# Diffusion in Biological Systems

class - 14 (16.10.24)

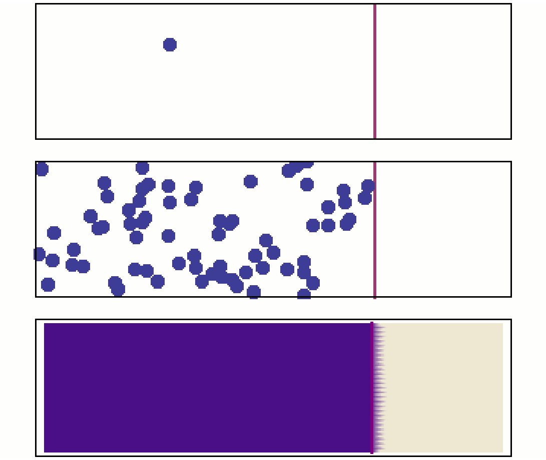
LS2103 (Autumn 2024)

Dr. Neelanjana Sengupta

Associate Professor, DBS

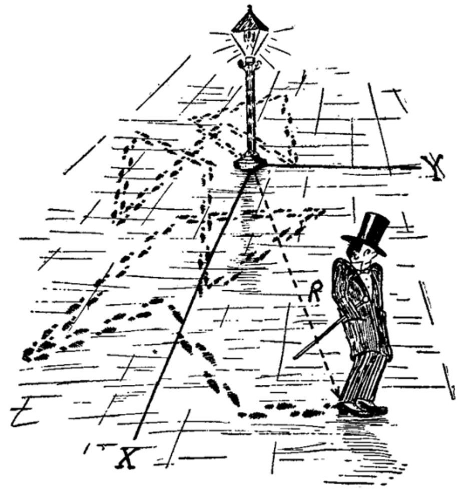
https://www.iiserkol.ac.in/~n.sengupta/

# In General: Random Biological Processes



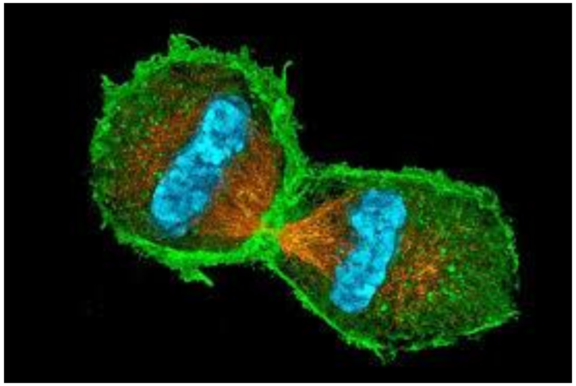
**Diffusion**

https://commons.wikimedia.org/w/index.php?curid=8995324



**Random Walk**

George Gamow, 1961

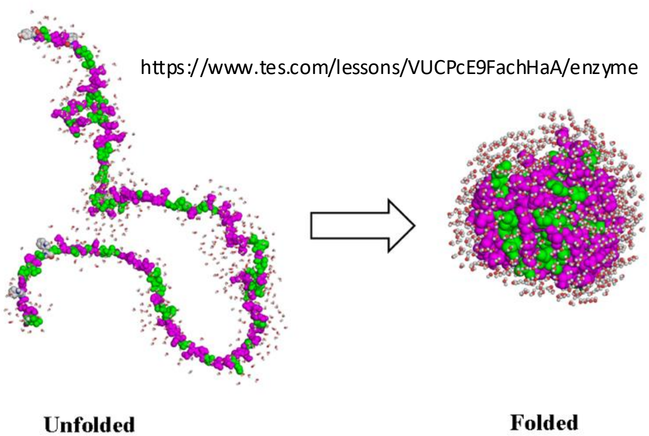


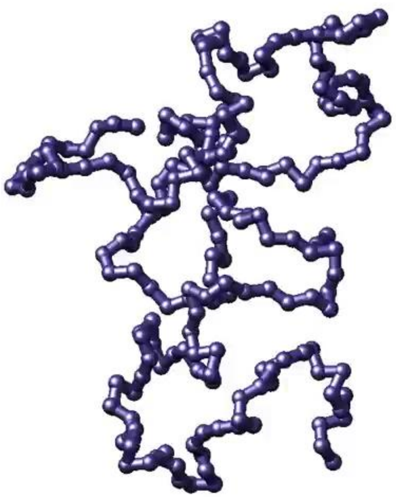
**Cell division**

https://www.thoughtco.com/mitosis-and-cell-division-quiz-4078417

**Polypeptide collapse**

https://www.tes.com/lessons/VUCPcE9FachHaA/enzyme

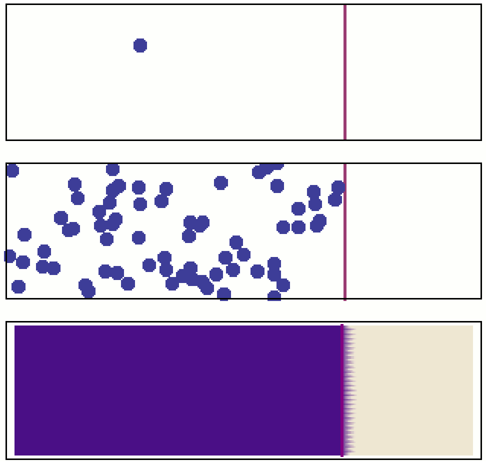


**Polymer collapse**

https://www.youtube.com/watch?v=ek9vd7_PDjk

# **Diffusion**: unbiased, random movement in space and time



$$\langle r_N^2 \rangle = (d)Na^2$$

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

T: total elapsed time

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

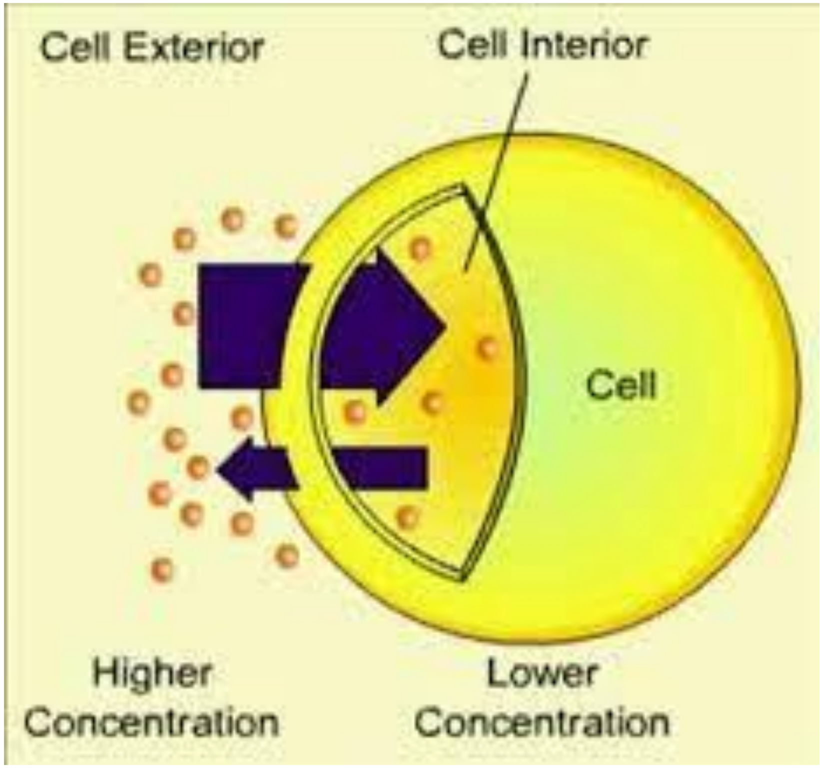
**Diffusion Coefficient:** $D \equiv \dfrac{a^2}{2\tau}$

**Diffusion Relationship:**

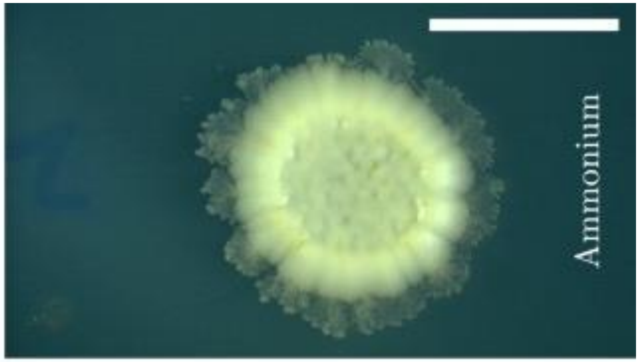
$$\boxed{\langle r_N^2 \rangle = (2d).D.(\text{elapsed time})}$$

# Examples: Diffusion within Biological Systems

**Molecular passage**



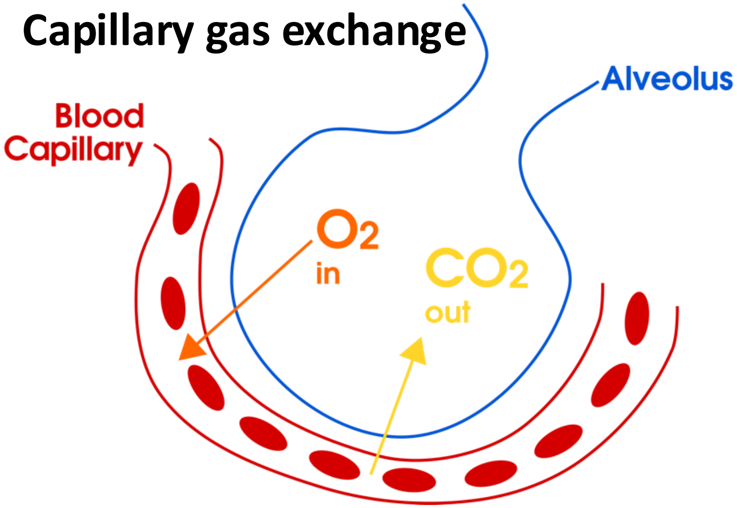

**Diffusion limited growth of microbial colonies**




(b) SLAD$^{-N}$ with ammonium added

Tronnolone et al., Scientific Reports 2018

**Capillary gas exchange**



# Examples: Diffusion within Biological Systems

## Apparent Diffusion Coefficient (ADC) as a Cancer Biomarker

OPEN ACCESS Freely available online PLOS | ONE

**Apparent Diffusion Coefficient (ADC) Value: A Potential Imaging Biomarker That Reflects the Biological Features of Rectal Cancer**

**Yiqun Sun[1¶], Tong Tong[1¶], Sanjun Cai[2], Rui Bi[3], Chao Xin[1], Yajia Gu[1*]**

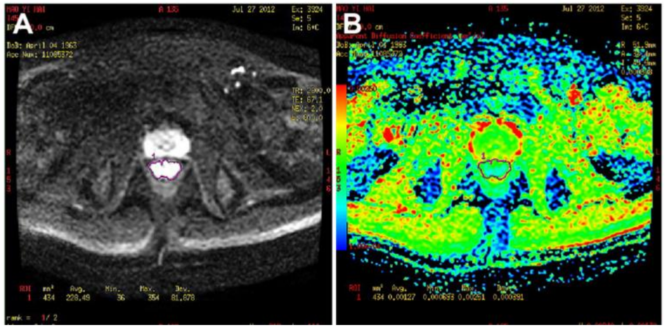
Int Urol Nephrol (2014) 46:555–561
DOI 10.1007/s11255-013-0557-1

UROLOGY - ORIGINAL PAPER

**Apparent diffusion coefficient value as a biomarker reflecting morphological and biological features of prostate cancer**

**Hyeyeol Bae · Soichiro Yoshida · Yoh Matsuoka · Hiroshi Nakajima · Eisaku Ito · Hiroshi Tanaka · Miyako Oya · Takayuki Nakayama · Hideki Takeshita · Toshiki Kijima · Junichiro Ishioka · Noboru Numao · Fumitaka Koga · Kazutaka Saito · Takumi Akashi · Yasuhisa Fujii · Kazunori Kihara**

**ADC maps**

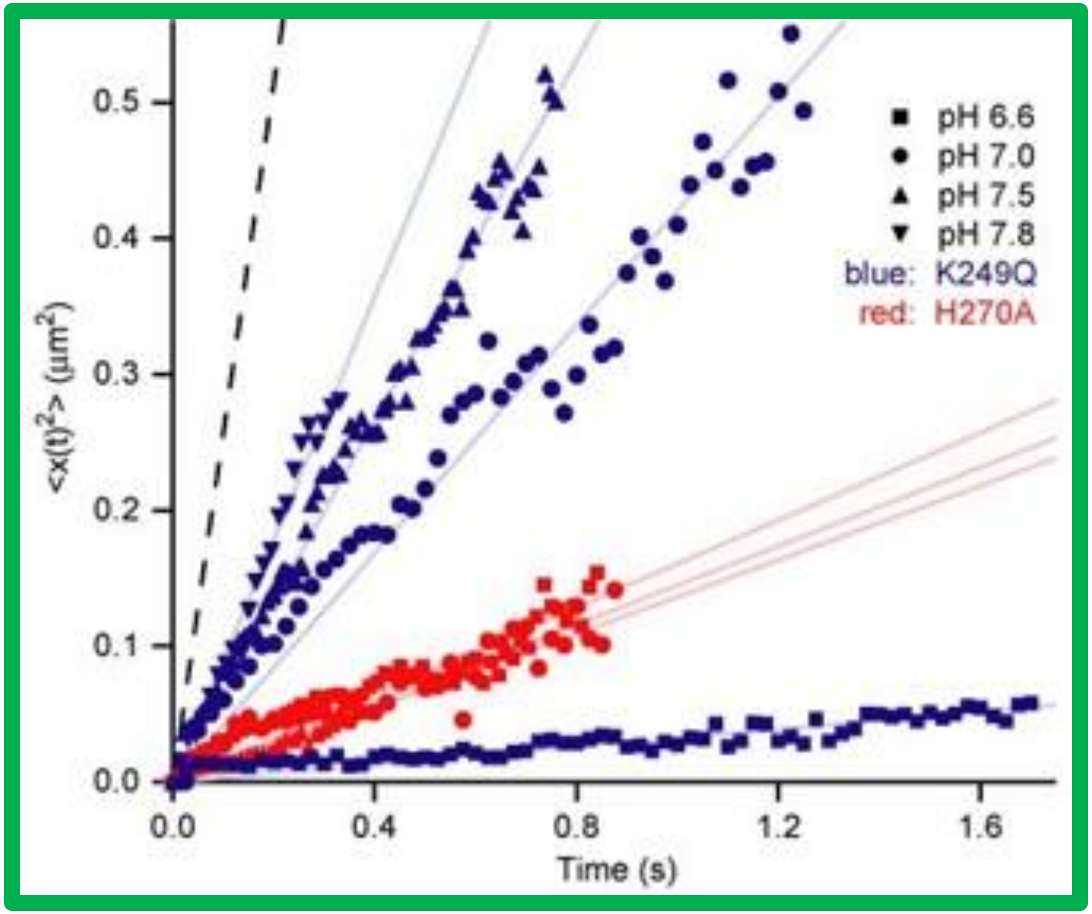



Diffusion Tensor

$$\mathcal{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

# Estimation of Diffusion Coefficient

"Single molecule" experiments




Sunny Xie Lab, Harvard Univ.

# detour: Binomial Distribution

Only **2 possible outcomes** of an event with ***N*** attempts:

- **Success**, probability ***s***
- **Failure**, probability ***f = (1 – s)***

Mean success, $\langle n \rangle = s . N$

***n*** = No. of success

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

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

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

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

# 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

Variance in success, $\sigma^2 = s(1-s)N$

Standard deviation, $\sigma = \sqrt{s(1-s)N}$

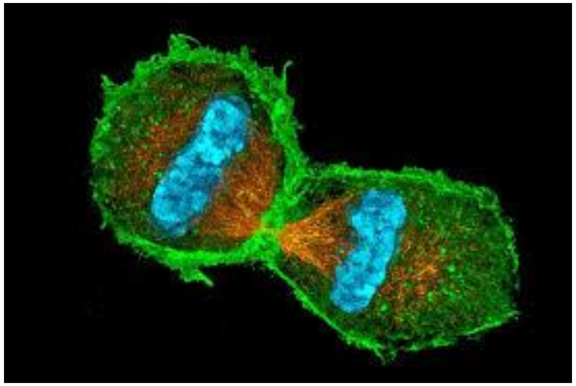
The ratio of std. dev. to mean $= \sqrt{\frac{1-s}{sN}} \propto \frac{1}{\sqrt{N}}$

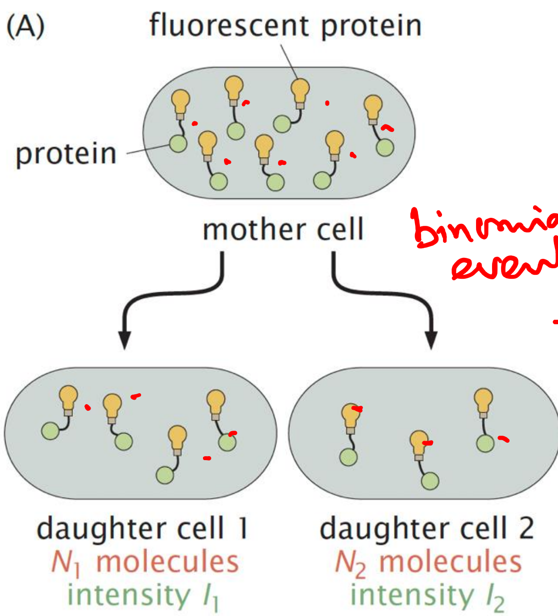
$r = \frac{\sigma}{\mu}$

# Molecular Partitioning During Cell Division: Binomial Events?

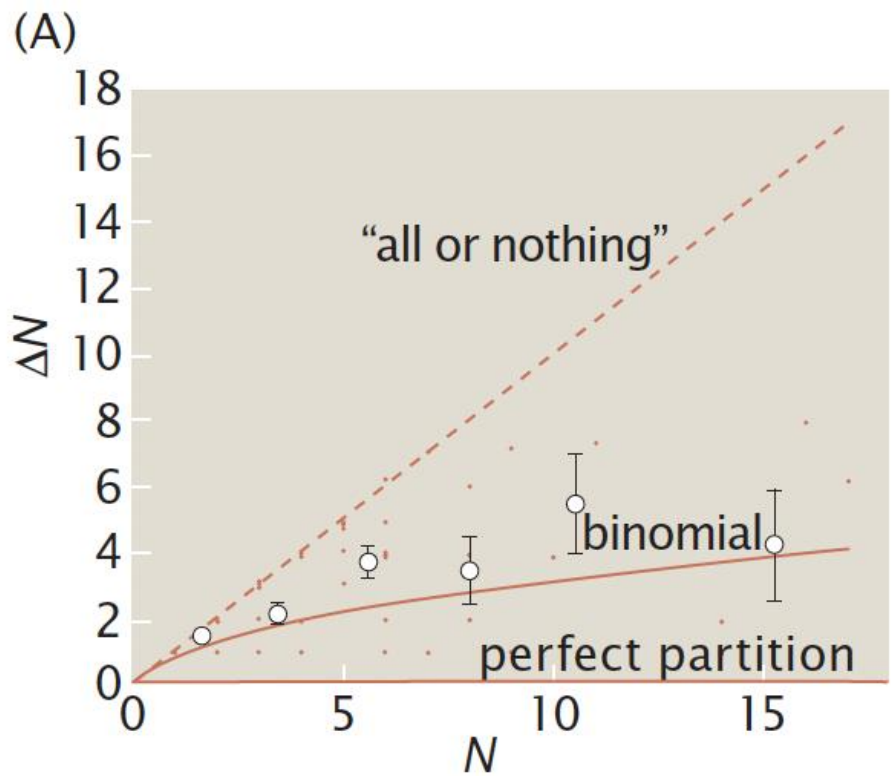
"Count" fluorescent proteins

$\Delta N = | N_{d(1)} - N_{d(2)} |$






binomial event

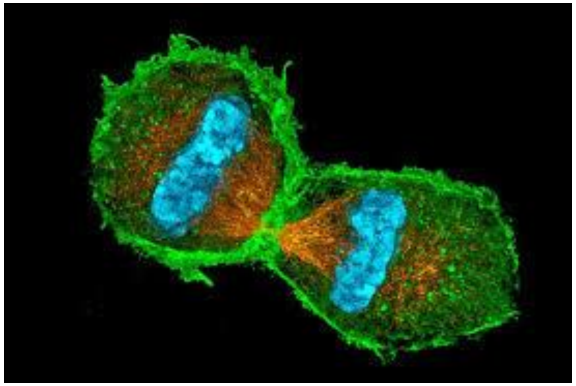


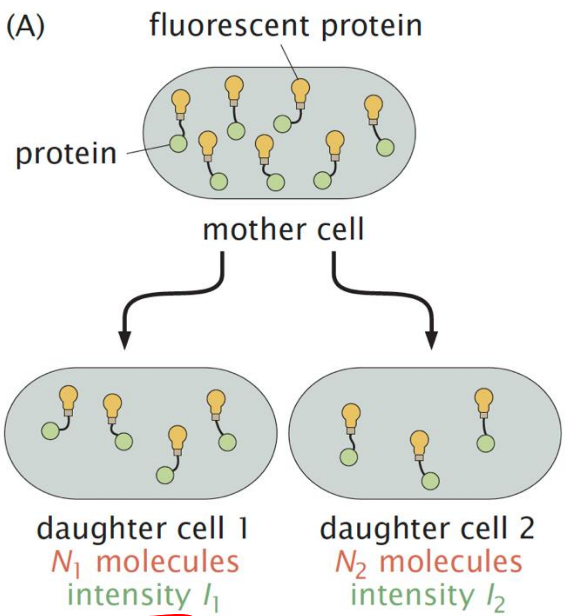

$N_1 + N_2 = N$

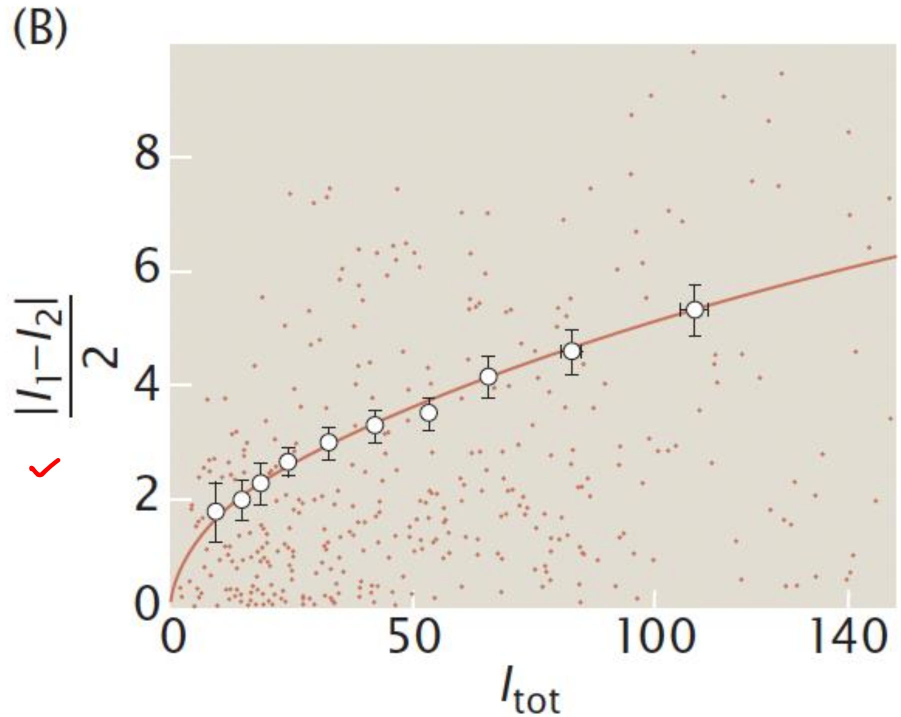
PBOC, Ch. 2

# Molecular Partitioning During Cell Division: Binomial Events?

"Count" fluorescent proteins





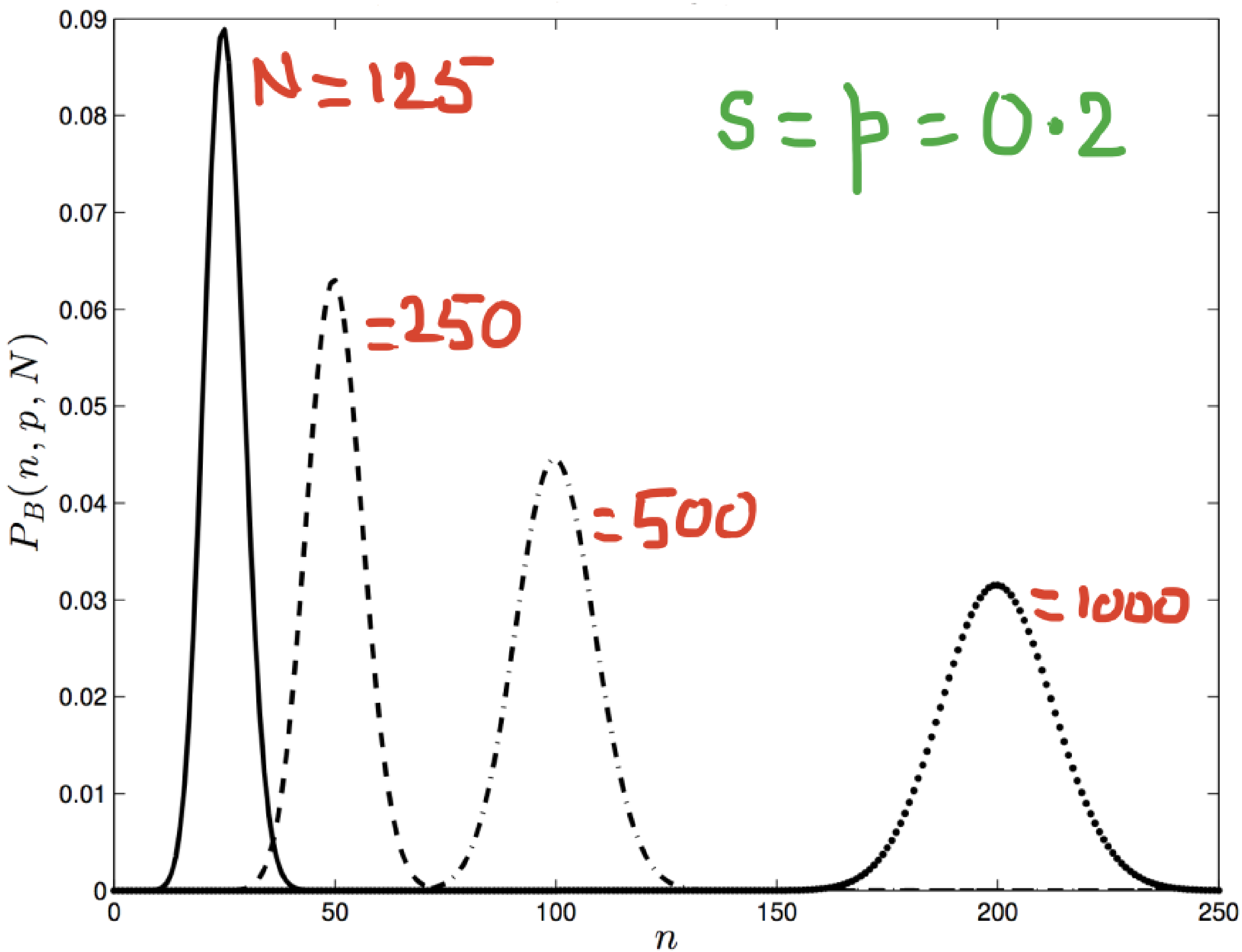




PBOC, Ch. 2

# Success (or failure) probability distribution

Only **2 possible outcomes** of an event with ***N*** attempts:

- **Success**, probability ***s (= p)***
- **Failure**, probability ***f = (1 – s)***

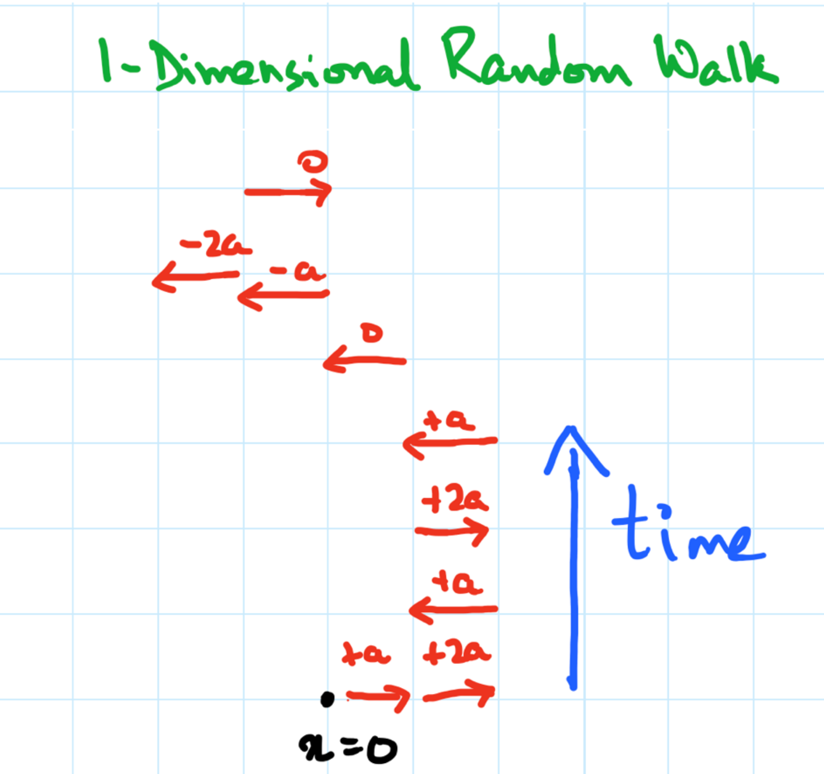


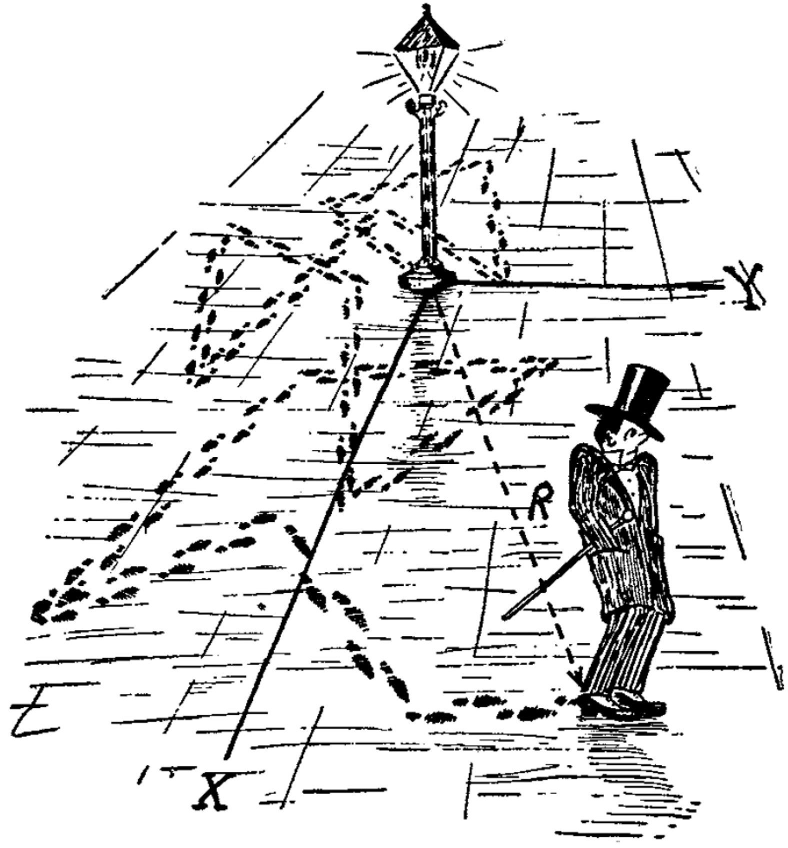

***n*** = No. of success

At large ***N***, Binomial disbn. approaches the Gaussian Disbn.

Proof:
not required;
request by email if interested

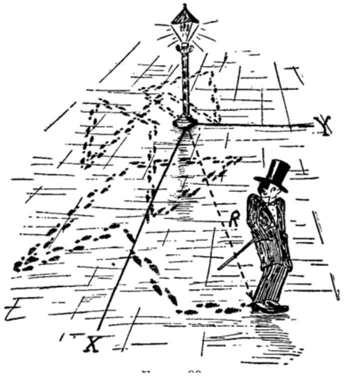
# Random Walk



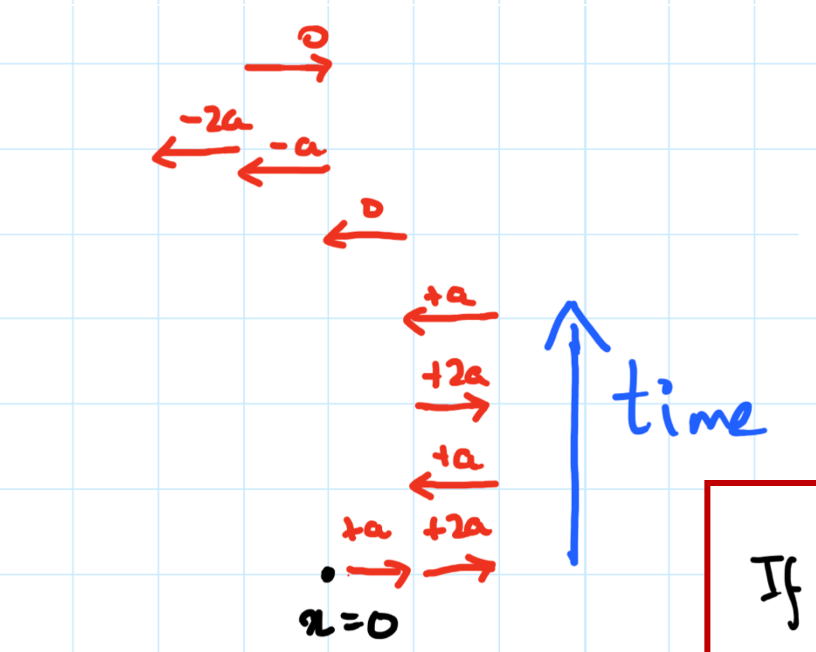




Biol. Physics, Nelson, Ch 2

# Random Walk



## 1-Dimensional Random Walk




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

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

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

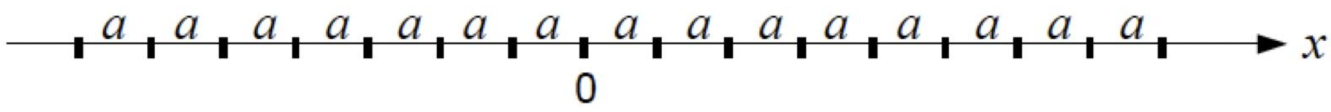
skipping steps

$$\equiv Na(2p-1)$$

If probability of front and back step are equal,

$$\boxed{\langle x\rangle = 0}$$

# 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 $P(k_n=1)=P(k_n=-1)=1/2$

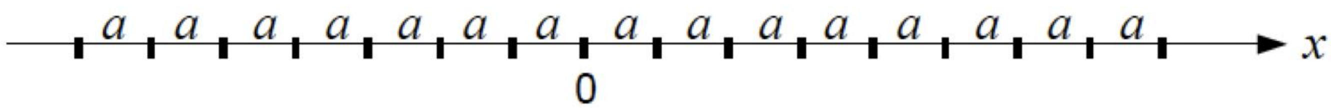
$k_n$ = +1 (right move)
= -1 (left move)

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

$$\begin{aligned}
\langle x_n \rangle &= \langle x_{n-1} + k_n a \rangle \\
&= \langle x_{n-1} \rangle + a\overset{\to 0}{\langle k_n \rangle} \\
&= \langle x_{n-2} \rangle + a\overset{\to 0}{\langle k_{n-1} \rangle} \\
&= \cdots \langle x_1 \rangle + a\overset{\to 0}{\langle k_1 \rangle}
\end{aligned}$$

$$\boxed{\langle x_n \rangle = \langle x_0 \rangle = 0}$$

# **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

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

$$= \langle x_{n-1}^2 \rangle + \langle k_n^2 \rangle a^2 + 2a \langle k_n x_{n-1} \rangle \rightarrow 0$$

$$= \langle x_{n-1}^2 \rangle + a^2 \quad = \langle x_{n-2}^2 \rangle + 2a^2$$

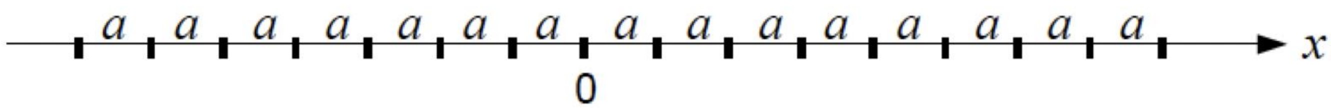
$$\langle k_n^2 \rangle = \frac{(+1)^2 + (-1)^2}{2} = 1$$

$$\langle k_n x_{n-1} \rangle = x_{n-1} \times (+1) \times P(+1) + x_{n-1} \times (-1) \times P(-1)$$

$$= x_{n-1} \left[ (+1) \times \left(\tfrac{1}{2}\right) + (-1) \times \left(\tfrac{1}{2}\right) \right]$$

$$= 0$$

# Mean squared displacement in 1-dimension




$a$---Length of each step

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

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

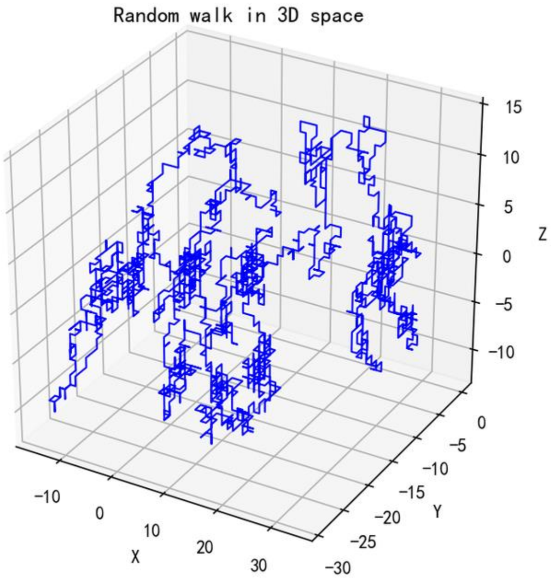
$$= \langle x_{n-1}^2 \rangle + \langle k_n^2 \rangle a^2 + 2a \langle k_n x_{n-1} \rangle$$

$$= \langle x_{n-1}^2 \rangle + \langle a^2 \rangle$$

By iteration, for ***N*** steps,

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

# **Mean squared displacement** in 2- or 3- dimensions




**HW**. Show that in '$d$' spatial dimensions, $\langle \mathbf{r}_N^2 \rangle = (d)Na^2$

Work out all steps.

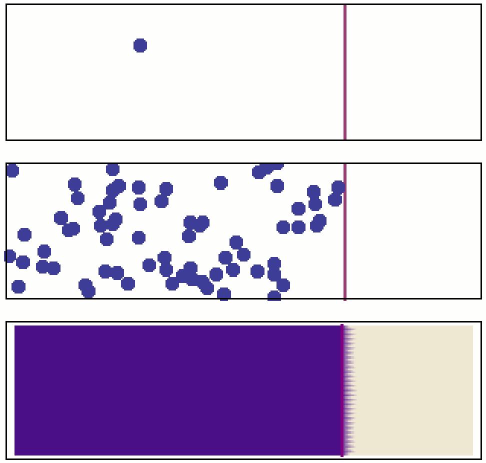
$$\langle r_N^2 \rangle = \langle x_N^2 + y_N^2 + z_N^2 \rangle$$

$$= \langle (x_{N-1} + k_{xN}a)^2 \rangle + \dots + \dots$$

$$= \left( \langle x_{N-1}^2 \rangle + 2a \overset{\to 0}{\langle x_{N-1} k_{xN} \rangle} + \langle k_{xN}^2 \rangle a^2 \right)$$

$$+ ( \dots ) + ( \dots )$$

# Diffusion: average spatio-temporal pattern of random walks



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

$\tau$ : time taken for step $(+a)$ *or* $(-a)$

T: total elapsed time

$\left.\right\}$ No. of steps, $N = \dfrac{T}{\tau}$

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

In 2-dimensions:

$$\langle r_N^2 \rangle = 2Na^2$$

$$= 2\left(\frac{T}{\tau}\right)a^2$$

$$= (2T)(2D)$$

**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

$$\zeta D = k_B T$$

Viscous Friction Coefficient

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

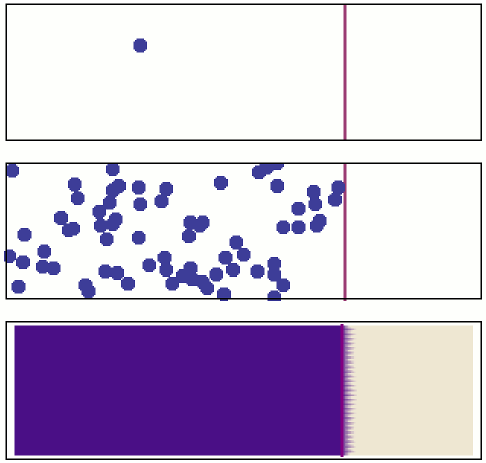
### STOKES-EINSTEIN RELATIONSHIP

viscosity

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

radius

# Diffusion: movement of particles in unbiased random walks in any dimension



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

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

T: total elapsed time

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

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

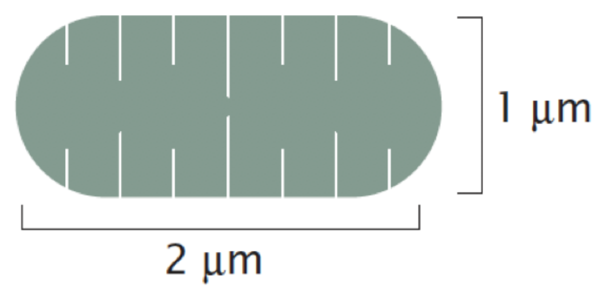
**Diffusion Relationship:**

$$\boxed{\langle \mathbf{r}_N^2 \rangle = (2d)D(t)}$$

**Stokes-Einstein (SE) Relationship:**

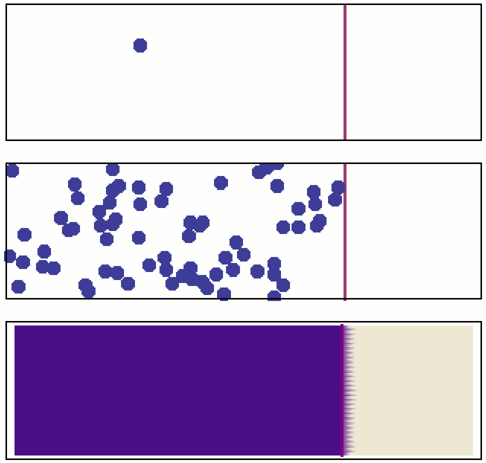
$$\boxed{6\pi\eta a D = k_B T}$$

- Consider a ~spherical protein of radius 15 nm diffusing ("wandering aimlessly") in water.
- How long will it take to transverse *E. coli* length?
- At 298 K, $\eta_{H_2O} = 8.9\times10^{-4}$ Pa-s $= 0.890$ centiPoise




approx. E. coli dimensions

# Diffusion: movement of particles in unbiased random walks in any dimension



$$\langle r_N^2 \rangle = (d)Na^2$$

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

T: total elapsed time

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

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

Problem (HW)

- Consider a ~spherical protein of radius 15 nm (= a) diffusing ("wandering aimlessly") in water.
- How long will it take to transverse *E. coli* length?
- At 298 K, $\eta_{H_2O} = 8.9 \times 10^{-4}$ Pa-s $= 0.890$ centiPoise

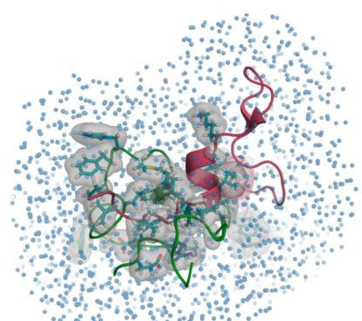
Pa.s : SI
centiPoise : CGS

**Diffusion Relationship:**

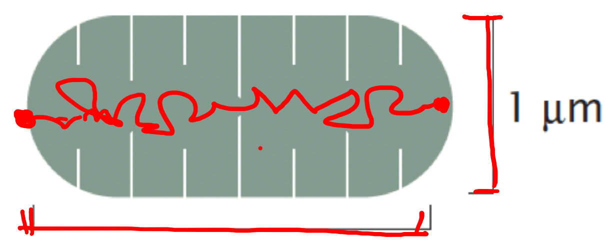
$$\boxed{\langle r_N^2 \rangle = (2d)D(t)}$$

**Stokes-Einstein (SE) Relationship:**

$$\boxed{6\pi\eta a D = k_B T}$$

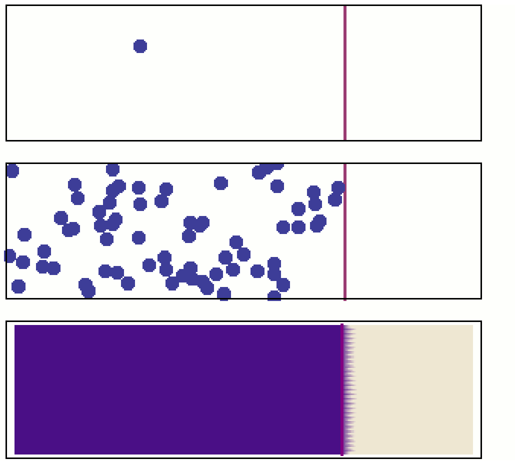


protein in water



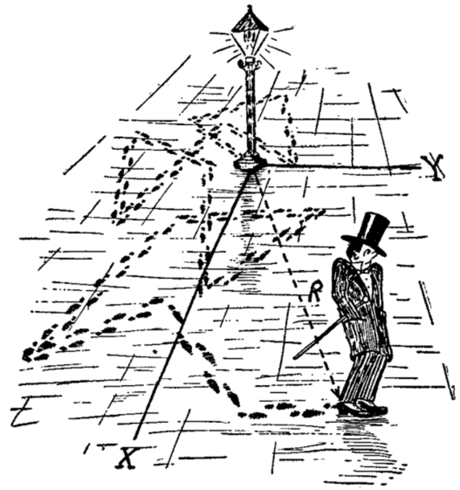

approx. E. coli dimensions

# In General: Random Biological Processes



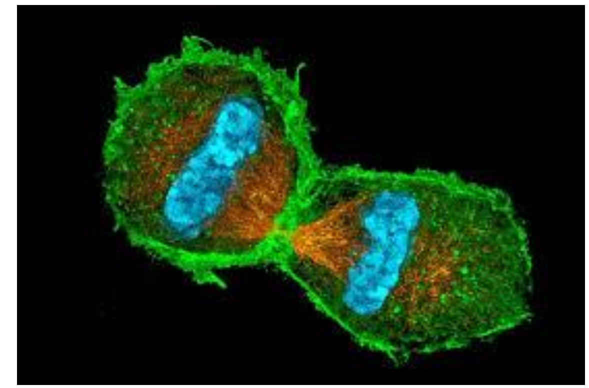
**Diffusion**

https://commons.wikimedia.org/w/index.php?curid=8995324



**Random Walk**

George Gamow, 1961

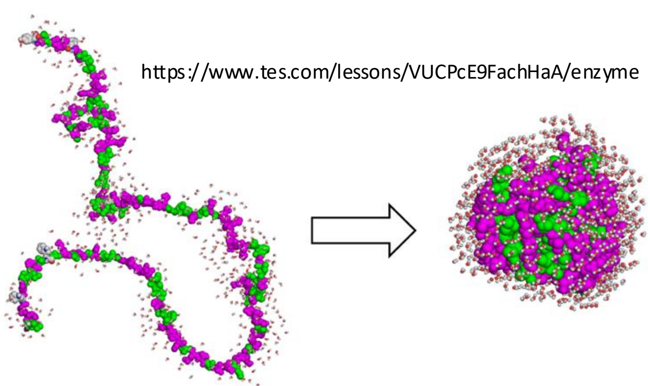


**Cell division**

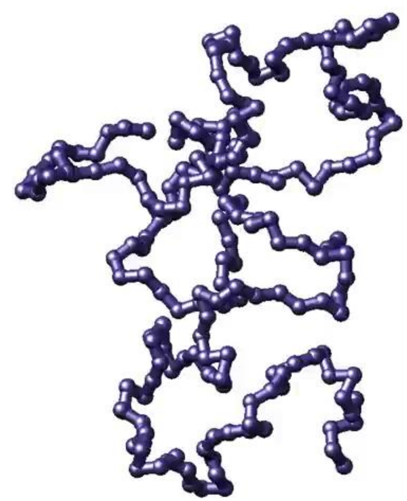
https://www.thoughtco.com/mitosis-and-cell-division-quiz-4078417

**Polypeptide collapse**

https://www.tes.com/lessons/VUCPcE9FachHaA/enzyme



**Unfolded** **Folded**

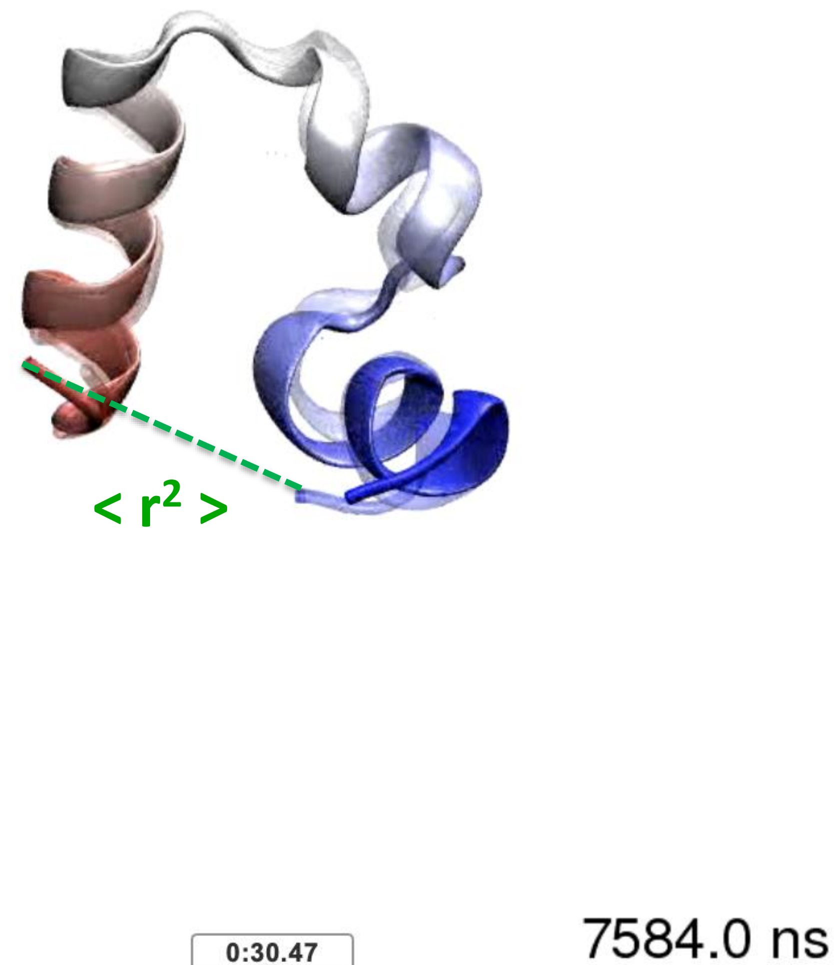


**Polymer collapse**

https://www.youtube.com/watch?v=ek9vd7_PDjk

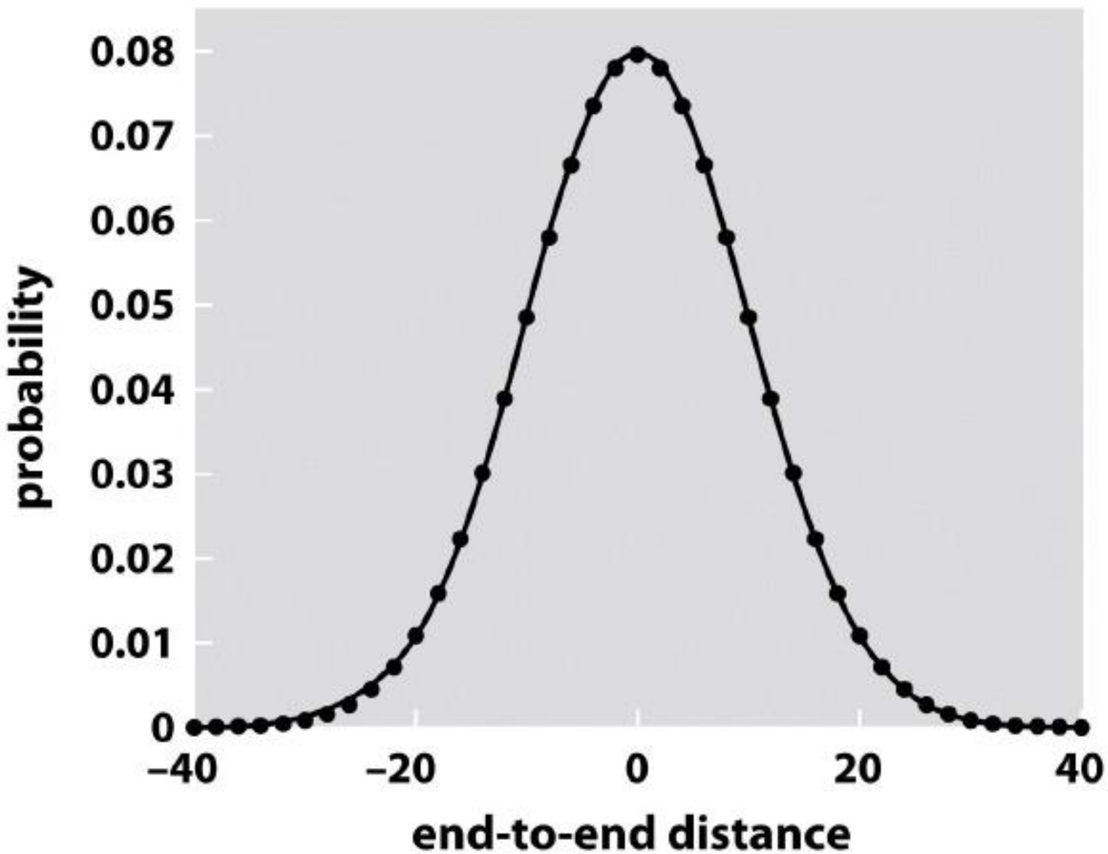
# Folding marker: **End-to-end distance**

Computationally folded structure superimposed on experimentally determined crystal structure



# End-to-end distance distribution of protein samples with ‘N’ amino acids

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




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

Line: Gaussian distribution

Dot: binomial distribution

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