

Diffusion in Biological Systems

class - 15 (17.10.24)

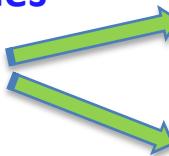
LS2103 (Autumn 2024)

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<https://www.iiserkol.ac.in/~n.sengupta/>

detour: Binomial Distribution

Only 2 possible outcomes
of an event with
 N attempts:



Success, probability s

Failure, probability $f = (1 - s)$

Mean success ,

$$\langle n \rangle = s \cdot N$$

n = No. of success

Probability of ['n' success and $(N-n)$ failure] is ,

pay attention
to the notation

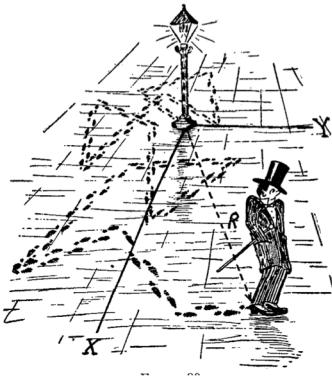
$$P(n, s, N) = \frac{N!}{n! (N-n)!} s^n (1-s)^{N-n}$$

The sum of probabilities for the (n, s, N) is 1.0, ie .

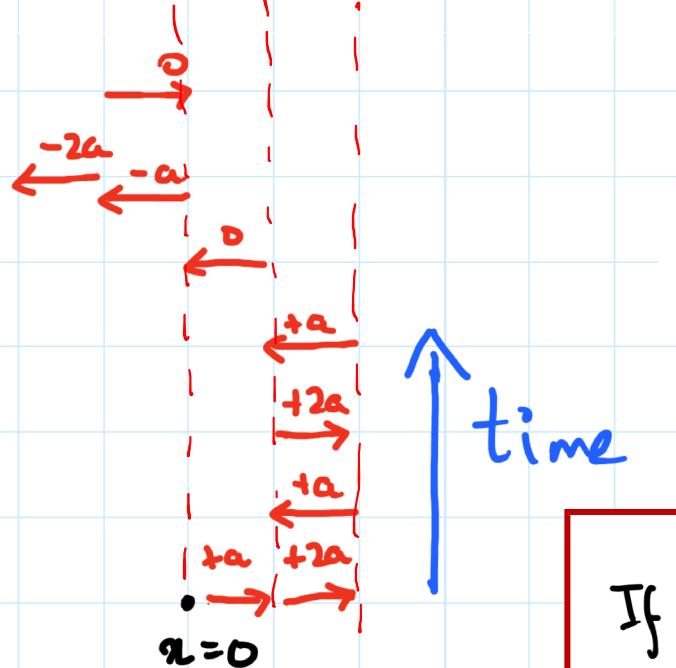
$$\sum_{n=0}^N P(n, s, N) = 1.0$$

Random Walk

Here, 'a' is the step length, and 'p' is the 'front step probability':



1-Dimensional Random Walk



$p = 0.5$ for a truly r. w.

Mean Displacement in "N" steps,
and "n" forward steps is,

$$\langle x \rangle = \sum_{n=0}^N P(n, p, N) [na - (N-n)a]$$

$$= a \sum_{n=0}^N \frac{N!}{n!(N-n)!} p^n (1-p)^{N-n} (2n-N)$$

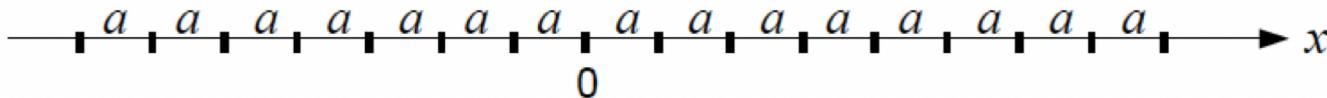
$$= \boxed{Na(2p-1)}$$

skipping steps

If probability of front and back step are equal,

$$\langle x \rangle = 0$$

Mean displacement in unbiased walk: a simpler argument



a ---Length of each step

$x_0=0$ ---start point

x_n ---position after the n -th step

$k_n a$ ---displacement of the n -th step with $P(k_n = 1) = P(k_n = -1) = 1/2$

$k_n = +1$ (right move)
 $= -1$ (left move)

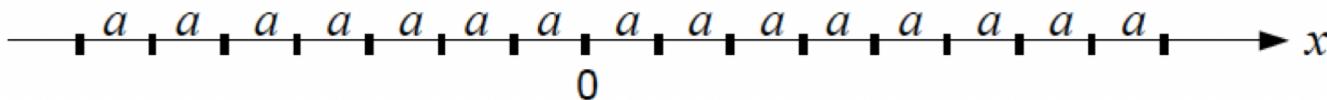
$$x_n = x_{n-1} + k_n a$$

$$\begin{aligned}\langle x_n \rangle &= \langle x_{n-1} + k_n a \rangle \\ &= \langle x_{n-1} \rangle + a \langle k_n \rangle \\ &= \langle x_{n-2} \rangle + a \langle k_{n-1} \rangle \\ &= \dots \langle x_1 \rangle + a \langle k_0 \rangle\end{aligned}$$

A truly random
walk.

$$\langle x_n \rangle = \langle x_0 \rangle = 0$$

Mean squared displacement in 1-dimension



a ---Length of each step

$x_0=0$ ---start point

x_n ---position after the n-th step

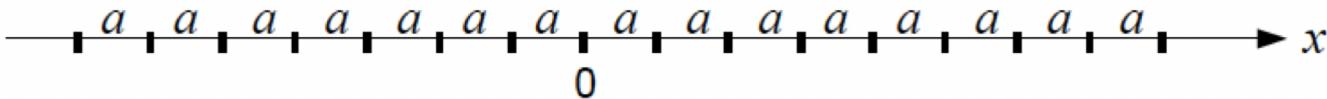
$k_n a$ ---displacement of the n-th step with $P(k_n=1)=P(k_n=-1)=1/2$

$$\begin{aligned}\langle x_n^2 \rangle &= \langle (x_{n-1} + k_n a)^2 \rangle \\&= \langle x_{n-1}^2 \rangle + \langle k_n^2 \rangle a^2 + 2a \langle k_n x_{n-1} \rangle \\&= \langle x_{n-1}^2 \rangle + a^2 = \langle x_{n-2}^2 \rangle + 2a^2\end{aligned}$$

$$\langle k_n^2 \rangle = \frac{(+)^2 + (-1)^2}{2} = 1$$

$$\begin{aligned}\langle k_n x_{n-1} \rangle &= x_{n-1} \times (+) \times P(+) \\&\quad + x_{n-1} \times (-) \times P(-) \\&= x_{n-1} [(+) \times (\tfrac{1}{2}) + (-) \times (\tfrac{1}{2})] \\&= 0\end{aligned}$$

Mean squared displacement in 1-dimension



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$x_0=0$ ---start point

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$k_n a$ ---displacement of the n-th step with $P(k_n=1)=P(k_n=-1)=1/2$

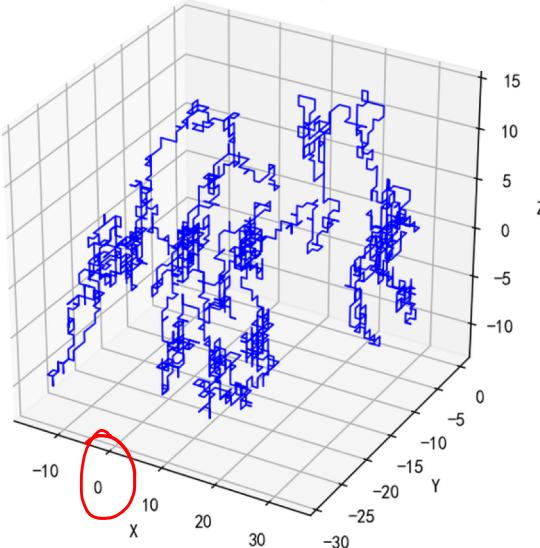
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By iteration, for N steps,

$$\boxed{\langle x_N^2 \rangle = N a^2}$$

Mean squared displacement in 2- or 3- dimensions

Random walk in 3D space

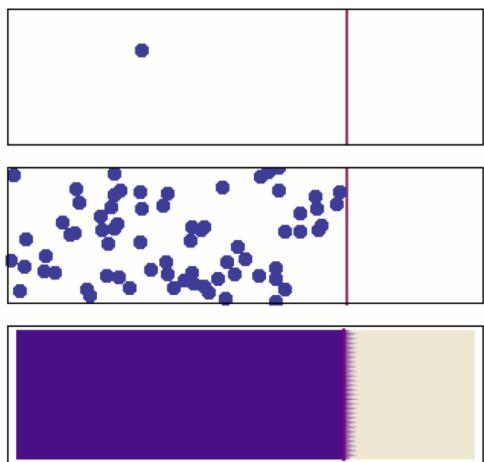


HW. Show that in 'd' spatial dimensions, $\langle r_N^2 \rangle = (d)Na^2$

Work out all steps.

$$\begin{aligned}\langle r_N^2 \rangle &= \langle x_N^2 + y_N^2 + z_N^2 \rangle \\ &= \langle (x_{N-1} + k_{xN}a)^2 \rangle + \dots + \dots \\ &= \left(\langle x_{N-1}^2 \rangle + 2a \langle x_{N-1} k_{xN} \rangle + \langle k_{xN}^2 \rangle a^2 \right) \\ &\quad + (\dots) + (\dots)\end{aligned}$$

Diffusion: average spatio-temporal pattern of random walks



$$\langle \mathbf{r}_N^2 \rangle = (d)Na^2$$

τ : time taken for step $(+a)$ or $(-a)$

T: total elapsed time

No. of steps, $N = \frac{T}{\tau}$

define **Diffusion Coefficient**: $D \equiv \frac{a^2}{2\tau}$

In 2-dimensions:

$$\begin{aligned}\langle r_n^2 \rangle &= 2Na^2 \\ &= 2\left(\frac{T}{\tau}\right)a^2 \\ &= (2T)(2D)\end{aligned}$$

Diffusion Relationship:

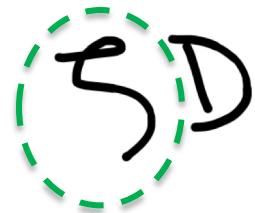
$$\boxed{\langle r_n^2 \rangle = 4DT}$$

HW. Generalize to ' d ' dimensions, ie. $\langle \mathbf{r}_N^2 \rangle = (2d)DT$

Diffusion: average spatio-temporal pattern of random walks

Diffusion is related to friction

EINSTEIN RELATIONSHIP



$$\xi_D = k_B T$$

Viscous Friction Coefficient

→ Result associated with
FLUCTUATION-DISSIPATION
Theorem.

At a given temperature, viscosity is inversely proportional to the diffusion coefficient.

STOKES-EINSTEIN RELATIONSHIP

$$6\pi \eta a D = k_B T$$

viscosity
radius

→ Strictly for a spherical particle of radius 'a'.

Structural Databases of mostly experimental protein structures:

The screenshot shows the homepage of the RCSB PDB (Protein Data Bank) website. At the top, there is a navigation bar with links for "Getting Started", "New Tab", and "(1) IISER Kolkata We...". Below the navigation bar is a dark blue header with the "RCSB PDB" logo and a "MyPDB" button. The main content area features a search bar with the placeholder "Search by PDB ID, author, macromolecule, sequence, or ligands" and a "Go" button. To the left is a sidebar with links for "Welcome", "Deposit", "Search", "Visualize", "Analyze", "Download", and "Learn". The central content area includes a section titled "A Structural View of Biology" with text about the 3D shapes of proteins, nucleic acids, and complex assemblies. It also features a banner for the "2018 Video Challenge for High School Students" and a "September Molecule of the Month" section featuring a large blue molecular model of Phytase with a red ligand.

Getting Started New Tab (1) IISER Kolkata We...

RCSB PDB Deposit Search Visualize Analyze Download Learn More

MyPDB

RCSB PDB PROTEIN DATA BANK 144042 Biological Macromolecular Structures Enabling Breakthroughs in Research and Education

PDB-101 Worldwide Protein Data Bank EMDDataBank Worldwide Protein Data Bank Foundation

Search by PDB ID, author, macromolecule, sequence, or ligands

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Go

Welcome

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A Structural View of Biology

This resource is powered by the Protein Data Bank archive-information about the 3D shapes of proteins, nucleic acids, and complex assemblies that helps students and researchers understand all aspects of biomedicine and agriculture, from protein synthesis to health and disease.

As a member of the wwPDB, the RCSB PDB curates and annotates PDB data.

The RCSB PDB builds upon the data by creating tools and resources for research and education in molecular biology, structural biology, computational biology, and beyond.

Award-Winning Videos on Antibiotic Resistance

2018 Video Challenge for High School Students

September Molecule of the Month

Phytase

Latest Entries As of Tuesday Sep 04 2018

Features & Highlights

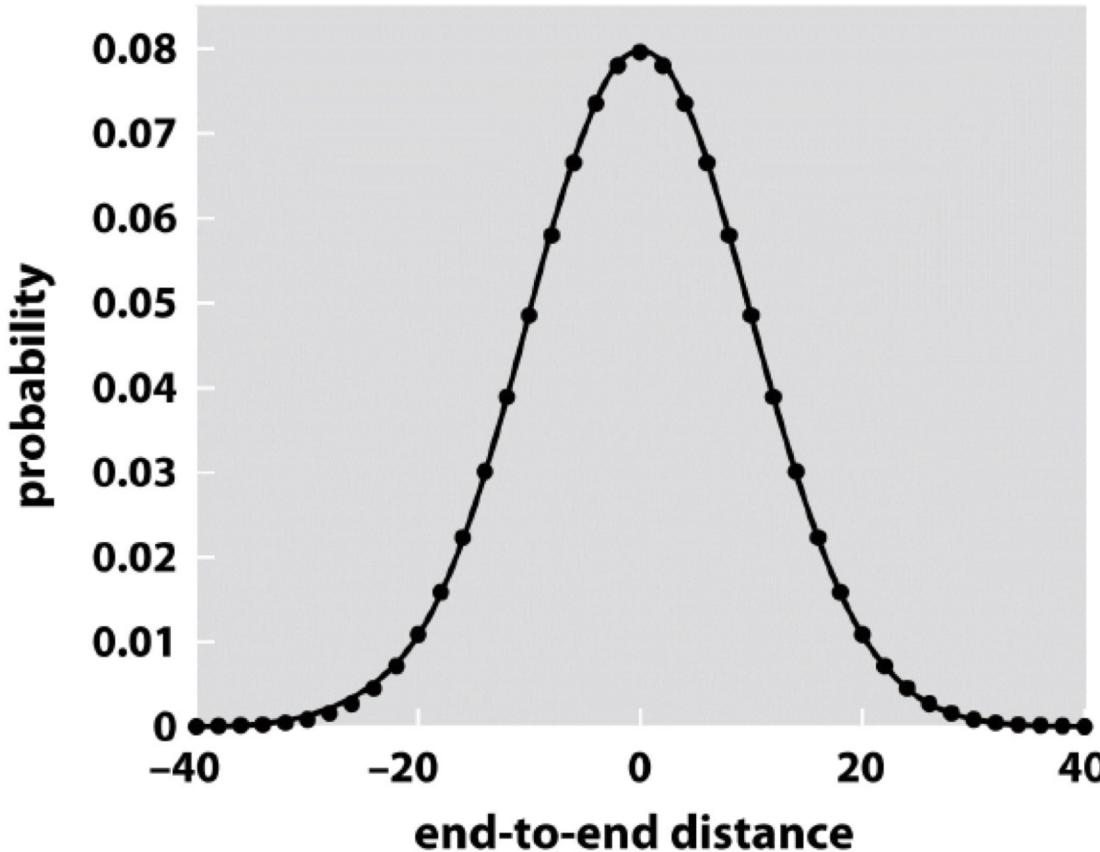
New Architecture and Services

News Publications

Folding has some similarities to a “diffusive process”

Distribution of end-to-end distance

$$P(R; N) = \frac{1}{\sqrt{2\pi Na^2}} e^{-R^2/2Na^2}$$



Parameter: $N=100, a=1/2$

Line: Gaussian distribution

Dot: binomial distribution



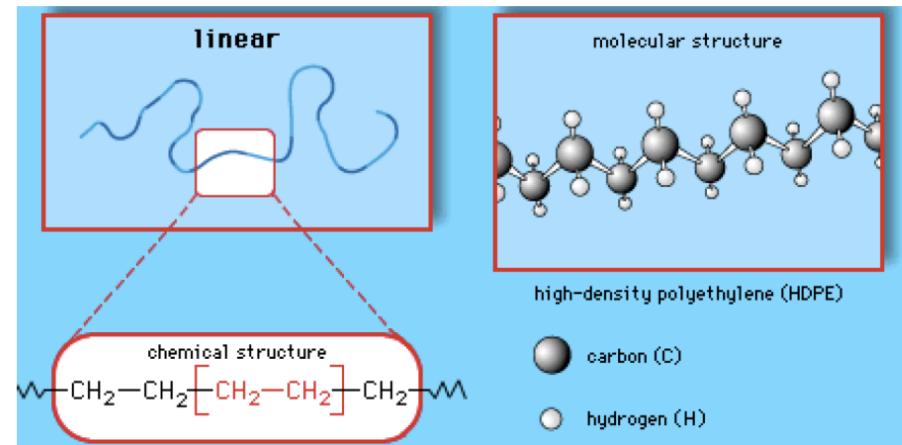
$$\langle R \rangle = 0, \quad \langle R^2 \rangle = Na^2$$

Structural Properties

Gross structure

Fine structure

Well approximated by harmonic approximation (when no chemical changes occur)



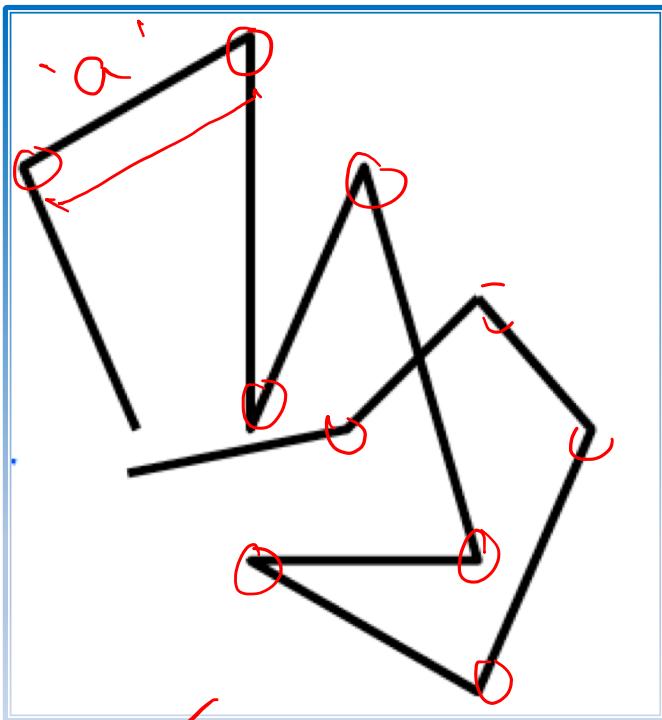
Bond length	$x_0=1.44\text{\AA}$	$k_1(x-x_0)^2/2$ $k_1 \sim 57\text{eV/\AA}^2$	$\sqrt{\langle(x-x_0)^2\rangle} \sim 10^{-2}\text{\AA}$
Bond angle	$\alpha_0=120^\circ$	$k_2(\alpha-\alpha_0)^2/2$ $k_2 \sim 84\text{eV}$	$\sqrt{\langle(\alpha-\alpha_0)^2\rangle} \sim 10^{-2}\text{rad}$

~2-3 order of magnitude greater than $k_B T$

Structural Properties

Gross structure

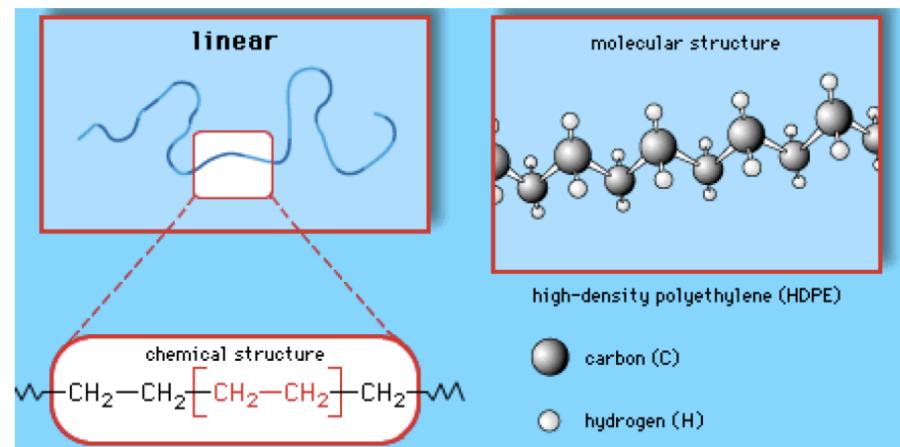
Relative stiffness determines gross structure



- Persistence length (ξ_p) is a measure of the extent of rigidity of the (bio)polymer
- Freely jointed hypothetical segments

Fine structure

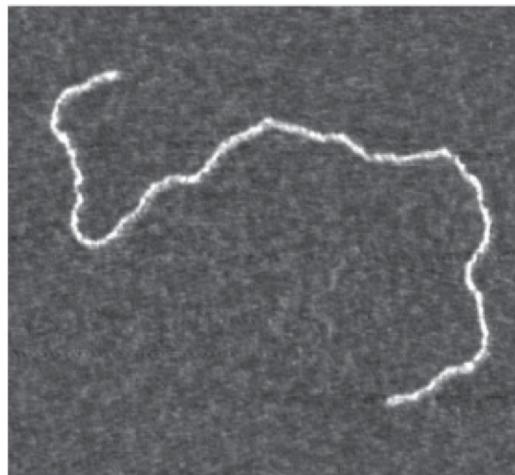
Well approximated by harmonic approximation (when no chemical changes occur)



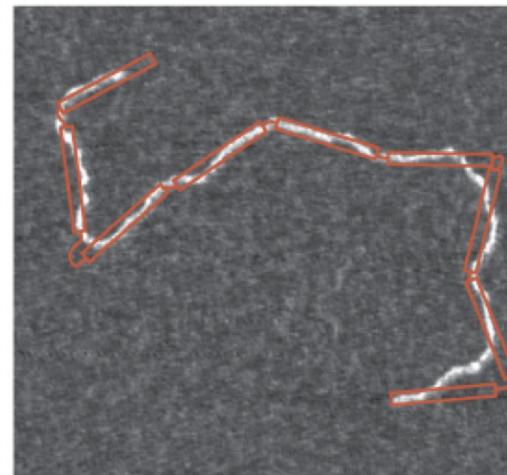
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~2-3 order of magnitude greater than $k_B T$

Bio-polymers: considered as rigid segments, connected via freely rotating hinges



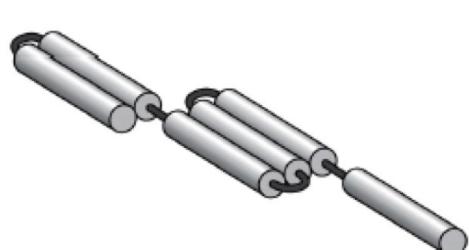
DNA on a surface (AFM image)



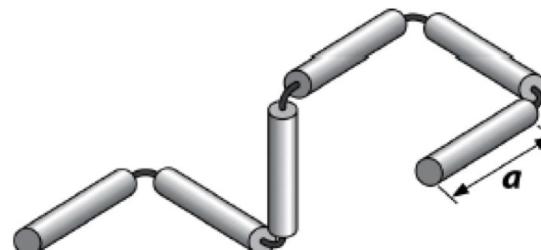
Representation of DNA as random walk

Condition: $L \gg \xi_p$

Wiggins et al.,
Nature Nanotech., 2006, 1, 37



1D random walk model



3D random walk model

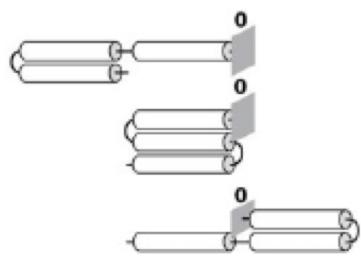
Folding has some similarities to a “diffusive process”

Distribution of end-to-end distance similar to random walk model:

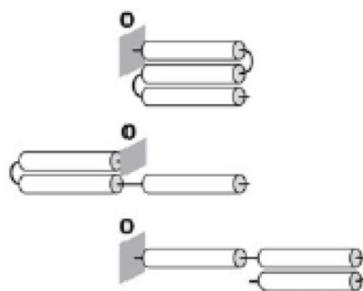
- **N steps, with n_r to the right**



$$] n_r=0, W=1$$



$$] n_r=1, W=3$$

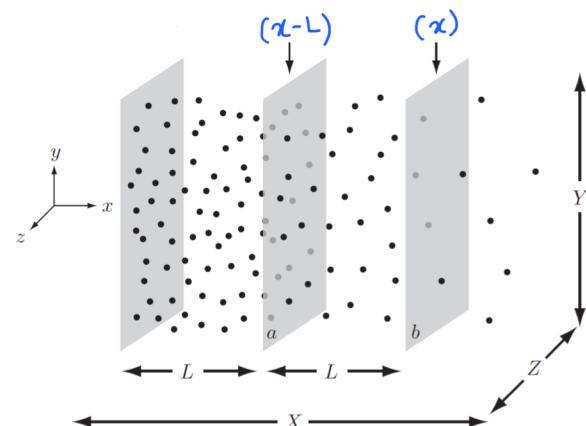
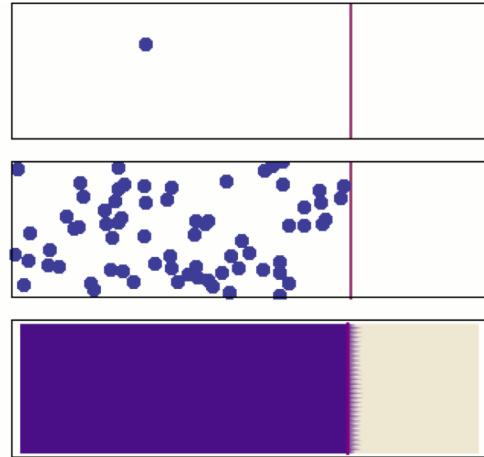


$$] n_r=2, W=3$$

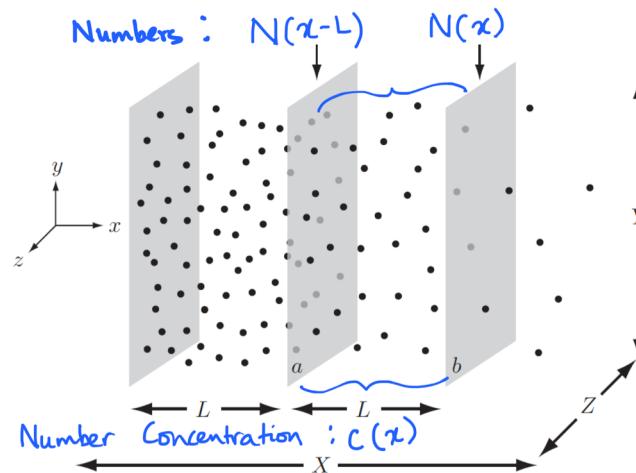
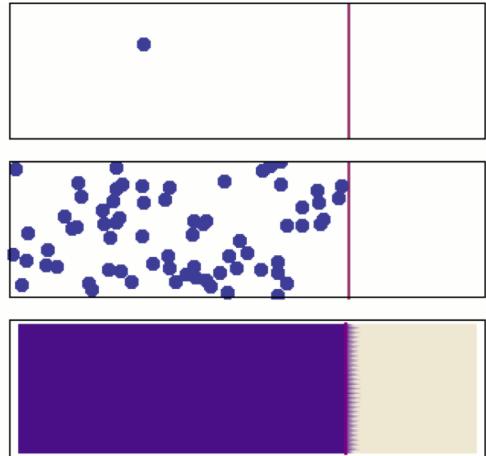


$$] n_r=3, W=1$$

Flux: movement of particles passing through unit area in unit time. Units?



What are the equations guiding flux?



Concentration does not vary along Y and Z

No. of particles ^{overall}
crossing Left \rightarrow Right

$$= \frac{1}{2} [N(x-L) - N(x)]$$

$$\lim_{L \rightarrow 0}$$

$$\frac{N(x-L) - N(x)}{L} = -\frac{dN}{dx}$$

$$= -\frac{d}{dx} [(Y \cdot Z \cdot L) c(x)]$$

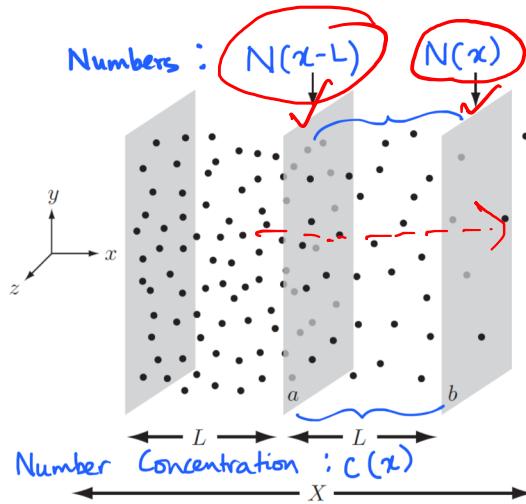
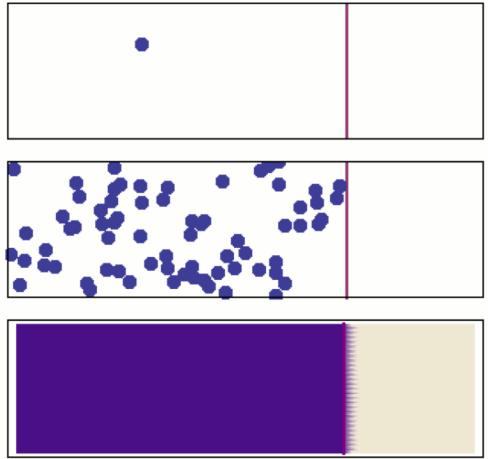
$$\lim_{L \rightarrow 0}$$

$$\frac{1}{2} [N(x-L) - N(x)]$$

$$= -\left(\frac{YZL^2}{2}\right) \frac{dc(x)}{dx}$$

✓ $N(x-L)$; N at the position $(x-L)$.

Flux (j): Number of particles passing through unit area in unit time



$$\text{Flux, } j = -\frac{(YZL^2)}{2(Y \cdot Z \cdot \Delta t)} \frac{dc}{dx}$$

$$D = L^2 / (2 \Delta t)$$

Fick's Law

$$j = -D \frac{dc(x)}{dx}$$

No. of particles crossing Left \rightarrow Right

$$= \frac{1}{2} [N(x-L) - N(x)]$$

$$\lim_{L \rightarrow 0}$$

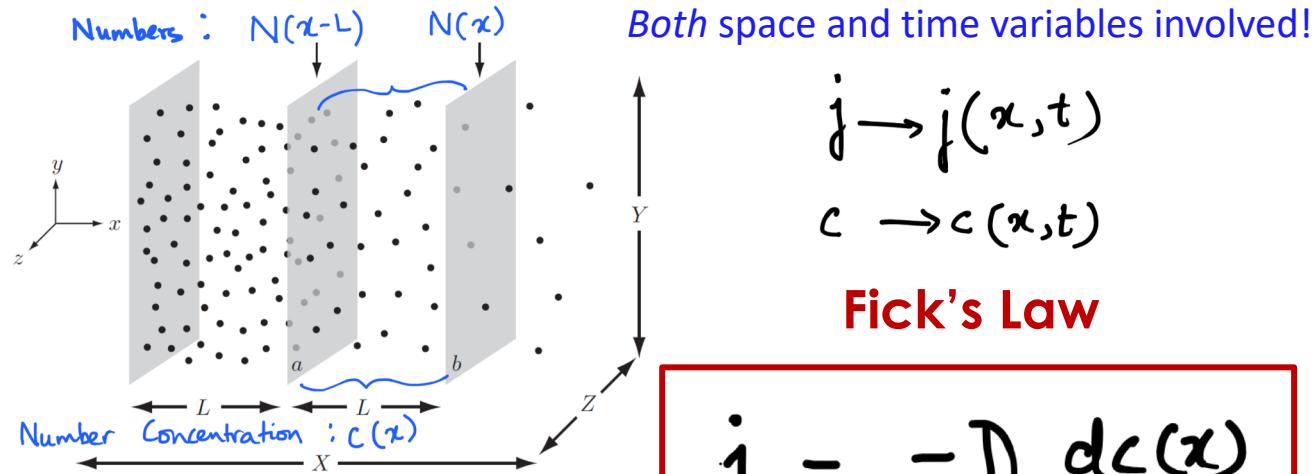
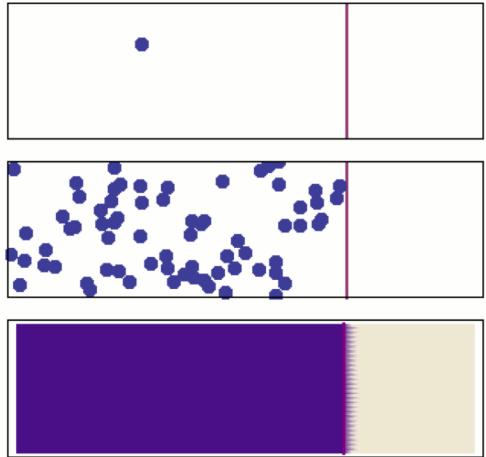
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$$\lim_{L \rightarrow 0} \frac{1}{2} [N(x-L) - N(x)]$$

$$= -\left(\frac{YZL^2}{2}\right) \frac{dc(x)}{dx}$$

Flux (j): Number of particles through unit area in unit time



(Proof not shown in class)

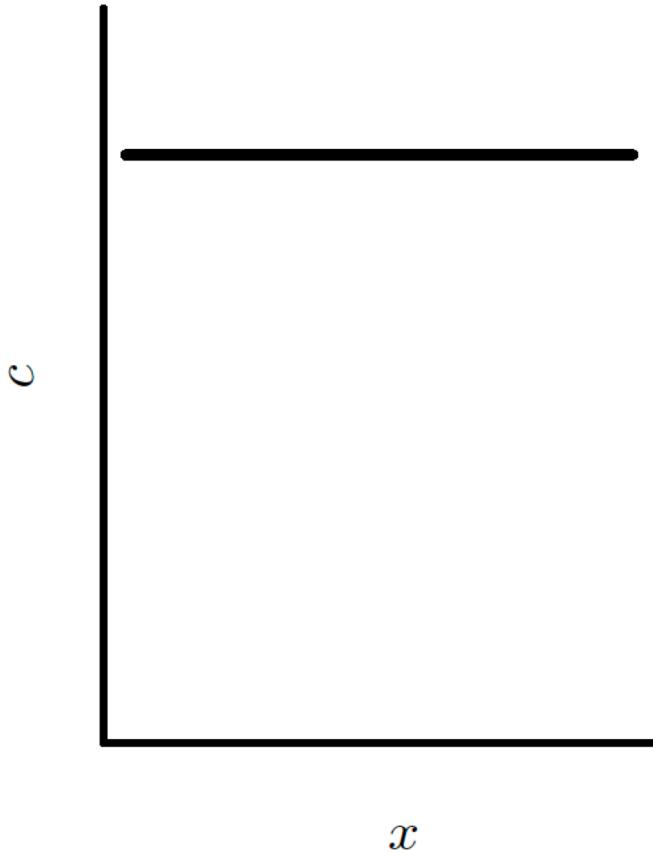
*Time derivative of concentration equals
Space derivative of flux*

Fick's Diffusion Equation

$$\frac{\partial c}{\partial t} \equiv - \frac{\partial j}{\partial x}$$

$$\frac{\partial c(x,t)}{\partial t} = +D \frac{\partial^2 c(x,t)}{\partial x^2}$$

How do the concentration profiles evolve in time?

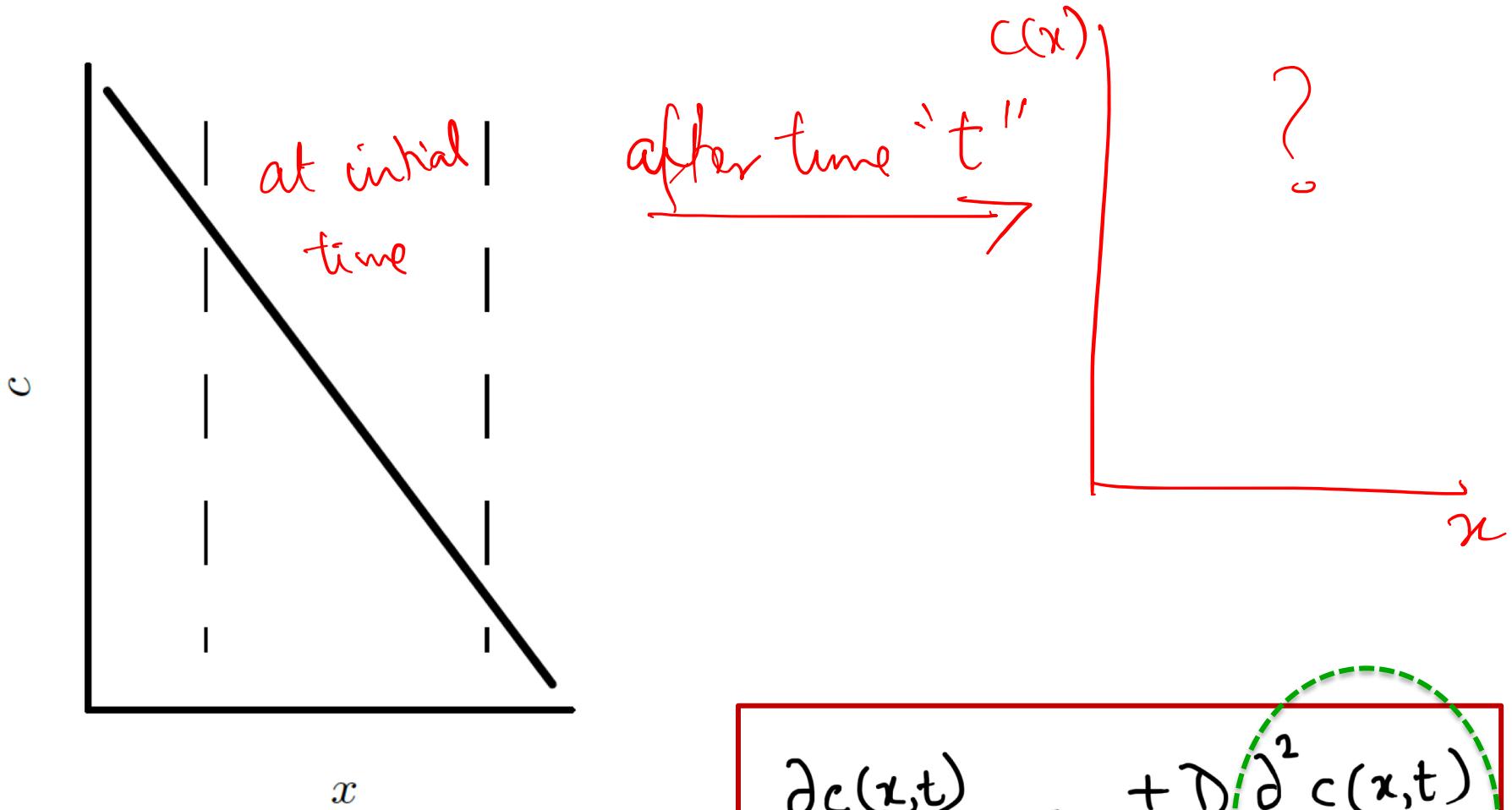


✓ Initial profile .

Curvature of conc. profile

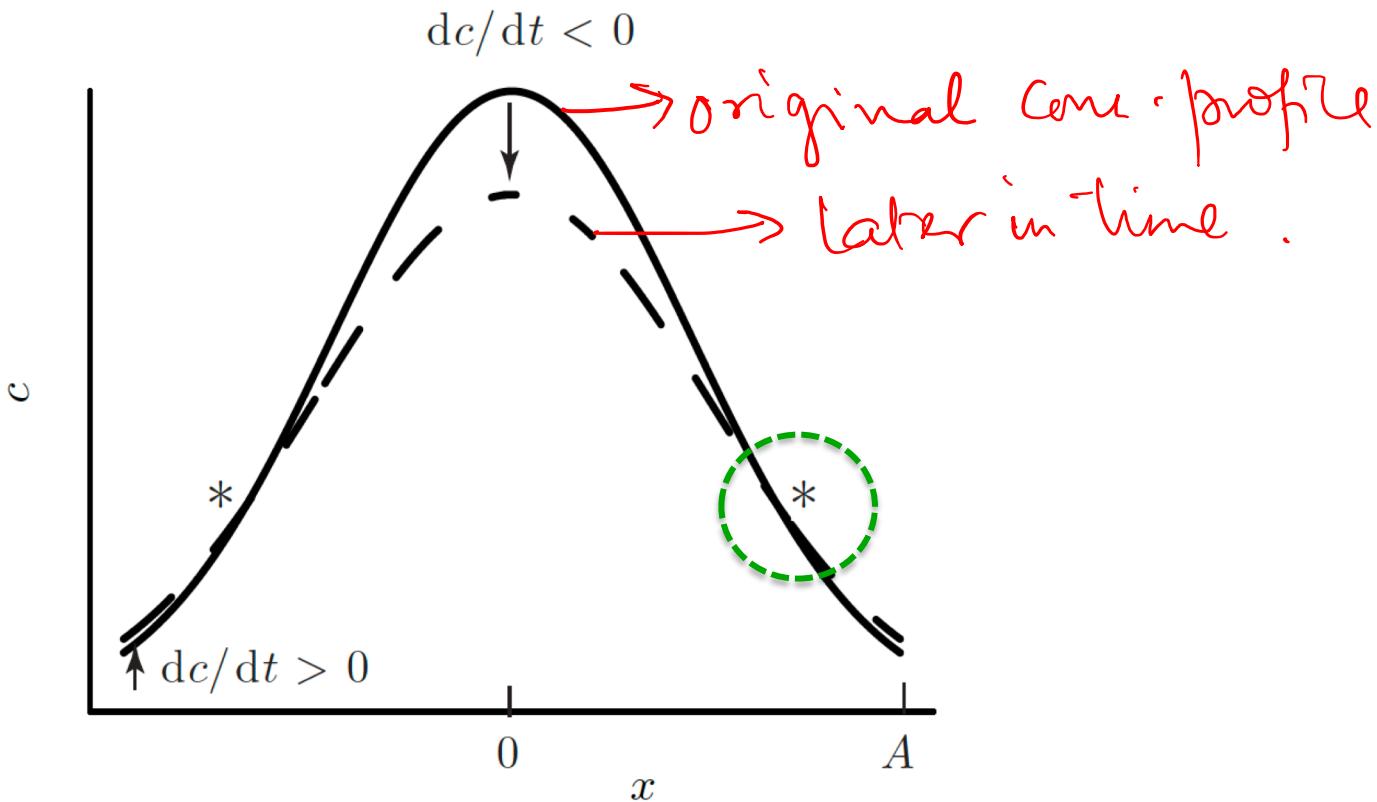
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