“Life” (or Molecular biology) exists at low Reynolds number, in salty water, and in a thermal bath!

What are the laws of physics and chemistry there?

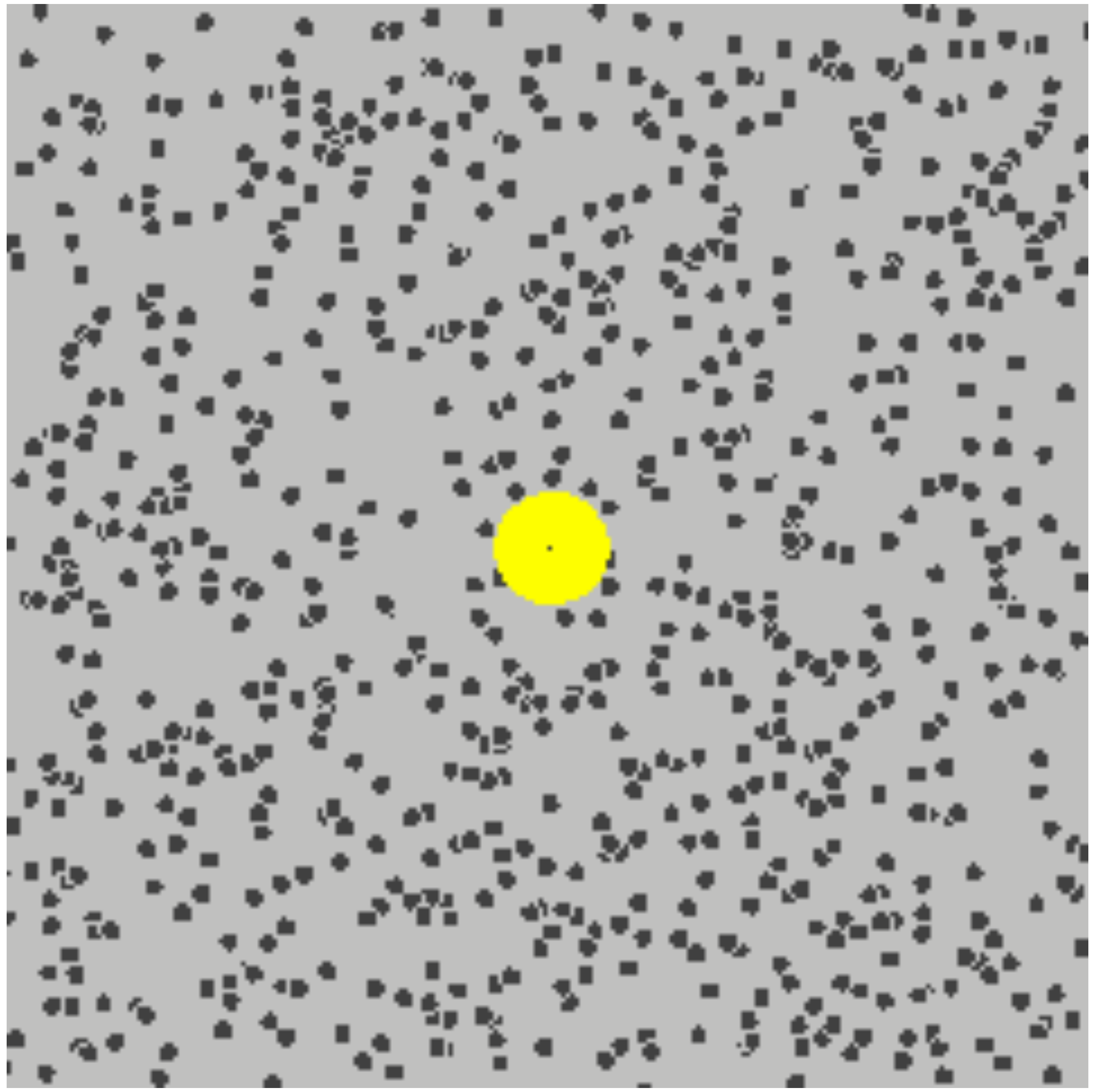
Thermal energy

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

Typical energy of these "kicks" is

"Thermal energy"

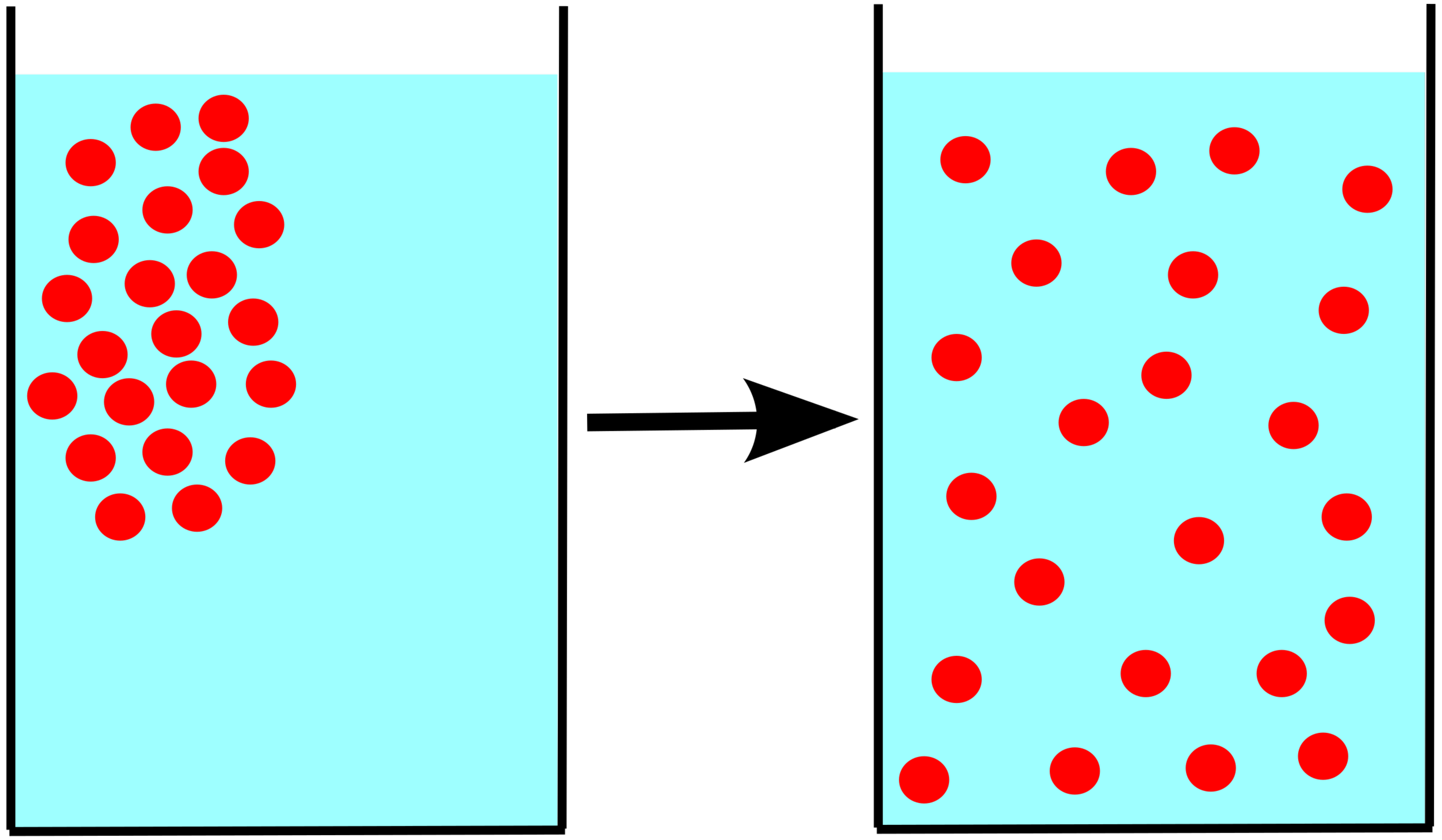
$$\text{Thermal Energy} \approx k_B T$$



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

What is the consequence of the thermal energy?

Diffusion



Each red particle will get randomly kicked due to thermal motion, resulting in diffusion

Image: https://simple.wikipedia.org/wiki/Diffusion#/media/File:Diffusion.svg

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

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Einstein’s PhD thesis, 1905

How far a protein of size "a" nanometer can diffuse?

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

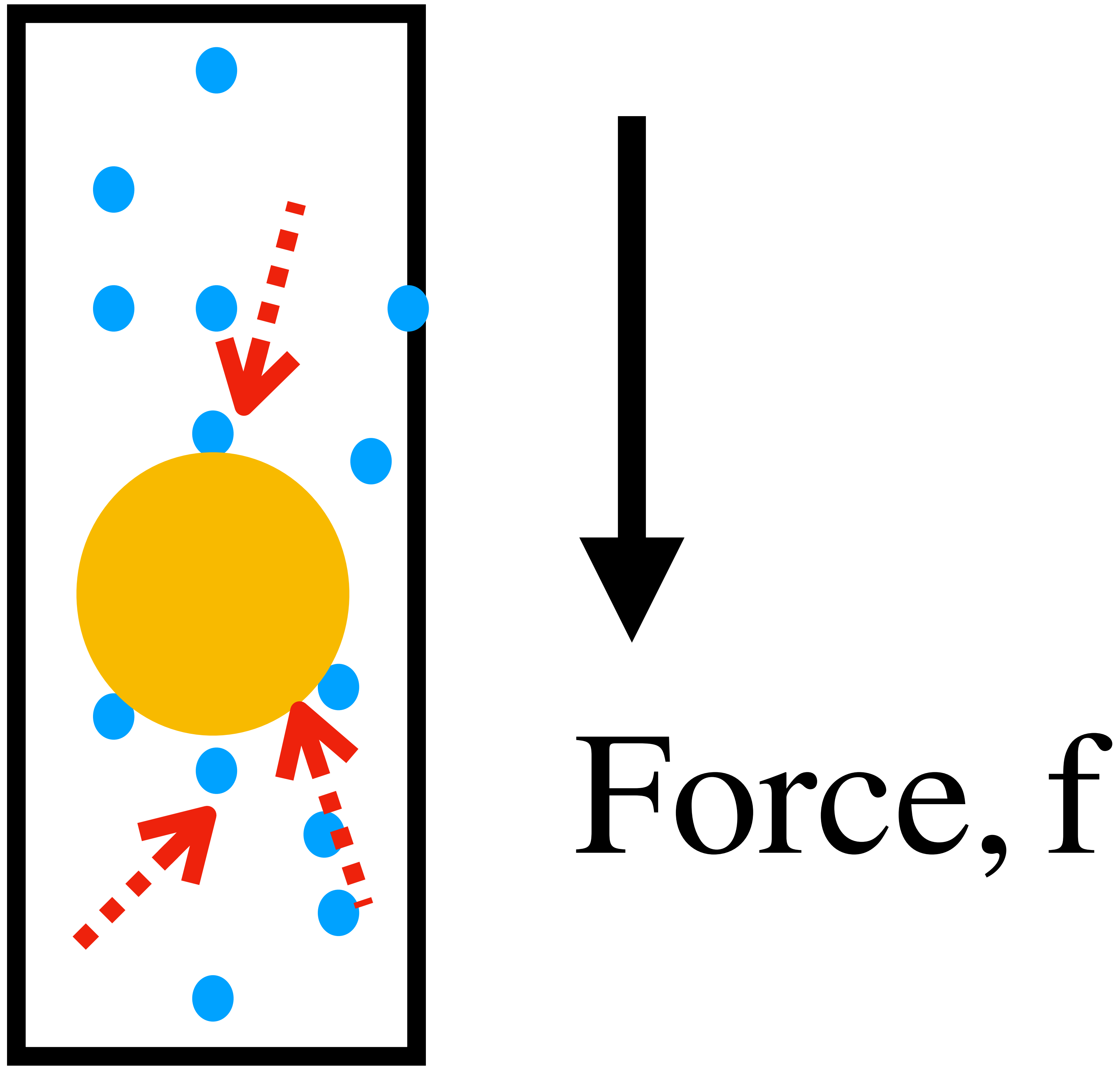
Mean distance diffused in time t

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

$$\eta = \text{viscosity of the medium}$$

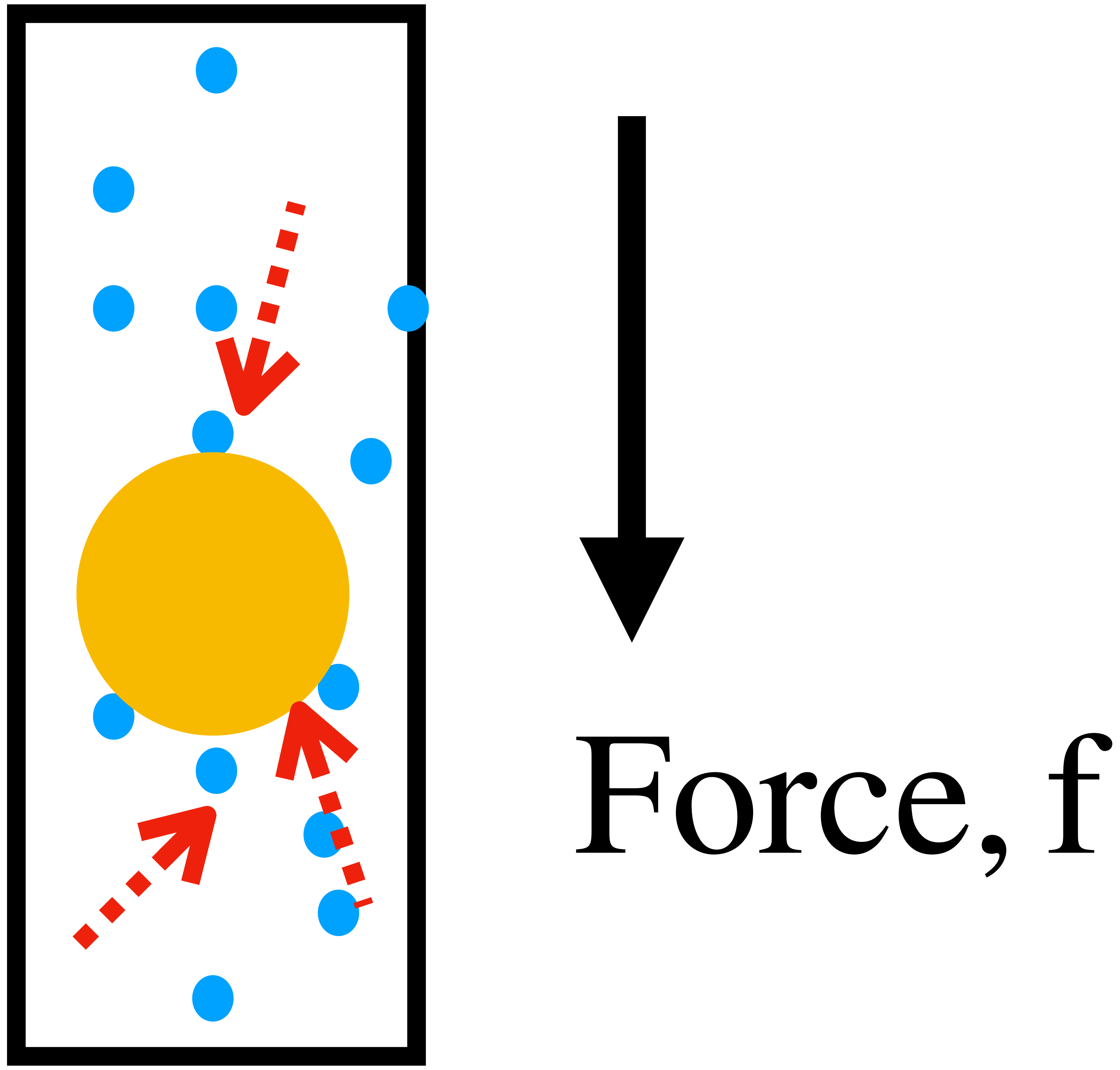
Need of probabilistic description

A cell or a biomolecule falling in a test tube under an external force (gravity or electric force)



Where will you find the cell?

A cell or a biomolecule falling in a test tube under an external force (gravity or electric force)

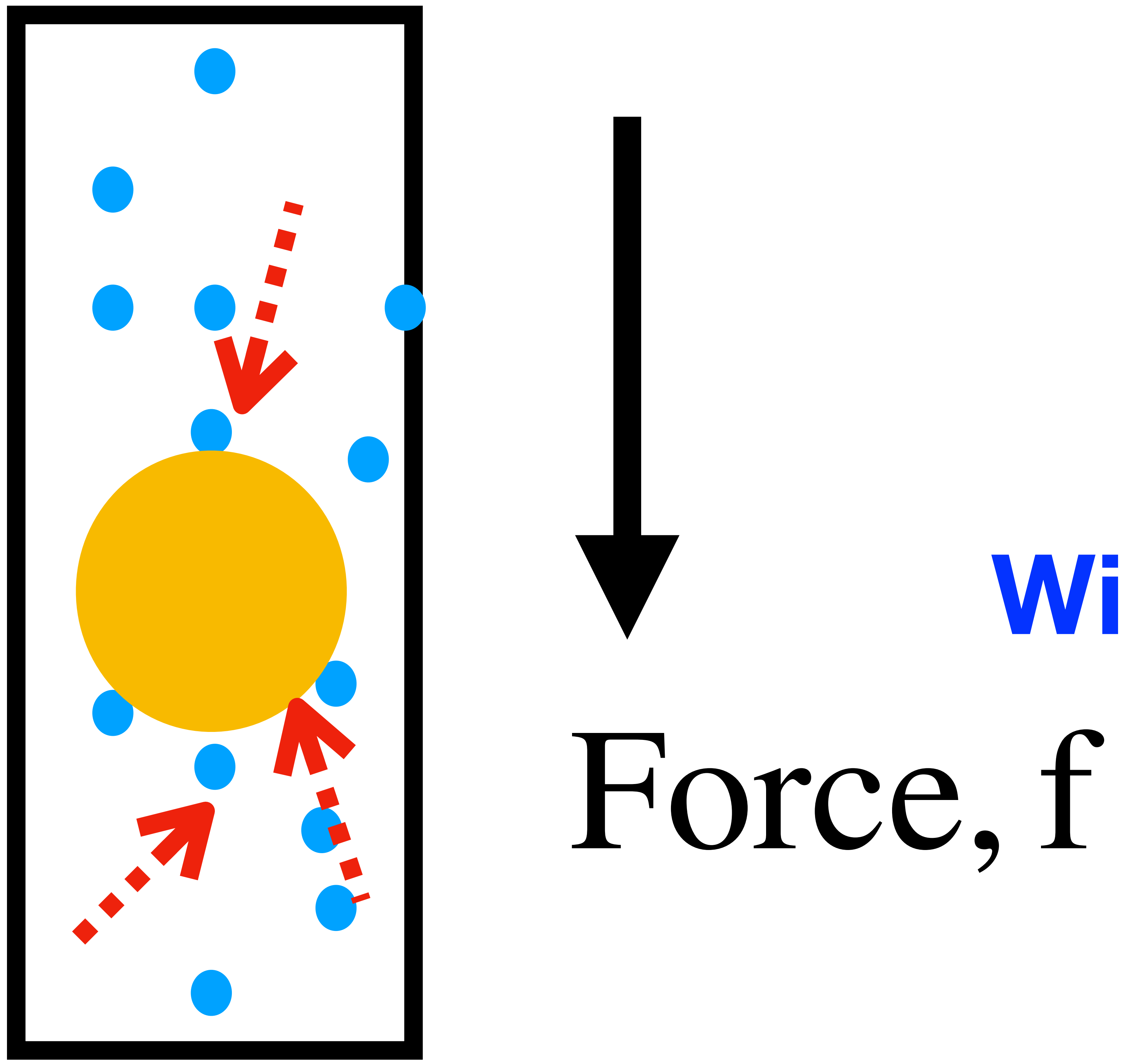


Where will you find the cell?

At the bottom

(old understanding; no thermal effect)

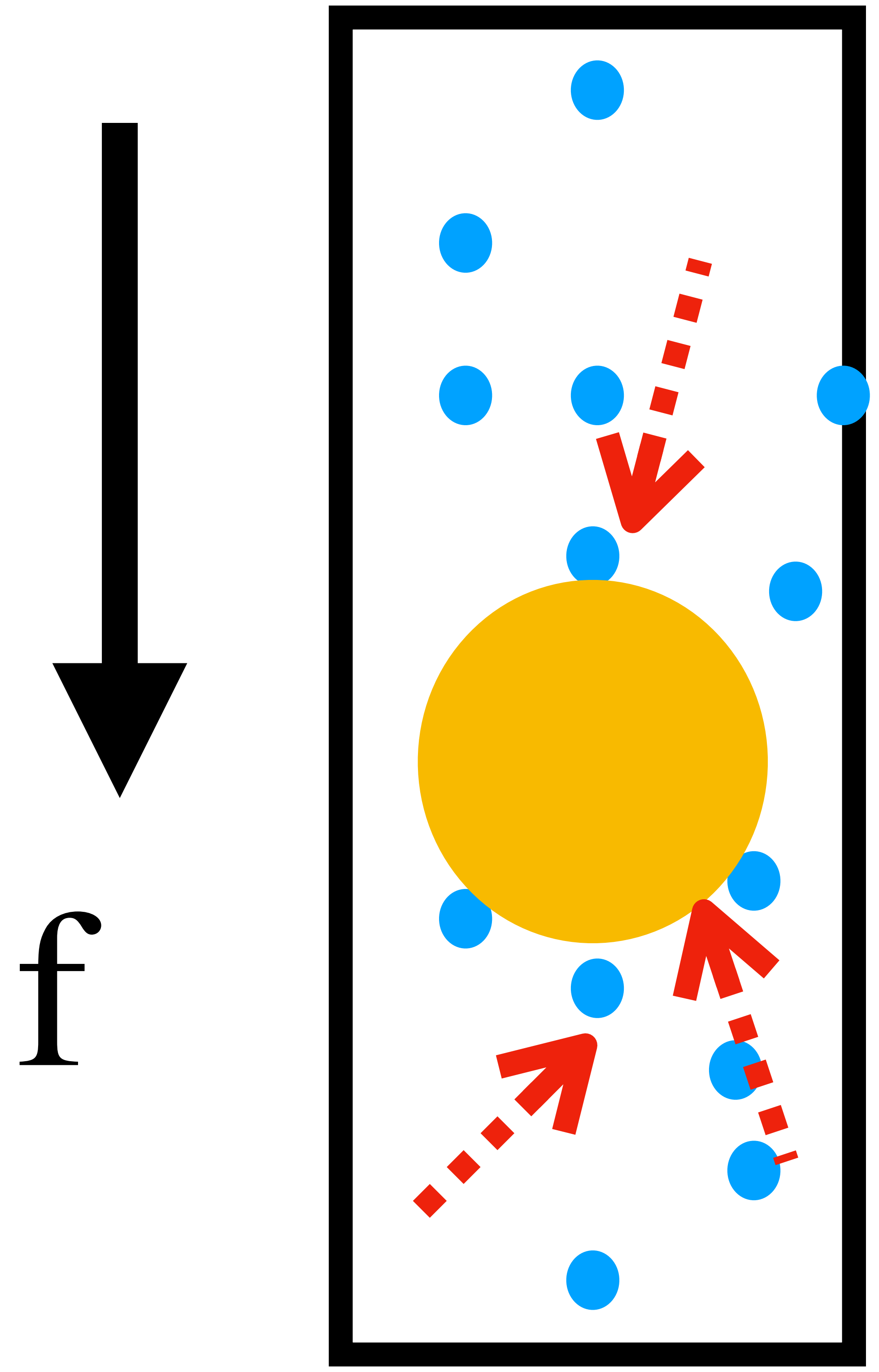
A cell or a biomolecule falling in a test tube under an external force (gravity or electric force)



Where will you find the cell?

With thermal kicks, it can be anywhere!

A cell or a biomolecule falling in a test tube under an external force (gravity or electric force)



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We cannot be certain! Hence we have to use “probability” ideas!

Biology => probabilistic; stochastic

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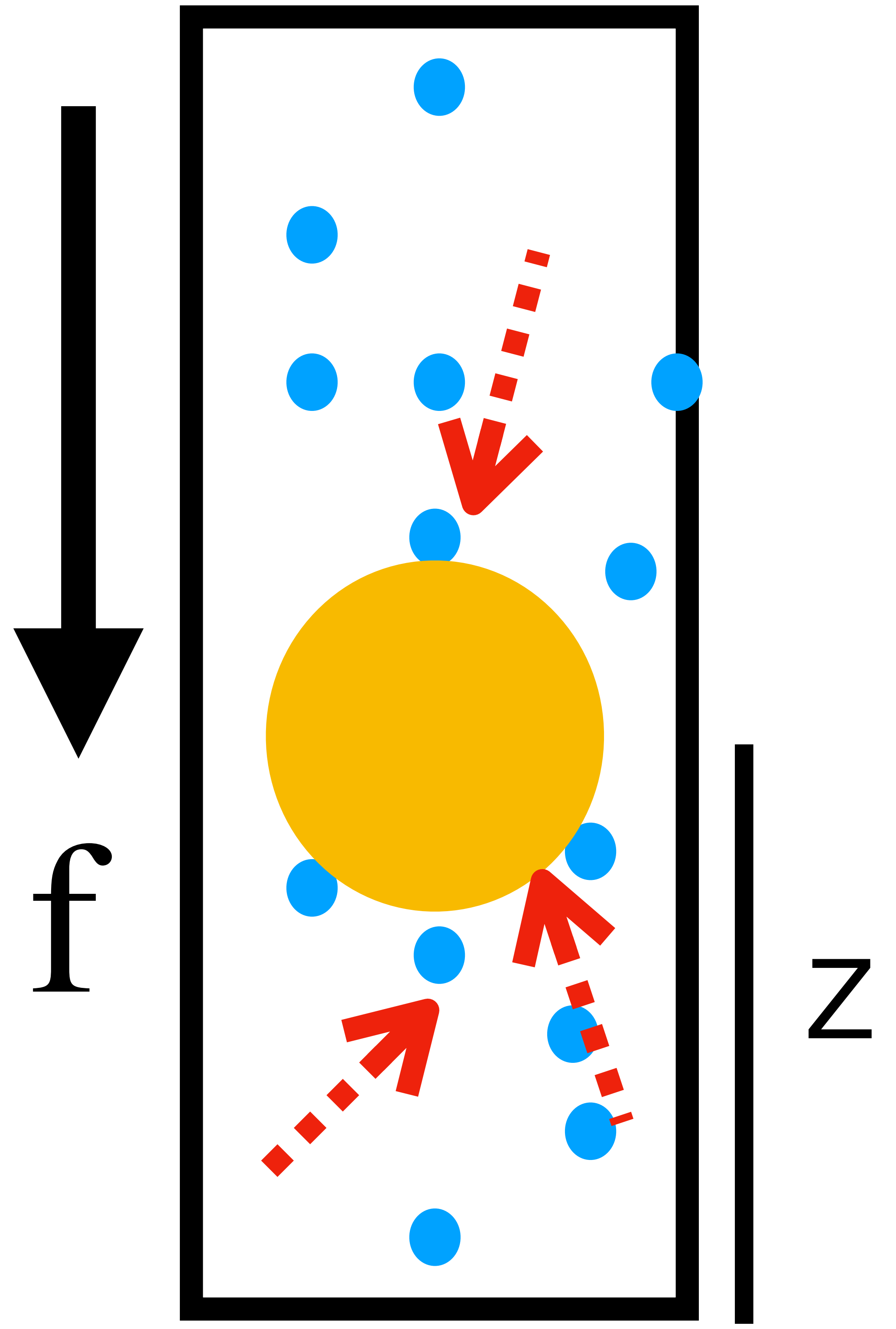


Probability of finding the a height, z

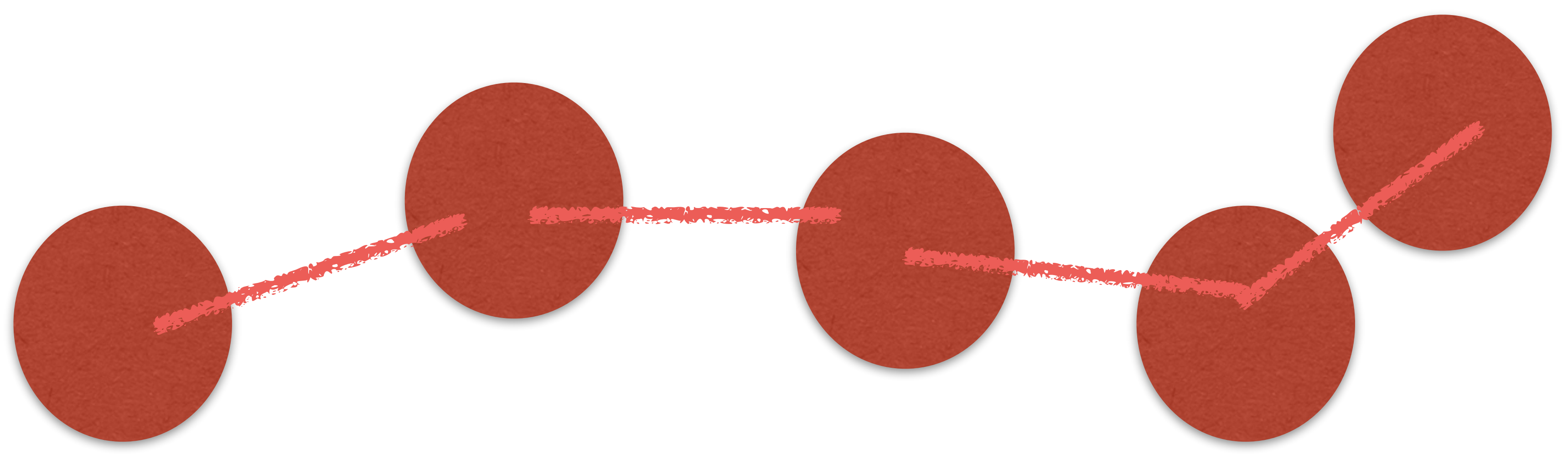
$$P(z) = A \exp\left(\frac{-E(z)}{k_B T}\right)$$

A = normalisation constant

Boltzmann probability

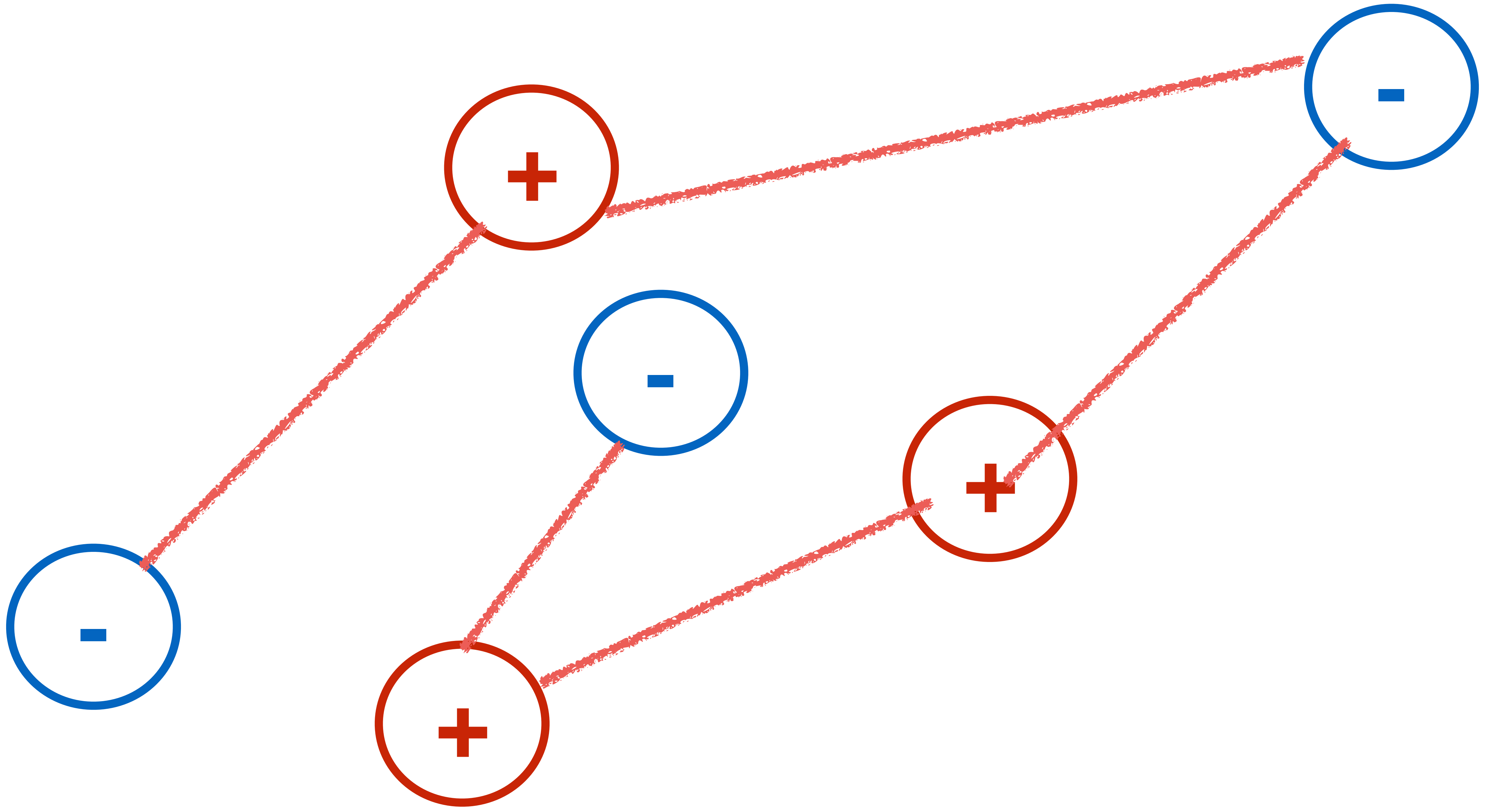
E(z)=Potential energy at height z

A protein is a small chain of molecules.



Proteins do their job by folding up to a nearly unique shape in 3D

What will be the preferred conformation of such proteins ?



Probability of finding protein in a conformation (say, conformation “n”)

$$P_n = \frac{\exp\left(\frac{-E_n}{k_{\mathrm{B}}T}\right)}{Z}$$

E_n is the total potential energy of the protein, in that conformation

Boltzmann probability

$$Z = \sum_n \exp\left(\frac{-E_n}{k_\mathrm{B}T}\right)$$

Z=partition function

Unlike what you learned so far, the system does not find itself in its minimum "energy" state!

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System (biomolecule, cells) can be in many different “states”.

Each has a certain probability

State = arrangements of atoms; also known as microstate

Dynamics: What is the equation of motion that you have studied?

In the world we see around us,

$$\text{force} \propto \text{acceleration}$$

JEE question: If I take a dead bacterium and leave it with an initial velocity “u”, in water, how far will it move?

(neglect thermal fluctuation; neglect gravity)

Assume bacterium to be a sphere of radius, a = 1 micrometer, filled with water.

$$m\frac{dv}{dt} = -6\pi\eta a v$$

$$v = u \exp\left(\frac{-6\pi\eta a}{m} t\right)$$

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$$\tau = \frac{m}{6\pi\eta a}$$

$$\text{mass}, m = \text{density} \times volume = 1000 \times \frac{4}{3}\pi(1\mu m)^3 \text{ SI units}$$

$$\approx 4 \times 10^{-15} kg$$

$$\tau = \frac{m}{6\pi\eta a} \approx \frac{4 \times 10^{-15}}{20 \times 10^{-3} \times 10^{-6}} = 2 \times 10^{-7} \text{ seconds}$$

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$$\text{Total distance moved by bacteriaum} = \int_0^\infty v dt = u\tau$$

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Total distance moved by the bacterium is smaller than the size of an atom!!

$$m\frac{dv}{dt} = -6\pi\eta a v \qquad u\tau \approx 10^{-6}(m/s) \times 10^{-7}s = 10^{-13}m$$

A bacterium without any external force, cannot even move the size of an atom!

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If you want to move (if you want velocity), apply force!

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$$m\frac{dv}{dt} + 6\pi\eta a v = f$$

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Intertial force

Viscous force

External force

For the parameters relevant to molecular biology, inertial force contribution is negligible compared to viscous force

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$$\Rightarrow \text{force} \propto \text{velocity}$$

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Intertial force

Viscous force

External force

$$\Rightarrow \text{force} \propto \text{velocity}$$

(Not acceleration!)

For the parameters relevant to molecular biology, inertial force contribution is negligible

$$\Rightarrow \text{force} \propto \text{velocity}$$

Experiments probing motion in biology will typically measure the relation between force and velocity

Force-Velocity relation

At low Reynolds number

$$\Rightarrow \text{force} \propto \text{velocity}$$

$$\text{Reynolds number, R} \approx \frac{u\tau}{a} \approx \frac{\rho u a}{\eta}$$

$$R = \frac{\text{Intertial forces}}{\text{Viscous forces}}$$

At low Reynolds numbers

$$\Rightarrow \text{force} \propto \text{velocity}$$

$$\text{Reynolds number, R} \approx \frac{\rho u a}{\eta} = \frac{10^3 ua}{10^{-3}} = 10^6 ua$$

	Typical speed, u	Typical size, a	Approximate R	R compared to 1
Bacterium in water	1 micron/s	Micron	10^{-6}	Low R
Molecular motor in water	1 micron/s	10 nm	10^{-8}	Low R
Fish in water	10cm/s	10cm	10^{4}	High R
Human in water	0.1 m/s	1m	10^{5}	High R
Human in tar (viscosity 100 billion times of water)	cm/s	1m	10^{-8}	Low R

Advanced reading recommendation

Life at low Reynolds number

E. M. Purcell
Lyman Laboratory, Harvard University, Cambridge, Massachusetts 02138
(Received 12 June 1976)

Summary

- Not minimum energy!
- Thermal force would make all configurations probable
- Some configurations are more probable than the others
- Boltzmann probability
- In the microscopic biology world, force is needed to maintain velocity
- Viscous forces are much larger than inertial forces.
- In the low Reynolod's number world, F is proportional to v.