Biology: measurements, quantification and models

Physics, engineering and mathematics to understand & explain living systems and processes

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Tests, tutorials etc

- Essentially the same way we had in the first half
- Tutorials every week. A short assignment question in every tutorial. Best 4 will be evaluated. Total 10 marks
- End-semester test (similar to mid-semester test)
- Adwaith (PhD scholar BSBE) will coordinate TA activities (office: 306 BSBE)
- 1)Kadambari 2) Priyanka 3) Aryan 4) Ilamathy 5) Dwiteeya
- After every lecture, I am available for 30 minutes (2 x 30 minutes = 1 hour per week) to clarify questions/any query/office hour
- Feel free to walk in to 306 BSBE any day.

In the first half, you learned many amazing phenomena occurring in living systems

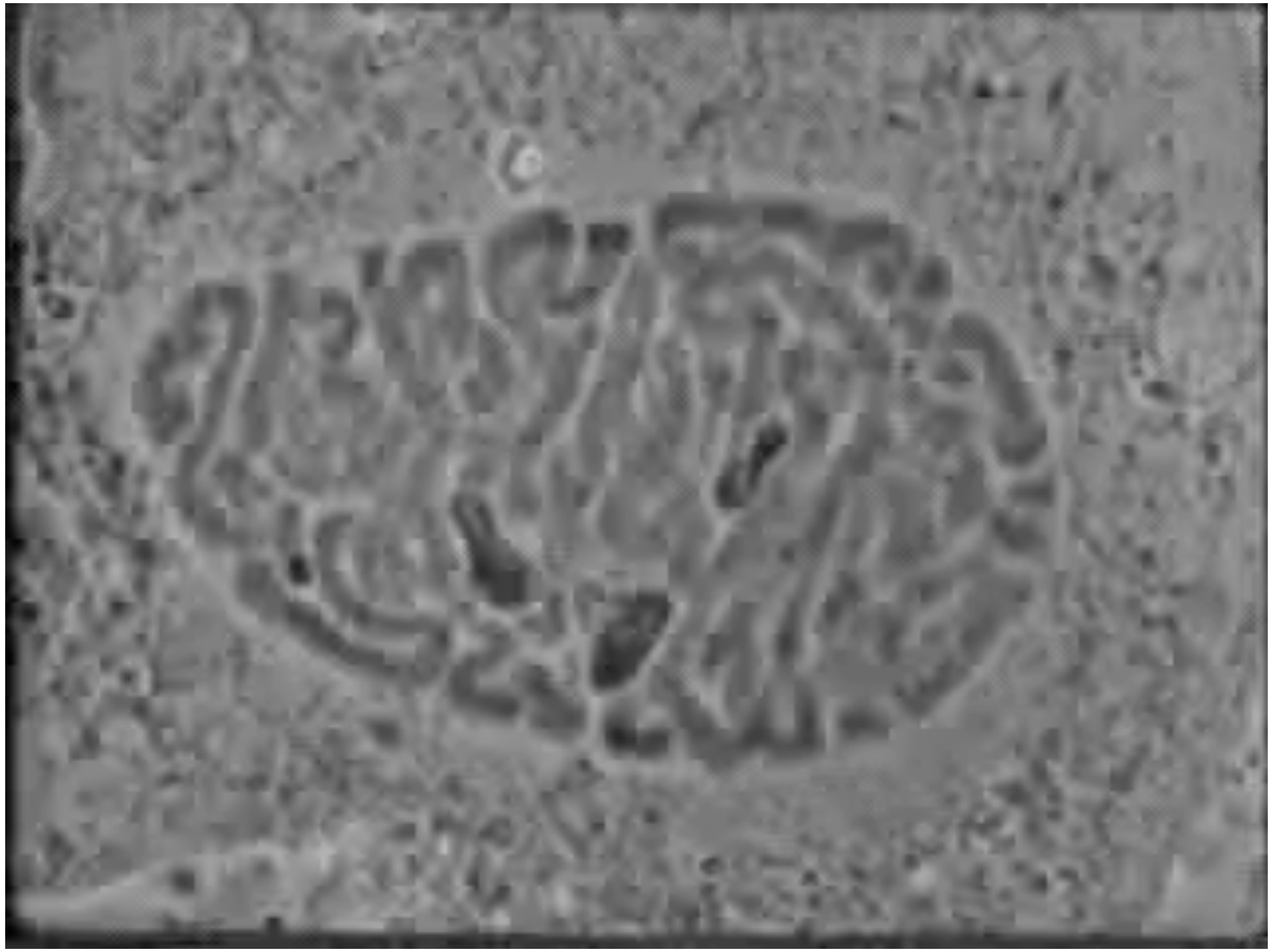
In this part, some new phenomena, a lot about measurement, quantification and models

Biology from a physics/engineering/quantitative science perspective

Living beings survive in this physical world, like other non-living objects!

Must obey laws of physics and chemistry!

Living beings are amazing machines: they must be evolved to implement some basic engineering principles!



(Movie source: Alberts et al supplementary movie)

In the next few lectures…

- **Predicting the future:** We can predict chemical reactions, planetary motion, Chandrayaan landing etc. In Living systems: What can we predict?
- **Randomness in life processes:** Temperature, thermal energy, randomness and stochasticity
- **How do we “see” biological structures and processes:** Making measurements to understand living systems
- **Motion & force in biology:** How molecular machines, cells and living organisms generate force and move. Is there a Newton’s equation of motion in
- **Interplay of structure and information, away from equilibrium!**
- **Pattern formation in biology:** from cells and fruit flies to Zebra lines and Tiger skins: patterns everywhere!
- (And other topics that will be added based on the feedback)

If you get a completely new object, what will you do to figure out what the object is?

Different ways you can "probe" the object

- You will "see" or "observe" — essentially use "light" or electromagnetic waves. Just observing it. Not really perturbing the system

- You will touch it and see; poke it — is it alive? Apply light pressure or force. Using force/pressure as a tool to perturb it. (Pressure vs volume)

- Pour some water on it? Put it in some solution? Chemical perturbation —vary concentration of molecules as a tool to perturb it (Chemical potential!)

- Heat it? Vary temperature. Temperature as a tool to perturb it. (Entropy)

- Temperature
- Pressure/force
- Volume
- Concentration

- Temperature
- Pressure/force
- Volume
- Concentration

When you hear these words, does any domain of science come into your mind?

What is temperature?

What happens when you increase the temperature?

Temperature <=> average kinetic energy

$$\langle \frac{1}{2} m v^2 \rangle = \frac{3}{2} k_B T$$

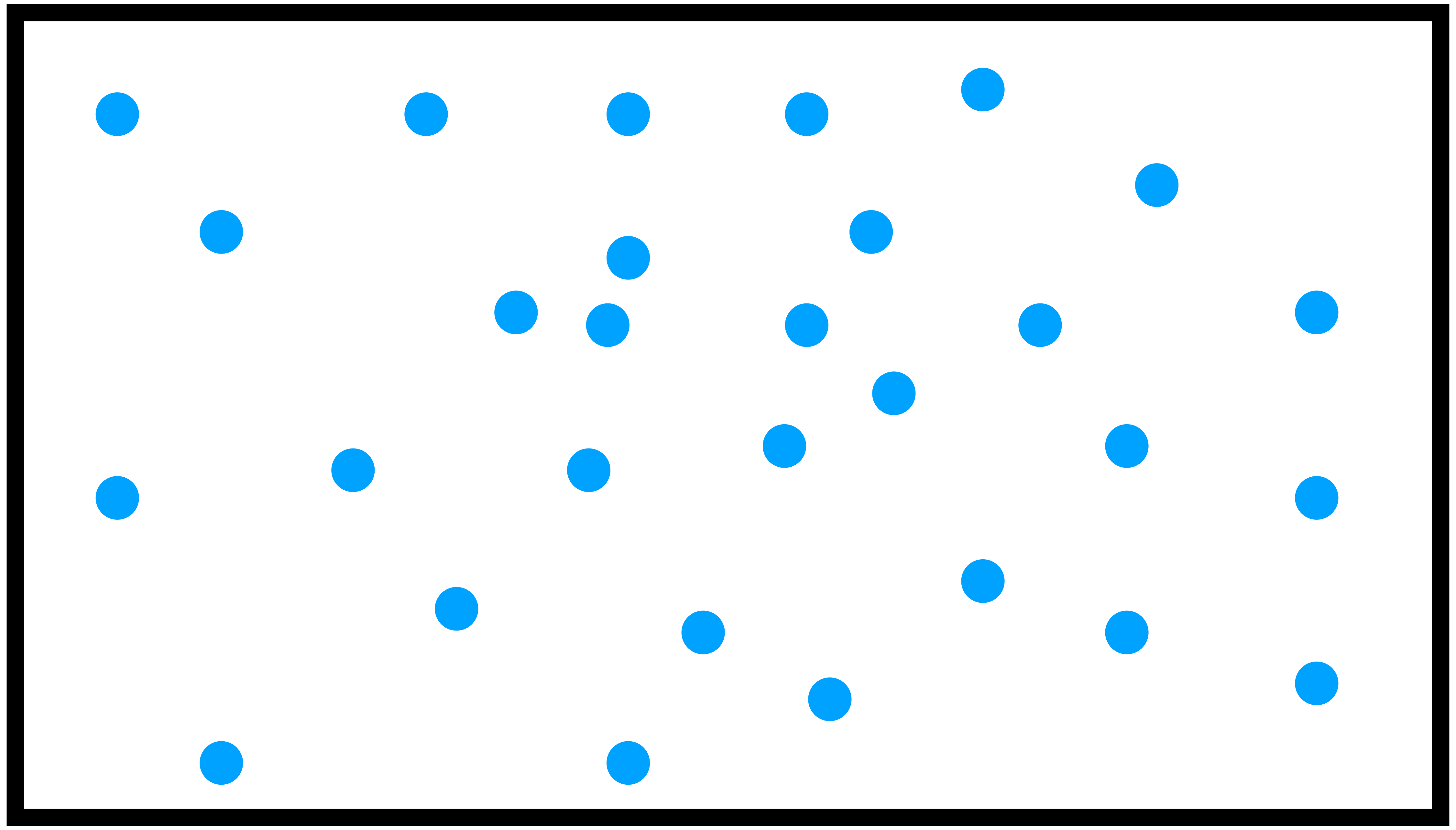
$$T = \frac{m\langle v^2 \rangle}{3k_B}$$

Temperature essentially related to the speed of the randomly moving molecules in the medium.

Water in the case of biomolecules

Kinetic energy is related to temperature

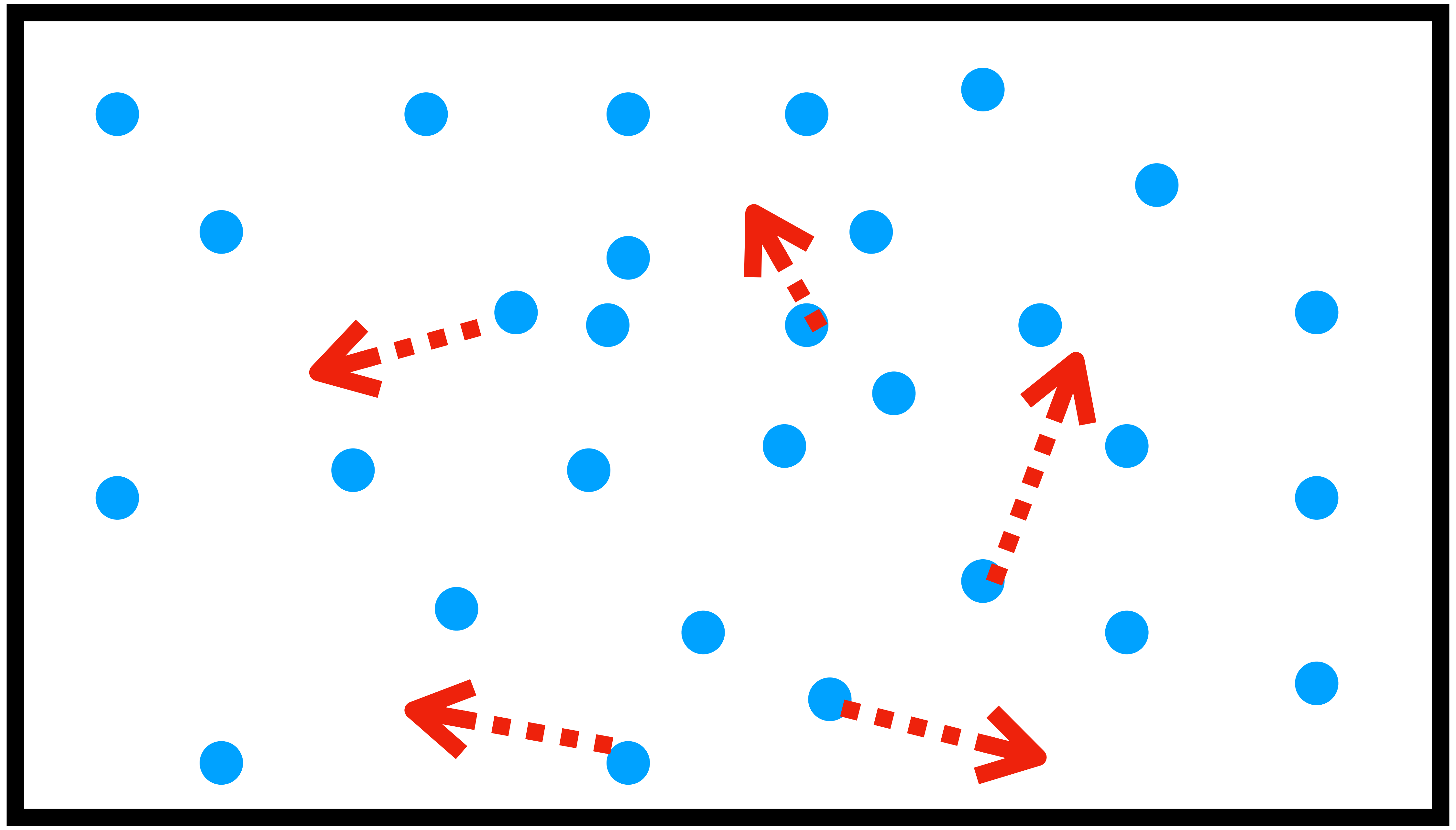
$$Average\ KE = \frac{3}{2} k_B T$$



Kinetic theory: Boltzmann, Maxwell and others (1850-1900)

Temperature is associated with random motion of molecules

$$Average\ KE = \frac{3}{2}k_B T$$



$$\frac{1}{2}m\frac{(\vec{v}_1^2 + \vec{v}_2^2 + \vec{v}_3^2 + \ldots \vec{v}_N^2)}{N} = \frac{3}{2}k_B T$$

Optional: advanced ideas to ponder

****Can we say something about the mean, standard deviation and distribution of velocities of these molecules?**

Water molecules in a beaker at 37 degree C
versus
Molecules inside a cell

Will they have similar behaviour**

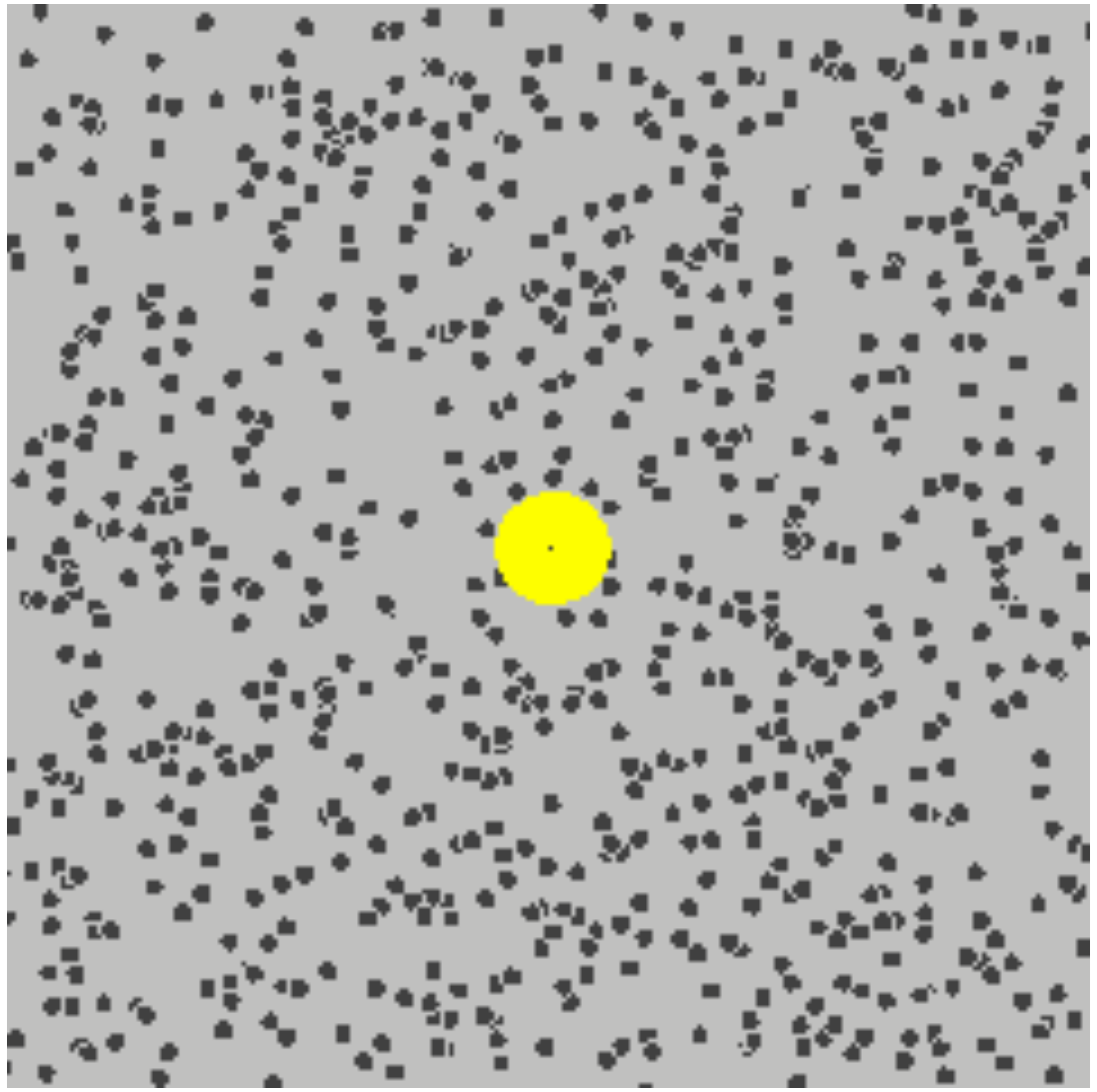
**** These are purely to stir your intellectual curiosity. We will not ask this in examination**

What are the implications of this “random movements” on the biomolecules?

Randomly jiggling water molecules kick other bigger molecules (proteins in water)

Make them randomly move around

Thermal fluctuation!



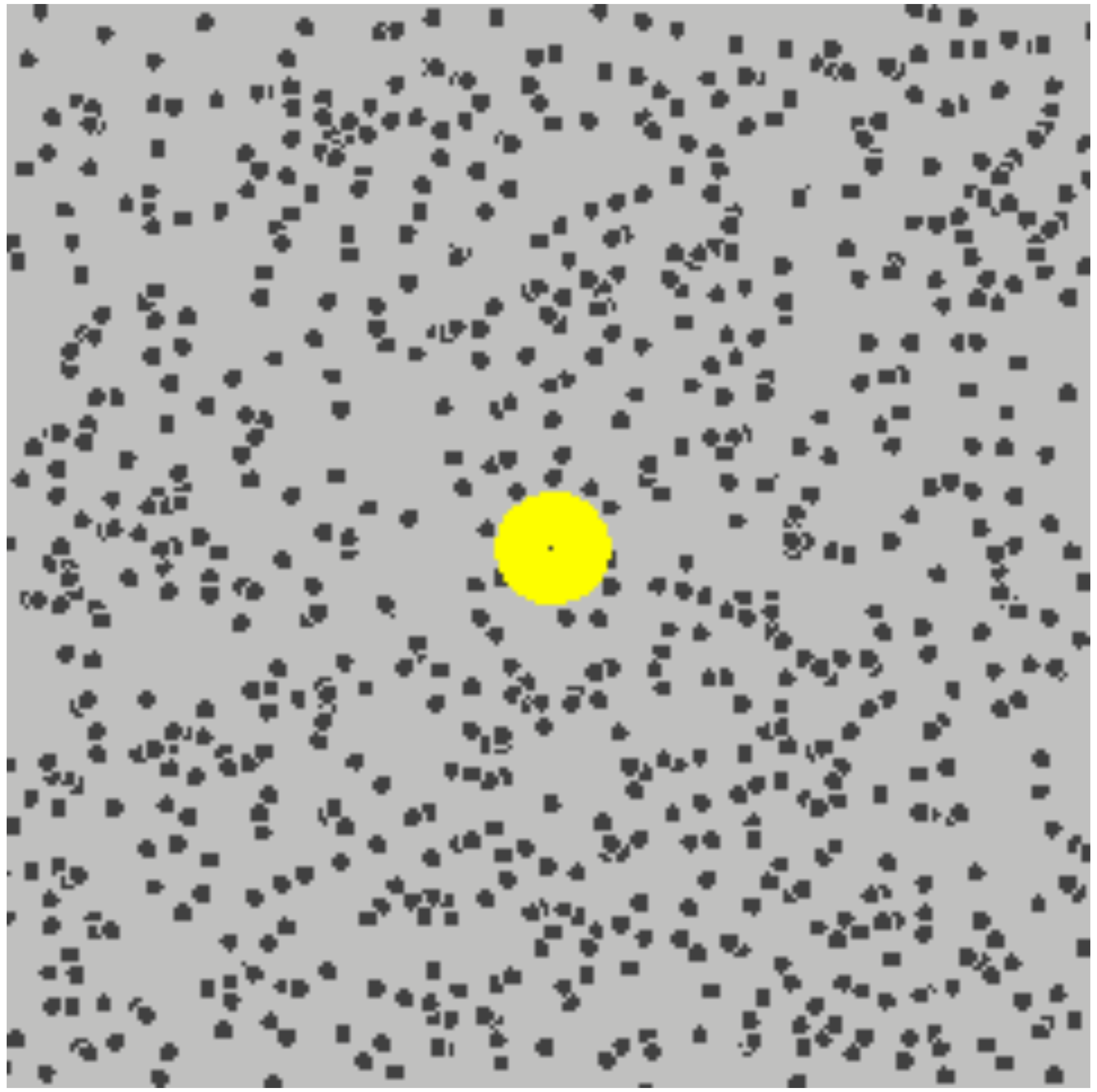
Source: https://en.wikipedia.org/wiki/Brownian_motion#/media/File:Brownian_motion_large.gif

Randomly jiggling water molecules kick other bigger molecules (proteins in water)

Make them randomly move around

Thermal fluctuation!

Very important idea.
Crucial to understand
diffusion, chemical reactions, biology



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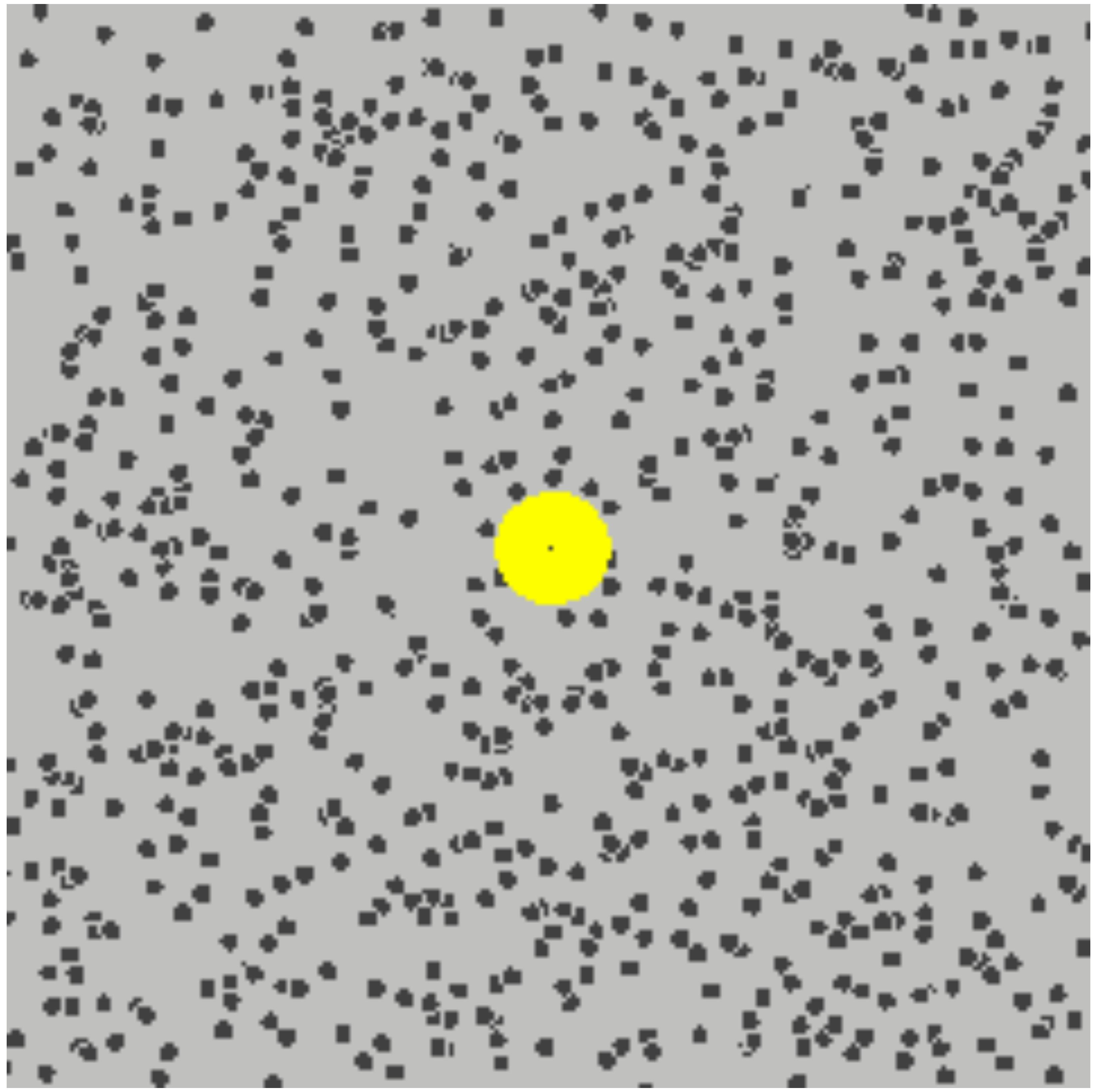
Brownian motion



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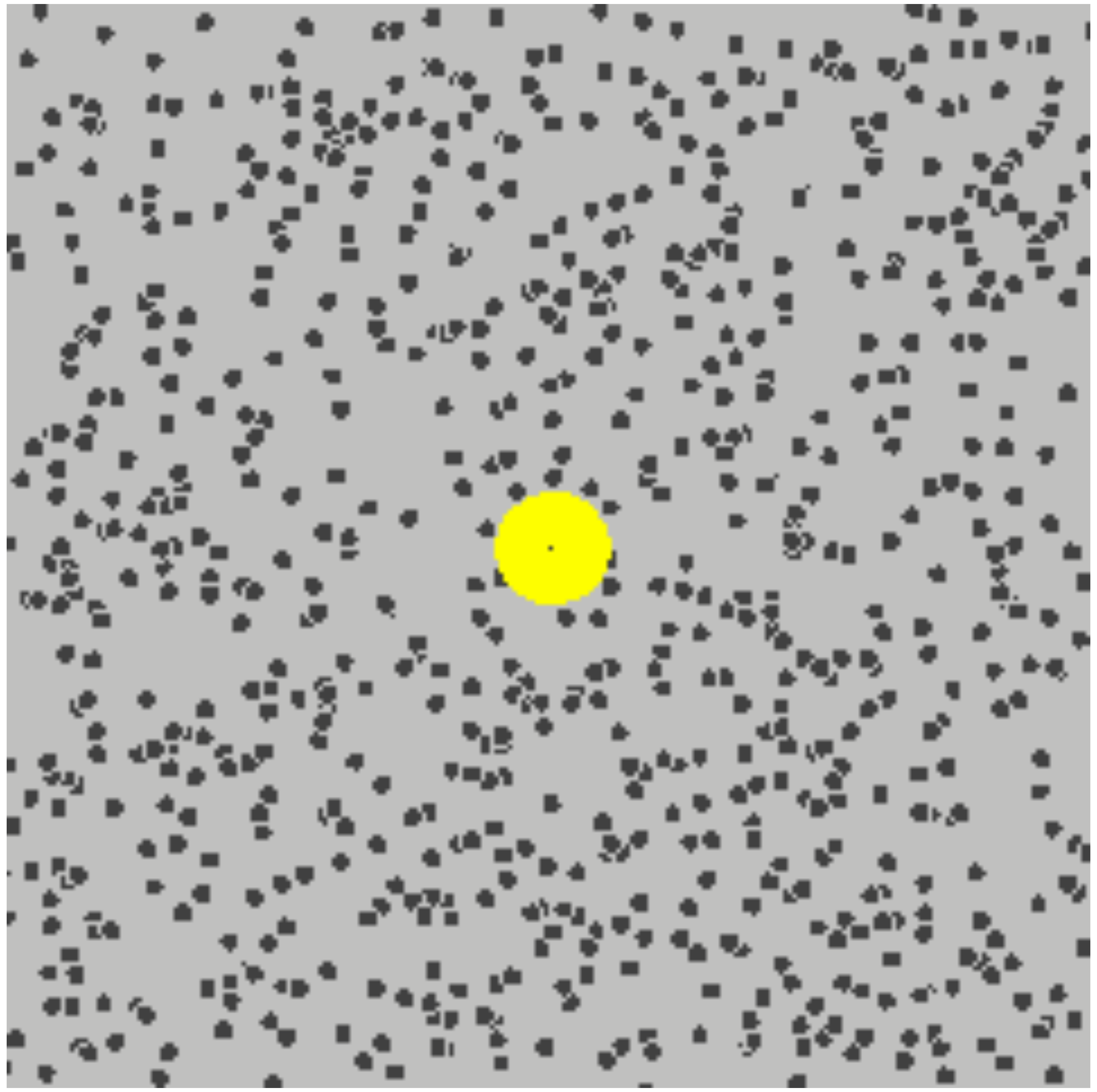
Brownian motion

In 1827, <u>Botanist</u> Robert Brown, using a microscope, observed pollen grains and other minute objects moving around in water. He wrote:

“…extremely minute particles of solid matter, whether obtained from organic or inorganic substances, when suspended in pure water, or in some other aqueous fluids, exhibit motions for which I am unable to account…”

(The miscellaneous botanical works of Robert Brown, Volume1, 1827,1828)



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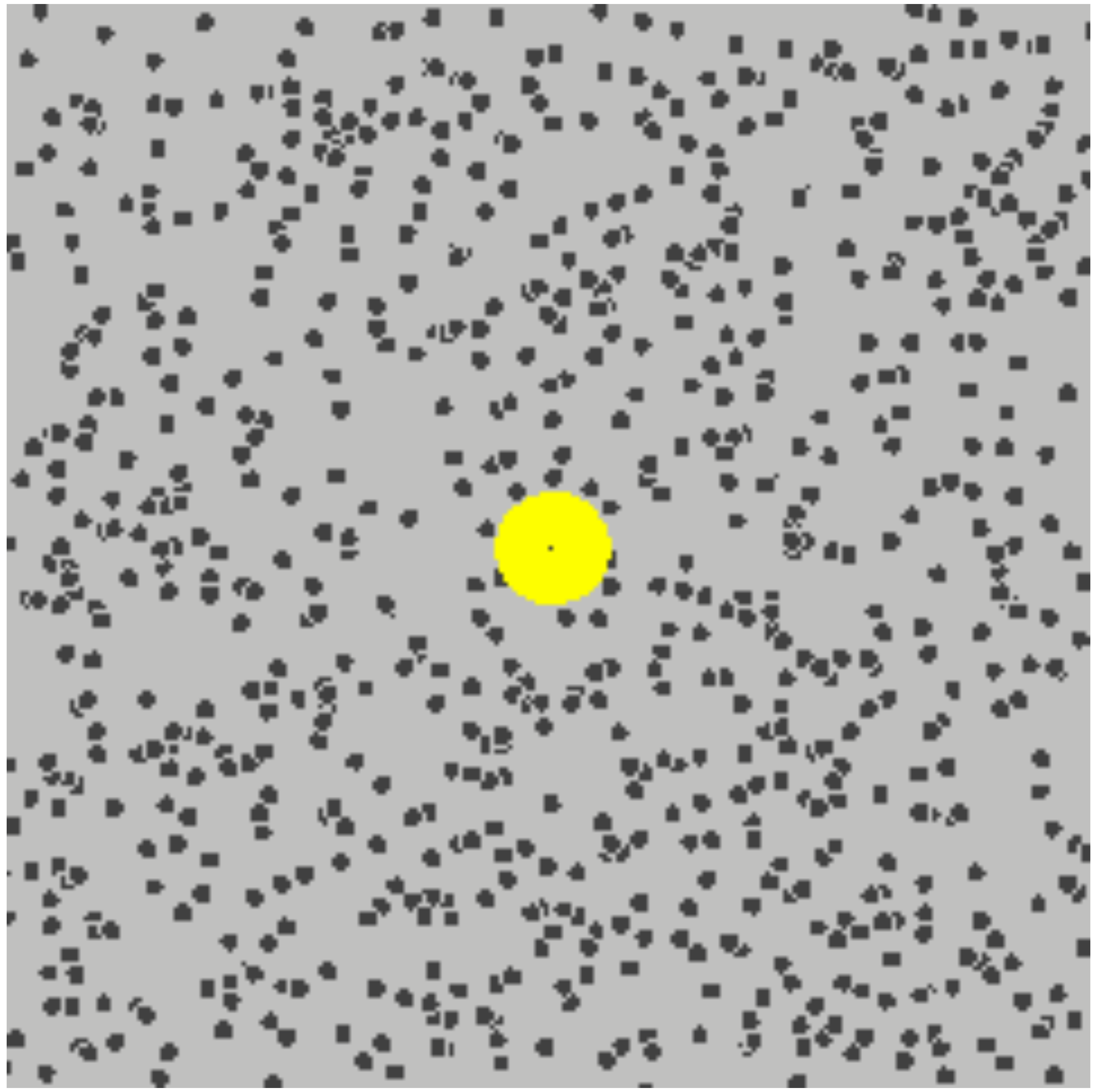
Biologist discovering a very important physics/chemistry/engineering idea!

Thermal energy

Randomly jiggling water molecules kick other bigger molecules (proteins in water)

Typical energy of these “kicks” is

“Thermal energy”



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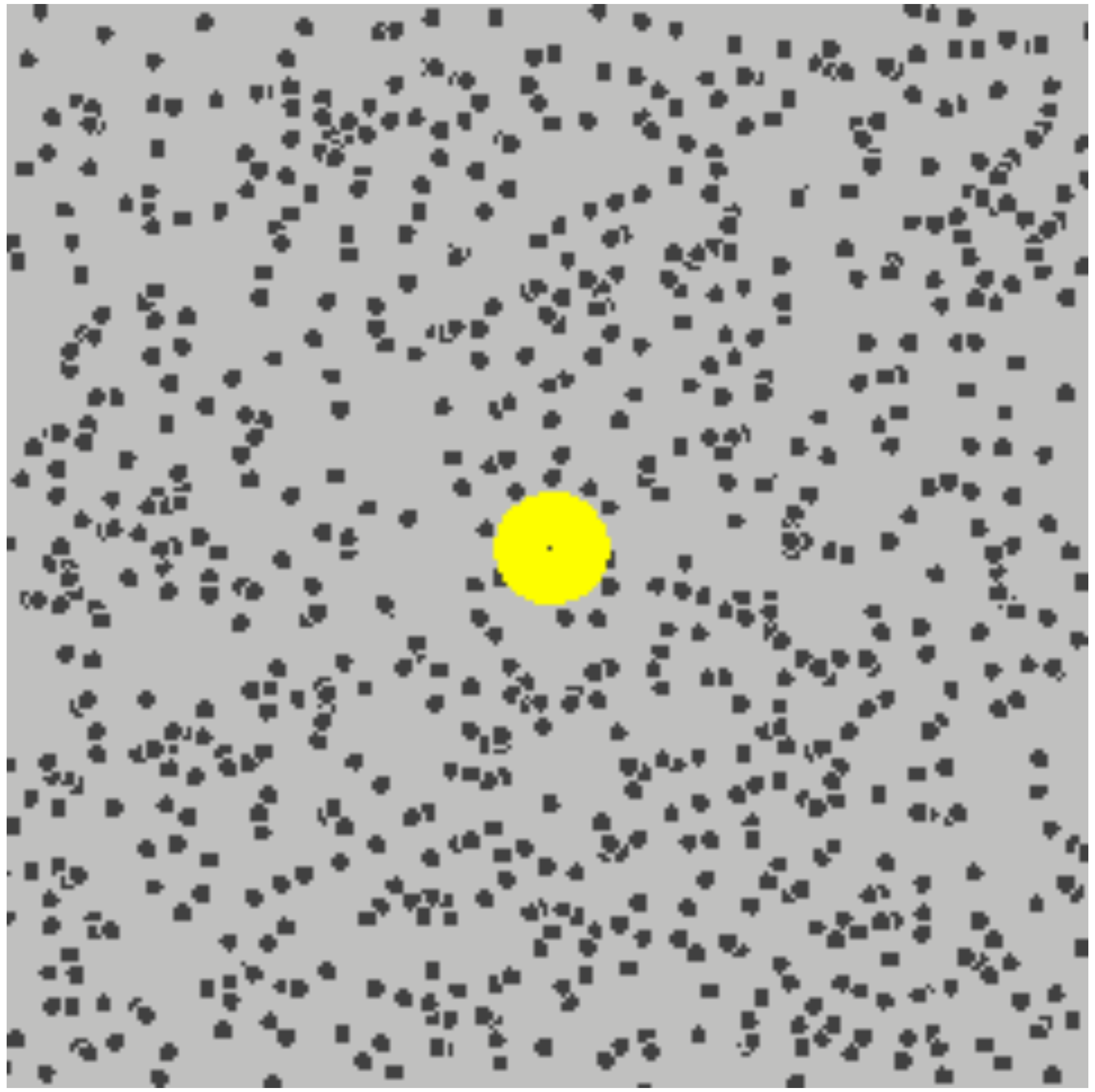
$$\text{Thermal Energy} \approx k_B T$$



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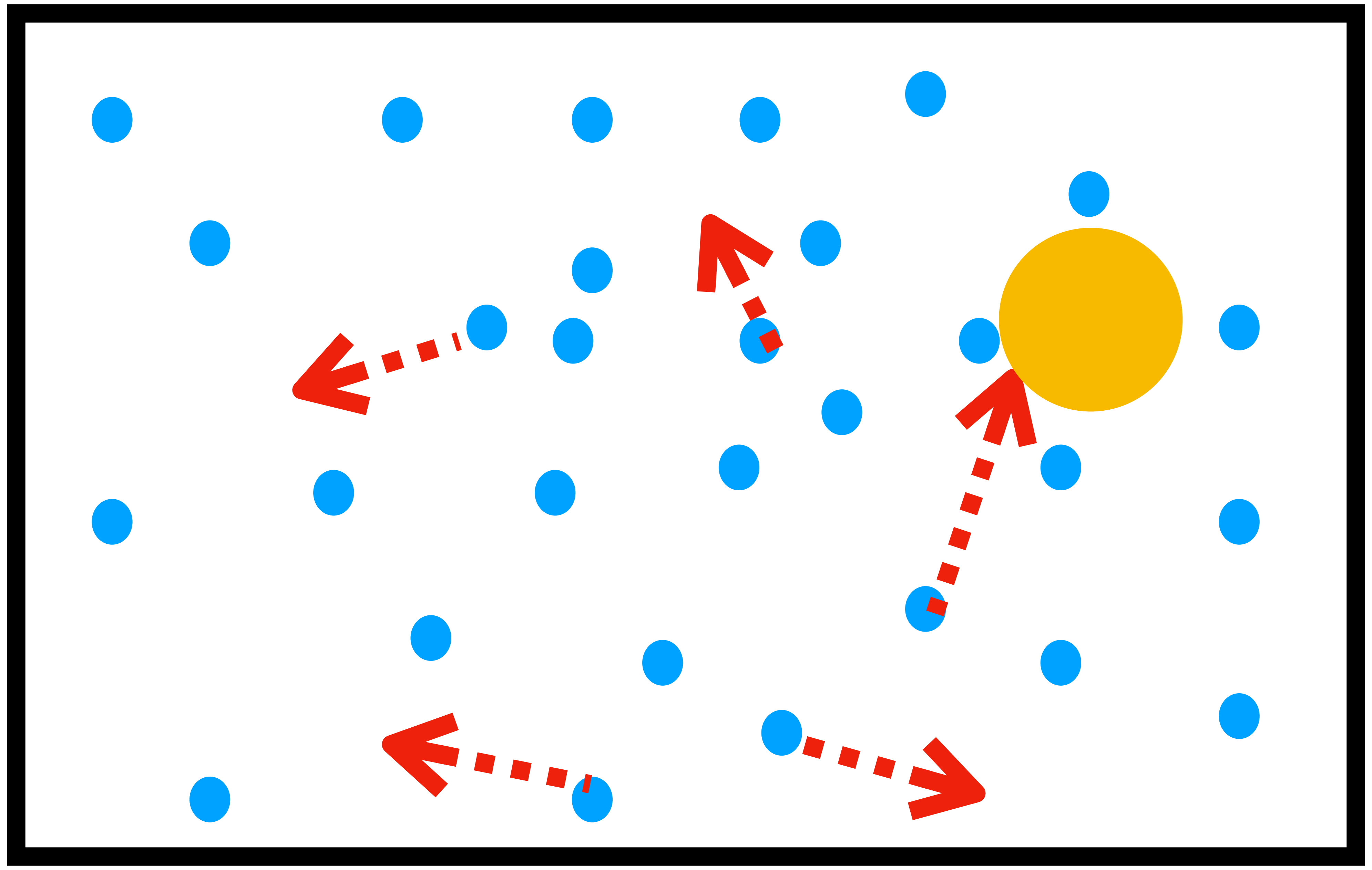
Thermal energy

$$\text{Thermal Energy} \approx \mathrm{k_B T}$$

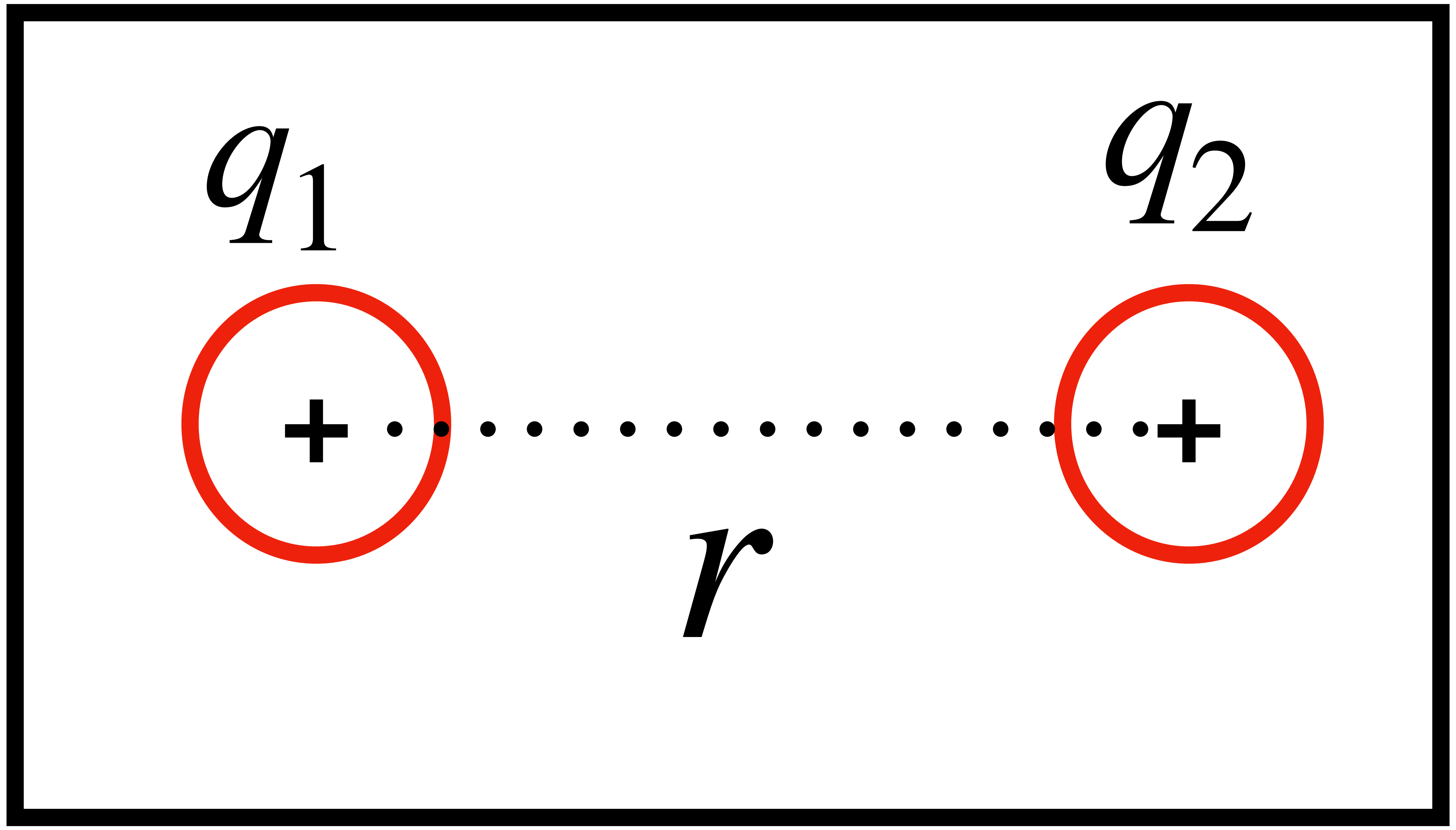
At room temperature (~300 K)



$$k_B T \approx 1.4 \times 10^{-23} J/K \times 300K$$

$$= 4.2 \times 10^{-21}\mathrm{J} \approx 0.6\mathrm{kcal/mol}$$

What is the electrostatic potential energy when two charges are nearby?



$$E_C = \frac{q_1 q_2}{4\pi\epsilon_0\epsilon_r r}$$

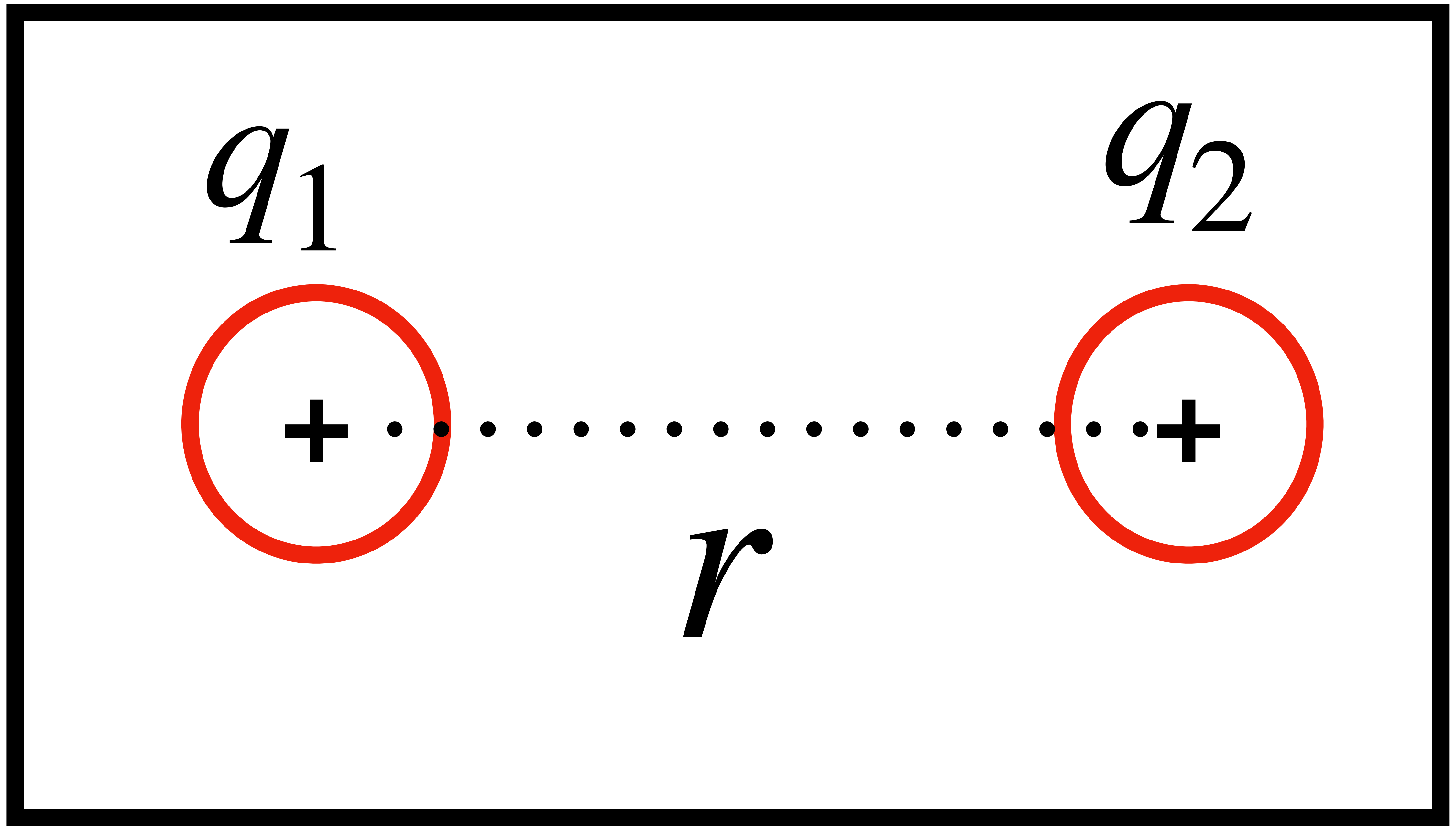
Based on the ideas developed Charles-Augustin de Coulomb (~1785)

Two unit charges in water: how big is the interaction energy?

$$q_1 = q_2 = e \approx 1.6 \times 10^{-19} C$$

$$\frac{1}{4\pi\epsilon_0} \approx 9 \times 10^9 \text{ SI units}$$

For water, $\epsilon_r \approx 80$ SI units



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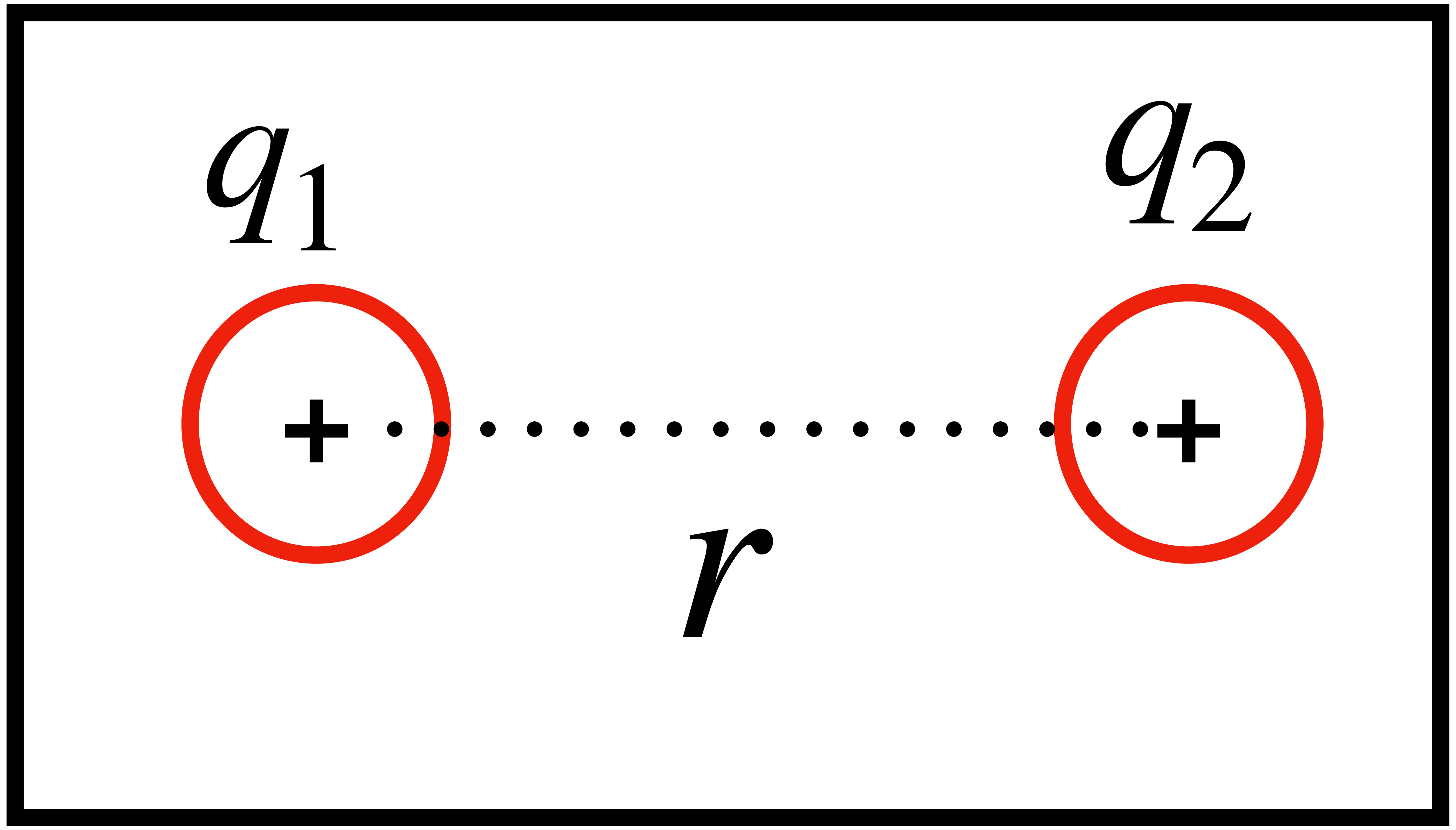
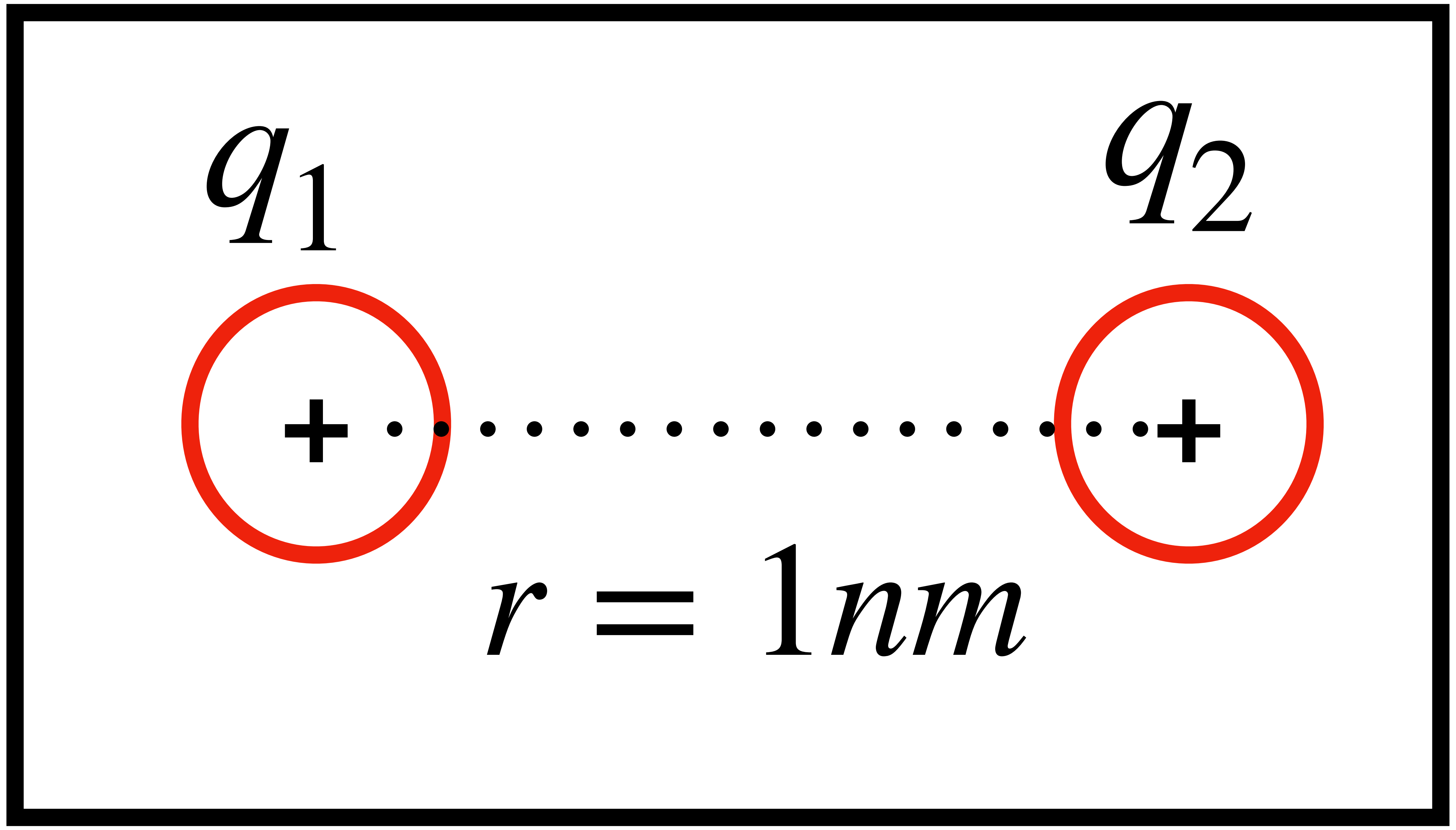


$$E_C = \frac{k}{r} \approx \frac{3 \times 10^{-30}}{r} J$$

Two unit charges in water: how big is the interaction energy?

In the case of biomolecules, $r \approx \text{nm} = 10^{-9}\text{m}$

$$E_C \approx 3 \times 10^{-21} J$$
$$\approx \frac{1}{2}\text{kcal/mol}$$



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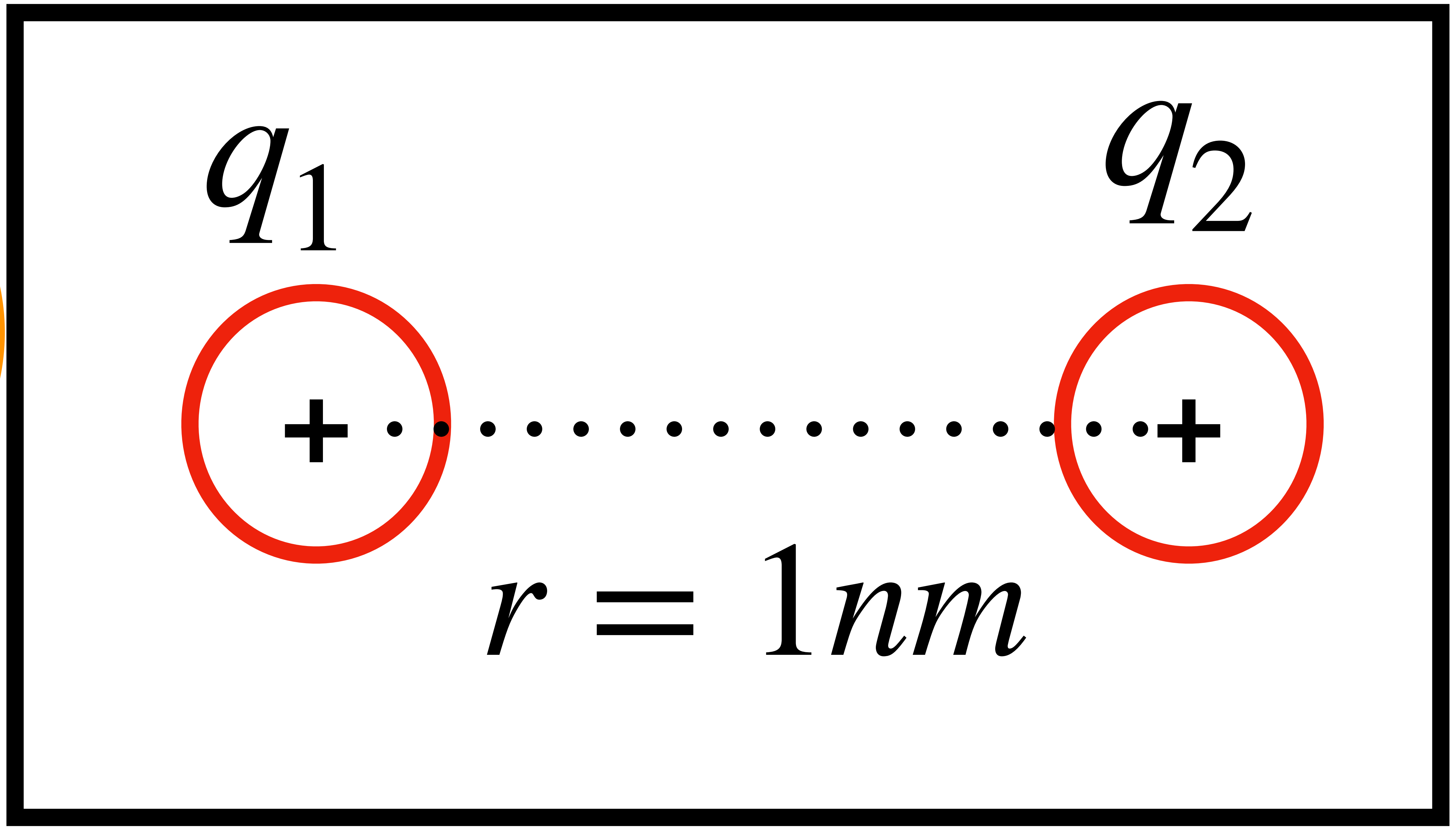


Electrostatic potential energy
Two charges in water 1nm away

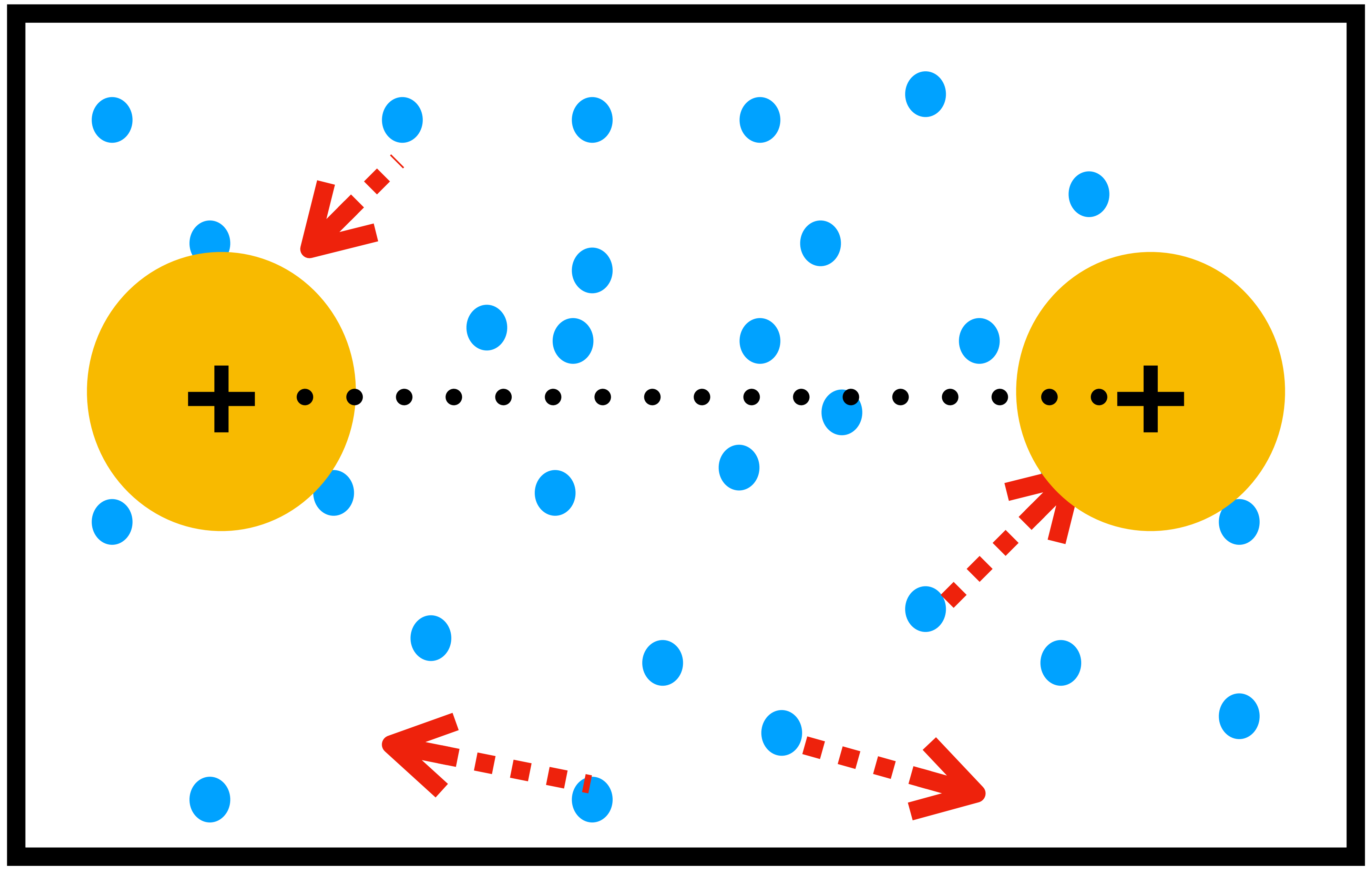
$$E_C \approx 3 \times 10^{-21} J$$
$$\approx \frac{1}{2}\text{kcal/mol}$$

How big is this compared to the other energies you know?
For example, energy of a hydrogen bond

Electrostatic energy is comparable to Thermal energy

$$\text{Thermal Energy} \approx \mathrm{k_B T_r} = 4.2 \times 10^{-21}\mathrm{J} \approx 0.6\mathrm{kcal/mol}$$

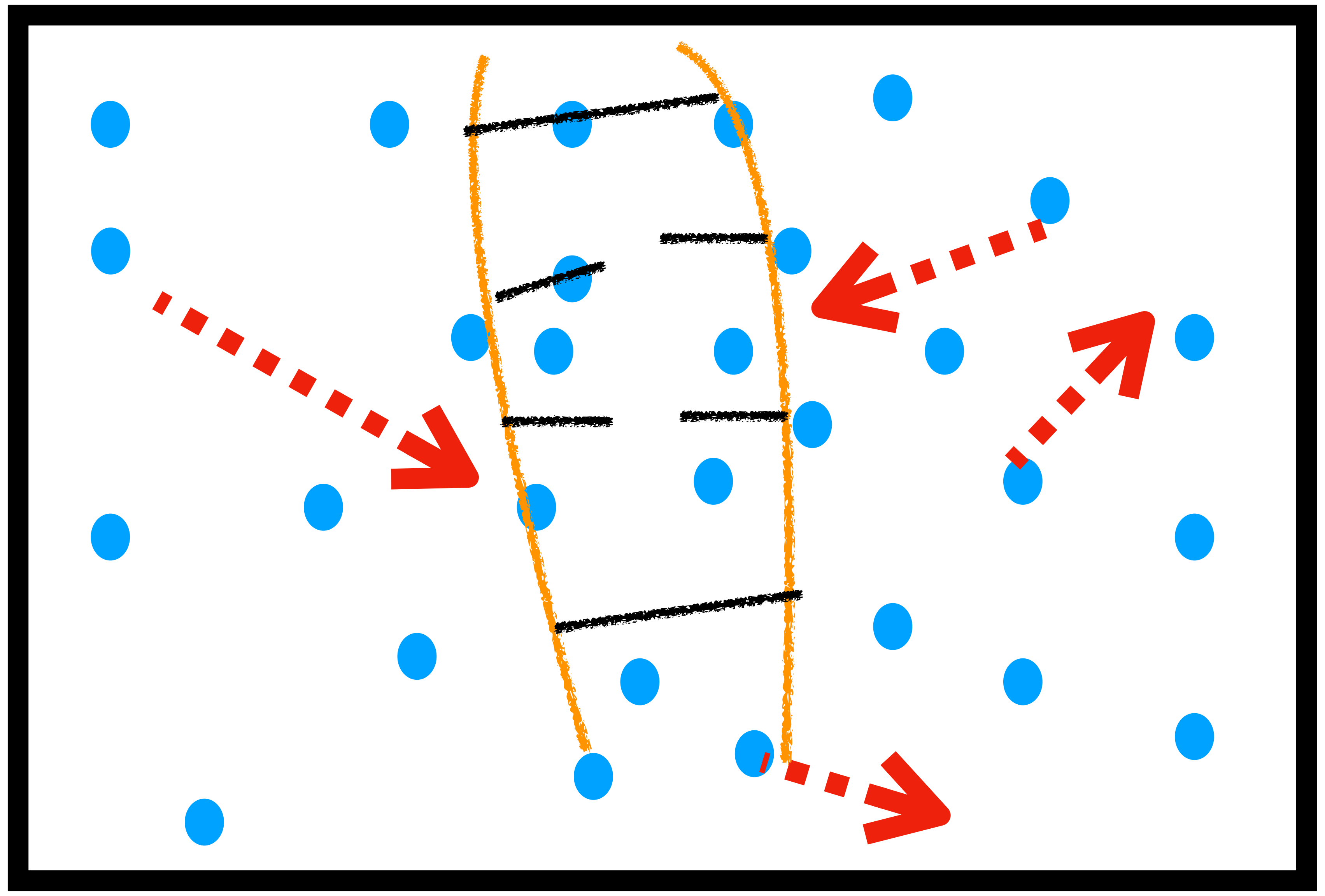
$$\text{Electrostatic Energy} = 3 \times 10^{-21}\mathrm{J} \approx 0.5\mathrm{kcal/mol} \approx k_B T_r$$



Thermal energy can destabilise bonds

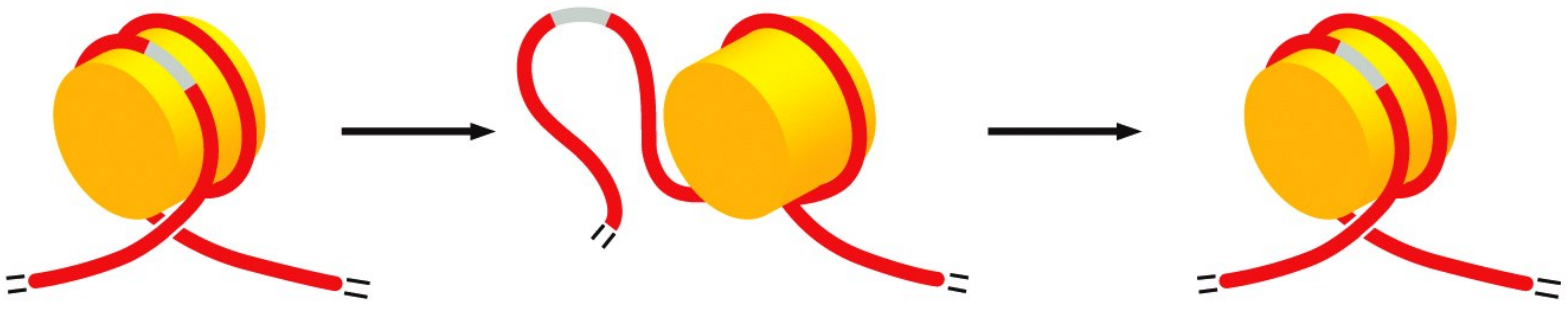
“DNA melting” due to temperature

Protein denaturation by heating



Get some sense of these numbers

Thermal energy can destabilise bonds



DNA from nucleosomes (DNA wrapped around histone proteins) can partially unwrap due to thermal fluctuations.

Wrapping/Unwrapping —> burying/exposing binding site—> gene regulation

Figure adapted from Molecular Biology of the Cell (Garland Science 2008)

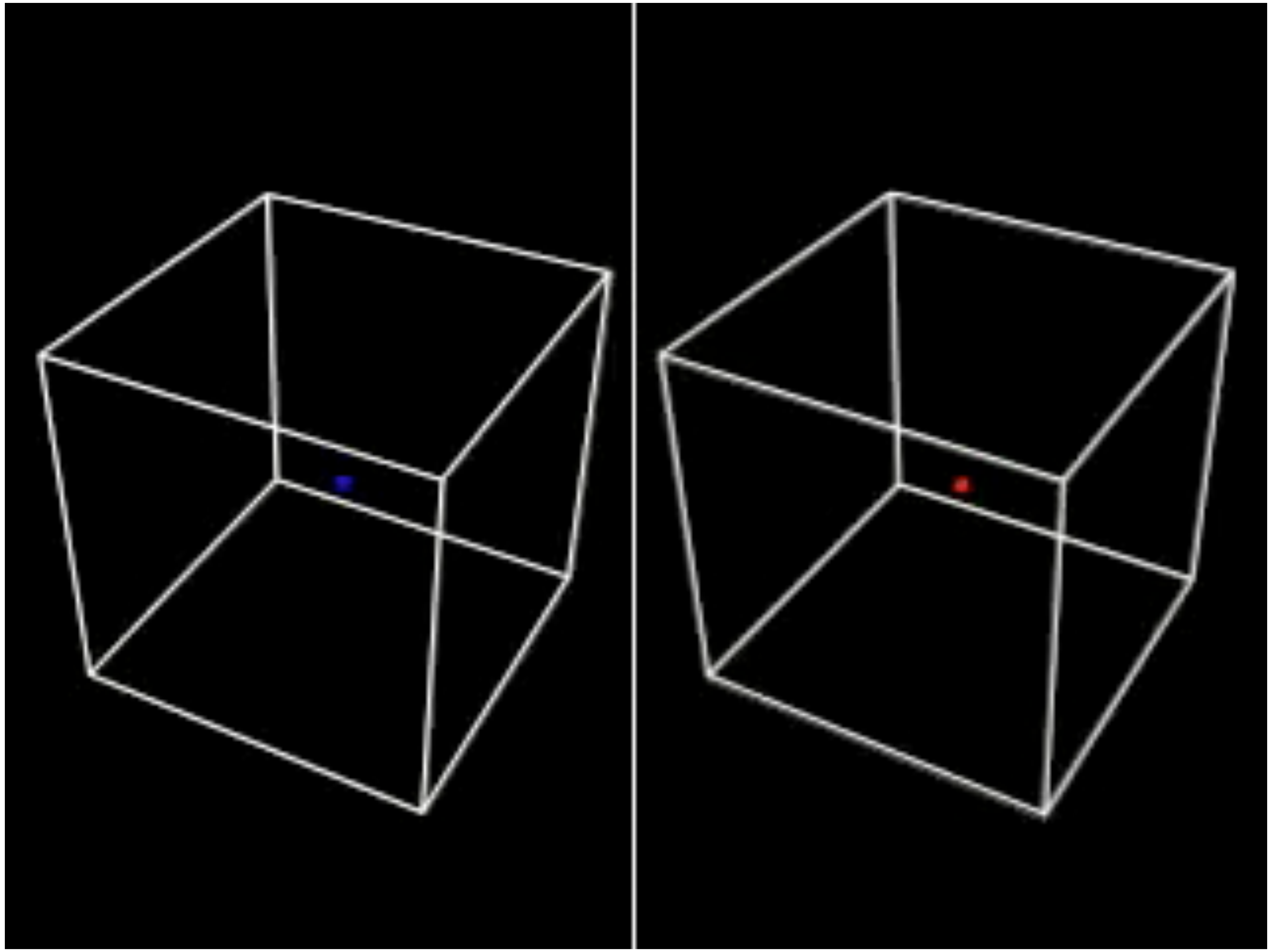
Discovery: J. Widom and others

“Random force” due to temperature => diffusion, random collision, chemical reaction!

“Errors” during chemical reaction! => mutation!

These random events/“errors”/ mutations lead to diversity, evolution!

Brownian motion: movement of a small sugar molecule versus a bigger protein in 1 second



<= Diffusion

How far a protein of size “a” nanometer can diffuse?

How far a protein of size “a” nanometer can diffuse?

Einstein’s PhD thesis, 1905

How far a protein of size “a” nanometer can diffuse?

$$\text{mean distance, r} = \sqrt{6Dt}$$

Mean distance diffused in time t

$$D = \frac{k_B T}{6\pi\eta a}, \text{Einstein relation}$$

η = viscosity of the medium

Optional: advanced ideas to ponder

Can you use Newton's equation to study Brownian motion of these particles? Why/why not?

Can we use that equation to predict the motion of a bacterium?

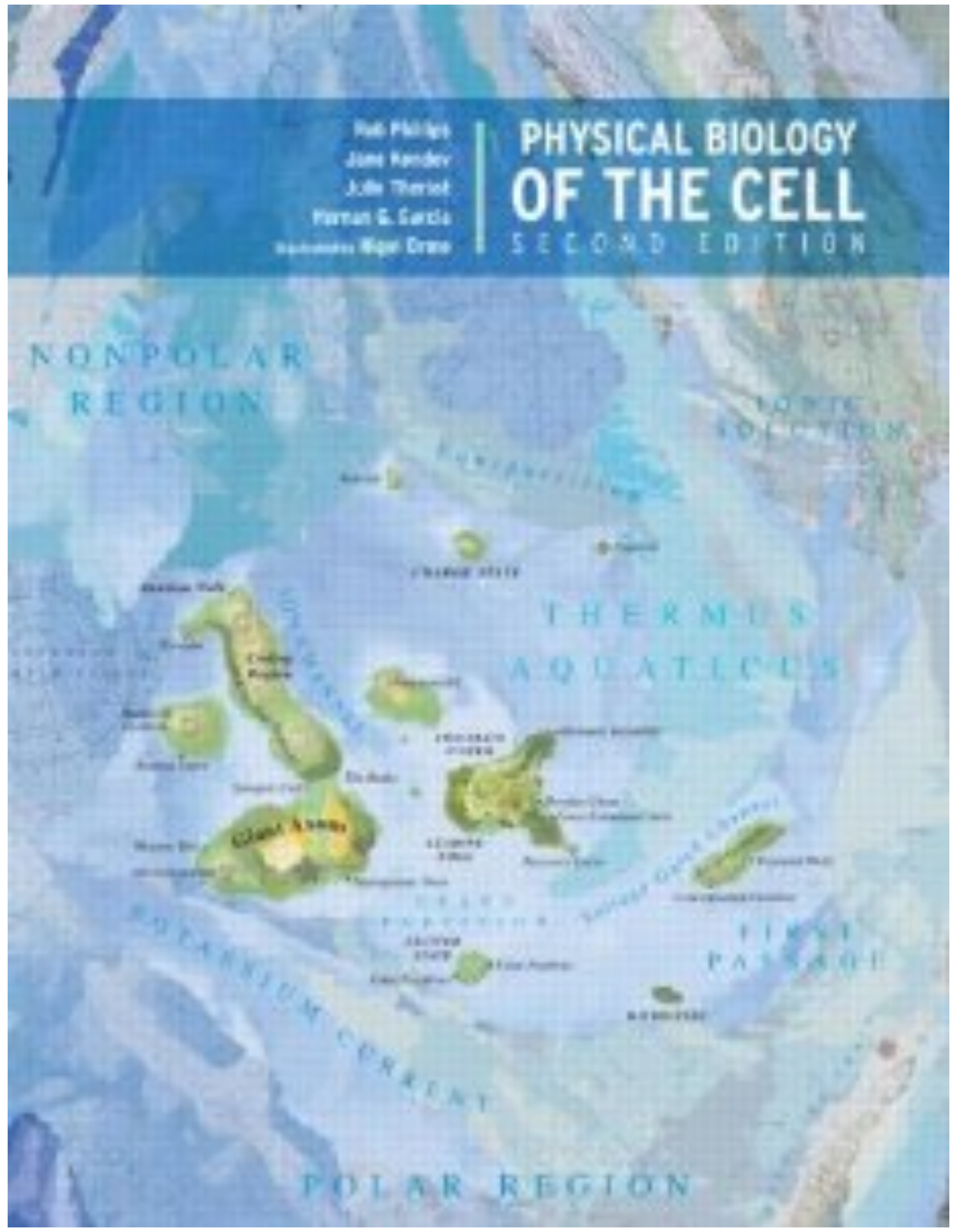
Can you take up the challenge of reading Einstein's
Brownian motion paper! It can be read by a UG student! (Available online free! Google)

Summary

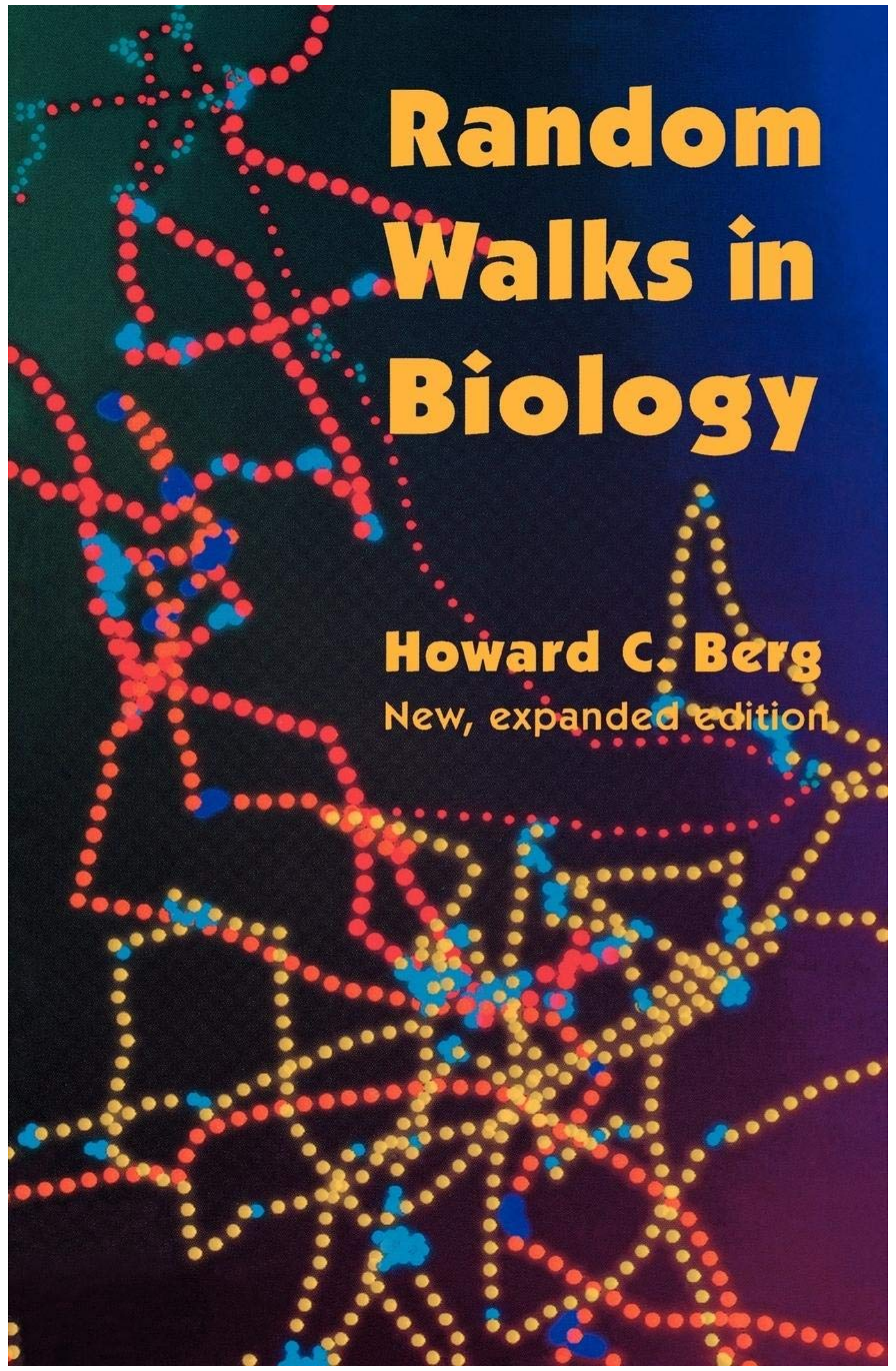
Book for reference

- Thermal energy
- Comparable to other energies
- Diffusion
- Einstein relation

Book references



Physical Biology of the cell
R. Phillips, J. Kondev…..
Publisher: Garland Science



Random walks in Biology
Howard Berg