Biophysics I (BPHS 3090)

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Website: http://www.yorku.ca/cberge/3090W2015.html

York University
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Lecture 3

Reference/Acknowledgement:
- TF Weiss (Cellular Biophysics)
- D Freeman

Diffusion Equation

1. Fick's First Law:

$$\phi = -D\frac{\partial c}{\partial x}$$

+

2. Continuity Equation:

$$\frac{\partial \phi}{\partial x} = -\frac{\partial c}{\partial t}$$

$$\boxed{\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}}$$

(Fick's Second Law)

Diffusion Processes

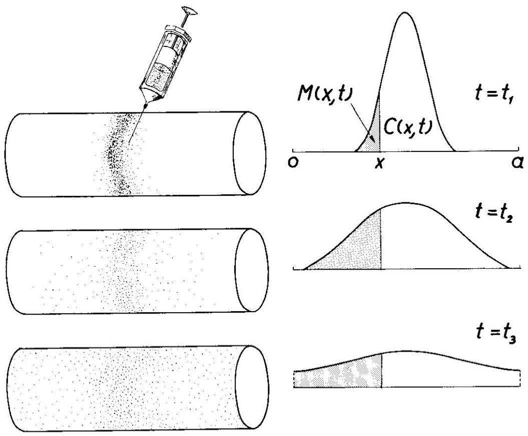
3. Impulse Response: Point-source of particles (n_o mol/cm^2) at t = 0 and x = 0 [Dirac delta function $\delta(x)$]

given the inital/boundary conditions:

$$c(x,t) = n_o \delta(x) \quad \text{at} \quad t = 0 \quad \text{where} \quad \int_{-\infty}^{\infty} \delta(x)\, dx = 1$$

need to solve:

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2}$$

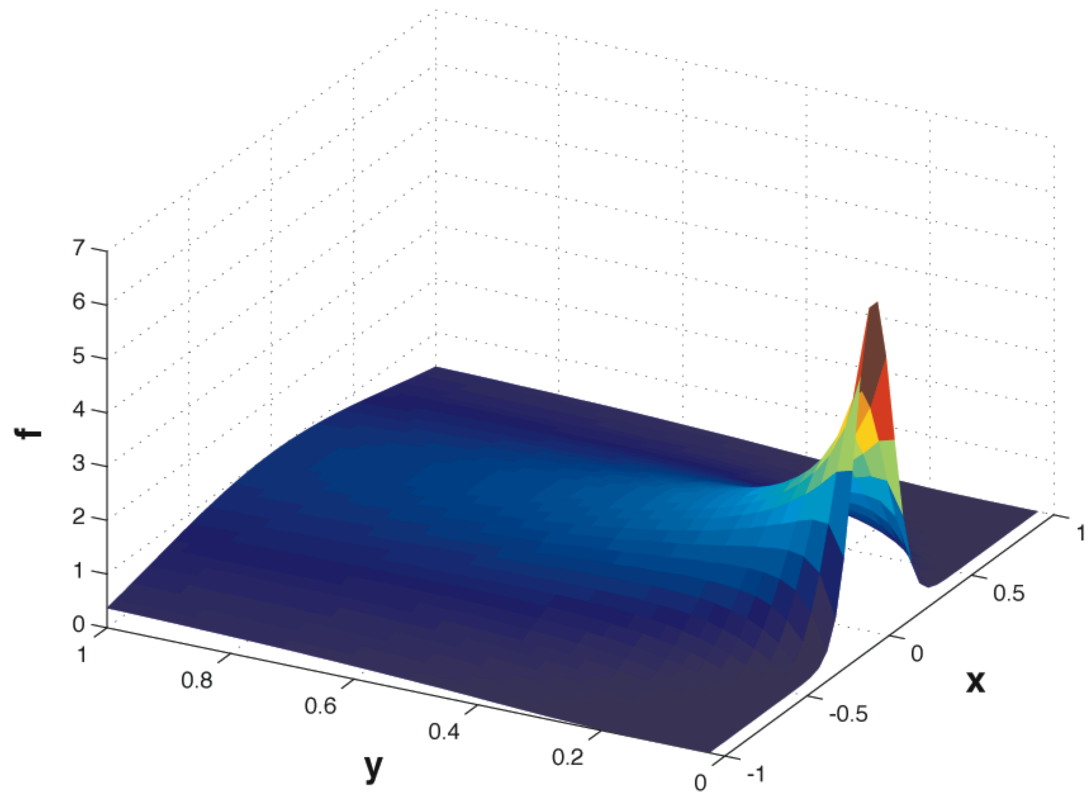


Batschelet Fig.12.5

[Aside: solution can be found by a # of different methods, one being by separation of variables and using a Fourier transform]

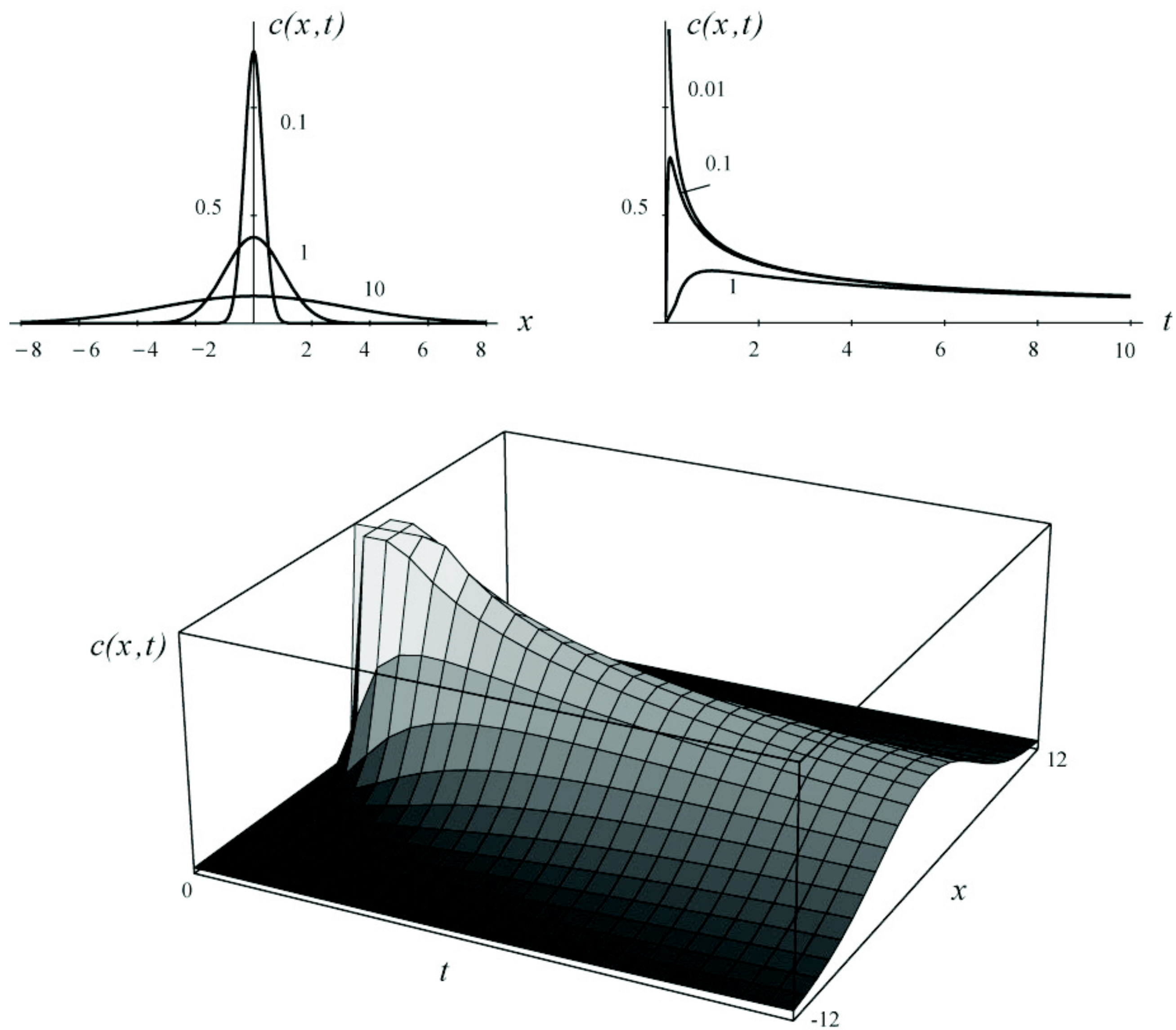
Solution
(for t > 0)

$$c(x,t) = \frac{n_o}{\sqrt{4\pi D t}} e^{-x^2/4Dt}$$



$$f(x, y) = \frac{1}{\sqrt{y}} e^{-x^2/y}$$

solution to
diffusion equation!



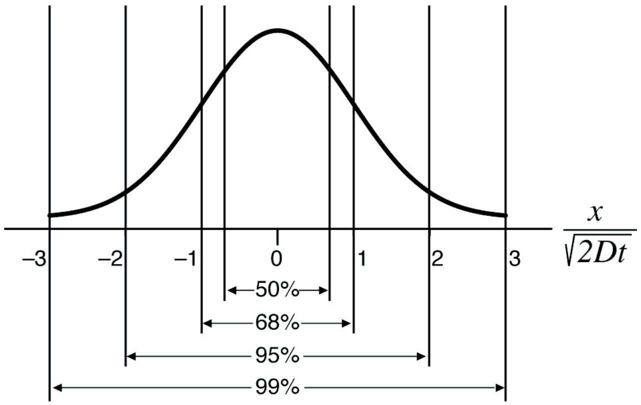
Weiss Fig.3.14 (modified)

Importance of Scale

$$c(x,t) = \frac{n_o}{\sqrt{4\pi D t}} e^{-x^2/4Dt}$$

Gaussian function with zero mean and standard deviation:

$$\sigma = \sqrt{2Dt}$$



Question: How long does it take ($t_{1/2}$) for ~1/2 the solute to move at least the distance $x_{1/2}$?

$$\frac{x_{1/2}}{\sqrt{2Dt_{1/2}}} \approx \frac{2}{3} \quad \Longrightarrow \quad \boxed{t_{1/2} \approx \frac{x_{1/2}^2}{D}}$$

For small solutes
(e.g. K^+ at body temperature)

$$D \approx 10^{-5} \ \frac{\mathrm{cm}^2}{\mathrm{s}}$$

	$x_{1/2}$	$t_{1/2}$
membrane sized	10 nm	$\frac{1}{10}$ µsec
cell sized	10 µm	$\frac{1}{10}$ sec
dime sized	10 mm	10^5 sec ≈ 1 day

Freeman

Exercise

At a junction between two neurons, called a synapse, there is a 20 nm cleft that separates the cell membranes. A chemical transmitter substance is released by one cell (the pre-synaptic cell), diffuses across the cleft, and arrives at the membrane of the other (post-synaptic) cell. Assume that the diffusion coefficient of the chemical transmitter substance is $D = 5 \times 10^{-6}$ cm^2/s.

→ Make a *rough estimate of the delay caused by diffusion of the transmitter substance across the cleft. What are the limitations of this estimate? Explain.*

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Answer

Consider the time it takes for ½ to cross the cleft, then we have approximately 1 us (1×10^{-6} s). However, this calculation:

- Ignores the cleft geometry (e.g., not infinite baths)
- There is nothing special about ½ the solute here (perhaps only a few molecules are needed, or perhaps a lot are)

Exercise

To wiggle your big toe, neural messages travel along a single neuron that stretches from the base of your spine to your toe. Assume that the membrane of this neuron can be represented as a uniform cylindrical shell that encloses the intracellular environment, which is represented as a simple saline solution. The diameter of the shell is 10 μm and the length is 1 m. Assume that 10^{-15} moles of dye are injected into the neuron at time $t = 0$ and at a point located in the center of the neuron, which we will refer to as the point $z = 0$. Assume that the dye diffuses across the radial dimension so quickly that the concentration of dye $c(z,t)$ depends only on the longitudinal direction z and time t. Assume that the diffusivity of the dye in the intracellular saline is $D = 10^{-7}$ cm²/s and that the membrane is impermeant to the dye.

→ Determine the amount of time t_1 required for 5% the injected dye to diffuse to points outside the region -1 mm$< z <$ 1 mm.

→ Determine the amount of time t_2 required for half the injected dye to diffuse to points outside the region -1 mm$< z <$ 1 mm. Determine the ratio of t_2 to t_1. Briefly explain the physical significance of this result.

→ Determine the amount of time t_3 required for 5% the injected dye to diffuse to points outside the region -10 mm$< z <$ 10 mm. Determine the ratio of t_3 to t_1. Briefly explain the physical significance of this result.

Answers

→ Determine the amount of time t_1 required for 5% the injected dye to diffuse to points outside the region −1 mm< z < 1 mm.

3.5 hours

→ Determine the amount of time t_2 required for half the injected dye to diffuse to points outside the region −1 mm< z < 1 mm. Determine the ratio of t_2 to t_1. Briefly explain the physical significance of this result.

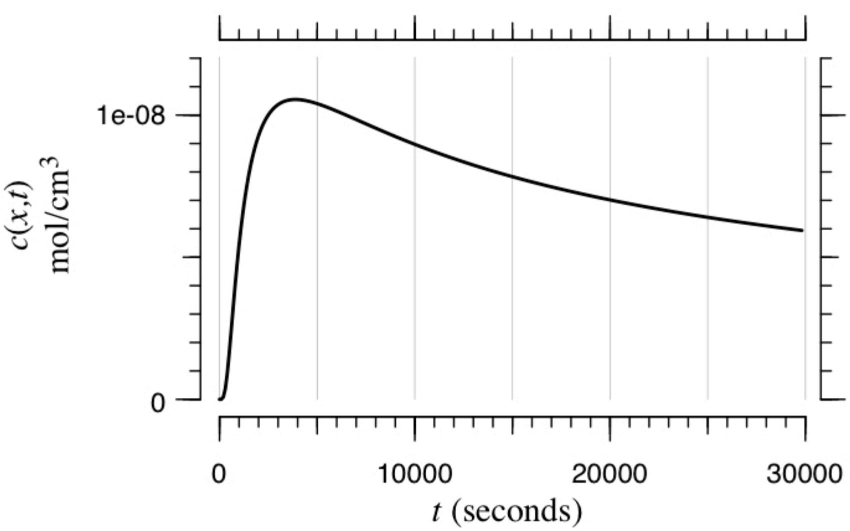
1.3 days

→ Determine the amount of time t_3 required for 5% the injected dye to diffuse to points outside the region −10 mm< z < 10 mm. Determine the ratio of t_3 to t_1. Briefly explain the physical significance of this result.

14.5 days

Exercise

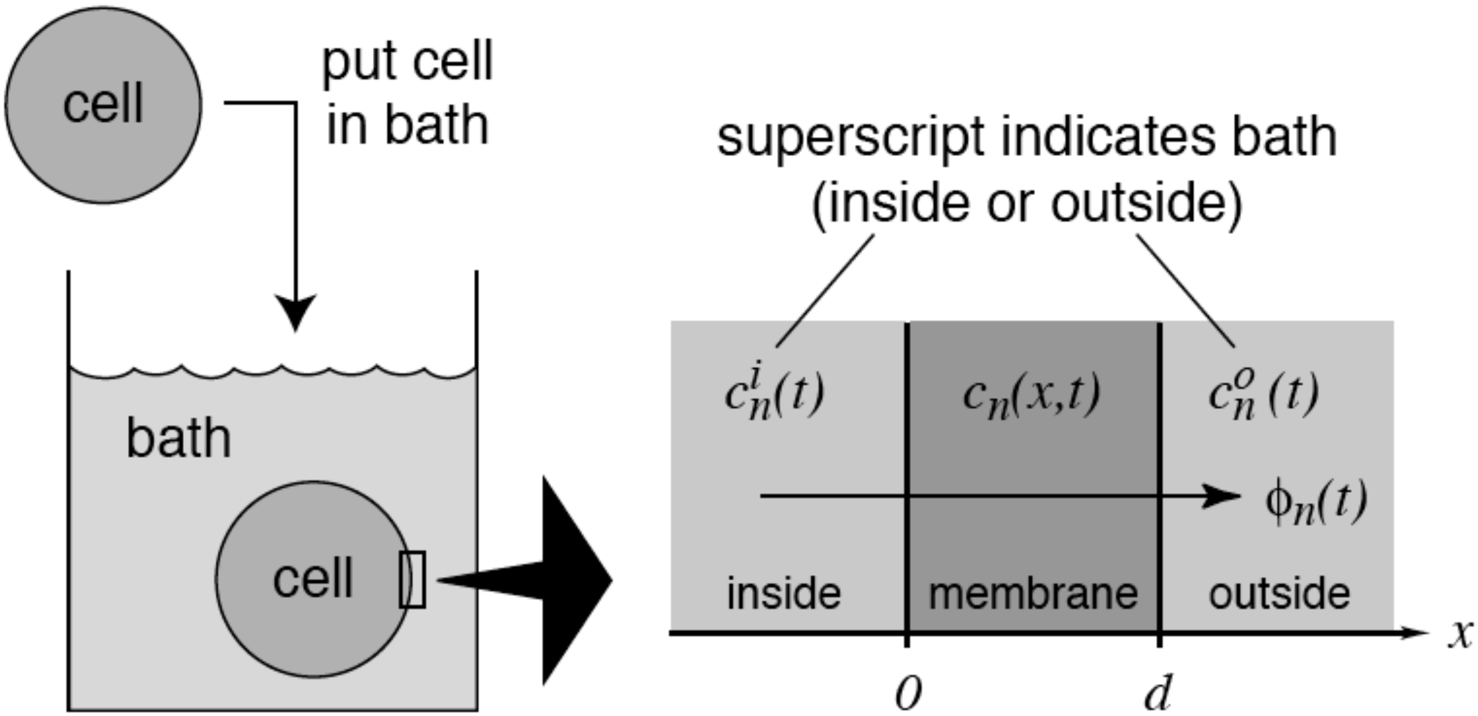
To wiggle your big toe, neural messages travel along a single neuron that stretches from the base of your spine to your toe. Assume that the membrane of this neuron can be represented as a uniform cylindrical shell that encloses the intracellular environment, which is represented as a simple saline solution. The diameter of the shell is 10 μm and the length is 1 m. Assume that 10^{-15} moles of dye are injected into the neuron at time t = 0 and at a point located in the center of the neuron, which we will refer to as the point z = 0. Assume that the dye diffuses across the radial dimension so quickly that the concentration of dye c(z,t) depends only on the longitudinal direction z and time t. Assume that the diffusivity of the dye in the intracellular saline is $D = 10^{-7}$ cm^2/s and that the membrane is impermeant to the dye.



The following plot shows the concentration of dye as a function of time for a particular point at z0 > 0.

→ Determine z0.

Membrane Diffusion: Two-Compartment Geometry



reference direction for flux is outward

Diffusion Through Cell Membranes: History 101

Diffusion through Cell Membranes

Charles Ernest Overton (late 1800s): first systematic studies
- qualitative:
  - put cell in bath with solute
  - wait, rinse, squeeze
  - analyze to see how much got in (+ = some; +++ = a lot)
- 100's of solutes, dozens of cell types
- surprising results: previously cell membranes had been thought to be impermeant to essentially everything but water

Overton's Rules:
- cell membranes are semi-permeable
- relative permeabilities of plant and animals cells are similar
- permeabilities correlate with solubility of solute in organic solvents
  → membrane is lipid (specifically cholesterol and phospholipids)
- certain cells concentrate some solutes → active transport
- potency of anesthetics correlated with lipid solubility
  → Meyer-Overton theory of narcosis
- muscles don't contract in sodium-free media

Diffusion through Cell Membranes

Paul Runar Collander (1920-1950): first quantitative studies
- large cells (cylindrical algae cells, 1 mm diameter, 1 cm long)
- bathe cell in solute for time t_1, squeeze out cytoplasm, analyze
- repeat with new cell and new time t_2
- plot intracellular quantity versus time
- fit with exponential function of time (two-compartment theory)
- infer permeability from time constant