Principles of Electronic Nanobiosensors

Unit 1: Introduction to Nanobiosensors

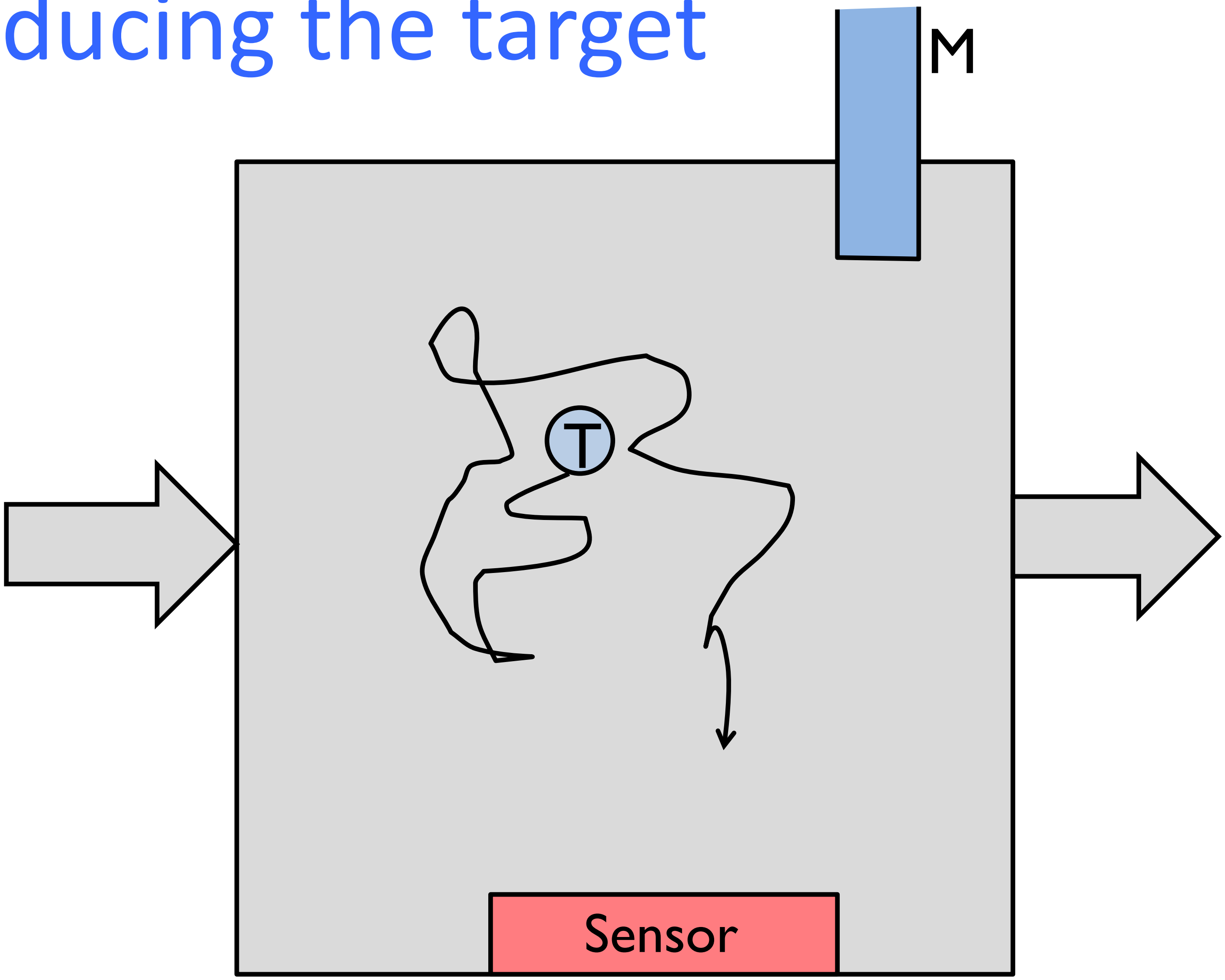
Lecture 1.2: Introductory Concepts: Biomolecules

By Muhammad A. Alam
Professor of Electrical and Computer Engineering
Purdue University
alam@purdue.edu

Outline

- How does a biosensor work
- Types of biomolecules: DNA, Protein, Virus
- Density of bimolecules
- Diffusion and capture of biomolecules
- Summary and conclusions

Introducing the target

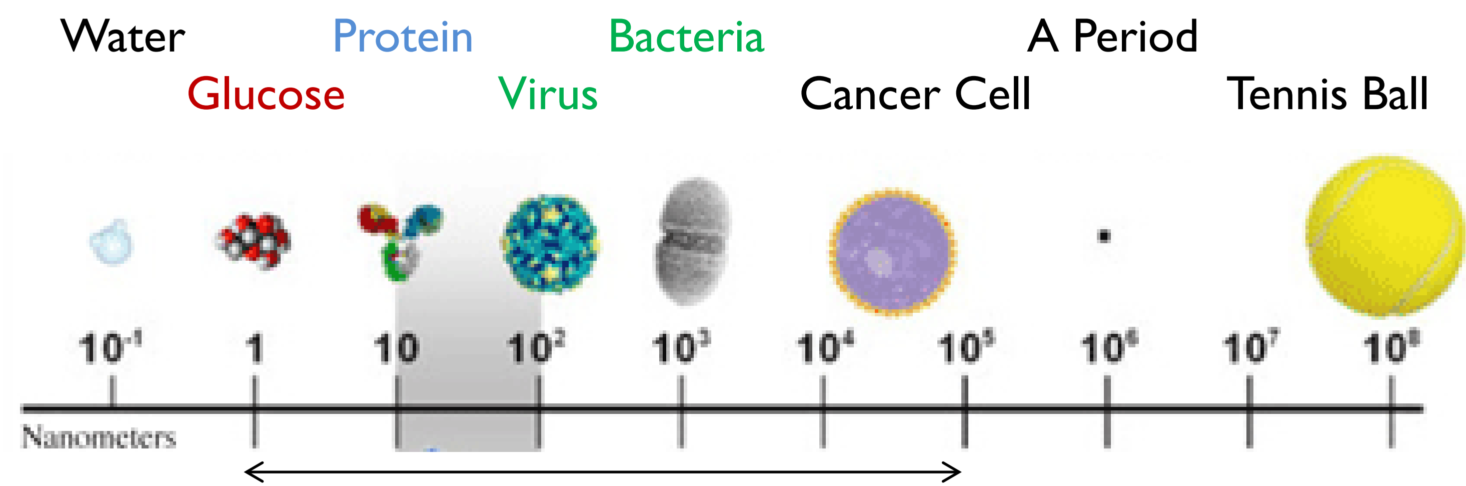


Biomolecules

- Chemical Indicators
  - Glucose (diabetes)
  - Nitric oxide (Parkinson)
- Elements of life
  - DNA (Genetic)
  - Protein (disorders)
- Invaders
  - Virus (infection)
  - Bacteria (infection)
  - DDT (disrupts cells function)

Charges
Mass
Redox potential
Optical index

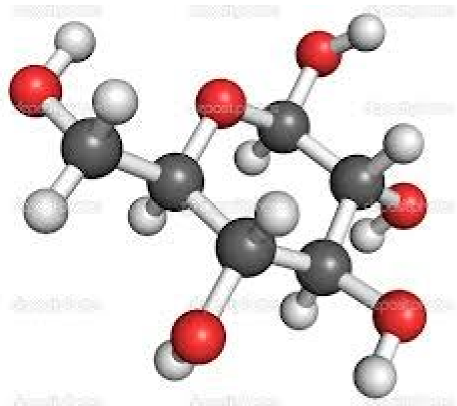
Variety of target biomolecules



They have different mass, charge, and electron affinity

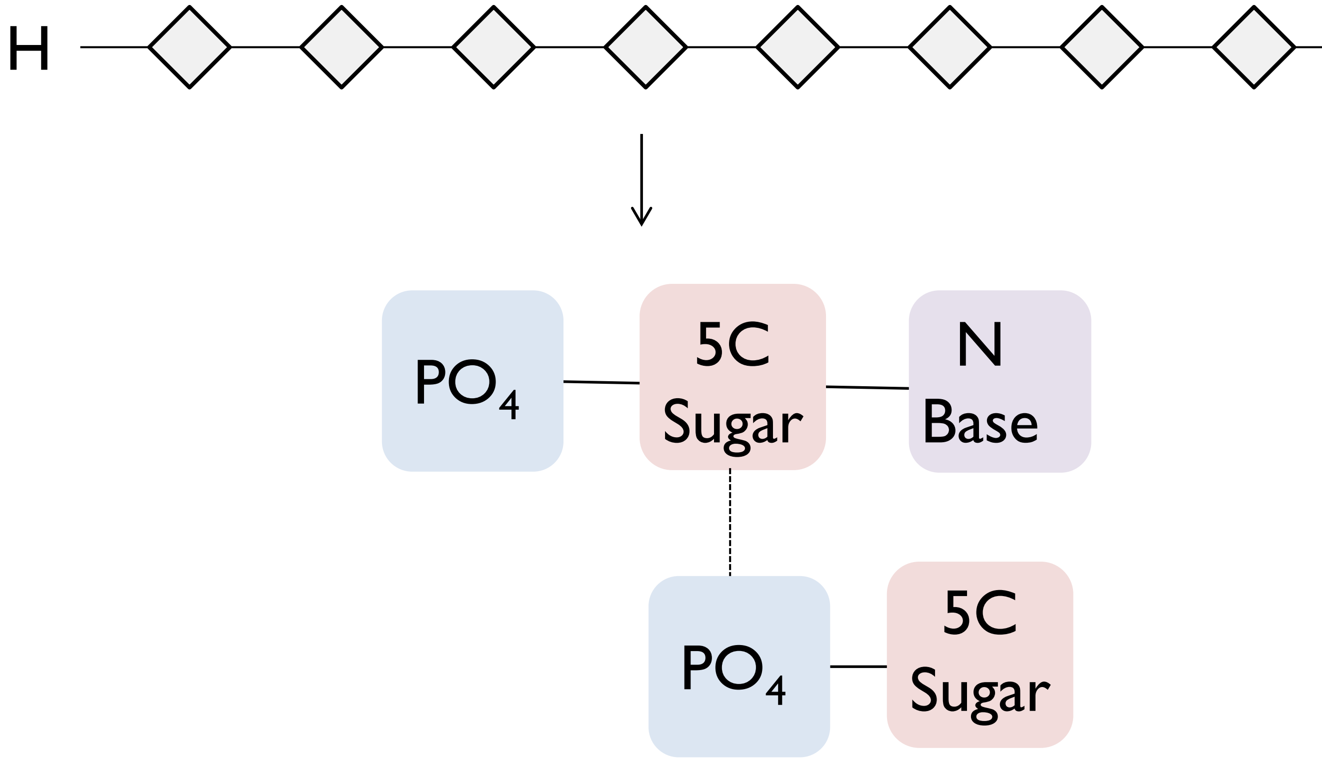
Small biomolecules: Glucose

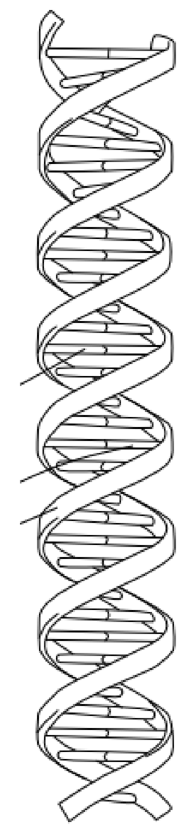
$C_6H_{12}O_6$



Mass .. 180 g mol^{-1}, Size ~ 1nm

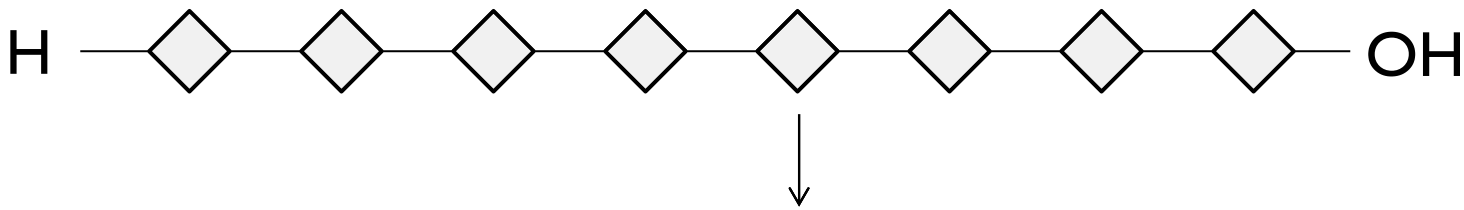
Biopolymers: DNA (deoxyribonucleic acid)

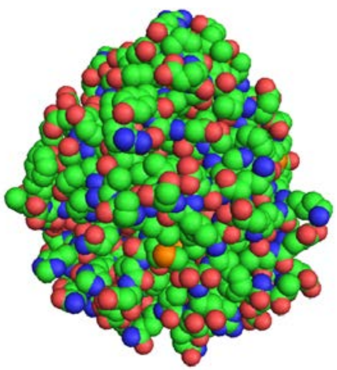


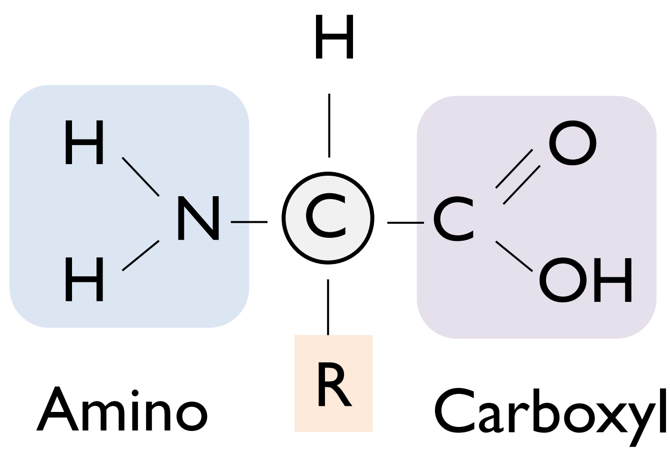


Charge ~q, Mass ~300 Dalton

Biopolymers: Protein







Enzymes
Hormones
Tissue
Transport molecules

Charge ..variable, Mass ~125 Dalton

Protein Biomarkers for Cancer

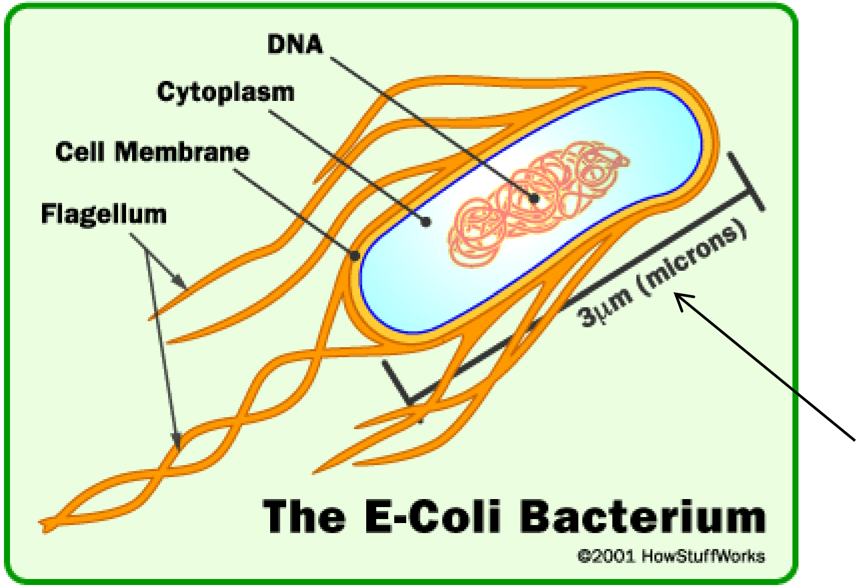
- PSA for prostrate cancer
- Cardiac Troprin T (CTnT) for heart attack
- Phosphorylation of histone protein (Y-HYAX) for ionizing exposure
- BRCA1 BRCA2 for breast & ovarian cancers

Viruses

~100 nm

No charges, but mass and tagging help identify them

Bacteria



1 mm^3 have tens of millions of bacteria
1 lb of our weight comes from bacteria

Example: How many molars in a 1000 mg Headache medicine?

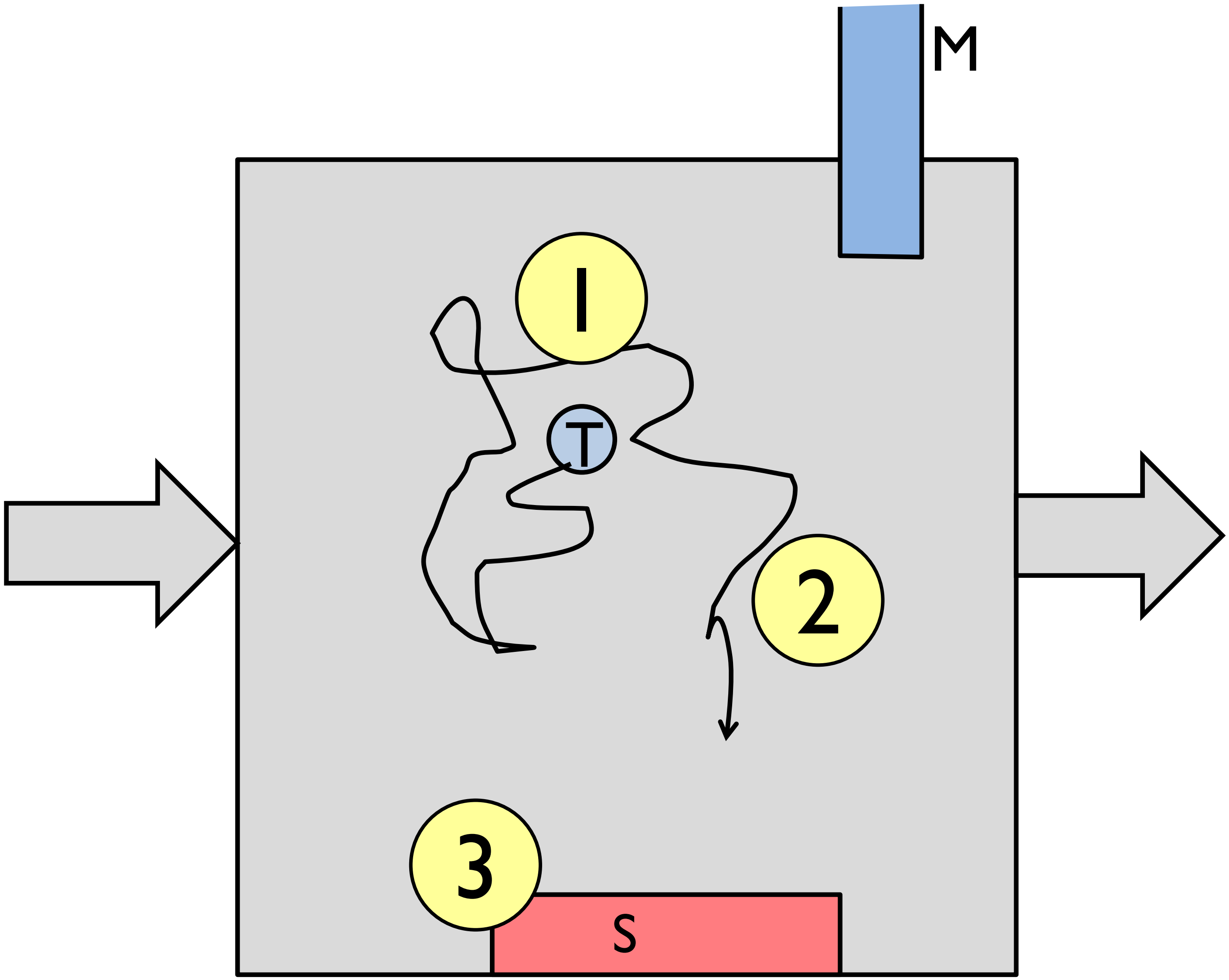
- Tylenol is $C_8H_9NO_2$. (C=12,H=1,N=14,O=16)
- 151.16 gm contains 6.023×10^{23} molecules.
- 1000 mg contains ~ 4×10^{21} molecules.
- Blood volume is 5 liters.
- Therefore, 8×10^{20} molecules/L, or the concentration is 8e20/6e23=1.32 mM.
- High concentration. Should work in minutes.

Example: Importance of Sample Volume

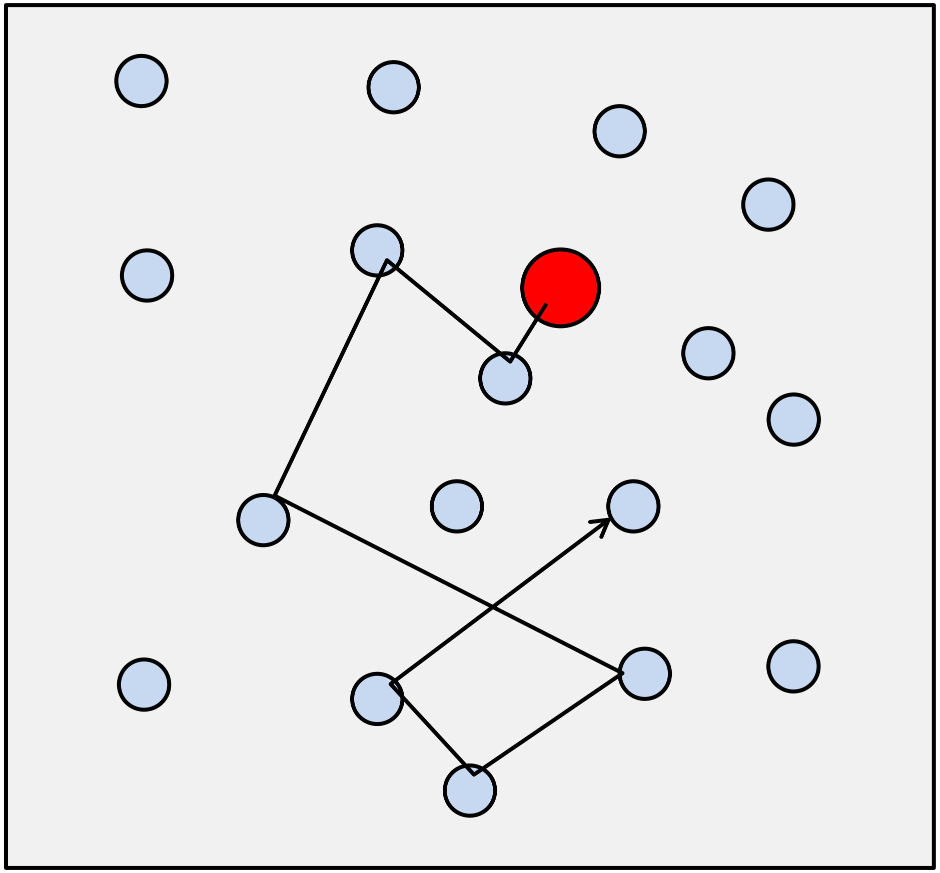
- A cancerous organ releases about 10000 cells that can be captured and lysed to detect the onset of the disease. Could a finger prick (mm^3 of blood) provide the same level of information as drawing blood (cm^3 of blood)?

- *Solution:* 1 cm^3 blood will contain $\sim 10^4/5000$ cm^3 $\sim$ 2 cells. A finger prick contains $10^4/(5000\times10^3) \sim$ 2e-3 cells – the statistical probability is close to zero that a finger prick will pick up the disease.
- Even for a cm^3 blood, the probability of detecting $x=2$ is the average. Any statistical sample will contain $P(n,x) = x^n \exp(-x)/n!$ number of particles – approximately $1/e^2 \sim 13\%$ of the time, the test will contain no diseased cell, i.e. $n=0$.

- **Sample volume is very important for any sensor analysis.**

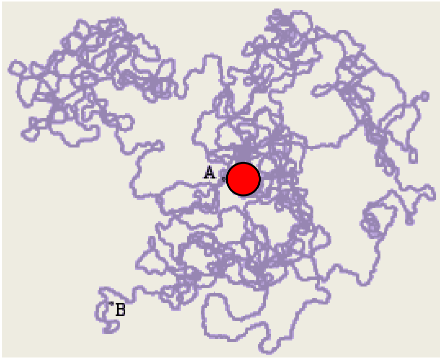

M
1
T
2
3
S

Diffusion Process – Why random walk



$$\frac{d\rho}{dt} = D\nabla^2\rho$$

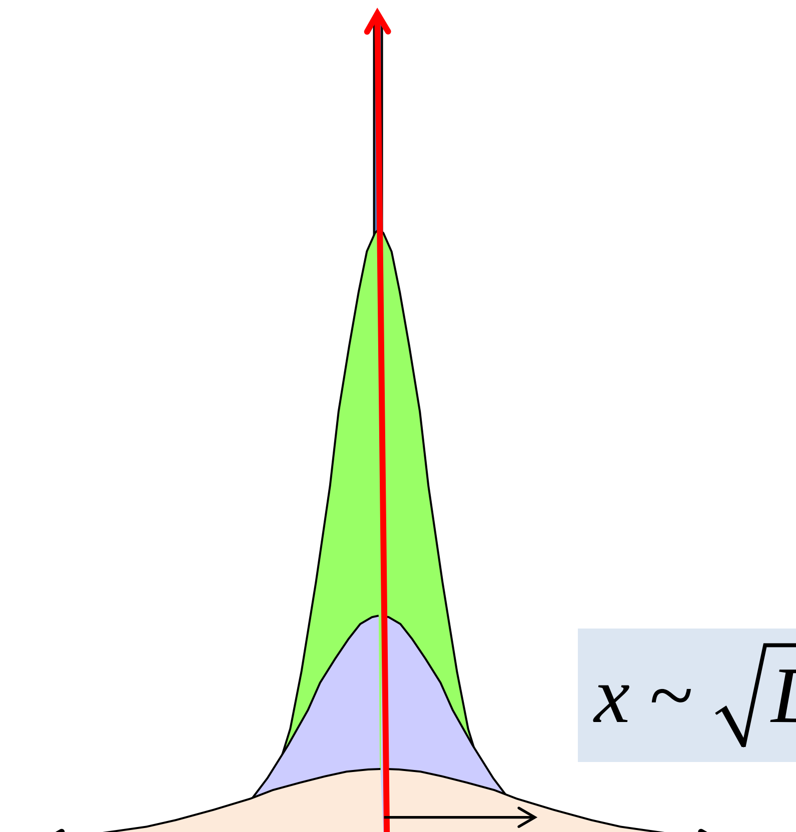
Diffusion Distance



$$\frac{d\rho}{dt} = D\nabla^2 \rho$$

$$\rho(x, t=0) = \delta(x=0)$$

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



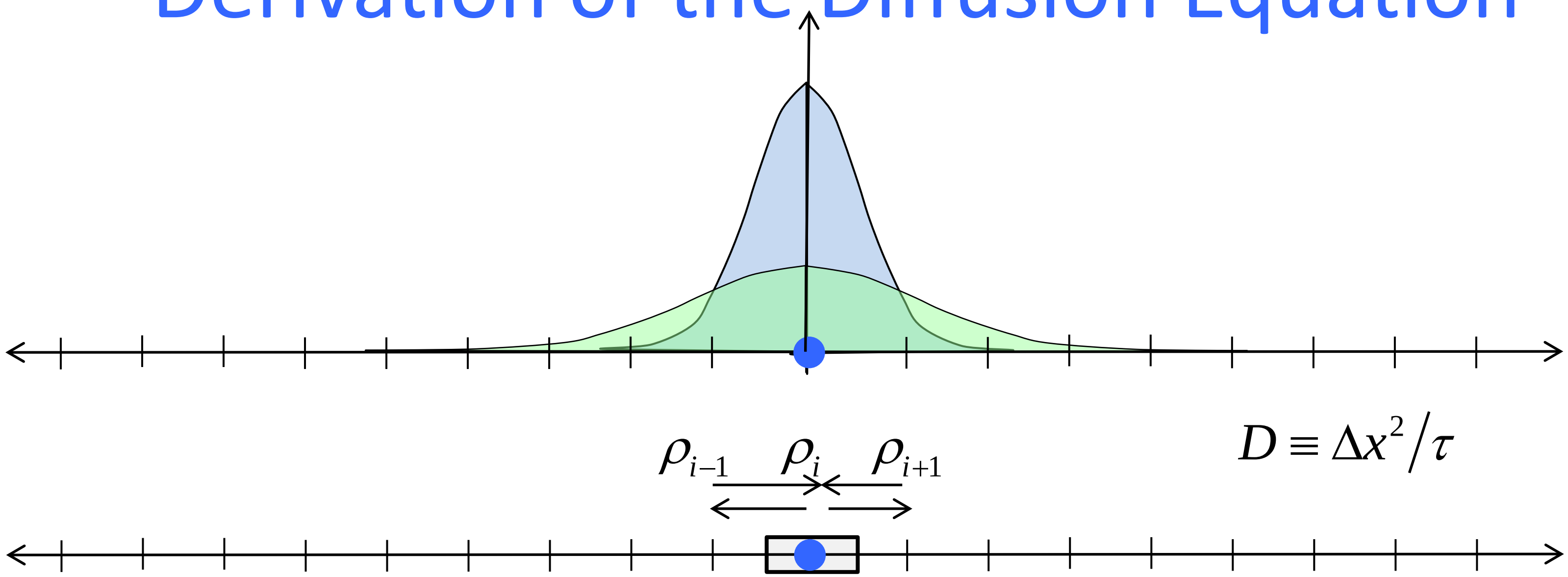
$$x \sim \sqrt{Dt}$$

$$\langle x^2 \rangle = \frac{\int_{-\infty}^{\infty} x^2 \rho(x,t)\,dx}{\int_{-\infty}^{\infty} \rho(x,t)\,dx} = 2Dt$$

Conclusions

- We are interested in broad range of biomolecules from glucose to DNA to bacteria.
- Typical sensors detect at mM range, nanobiosensors may detect at fM range.
- Classical theory of diffusion suggests that a molecule diffuses a distance of $\sim(Dt)^{1/2}$.

Appendix: Derivation of the Diffusion Equation



$$D \equiv \Delta x^2 / \tau$$

$$\rho_i(t+\Delta t) - \rho_i(t) = \frac{\Delta t}{\tau}\left[\frac{1}{2}\rho_{i-1}(t) + \frac{1}{2}\rho_{i+1}(t) - \frac{1}{2}\rho_i(t) - \frac{1}{2}\rho_i(t)\right]$$

$$\frac{\rho_i(t+\Delta t) - \rho_i(t)}{\Delta t} = D\left[\frac{\rho_{i-1}(t) + \rho_{i+1}(t) - 2\rho_i(t)}{2\Delta x^2}\right]$$

$$D \equiv \frac{(\Delta x)^2}{\tau}$$

$$\frac{d\rho}{dt} = D\frac{d^2\rho}{dx^2} = D\nabla^2\rho$$