\delta_x^2}{2\tau}$$

- The usual form of Fick's first law:

$$J = -D\frac{dC}{dx}$$

- D can be experimentally determined, without knowing anything about the microscopic random walk steps.

Clicker Question #1

What are the units of the diffusion coefficient: $D = \frac{\delta_x^2}{2\tau}$?

A) mol/s

B) m^2/s

C) $\text{mol}/\text{m}/\text{s}$

D) m/s

Clicker Question #2

What are the units of the concentration gradient: $\frac{dC}{dx}$?

A) $\mathrm{mol/m}$

B) $\mathrm{mol/m^2}$

C) $\mathrm{mol/m^3}$

D) $\mathrm{mol/m^4}$

Dimensional Analysis of Fick's First Law

- The diffusion coefficient: $D = \frac{\delta_x^2}{2\tau}$, units: m^2/s
- The concentration gradient: $\frac{dC}{dx}$

  C (concentration) units: $\mathrm{moles}/\mathrm{m}^3$
  x (distance) units: m

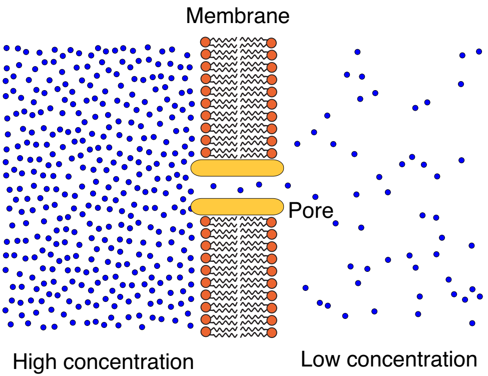
  $$\frac{dC}{dx} \text{ has units of } \frac{\mathrm{moles}/\mathrm{m}^3}{\mathrm{m}} = \frac{\mathrm{moles}}{\mathrm{m}^4}$$

- Flux, J

  $$J = -D\frac{dC}{dx} = \frac{\mathrm{m}^2}{\mathrm{s}}\frac{\mathrm{moles}}{\mathrm{m}^4} = \frac{\mathrm{moles}}{\mathrm{s}\cdot\mathrm{m}^2}$$

  moles per unit time per unit area, as originally defined.

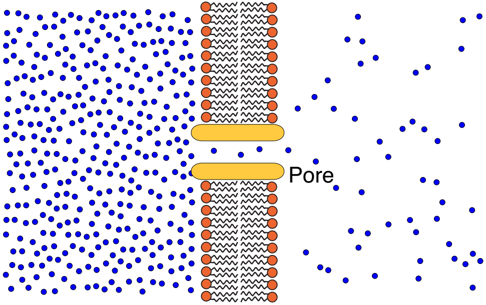
Diffusion of Molecules Across a Cellular Membrane



Some plausible values:

- Diffusion coefficient for a small molecule: $\approx 10^{-10}\,\mathrm{m}^2/\mathrm{s}$ (to be considered later)
- Thickness of a biological membrane: $\approx 3\,\mathrm{nm}$
- Diameter of a molecular pore: $\approx 1\,\mathrm{nm}$
- Concentrations: 50 mM and 5 mM

Clicker Question #3



- Thickness of membrane: $\approx 3\,\text{nm}$
- Diameter of pore: $\approx 1\,\text{nm}$
- Concentrations: 50 mM and 5 mM

Estimate the concentration gradient:

$$\frac{dC}{dx} \approx \frac{\Delta C}{\Delta x}$$

A) 1.5×10^{3} moles/m^4

B) 1.5×10^{6} moles/m^4

C) 1.5×10^{9} moles/m^4

D) 1.5×10^{10} moles/m^4

E) 4.5×10^{10} moles/m^4

Applying Fick's First Law

- Approximate the concentration gradient:

$$\frac{dC}{dx} \approx \frac{\text{concentration difference}}{\text{membrane thickness}} = \frac{50\,\text{mM} - 5\,\text{mM}}{3\,\text{nm}} = 15\,\text{mM}/\text{nm}$$

- Convert this to units with moles and meters:

$$15\,\text{mM}/\text{nm} = \frac{0.015\,\text{moles}/\text{L}}{10^{-9}\,\text{m}} \times \frac{10^{3}\,\text{L}}{\text{m}^{3}} = 1.5 \times 10^{10}\,\text{moles}/\text{m}^{4}$$

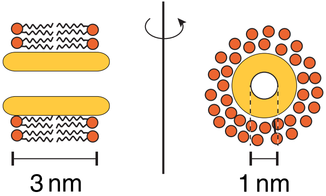
- Flux from Fick's first law:

$$J = -D\frac{dC}{dx} = -10^{-10}\,\text{m}^{2}/\text{s} \times 1.5 \times 10^{10}\,\text{moles}/\text{m}^{4} = -1.5\,\text{moles}/(\text{s} \cdot \text{m}^{2})$$

Negative sign indicates that diffusion is in the direction opposite to the concentration gradient.

Diffusion Through a Membrane Pore

- The pore:



Diameter = 1 nm

Area = $\pi r^2 = \pi(0.5\,\text{nm})^2 = 7.8 \times 10^{-19}\,\text{m}^2$

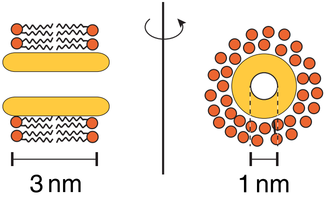
- Flux:

$$J = -1.5\,\text{moles}/(\text{s}\cdot\text{m}^2)$$

- Moles per second through the pore:

$$1.5\,\text{moles}/(\text{s}\cdot\text{m}^2) \times 7.8 \times 10^{-19}\,\text{m}^2 = 1.2 \times 10^{-18}\,\text{moles}/\text{s}$$

Diffusion Through a Membrane Pore



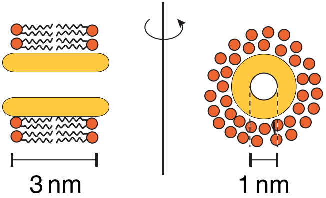
- Moles per second through the pore:

$$1.5\,\text{moles}/(\text{s}\cdot\text{m}^2) \times 7.8 \times 10^{-19}\,\text{m}^2 = 1.2 \times 10^{-18}\,\text{moles}/\text{s}$$

- Molecules per second through the pore:

$$1.2 \times 10^{-18}\,\text{moles}/\text{s} \times 6.02 \times 10^{23}\,\text{molecules}/\text{mole} = 7 \times 10^{5}\,\text{molecules}/\text{s}$$

How Many Molecules are in the Pore?



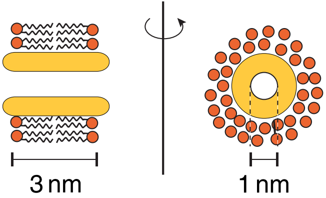
- Pore volume:

$$V = \pi r^2 \times l = \pi(0.5\,\mathrm{nm})^2 \times 3\,\mathrm{nm}$$
$$= 2.4\,\mathrm{nm}^3 \times (10^{-9}\,\mathrm{m/nm})^3 = 2.4 \times 10^{-27}\,\mathrm{m}^3$$
$$= 2.4 \times 10^{-27}\,\mathrm{m}^3 \times 10^3\,\mathrm{L/m}^3 = 2.4 \times 10^{-24}\,\mathrm{L}$$

- Assume that the concentration in the pore is the mean of the concentrations on the two sides:

$$C = (50\,\mathrm{mM} - 5\,\mathrm{mM})/2 = 22\,\mathrm{mM} = 0.022\,\mathrm{moles/L}$$

How Many Molecules are in the Pore?



- Concentration: 0.022 moles/L
- Moles in pore:

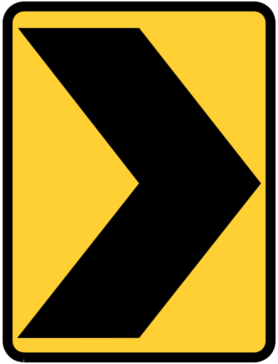
$$0.022\,\text{moles}/\text{L} \times 2.4 \times 10^{-24}\,\text{L} = 5.3 \times 10^{-26}\,\text{moles}$$

- Molecules in pore:

$$5.3 \times 10^{-26}\,\text{moles} \times 6.02 \times 10^{23}\,\text{molecules}/\text{mole} \approx 0.03\,\text{molecules}$$

Most of the time, the pore is “empty”!

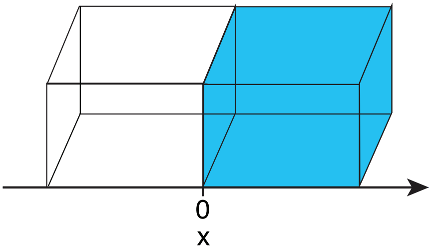
Warning!

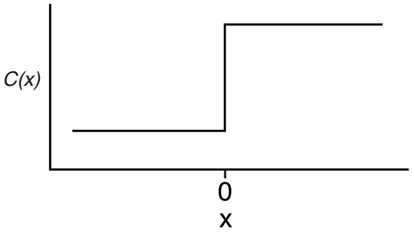


Direction Change

Change in Concentration with Time

An Idealized Macroscopic Diffusion Experiment

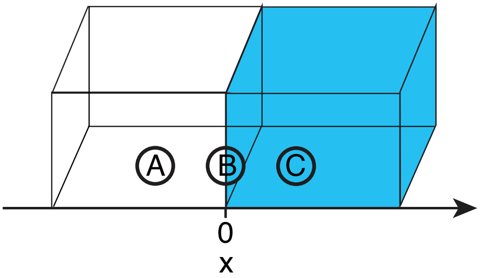


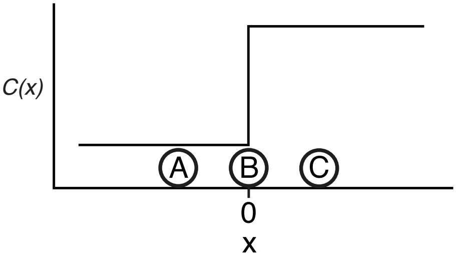


- How will plot of $C(x)$ versus x change with time?

Clicker Question #4

Where will the flux, *J*, be greatest?



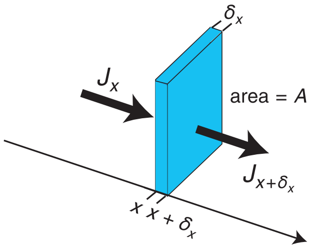


- At point B, where the concentration gradient is greatest.
- But, the molecules move at the same rate everywhere!

Fick's Second Law of Diffusion

- How does the concentration at a given point change with time?
- Net number of molecules moving to the right at two sides of a slice, during interval dt:

$$N_x = J_x A dt$$
$$N_{x+\delta_x} = J_{x+\delta_x} A dt$$



- Change in number of molecules in the slice:

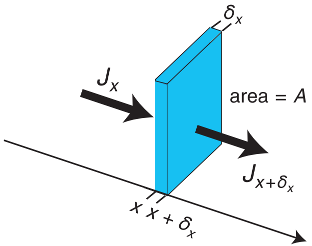
$$\begin{aligned} dN &= N_x - N_{x+\delta_x} \\ &= AJ_x dt - AJ_{x+\delta_x} dt \\ &= Adt\left(J_x - J_{x+\delta_x}\right) \end{aligned}$$

Fick's Second Law of Diffusion

- Change in concentration in the slice:

$$dC = \frac{dN}{A\delta_x} = \frac{Adt\left(J_x - J_{x+\delta_x}\right)}{A\delta_x}$$

$$= -dt\frac{J_{x+\delta_x} - J_x}{\delta_x}$$



- In the limit of small dt and small δ_x:

$$\frac{dC}{dt} = -\frac{J_{x+\delta_x} - J_x}{\delta_x} = -\frac{dJ}{dx}$$

- How does J change with x?

Fick's Second Law of Diffusion

- Fick's first law:

$$J = -D\frac{dC}{dx}$$

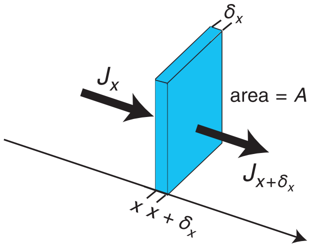
- Derivative of J with respect to x:

$$\frac{dJ}{dx} = -D\frac{d^2C}{dx^2}$$

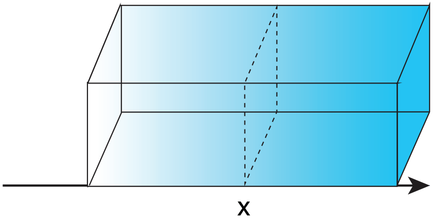
- Fick's second law:

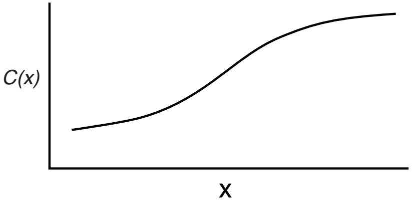
$$\frac{dC}{dt} = -\frac{dJ}{dx} = D\frac{d^2C}{dx^2}$$

Also called the diffusion equation.
What is it good for? How do we use it?



Fick's First and Second Laws of Diffusion





- First law:

$$J = -D\frac{dC}{dx}$$

- Flux, J, at position x is proportional to the concentration gradient at that position.

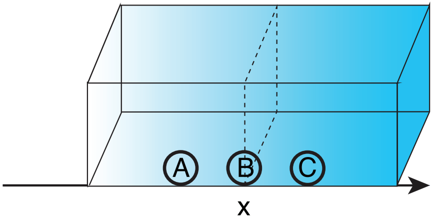
- Second law:

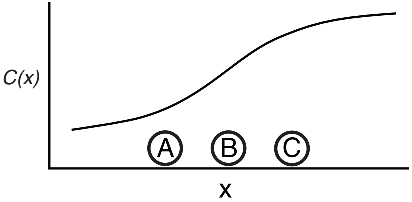
$$\frac{dC}{dt} = D\frac{d^2C}{dx^2}$$

- Rate of change in concentration at position x is proportional to the derivative of the concentration gradient.

Clicker Question #5

Where will the concentration increase most rapidly?





At point A, where the concentration gradient increases most rapidly with respect to x.

Fick's Second Law of Diffusion

$$\frac{dC}{dt} = D\frac{d^2C}{dx^2}$$

- A "second-order differential equation".
- The solution to the equation is a function:

$$C = f(x,t)$$

  that satisfies the equation:

$$\frac{df(x,t)}{dt} = D\frac{d^2f(x,t)}{dx^2}$$

- The trick is to find $C = f(x,t)$.
- The solution depends on the shape of the volume and the initial concentrations, the *boundary conditions*.