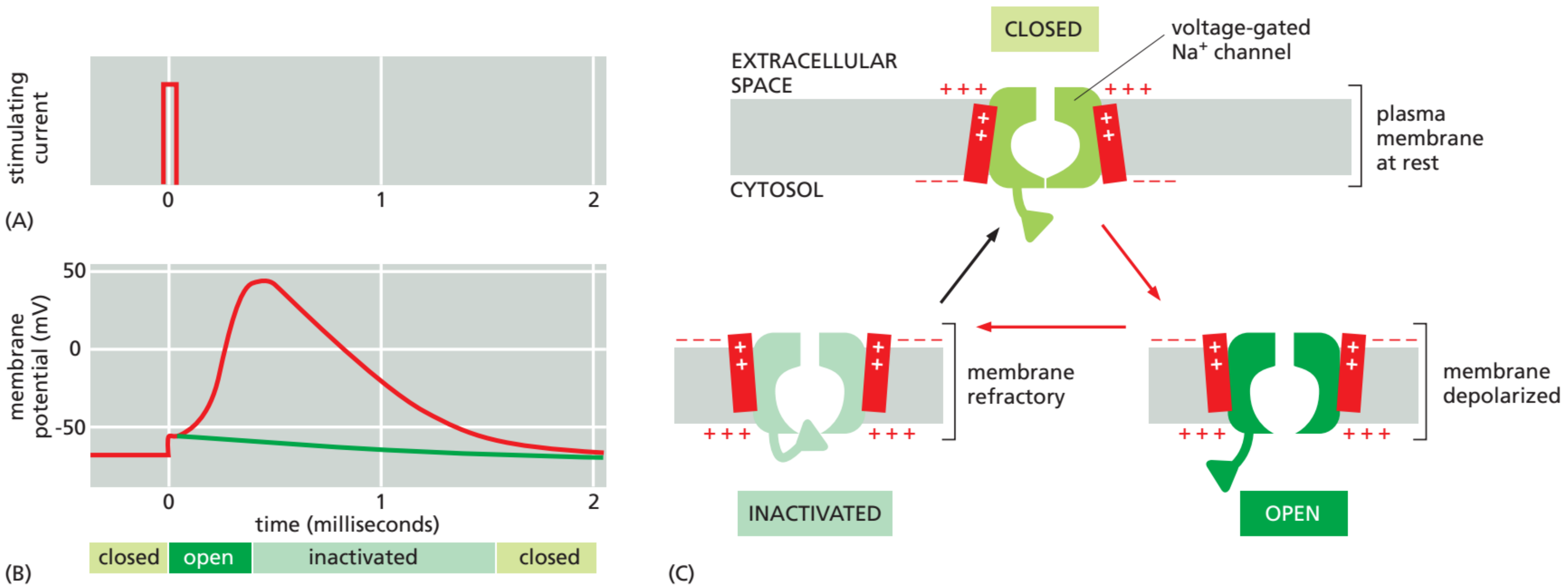

stimulating current
0
1
2
(A)
50
0
-50
membrane potential (mV)
0
1
2
time (milliseconds)
closed
open
inactivated
closed
(B)
CLOSED
voltage-gated
Na+ channel
EXTRACELLULAR SPACE
CYTOSOL
plasma membrane at rest
membrane refractory
membrane depolarized
INACTIVATED
OPEN
(C)

11–9 In a subset of voltage-gated K^+ channels, the N-terminus of each subunit acts like a tethered ball that occludes the cytoplasmic end of the pore soon after it opens, thereby inactivating the channel. This "ball-and-chain" model for the rapid inactivation of voltage-gated K^+ channels has been elegantly supported for the *shaker* K^+ channel from *Drosophila melanogaster*. (The *shaker* K^+ channel in *Drosophila* is named after a mutant form that causes excitable behavior—even anesthetized flies keep twitching.) Deletion of the N-terminal amino acids from the normal *shaker* channel gives rise to a channel that opens in response to membrane depolarization, but stays open instead of rapidly closing as the normal channel does. A peptide (MAAVAGLYGLGEDRQHRKKQ) that corresponds to the deleted N-terminus can inactivate the open channel at 100 μM.

Is the concentration of free peptide (100 μM) that is required to inactivate the defective K^+ channel anywhere near the local concentration of the tethered ball on a normal channel? Assume that the tethered ball can explore a hemisphere [volume = $(2/3)\pi r^3$] with a radius of 21.4 nm, which is the length of the polypeptide "chain" (**Figure Q11–2**). Calculate the concentration for one ball in this hemisphere. How does that value compare with the concentration of free peptide needed to inactivate the channel?

CHAPTER 11 END-OF-CHAPTER PROBLEMS

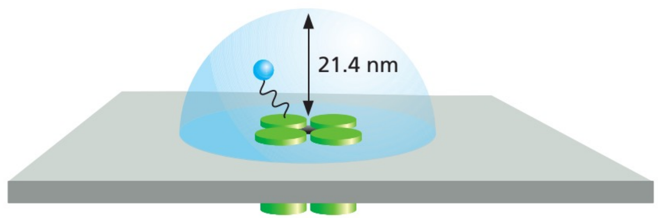


Figure Q11–2 A "ball" tethered by a "chain" to a voltage-gated K^+ channel (Problem 11–9).

Help design an experiment - 1

- Ion channel inactivation mechan

Is the concentration of free peptide (100 μM) that is required to inactivate the defective K^+ channel anywhere near the local concentration of the tethered ball on a normal channel? Assume that the tethered ball can explore a hemisphere [volume = $(2/3)\pi r^3$] with a radius of 21.4 nm, which is the length of the polypeptide "chain" (**Figure Q11–2**). Calculate the concentration for one ball in this hemisphere. How does that value compare with the concentration of free peptide needed to inactivate the channel?

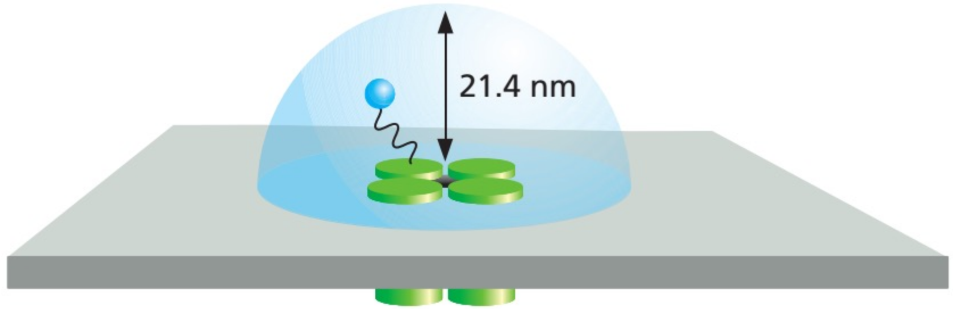


Figure Q11–2 A "ball" tethered by a "chain" to a voltage-gated K^+ channel (Problem 11–9).

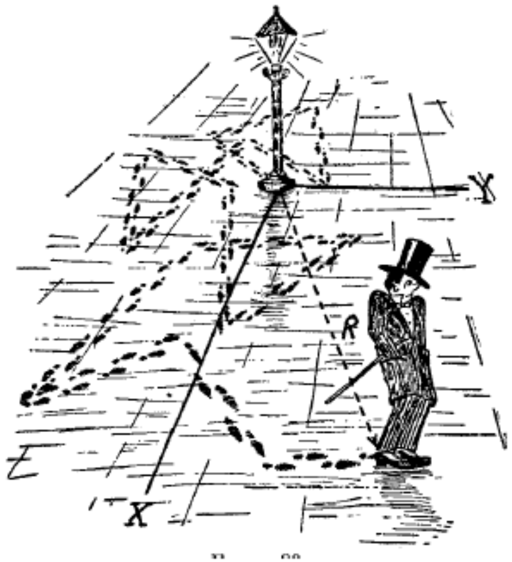
https://www.science.org/doi/10.1126/science.2122520?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

Why single-celled organisms are small

- Oxygen uptake increases with size – but a power of R
- Oxygen consumption (requirement) expected to increase as volume hence power of R^3
- For large R – cell would suffocate if its dependent on diffusion to get transport oxygen

MICROSCOPIC ORIGIN

- Understanding diffusion as random walk.
- Random??



Brown: 1828
Einstein: 1905
Perrin: 1913

Fick: 1855

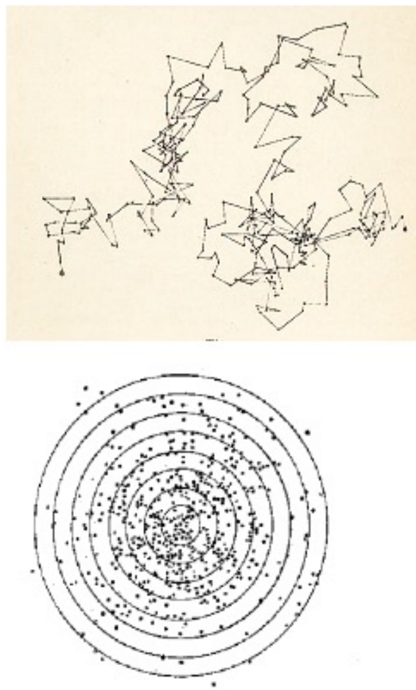
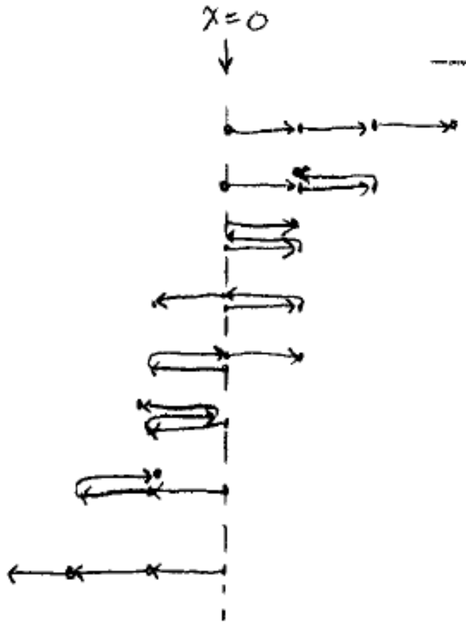


Fig 3. Brownian motion, after Jean Perrin [12]: An example of a trajectory (above) and statistical distribution of displacements (below, the circles correpond to fractions and multiples of the square root of the mean square displacement $<X^2>$)

Molecules move at 10^3 ms^{-1}
Collision rate : 10^{12} collisions per sec

MICROSCOPIC ORIGIN



$\{x_1, x_2, x_3\}$, cm	$x_2 \times k_3$, cm	
1, 2, 3	+2	0
1, 2, 1	−2	
1, 0, 1	0	0
1, 0, −1	0	
−1, 0, 1	0	0
−1, 0, −1	0	
−1, −2, −1	−2	0
−1, −2, −3	+2	

$$\langle x_3 \rangle = \frac{1}{8} \sum x_3 = 0$$

$$\langle x_2 k_3 \rangle = 0$$

$$\langle (x_3)^2 \rangle = \frac{1}{8} \sum (x_3)^2 = \frac{1}{8} \cdot 24 = 3$$

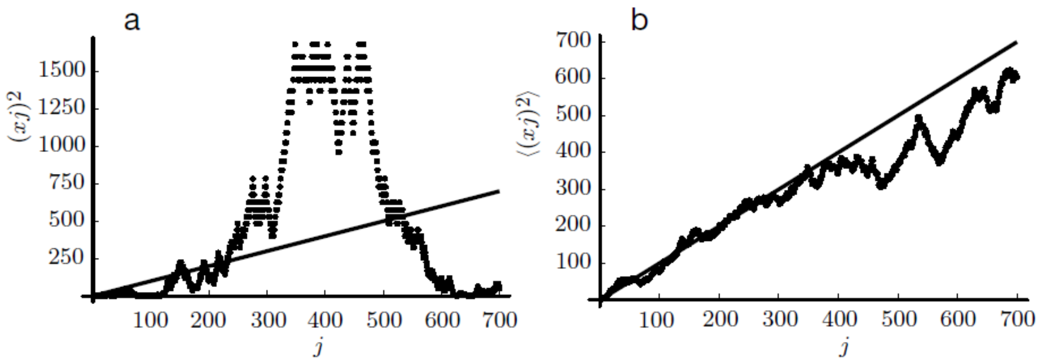
$$\langle (x_N)^2 \rangle = \langle (x_{N-1} + k_N L)^2 \rangle = \langle (x_{N-1})^2 \rangle + 2L\langle x_{N-1} k_N \rangle + L^2 \langle (k_N)^2 \rangle.$$

Position after Nth step

$$\langle (x_N)^2 \rangle = NL^2.$$

$$N = t/\Delta t \qquad D = L^2/2\Delta t \quad \rightarrow \quad \langle (x_N)^2 \rangle = 2Dt$$

One dimensional random walk



Thirty walks

Figure 4.5: (Mathematical functions.) (**a**) Squared deviation $(x_j)^2$ for a single, one-dimensional random walk of 700 steps. Each step is one unit long. The solid line shows j itself; the graph shows that $(x_j)^2$ is not at all the same as j. (**b**) As (a), but this time the dots represent the *average* $\langle (x_j)^2 \rangle$ over thirty such walks. Again the solid line shows j. This time $\langle (x_j)^2 \rangle$ does resemble the idealized diffusion law (Equation 4.4).

From: Nelson

Discuss how do we get information out of SINGLE walk?