Current Topics in Biophysics (BPHS 2090)

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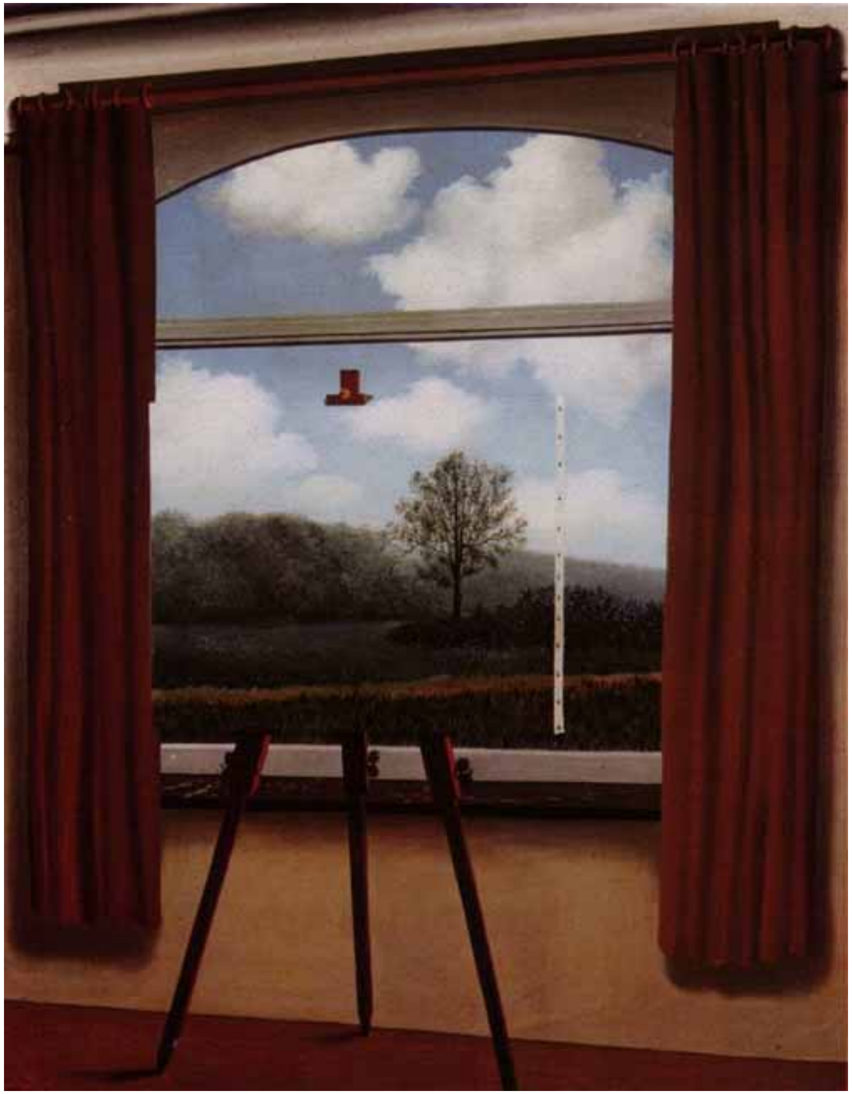
Website: http://www.yorku.ca/cberge/2090F2015.html

References/Acknowledgement:
- Bialek (2012)
- Weiss (1996)
- Berg (1993)
- Dusenbery (2009)
- Nelson (2004)

York University
Fall 2015 (11/10/15)

What is *biophysics*?



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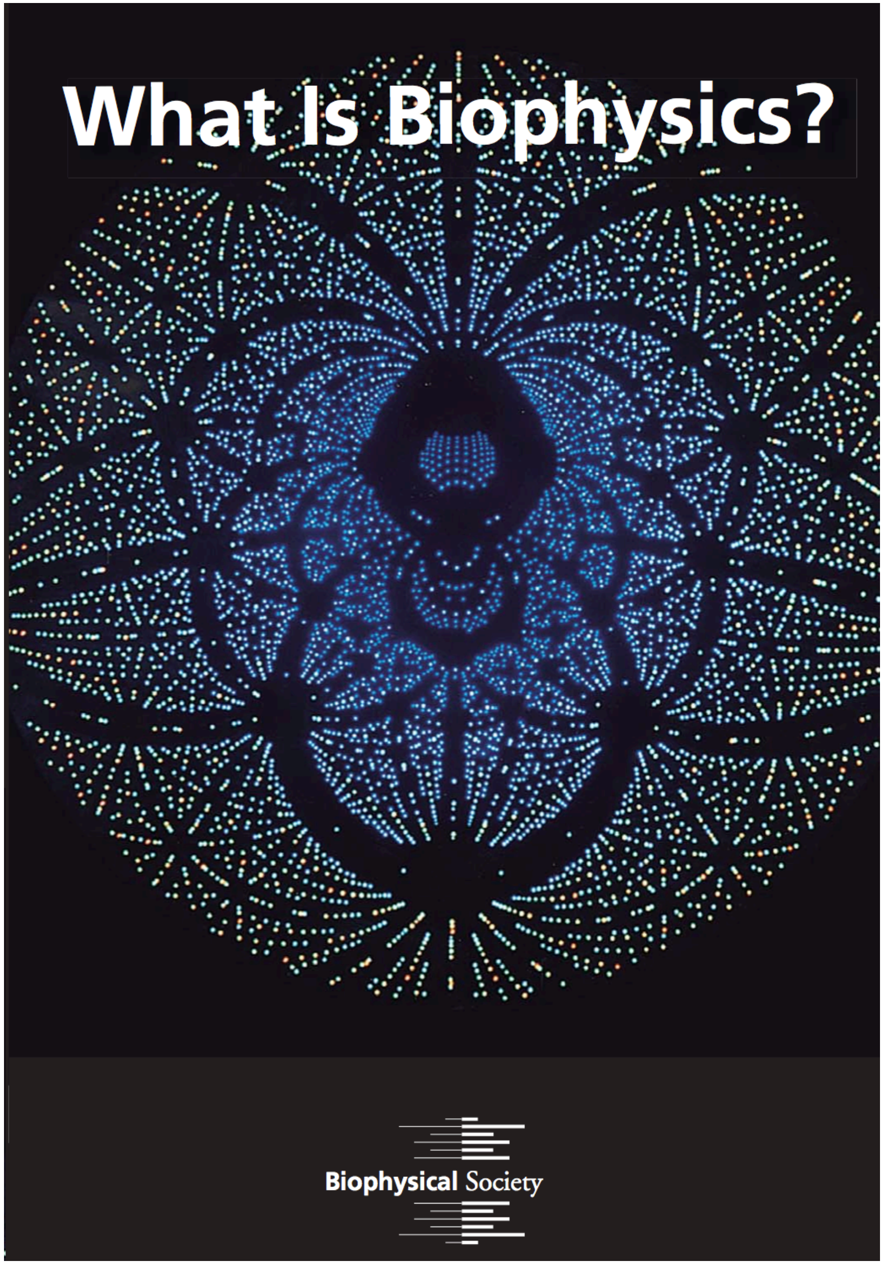
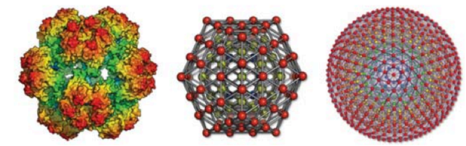


Biophysics is a bridge between biology and physics.

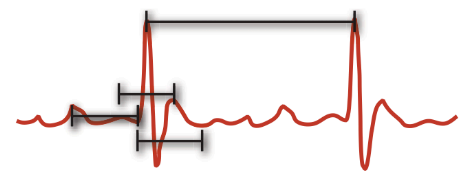
Biology studies life in its variety and complexity. It describes how organisms go about getting food, communicating, sensing the environment, and reproducing. On the other hand, physics looks for mathematical laws of nature and makes detailed predictions about the forces that drive physical systems. Spanning the distance between the complexity of life and the simplicity of physical laws is the challenge of biophysics. Looking for the patterns in life and analyzing them with math and physics is a powerful way to gain insights.

Biophysics looks for principles that describe patterns. If the principles are powerful, they make detailed predictions that can be tested.



Yang, A., Bahar, I. and Widom, M., Biophysical Journal, Volume 96, Issue 11, 4438-4448, 3 June 2000.

The natural symmetries of viral shell molecules contribute to their strength and flexibility. These properties are vital to their life cycles, and also provide principles for devising strong, flexible materials for manufacture.



The patterns and quantities in an electrocardiogram describe the functioning of the human heart.

Shining X-rays on protein creates a diffraction pattern revealing its structure (cover image). This false-color pattern of a protein from peas was created using data from the world's first dedicated high energy synchrotron, the Synchrotron Radiation Source. Biophysicists analyze diffraction patterns to determine the positions of the atoms in proteins, DNA and other important molecules. Understanding the atomic structures is an important step toward understanding how molecules work together to sustain life.

Daresbury Laboratory, UK. © STFC.

http://www.biophysics.org/portals/1/pdfs/what%20is%20biophysics%20brochure.pdf

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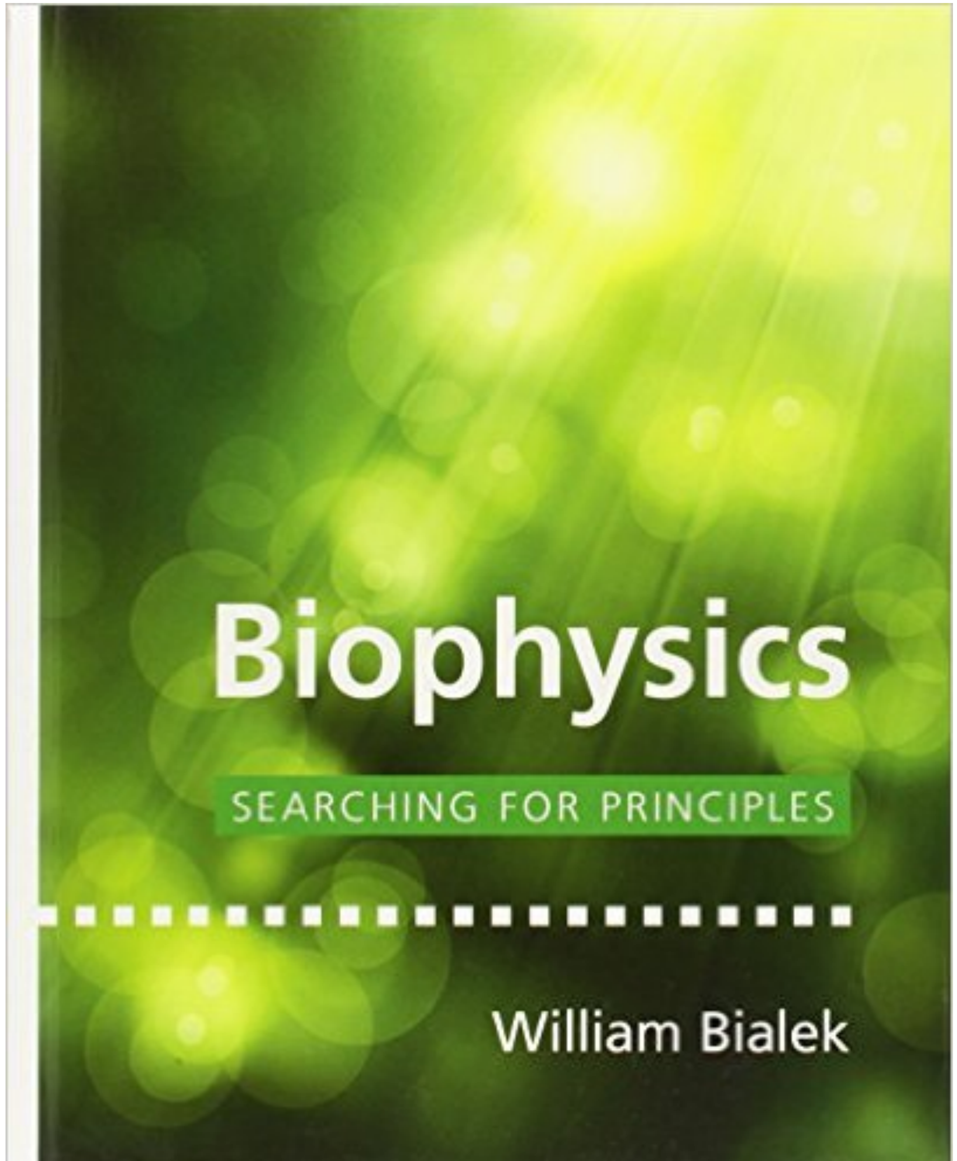

Bialek (2012)

What is biophysics? (Bialek-ian viewpoint)

“I believe that much has been lost in the emergence of the conventional views about the nature of the interaction between physics and biology. By focusing on methods, we miss the fact that, faced with the same phenomena, physicists and biologists will ask different questions. In speaking of biological importance, we ignore the fact that physicists and biologists have different definitions of understanding. By organizing ourselves around structures that come from the history of biology, we lose contact with the dreams of our intellectual ancestors that the dramatic qualitative phenomena of life should be clues to deep theoretical insights, that there should be a physics of life and not just the physics of this or that particular process”

Bialek (2012)

<u>What is biophysics?</u> (Bialek-ian viewpoint)

"In each area of physics we have a set of general theoretical principles, all interconnected, which define what is possible; the path to confidence in any of these principles is built on a series of beautiful, quantitative experiments that have extended the envelope of what we can measure and know about the world. Beyond providing explanations for what has been seen, these principles provide a framework for exploring, sometimes playfully, *<u>what ought to be seen</u>*."

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“Can we imagine a physics of biological systems that reaches the level of predictive power that has become the standard in other areas of physics?

Can we reconcile the physicists’ desire for unifying theoretical principles with the obvious diversity of life’s mechanisms?

Could such theories engage meaningfully with the myriad experimental details of particular systems, yet still be derivable from succinct and abstract principles that transcend these details?”

Bialek (2012)

What is biophysics? (Bialek-ian viewpoint)

"Although physics has subfields, to a remarkable extent the physics community clings to the romantic notion that Physics is one subject. Not only is the book of Nature written in the language of mathematics, but there is only one book, and we expect that if we really grasped its content it could be summarized in very few pages. Where does biophysics fit into this view of the world?"

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"At present, most questions about how things work in biological systems are viewed as questions that must be answered by experimental discovery."

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“At present, most questions about how things work in biological systems are viewed as questions that must be answered by experimental discovery.”

“It is a remarkable thing that, pulling on the threads of one biological phenomenon, we can unravel so many general physics questions.”

Bialek (2012)

What is biophysics? (Bialek-ian viewpoint)

“ ...and perhaps the greatest success of molecular biology is the discovery that many of these basic molecules of life are universal, shared across organisms separated by hundreds of millions of years of evolutionary history. Where classical biology emphasized the complexity and diversity of life, the first generation of molecular biologists emphasized the simplicity and universality of life’s basic mechanisms, and it is not hard to see this as an influence of the physicists who came into the field at its start.”

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“What is special about the state of matter that we call life? How does it come to be this way? Different generations of physicists have approached these mysteries in different ways. [...] Some of their forays into the phenomena of life were driven by a desire to test the universality of physical laws, such as the conservation of energy.”

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“... insistence that the community should focus (as the physics tradition teaches us) on the simplest examples of crucial biological phenomena”

Bialek (2012)

<u>What is biophysics?</u> (Bialek-ian viewpoint)

"The challenge is not to find the most important or 'fundamental' phenomenon, but rather to see through any one of many interesting and beautiful phenomena to the deep physics problems that are hiding underneath the often formidable complexity of these systems."

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“In order to survive in the world, organisms do indeed have to solve a wide variety of problems. Many of these are really physics problems: converting energy from one form to another, sensing weak signals from the environment, [...]. While it’s obvious that everything which happens in living systems is constrained by the laws of physics, these physics problems in the life of the organism highlight these constraints and provide a special path for physics to inform our thinking about the phenomena of life.”

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"Perhaps surprisingly, many biologists share the expectation that their measurements will be noisy. Indeed, some biologists insist that physicists have to get used to this, and that this is a fundamental difference between physics and biology. Certainly it is a difference between the sciences as they are practiced, but the claim that there is something essentially sloppy about life is deeper, and deserves more scrutiny."

Bialek (2012)

What is biophysics? (Bialek-ian viewpoint)

"Many students are given the impression, implicitly or explicitly, that to do biophysics one can get away with knowing less 'real physics' than in other subfields, and I think this is a disastrous misconception."

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"No matter how much we may be searching for deep theoretical principles, in the physics tradition, we do need a grasp of the facts. But when we teach particle physics we don't start by reading from the particle data book, so similarly I don't start by reciting the 'biological background.' Rather, we plunge right in..."

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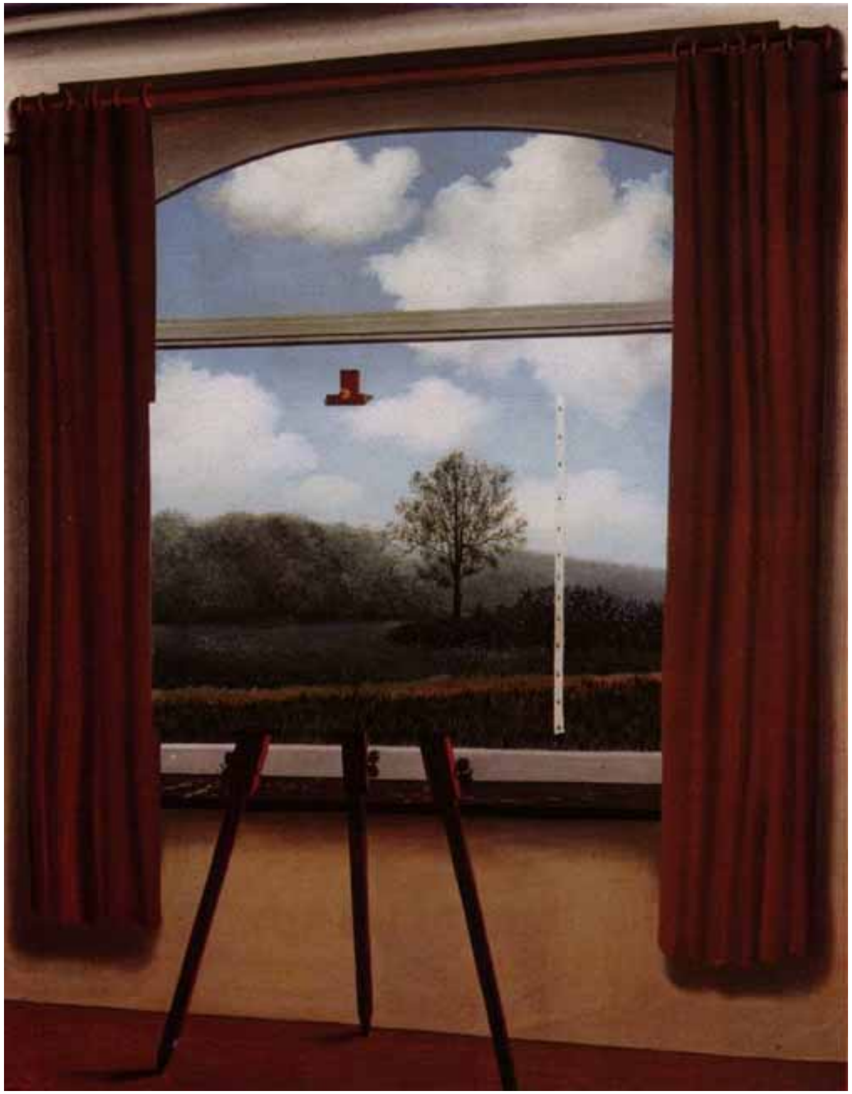
"I think we should avoid talking about how 'physicists need to learn the biology,' since 'biology' could mean either the study of living systems or the academic discipline practiced in biology departments, and these need not be the same thing. We must know what has been measured, assess these data with informed skepticism, and use the results to guide our thinking as we ask our own new and interesting questions."

Bialek (2012)

So what is *biophysics*?



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Plan for the last 1/3 of BPHS 2090 (F15)

1. Intro, Diffusion

2. Diffusion (cont.), Bacterial swimming, Fluid dynamics

3. Fluid dynamics (cont.), Microfluidics (& Low Reynold's #)

4. Ion channels, Neurons & Neurotransmitter

5.Sensory biophysics: Hearing & Vision

6. X-ray crystallography

7. Smorgasboard of "current topics"

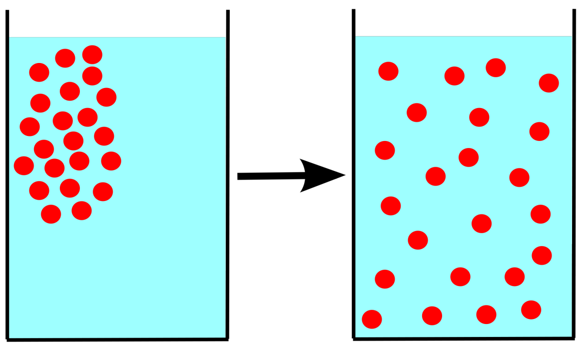
8. Midterm (12/3)

Note: Many of these topics will appear in varying depths in BPHS 3090 (now 4080) and 4090

<u>Diffusion</u>

- According to the dictionary....

- According to wikipedia....



- According to history....

diffusion

[dih-**fyoo**-zh*uh* n]

Spell Syllables

Examples Word Origin

noun

1. act of diffusing; state of being diffused.

2. prolixity of speech or writing; discursiveness.

3. *Physics.*
   a. Also called **migration**. an intermingling of molecules, ions, etc., resulting from random thermal agitation, as in the dispersion of a vapor in air.
   b. a reflection or refraction of light or other electromagnetic radiation from an irregular surface or an erratic dispersion through a surface; scattering.

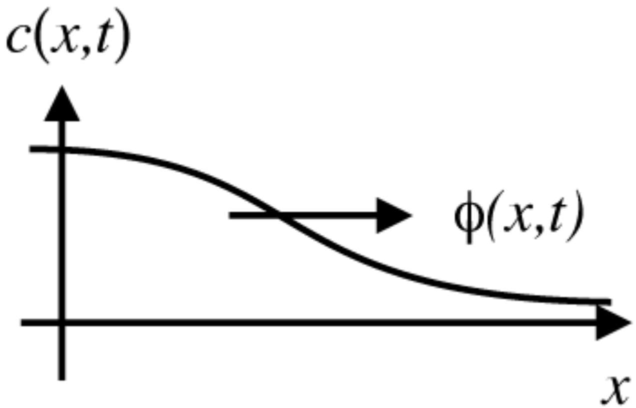
4. *Movies.* a soft-focus effect resulting from placing a gelatin or silk plate in front of a studio light or a camera lens, or through the use of diffusion filters.

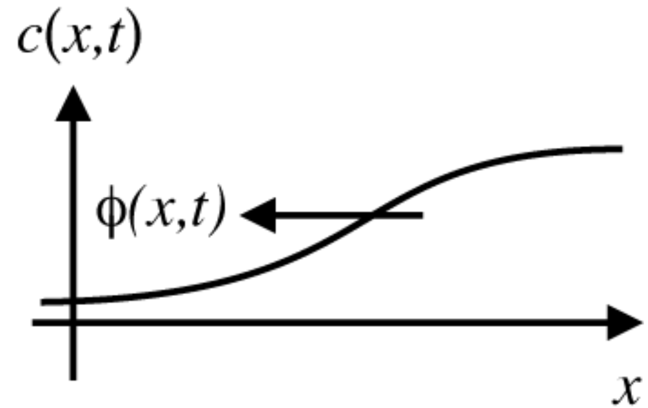
5. *Meteorology.* the spreading of atmospheric constituents or properties by turbulent motion as well as molecular motion of the air.

6. *Anthropology, Sociology.* Also called **cultural diffusion**. the transmission of elements or features of one culture to another.

Diffusion

From Graham's observations (~1830):





"A few years ago, Graham published an extensive investigation on the diffusion of salts in water, in which he more especially compared the diffusibility of different salts. It appears to me a matter of regret, however, that in such an exceedingly valuable and extensive investigation, the development of a fundamental law, for the operation of diffusion in a single element of space, was neglected, and I have therefore endeavoured to supply this omission."

- A. Fick (1855)

Diffusion

$$\phi(x,t) = -D\frac{\partial c(x,t)}{\partial x}$$

(Fick's Law)

- diffusion constant is always positive (i.e., $D > 0$)
- determines time it takes solute to diffuse a given distance in a medium
- depends upon both solute and medium (solution)
- *Stokes-Einstein relation* predicts that D is inversely proportional to solute molecular radius

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

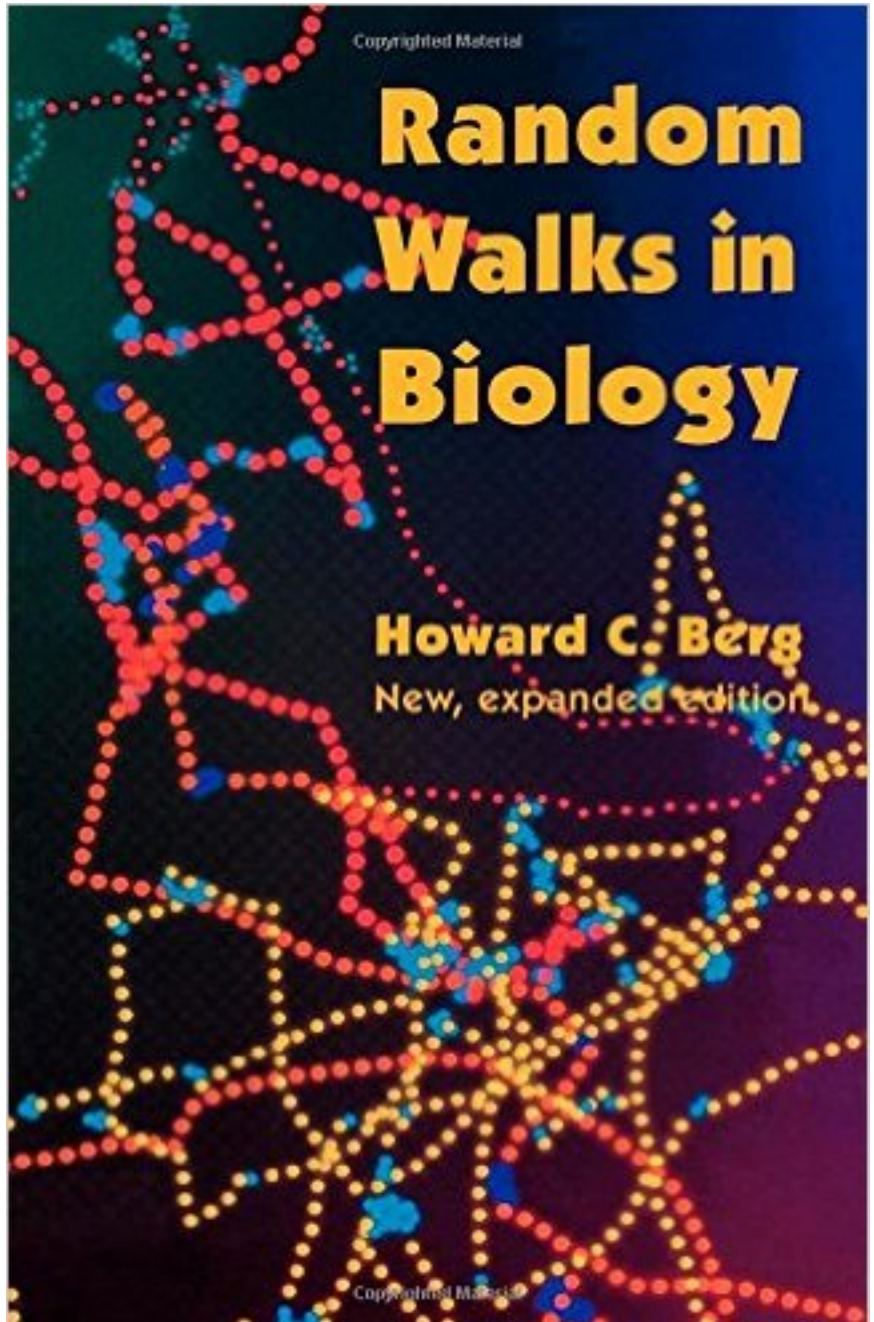
(Diffusion equation)

Note: This is a PDE(!!)

In short, there is a net movement down a concentration gradient

→ We'll derive all this in detail come BPHS 4080....

Diffusion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Chapter 1

Diffusion: Microscopic Theory

Diffusion is the random migration of molecules or small particles arising from motion due to thermal energy. A particle at absolute temperature T has, on the average, a kinetic energy associated with movement along each axis of $kT/2$, where k is Boltzmann's constant. Einstein showed in 1905 that this is true regardless of the size of the particle, even for particles large enough to be seen under a microscope, i.e., particles that exhibit Brownian movement. A particle of mass m and velocity v_x on the x axis has a kinetic energy $mv_x^2/2$. This quantity fluctuates, but on the average $\langle mv_x^2/2 \rangle = kT/2$, where $\langle \; \rangle$ denotes an average over time or over an ensemble of similar particles. From this relationship we compute the mean-square velocity,

$$\langle v_x^2 \rangle = kT/m, \qquad (1.1)$$

and the root-mean-square velocity,

$$\langle v_x^2 \rangle^{1/2} = (kT/m)^{1/2}. \qquad (1.2)$$

We can use Eq. 1.2 to estimate the instantaneous velocity of a small particle, for example, a molecule of the protein lysozyme. Lysozyme has a molecular weight 1.4×10^4 g. This is the mass of one mole, or 6.0×10^{23} molecules; the mass of one molecule is $m = 2.3 \times 10^{-20}$ g. The value of kT at 300°K (27°C) is 4.14×10^{-14} g cm^2/sec^2. Therefore, $\langle v_x^2 \rangle^{1/2} = 1.3 \times 10^3$ cm/sec. This is a sizeable speed. If there were no obstructions, the molecule would cross a typical classroom in about 1 second. Since the protein is not in a vacuum but is immersed in an aqueous medium, it does not go very far before it bumps into molecules of

Berg (1993)

Diffusion

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Some (remarkably deep) ideas right off the bat:

- Random walkers
- Temperature, Boltzmann's constant
- Einstein and 1905
- Mean-squared velocity, "ensemble"
- "Brownian movement"
- "Microscopic theory" (ch.2 is "Macroscopic theory")

→ A kernel of a deep idea is here, the distinction between "lots of little things" versus "big things"

[statistical mechanics being the thread tying things together]

Berg (1993)

Diffusion: Microscopic

- Random walking (in 1-D for simplicity)
  - independent of one another
  - equal probability either way

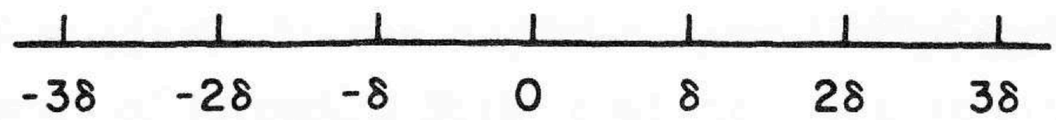


Fig. 1.2. Particles executing a one-dimensional random walk start at the origin, 0, and move in steps of length δ, occupying positions 0, $\pm\delta$, $\pm 2\delta$, $\pm 3\delta$, ...

Position of i'th walker:

$$x_i(n) = x_i(n-1) \pm \delta.$$

Mean displacement:

$$\langle x(n) \rangle = \frac{1}{N} \sum_{i=1}^{N} x_i(n)$$

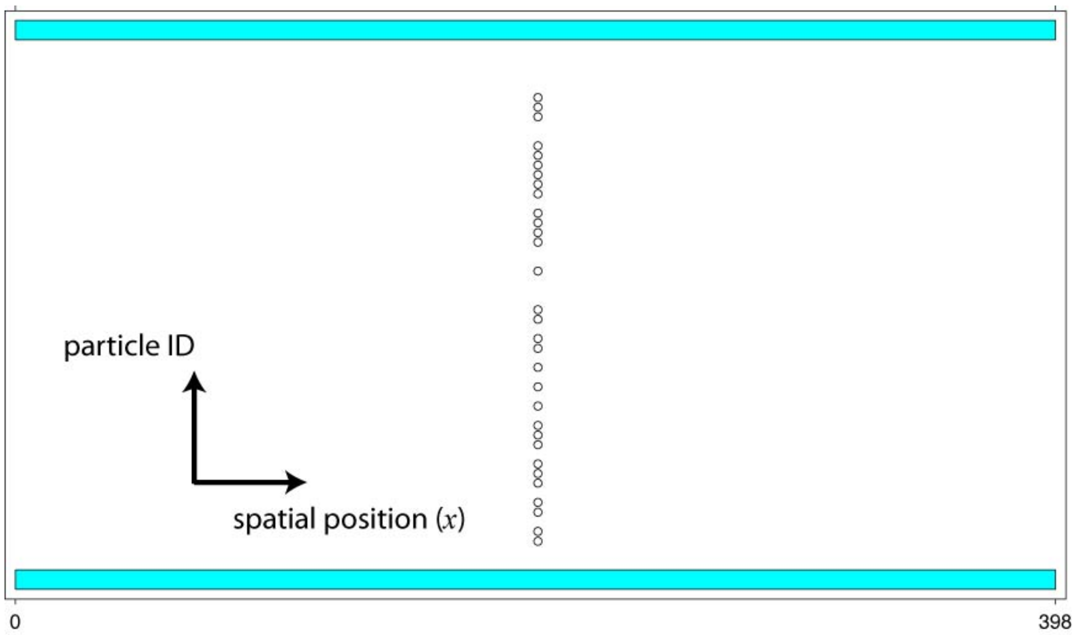
$$\langle x(n) \rangle = \frac{1}{N} \sum_{i=1}^{N} [x_i(n-1) \pm \delta]$$

$$= \frac{1}{N} \sum_{i=1}^{N} x_i(n-1) = \langle x(n-1) \rangle$$

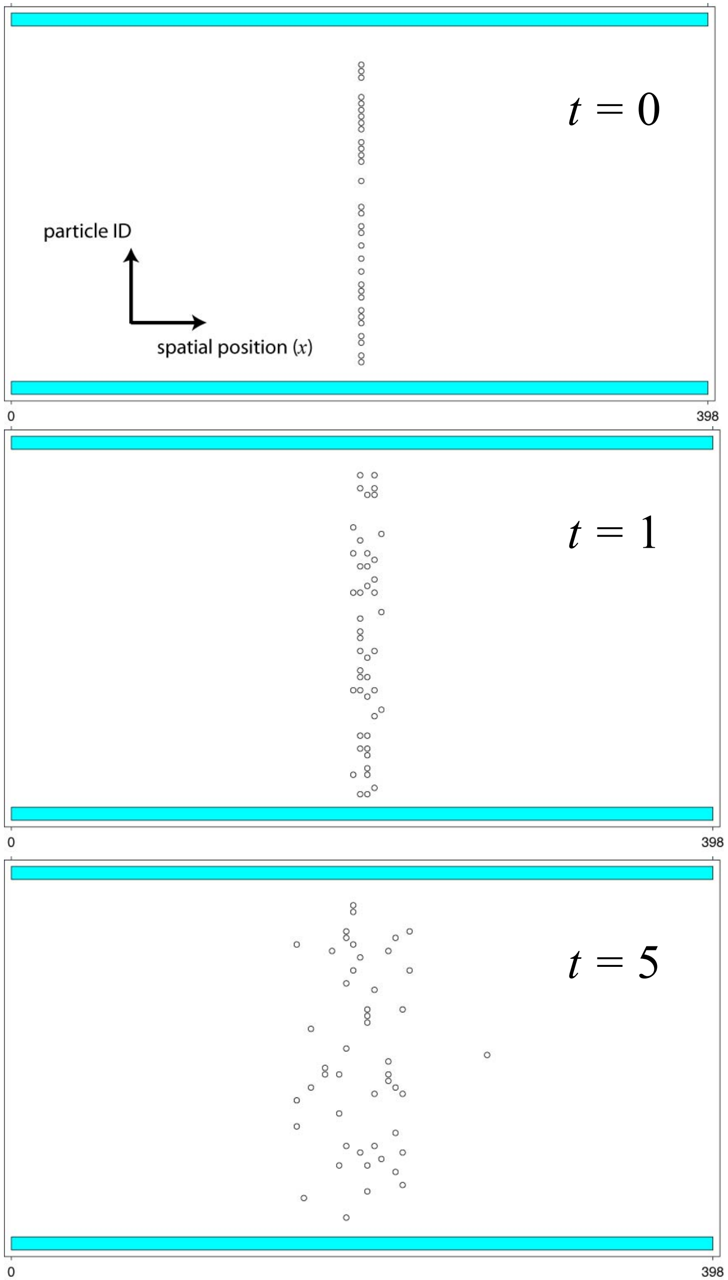
→ On average, they don't go anywhere(!)

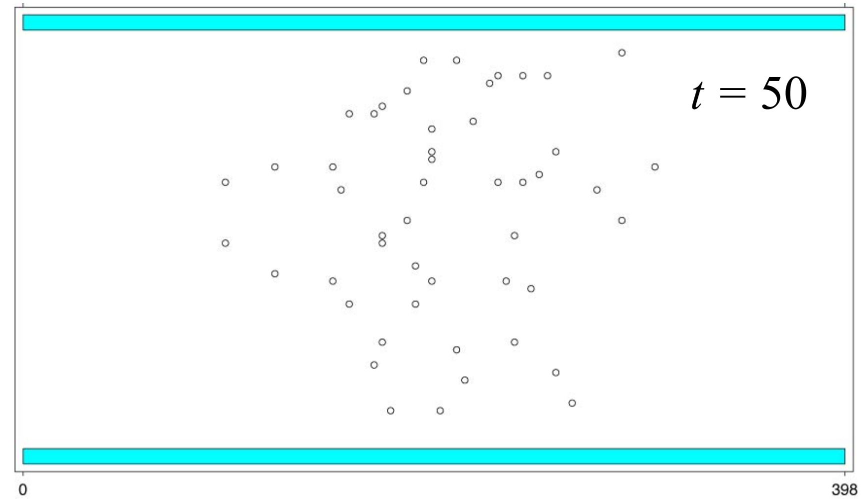
Berg (1993)

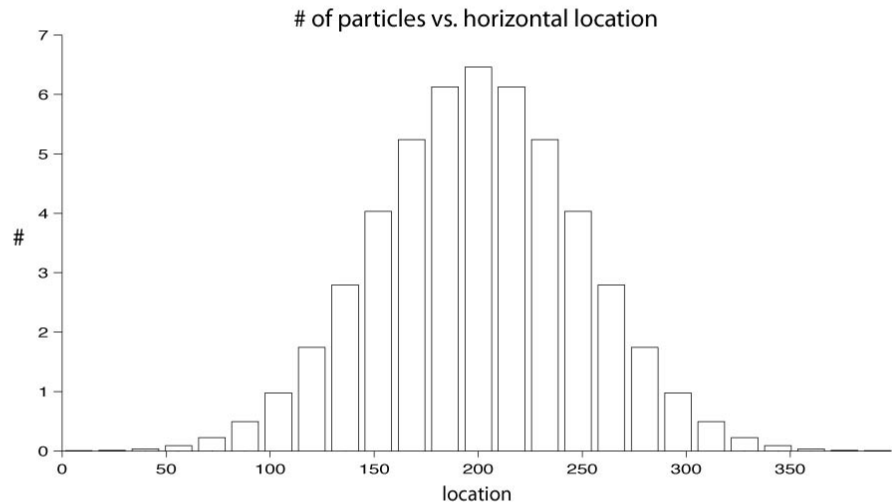
Ensemble of Random Walkers



Diffusion: Microscopic

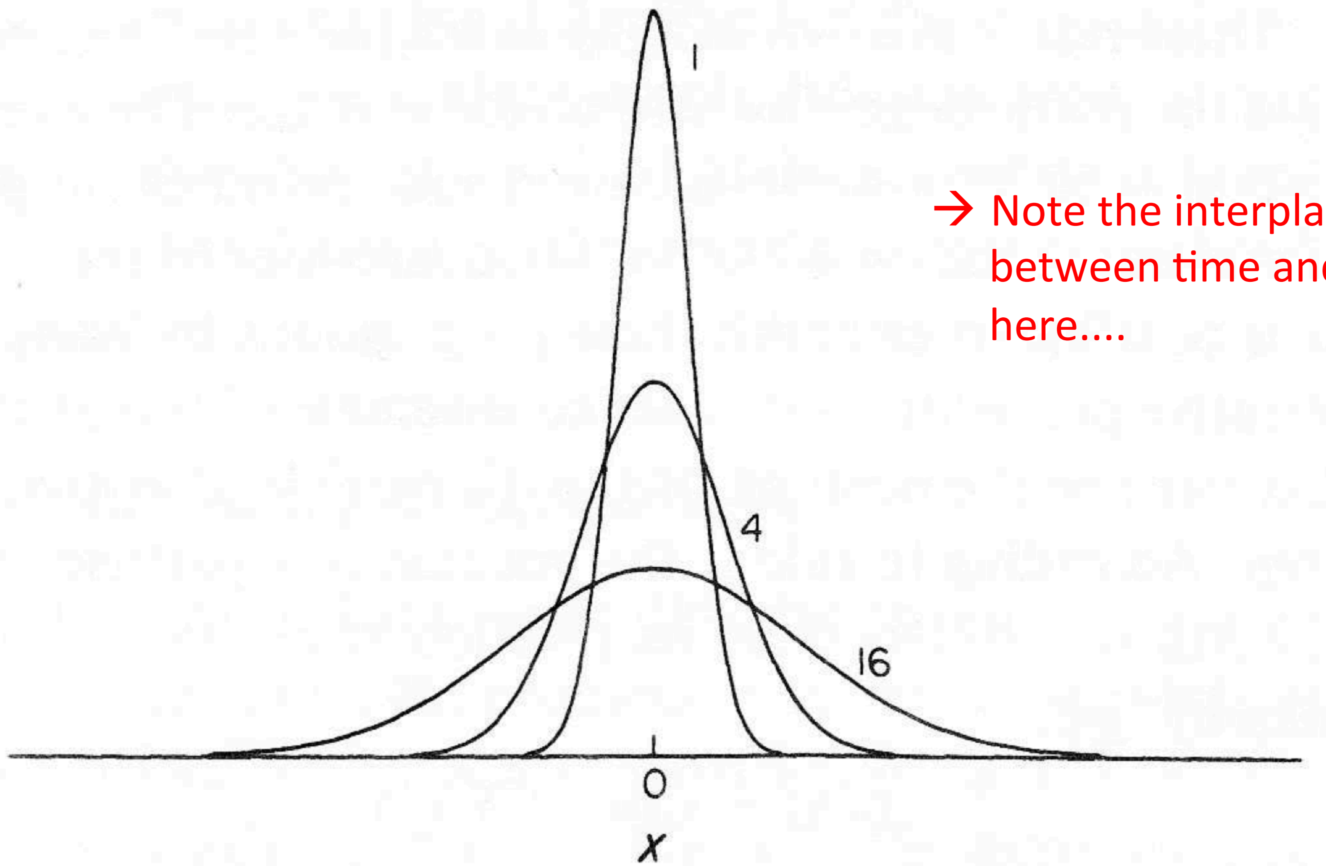






→ On average, they don't go anywhere... but they do "spread out" with time

Diffusion: Microscopic → Macroscopic



→ Note the interplay between time and space here....

Fig. 1.3. The probability of finding particles at different points x at times $t = 1, 4$, and 16. The particles start out at position $x = 0$ at time $t = 0$. The standard deviations (root-mean-square widths) of the distributions increase with the square-root of the time. Their peak heights decrease with the square-root of the time. See Eq. 1.22.

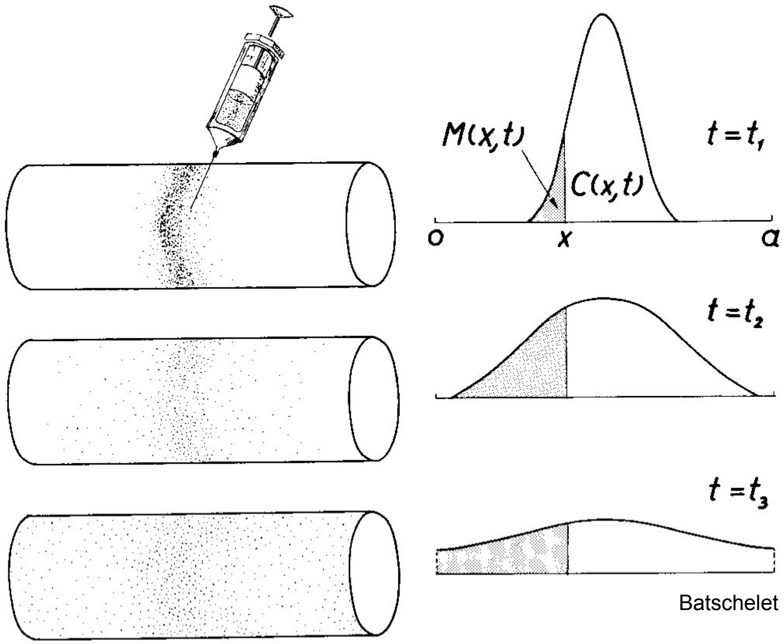
Berg (1993)

Diffusion Processes

→ You have intuition for this already....

- "Impulse response" → Point-source of particles (n_o mol/cm^2) at t = 0 and x = 0

[Dirac delta function $\delta(x)$]



Batschelet Fig.12.5

Mathematically, this can be described as:

need to solve:

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

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

[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)

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