Physics 3A: Physics for the Life Sciences

Chapter 1: Diffusion and Proportional Reasoning

What is Root Mean Square (RMS) and Why We Use It?

1. **Molecule Jiggling (Brownian Motion)** - A protein or drug molecule in water moves randomly: forward, backward, left, right. Average displacement $= 0$ (it cancels out). Average doesn't tell us the typical distance travelled.

2. **Nerve Signals (Oscillating Currents)** - A neuron's voltage signal fluctuates above and below zero. Average could look like zero.

3. **Breathing In and Out** - Lung volume goes up (inhalation) and down (exhalation). Average change could be near zero if you breathe symmetrically.

4. **Heartbeat (ECG Signal)** - The ECG trace oscillates above and below baseline. Average ≈ 0, but we clearly feel the heartbeat!

So, we need something that quantifies the typical changes!

- RMS = take **square** $\rightarrow$ take **mean** $\rightarrow$ take square **root**
  - **Squaring** gets rid of negatives.
  - **Taking the mean** tells us the typical size.
  - **Square root** brings the size back to the original units.
- e.g. for neuron voltage: $V_{rms} = \sqrt{\langle V^2 \rangle}$, or protein travel distance: $r_{rms} = \sqrt{\langle r^2 \rangle}$

The RMS displacement tells you the typical distance the protein wandered away from where it started.
The RMS voltage tells you the real "strength" of the signal.
The RMS change of lung volume tells you the typical size of your breathing motion.
The RMS value of ECG measures the "power" of the heart's electrical activity.

Brownian Motion

- **1827 – Robert Brown (Botanist)** While looking at pollen grains under a microscope, he noticed they jittered randomly in water. At first, he thought it might be due to "life forces." Later, he tested dust and sand particles and saw the same effect — so it wasn't just biology.
- **Mid–1800s – Hypotheses** Some scientists suggested it was due to currents in the water or "internal vibrations" of the particles. Others speculated invisible molecules in motion might be responsible — but no one could prove it.
- **1905 – Albert Einstein** Published a famous paper giving a statistical theory of Brownian motion. He showed that the random motion of particles could be explained as collisions with fast-moving water molecules. Importantly, he derived equations linking the diffusion of particles to Avogadro's number.
- **Importance in Biology:** Diffusion is vital in biology because it's the passive movement of molecules (like oxygen, carbon dioxide, water, and small nutrients) across cell membranes and throughout the body, ensuring gas exchange, waste removal, and nutrient distribution without the cell expending energy.

Diffusion — The Core Idea

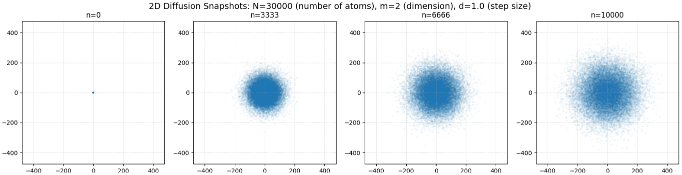
- Particles jiggle randomly because of random collisions between them.
- Clumps (high concentration) naturally spread into emptier regions (low concentration) because fewer particles come toward the high concentration than the other way around.

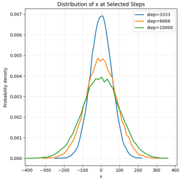
- No stirring is needed—the mixing emerges from countless random steps.
- Occurs in gases, liquids, and even solids (e.g., dye in water, smells in air, ions across membranes).
- Mathematically, one can model diffusion with a random walk (random steps)

Summary: Random motion smooths out concentration differences over time.

2D Diffusion: Snapshots and Theory Check

- Random walk of N atoms in $m = 2$ dimensions with step size d, after n steps:

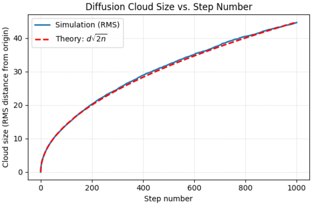


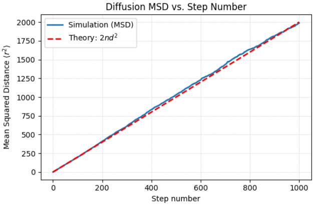


Snapshots and distributions at equally spaced times

- The root mean square (RMS) and the mean squared displacement (MSD) cloud radius:

$$r_{\text{rms}} = d\sqrt{mn} \quad \text{and} \quad r_{\text{rms}}^2 = d^2 mn$$





Applied Problem: Ciprofloxacin Diffusion

Ciprofloxacin is an antibiotic that blocks bacterial DNA replication and transcription. After crossing the cell membrane, it diffuses rapidly through the cytoplasm to the nucleoid, where it binds DNA enzymes, prevents proper DNA synthesis and ultimately kills the bacterium.

- A typical bacterium has diameter $\sim 2\,\mu$m, and they are in 3 dimensions ($m = 3$).
- Assume that the effective step size of diffusion in cytoplasm: $d = 0.3$ nm.
- Assume that the collision (step) time: $\tau \approx 1.5 \times 10^{-8}$ s.
- Question:
  1. How many steps are needed to reach the DNA (for the RMS to be 1 μm)?
  2. How long does it take for ciprofloxacin to arrive?

Solution: Ciprofloxacin Diffusion

- In 3D, the RMS displacement is:

$$r_{\mathrm{rms}} = d\sqrt{mn}$$

- With $m = 3$, $d = 0.3$ nm, and RMS displacement $1\,\mu$m $= 1000$ nm:

$$1000 = 0.3\sqrt{3n}$$

- Solve for the number of steps (n):

$$\sqrt{3n} \approx 3333 \quad \Rightarrow \quad n \approx 3.7 \times 10^{6}$$

- Time estimate (with $\tau = 1.5 \times 10^{-8}$ s):

$$t = n \cdot \tau \approx 3.7 \times 10^{6} \times 1.5 \times 10^{-8}\,\mathrm{s} \approx 5.6 \times 10^{-2}\,\mathrm{s} \approx 56\,\mathrm{ms}$$

With realistic cytoplasmic diffusion, antibiotics reach DNA in tens of milliseconds — rapid compared to cellular processes.

Example: Random Walk Diffusion

Problem. After 10^3, 10^5, and 10^9 steps, what fraction of the maximum straight-line distance does a diffusing particle typically reach?

Setup. If every step pointed in the same direction, the particle would move

$$x_{\text{max}} = nd,$$

where n is the number of steps and d is the step length. In a random walk, the average displacement grows more slowly, as we already know:

$$x_{\text{diff}} = \sqrt{n}\, d.$$

Calculation. The ratio is

$$\frac{x_{\text{diff}}}{x_{\text{max}}} = \frac{\sqrt{n}\, d}{nd} = \frac{1}{\sqrt{n}}.$$

For the chosen step counts:

$$\frac{x_{\text{diff}}}{x_{\text{max}}} = \begin{cases} 10^{-1.5}, & n = 10^3, \\ 10^{-2.5}, & n = 10^5, \\ 10^{-4.5}, & n = 10^9. \end{cases}$$

Interpretation. Even though the particle takes many steps, its typical displacement is tiny compared with the maximum straight-line distance. Random motion makes spreading very slow: after 10^9 steps, the diffusive distance is only about one thirty-thousandth of the maximum possible.

Diffusion Coefficient D

- In biology diffusion is how molecules like oxygen, glucose, or drugs spread inside cells and tissues. We know that $r_{\text{rms}} = \sqrt{n}d$, but we can't measure n nor d easily - because we can't see them in sufficient detail. We can only measure r_{rms} and t directly.
- We want a single number that absorbs the microscopic details into a single effective coefficient and relates:

$$r_{\text{rms}} \quad \longleftrightarrow \quad t$$

  so we can predict how far molecules travel in a given time. That's what matters!
- To capture this, we define the **diffusion coefficient**:

$$\boxed{D = \tfrac{1}{2} v d}$$

- Use $n = t/\Delta t$ and $v = d/\Delta t$:

$$r_{\text{rms}} = d\sqrt{mn} = d\sqrt{m\frac{t}{\Delta t}} = \sqrt{md^2\frac{t}{\Delta t}} = \sqrt{mdt\frac{d}{\Delta t}} = \sqrt{mvd\, t}$$

- With this definition:

$$\boxed{r_{\text{rms}} = \sqrt{2mDt}}$$

- **Take-home:** D packages all microscopic motion into one effective constant that links measurable quantities (distance and time).

Example: Diffusion Times

- **Medical context:** Molecules like oxygen or glucose spread by diffusion. Works very fast over single-cell distances, but far too slow over tissue or organ scales.
- **Model:**

$$r_{\text{rms}} = \sqrt{6Dt} \quad \Rightarrow \quad t = \frac{r_{\text{rms}}^2}{6D}$$

- Assume $D \approx 1 \times 10^{-9}\ \text{m}^2/\text{s}$ for oxygen in fluid.
- **Across a cell:** $r_{\text{rms}} = 20\,\mu\text{m} = 2 \times 10^{-5}\ \text{m}$

$$t \approx \frac{(2 \times 10^{-5})^2}{6(1 \times 10^{-9})} \approx 0.07\,\text{s}$$

- **Across a small organ:** $r_{\text{rms}} = 5\,\text{cm} = 0.05\,\text{m}$

$$t \approx \frac{(0.05)^2}{6(1 \times 10^{-9})} \approx 4 \times 10^5\ \text{s} \approx 5\,\text{days}$$

- **Conclusion:** Diffusion alone is sufficient within cells or over a few microns, but is much too slow across whole organs — hence the need for circulatory systems.

- **Linear proportionality:** (orange line)

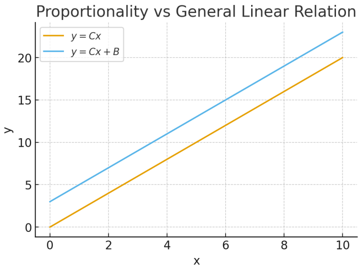
$$y \propto x \quad \Rightarrow \quad \Rightarrow \quad \boxed{y = Cx}$$

  - C is the proportionality constant (slope).
  - Graph is a straight line *through the origin*.

- **Ratio reasoning:** If $y = Cx$, then ratios cancel C:

$$\frac{y_2}{y_1} = \frac{Cx_2}{Cx_1} \quad \Rightarrow \quad \boxed{\frac{y_2}{y_1} = \frac{x_2}{x_1}}$$

  - Doubling x doubles y. Halving x halves y, etc.



- **Examples:**
  - Oxygen uptake $\propto$ surface area of alveoli in lungs.
  - Diffusion time $\propto$ distance^2 for molecules crossing cell membranes.
  - Mass (m) $\propto$ volume (V): $m = \rho V$. Surface area (A) $\propto$ radius^2: $A = 4\pi r^2$, etc.

- **Important:** Proportionality is stronger than a general linear relation ($y = Cx + B$, blue line). Ratio reasoning works only if $B = 0$:

$$\frac{y_2}{y_1} = \frac{Cx_2 + B}{Cx_1 + B} \neq \frac{x_2}{x_1}$$

Why Ratio Reasoning Does Not Apply To General Linear Relation

Neuron Firing Rate

- Neurons need a threshold input current before firing.
- Above threshold, firing rate (ν) grows roughly linearly with input current (I):
$$\nu = C \cdot I + B$$
- Doubling I does not double ν, because B shifts the ratio.
- Read two clear points from the nearly linear region (e.g., around $I \in [0.5, 2.0]$). For instance, from the graph:
$$(I_1, \nu_1) \approx (0.5,\ 30), \qquad (I_2, \nu_2) \approx (2.0,\ 100).$$
- Between these points, I increases by a factor of 4. If the relation were strictly proportional, the firing rate would rise from about 30 Hz to 120 Hz. In reality, it only reaches about 100 Hz.

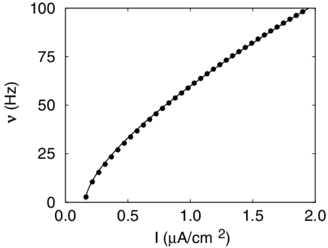


Figure: More at: *Asynchronous States and the Emergence of Synchrony in Large Networks of Interacting Excitatory and Inhibitory Neurons*, DOI:10.1162/089976603321043685

- Compute slope C and intercept B:

$$C = \frac{\nu_2 - \nu_1}{I_2 - I_1} = \frac{100 - 30}{2.0 - 0.5} = \frac{70}{1.5} \approx 46.7 \quad \frac{\text{Hz}}{\mu\text{A/cm}^2}$$

$$B = \nu_1 - C\, I_1 = 30 - C(0.5) \approx 30 - 23.3 \approx 6.7 \text{ Hz}.$$

Q&A 1. What drives diffusion, and why does it always spread from high to low concentration without external help?

- Molecules are constantly *jiggling* because of thermal energy (collisions with other molecules).
- In a high-concentration region, there are more molecules bouncing out than bouncing in.
- This imbalance leads to a net flow toward the low-concentration side.
- No stirring or pumping is needed — diffusion is powered by randomness.
- **In biology:** this explains why oxygen naturally moves into cells where it is lower, and CO_2 leaves where it is higher.

Takeaway: Diffusion is driven by random molecular motion, and "high to low" just means probability favors leveling things out.

Q & A 2. How does the math of random walks explain why diffusion is so much slower than straight-line motion, and why does time scale with distance squared?

- In a straight line: distance $\propto$ steps (linear).
- In a random walk: steps partly cancel each other, so net distance $\propto \sqrt{\text{steps}}$.
- If each step takes time τ, then the number of steps is $n = t/\tau \quad \Rightarrow \quad$ displacement grows with $\sqrt{t}$.
- Rearranged:

$$t \;\propto\; (\text{distance})^2$$

- **Biological meaning:** crossing $20\,\mu$m (a cell) is fast (fractions of a second), but crossing 5 cm (an organ) would take days.

Takeaway: Random wandering is inefficient — distance grows with the square root of time, making diffusion painfully slow over large distances.

Q & A 3. What is the diffusion coefficient (D), how is it measured, and why is it more useful than step size and time in biology?

- **Definition:** D condenses microscopic motion (step size & step time) into a single constant.
- **Relation:**

$$r_{\text{rms}} = \sqrt{2mDt}$$

- **Measurement:** We measure D experimentally by observing how far molecules spread in a known time (e.g., fluorescence microscopy, tracer molecules).
- **Why useful:** We cannot see individual molecular steps, but we can measure how far a dye or drug cloud spreads.
- **Typical values:** Oxygen in water $\approx 10^{-9}\,\text{m}^2/\text{s}$.

Takeaway: D is the practical "speed of spreading" number for molecules, letting us predict transport inside cells and tissues.

Q & A 4. Why is diffusion fast enough for single cells but far too slow across organs, and how do organisms solve this problem?

- **Inside a cell (tens of μm):** diffusion is quick (fractions of a second).
- **Across an organ (cm):** diffusion would take days.
- **Evolutionary solution:** circulatory systems and lungs move materials by bulk flow, then diffusion takes over only across microscopic distances.
- **Example:** Oxygen diffuses from alveoli $\rightarrow$ blood (microns), but blood circulation handles cm-level transport.

Takeaway: Diffusion is nature's solution for micrometer scales, but living systems need pumps, blood, and lungs to cover macroscopic distances.

Q & A 5. When can we use proportional reasoning in biology and medicine, and why does it sometimes fail (like in neuron firing)?

- **Proportionality ($y \propto x$):** doubling x doubles y. Works when the relation passes through the origin (no offset).
- **Examples where it works:**
  - Diffusion time $\propto$ distance^2
  - Drug dose $\propto$ body mass
- **Failure case:** If there is a threshold or offset ($y = Cx + B$), doubling does not hold.
- **Example:** Neurons need a minimum current before firing; above threshold, firing rate grows but not strictly proportionally.
- **In medicine:** dosing by body mass works (proportional), but neuron firing or enzyme activation often has thresholds (non-proportional).

Takeaway: Ratio reasoning is powerful but only works when the relationship is truly proportional — biology often adds offsets or thresholds.