Mahidol University
Faculty of Science

60 YEARS MAHIDOL UNIVERSITY SCIENCE

SCPY508 Contemporary Physics

Contemporary Biophysics

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PHYSICS meets BIOLOGY

Simulations in Biology and Biophysics

How to bring Physics to Life?

Careers in Biophysics

Job Market:

Universities

Industry

Medical Centers

Research Institutes

Government

Impact on biotechnology and medicine & Innovation

Divisions of Biophysics:

Molecular biophysics

Biomechanics

Membrane Biophysics

Bio-electrochemistry

Environmental Biophysics

Theoretical Biophysics

History of Biophysics

First Biophysicists

Heraclitus 5th century B.C. – earliest mechanistic theories of life processes, insight into dynamic.

“Change is central to Universe”.

“Logos is the fundamental order of all “on Nature” changes of objects with the flow of time”

“You can not step twice into the same river”

First Biophysicists

Epicurus 3rd century B.C. – atom. Living organisms follow the same laws as non-living objects.

Galen 2th century AD – physician, most accomplished medical researcher of the Roman period. His theories dominated Western medicine for over millennium.

Better anatomy only by Vesalius in 1543
Better understanding of blood and heart in 1628

Leonardo da Vinci 16th century – mechanical principles of bird flight (to use for engineering design) - bionics

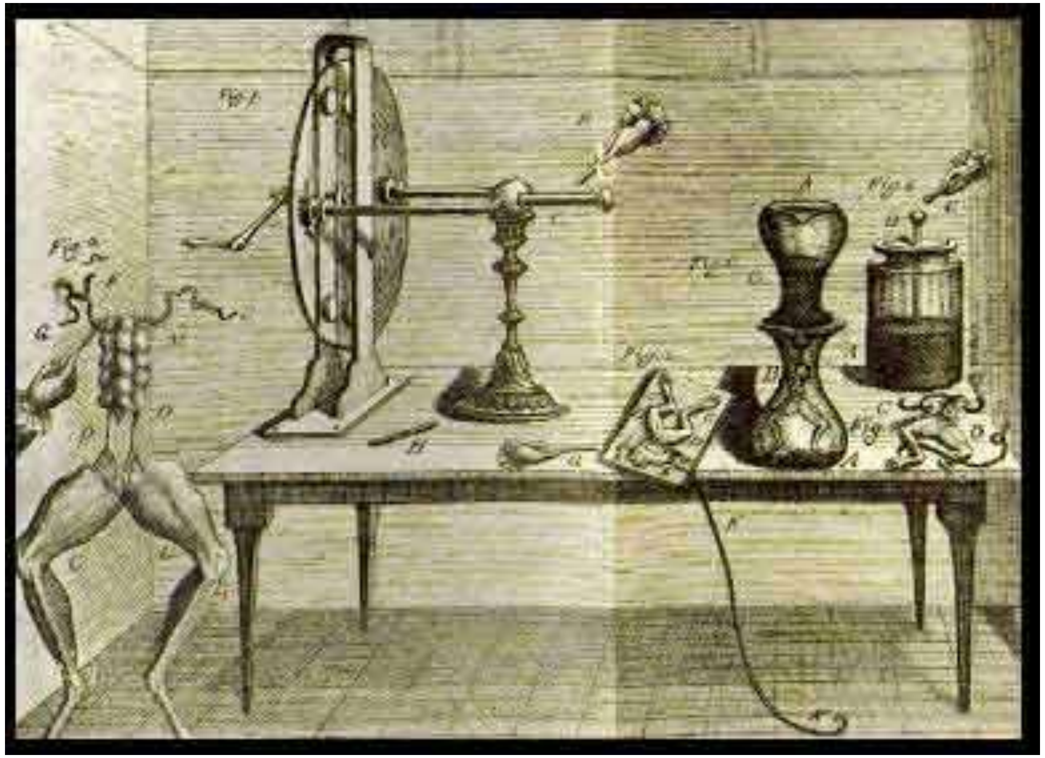
Borelli farther of biomechanics

Giovanni Alfonso Borelli 17th century- related animals to machines and utilized mathematics to prove his theories.

De Motu Animalium – comprehensive biomechanical description of limb’s mobility, bird’s flight, swimming movement, heart function.

Luigi Galvani / Alessandro Volta
Bio-electrochemistry

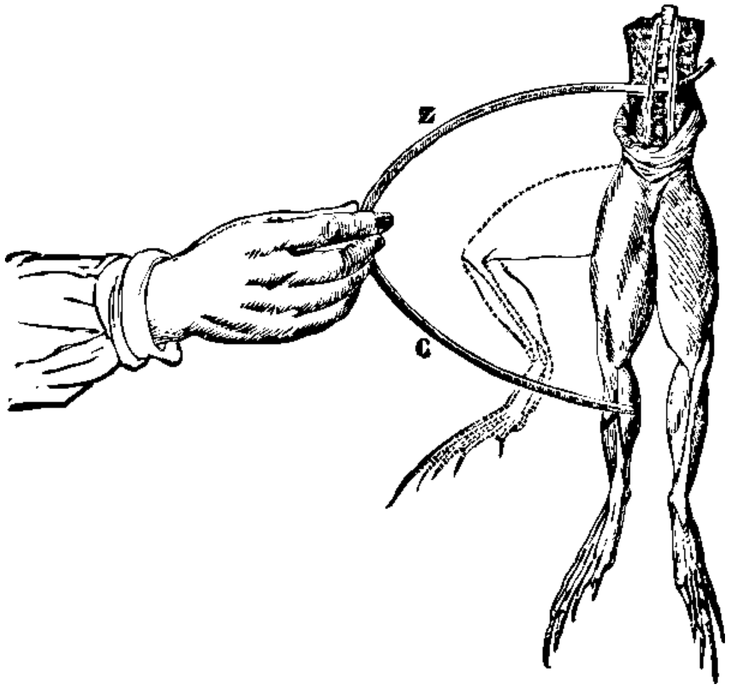
18th (1771) Galvani touched frog nerve with charged scalpel.



Signal transduction in neurons and communication between neurons and muscle has electrical nature.

Luigi Galvani / Alessandro Volta

From frog leg to first battery.



With two different metals effect is stronger.

Contact potential !!

Electric circuit = two different metals + sciatic nerve of the frog
Nerve of the frog's leg = electrolyte and sensor
Metals = electrodes
If close the circuit dead leg will twitch.

Volta created first battery by substituting frog leg with electrolyte.

History of discoveries in Biophysics:

First law of thermodynamic

Optical aspects of the human eye

Theory of hearing

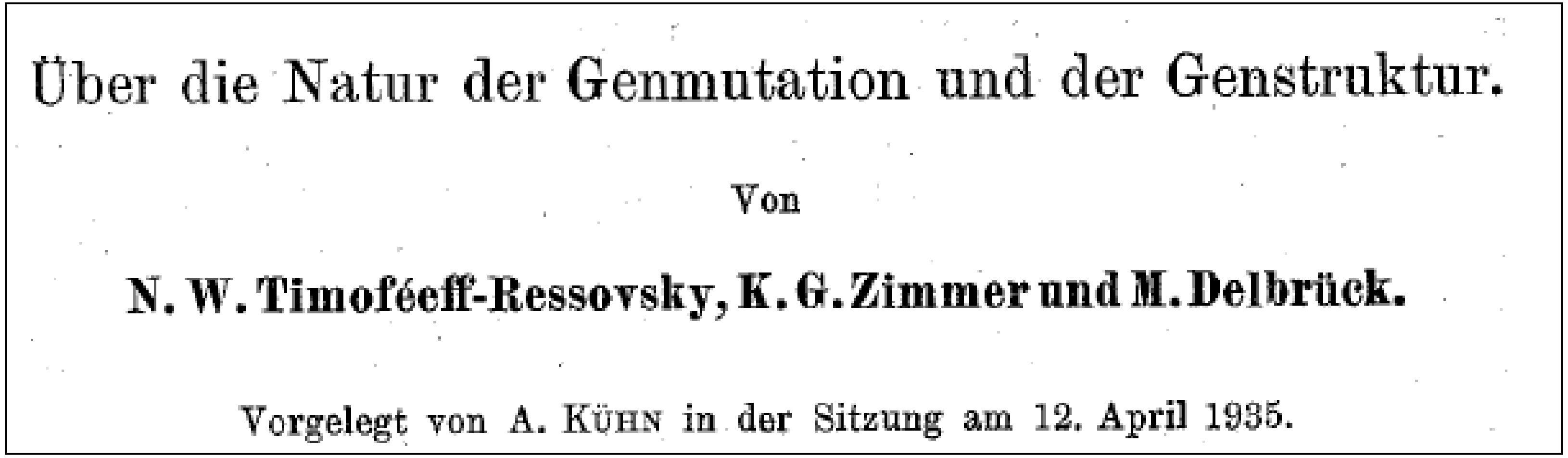
Brown’s motion

Osmotic process

Nonequilibrium thermodynamics

Discovery of X-rays – emergence of radiation biophysics

Transmission of order from one organism to it’s descendants



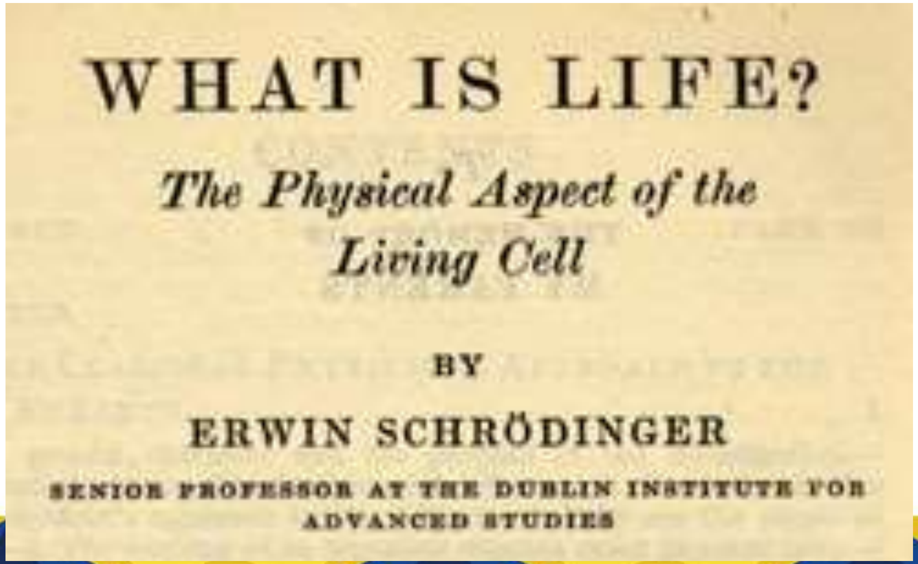
Über die Natur der Genmutation und der Genstruktur.

Von

N. W. Timoféeff-Ressovsky, K. G. Zimmer und M. Delbrück.

Vorgelegt von A. Kühn in der Sitzung am 12. April 1935.

The major advance in understanding the nature of gene mutation and gene structure. The work was a keystone in the formation of molecular genetics.



WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

ERWIN SCHRÖDINGER

SENIOR PROFESSOR AT THE DUBLIN INSTITUTE FOR ADVANCED STUDIES

History of discoveries in Biophysics:

Discovery of DNA structure

Information theory

Statistical physics of biopolymers

What is Biophysics?

It is neither “physics for biologists”, nor “physical methods applied to biology”

It is a modern, interdisciplinary field of science leading to new approaches for our understanding of biological functions.

Mathematics +Physics +Biology + Chemistry

“Biological system is not simply the sum of its molecular components but is rather their functional integration” –example biological membrane.

Scale from organism to single molecule
Time scales from years to femtoseconds (10^{-15}), 1/1000 ps

Examples of problems to solve:

How brain processes and stores information?

How the heart pumps blood?

How muscles contract?

How plants use light for grow in photosynthesis?

How genes are switched on and off?

Biophysics discovers how atoms are arranged to work in DNA and proteins.

Protein molecules perform the body’s chemical reactions.

Proteins make the parts of your eyes, ears, nose, and skin that sense your environment.

They turn food into energy and light into vision.

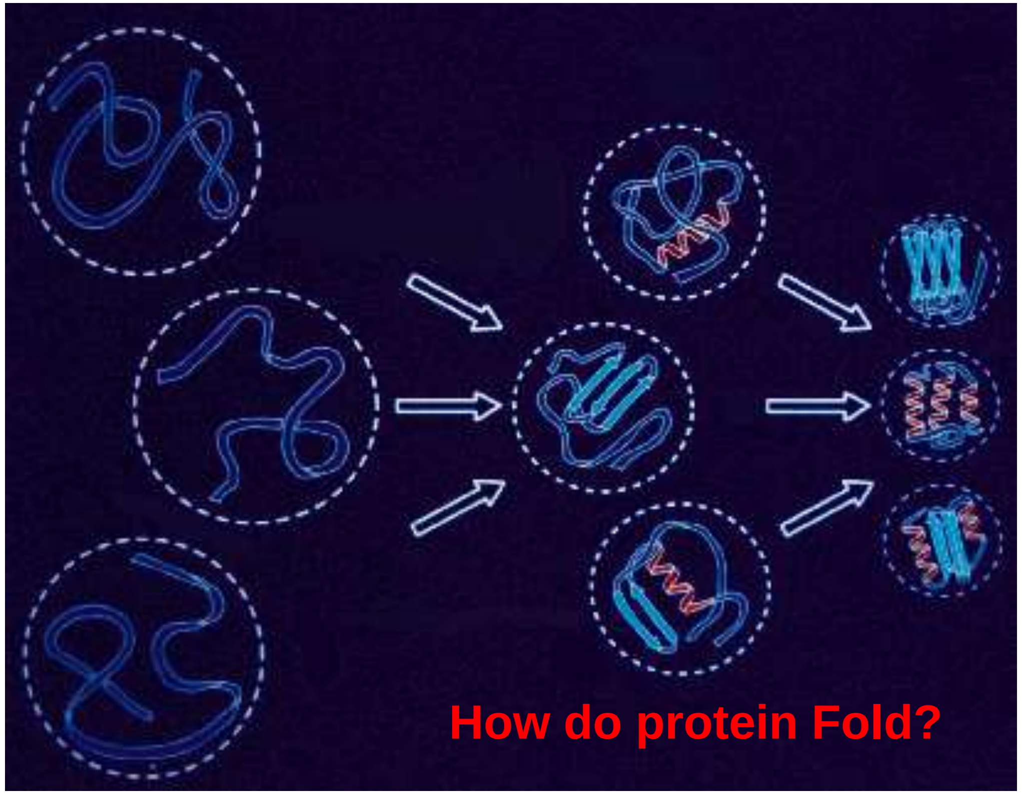
They provide immunity to illness.

Proteins repair what is broken inside of cells, and regulate growth.

They fire the electrical signals in your brain.

They read the DNA blueprints in your body and copy the DNA for future generations.

Question biophysicists ask:



How three-dimensional structure determines function? Why do molecules and parts of molecules assume the shapes they do? How do they fold into these shapes, and how do they change their structure under changing conditions? The shapes molecules take depend on the physical and chemical forces acting upon them and within them.

X-ray crystallography, nuclear magnetic resonance spectroscopy and scanning probe microscopy, recombinant DNA, computation.

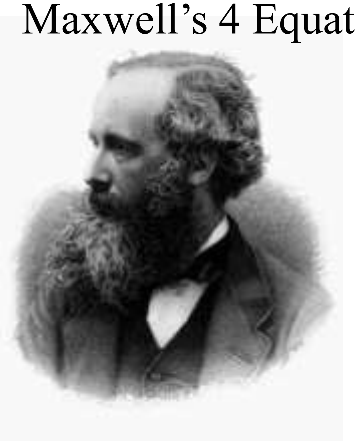
Physics is about great laws

Some examples…

Newton’s 3 Laws (Mechanics)

Isaac Newton
1642-1727

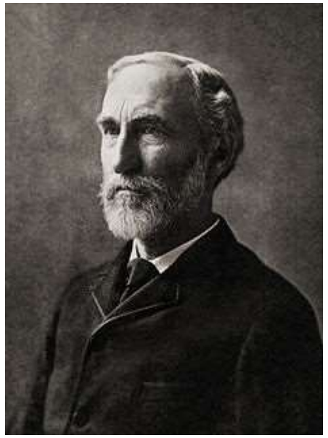
(Electricity & Magnetism)
Maxwell’s 4 Equations



James Clerk Maxwell
1831-1879

(Thermodynamics)

Gibb’s Free Energy



J. Willard Gibbs
1839-1903

(Quantum Mechanics)
Schrodinger’s Eq’n

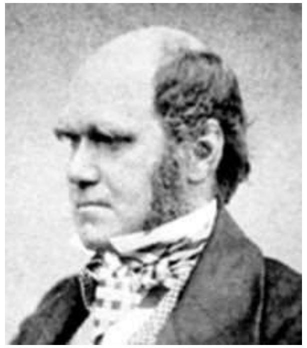
Erwin Schrödinger
1887-1961

Ludwig Boltzmann
1844-1906

(Stat. Mechanics
of Entropy)

S= k·log W

Does Biology have any great theories/laws?



Charles Darwin, Age 51, 1860,
On the Origin of Species

Evolution

-- Life evolved from simpler forms

--One of the best tested scientific theories around

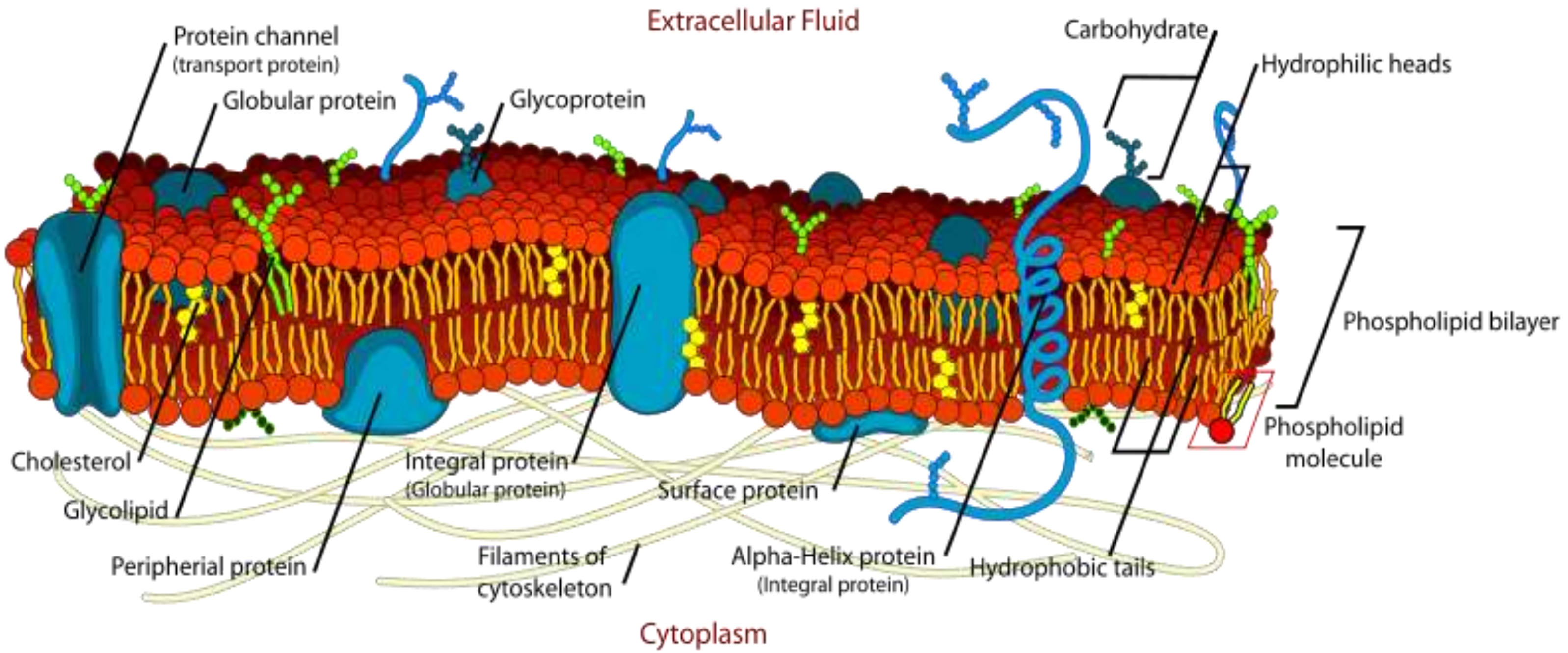
Evolution is a series of tricks/random events

Build complex beings from simpler parts

Often many ways of doing this
Our life form is just one.

Cellular Biophysics

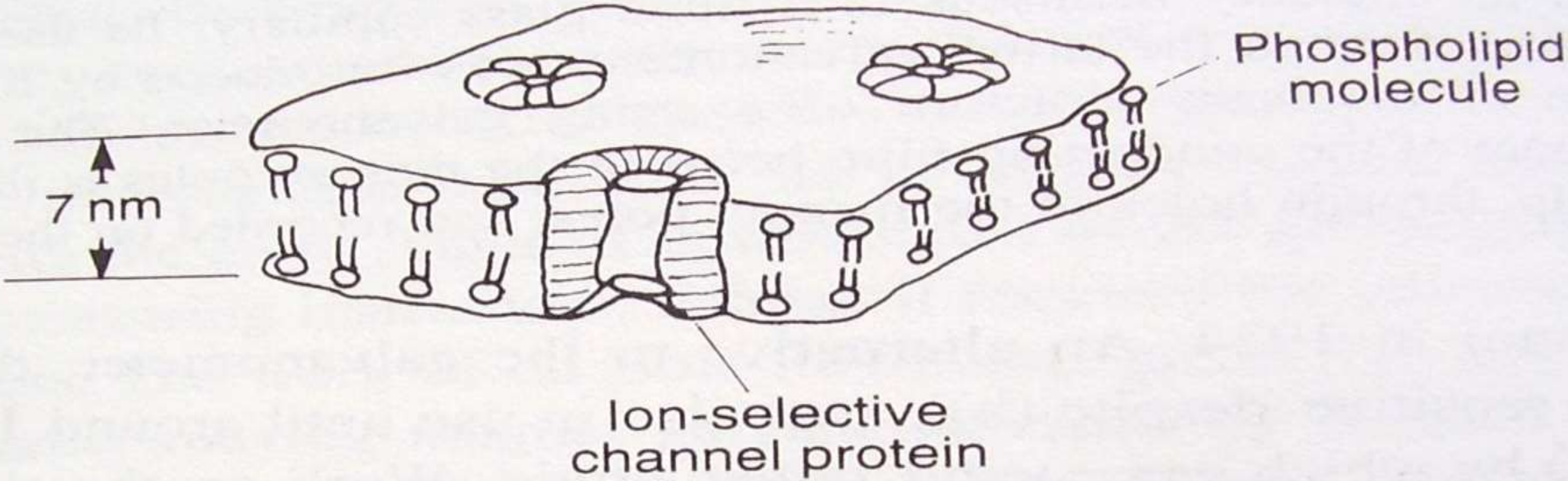
Biological Membrane



Highly organized anisotropic structure

Relationship structure–function are central to biophysics

SURFACE MEMBRANE



(b) Cut-away view of a segment of neuron membrane showing the arrangement of phospholipid molecules and ion-selective channel proteins.

Diffusion

- What is diffusion?
  - The random movement of molecules due to thermal energy
- The fundamental principle underlying all life processes!
  - Determines the rate of enzyme reactions
  - Determines the size and shape of cells
  - Determines the speed of signal transduction

History

- Until the early 1900’s, the idea of molecules was controversial
- In 1828, Robert Brown observed movement of pollen particles in suspension (Brownian motion)
- What was driving the motion?
  - Hypothesis 1- they were alive
    - But they never stopped!
    - Lifeless particles (soot) did the same

- Hypothesis 2 (1860’s)- movement was caused by collisions of water molecules with the pollen
- At higher temperatures, they moved faster!
  - But- particles are much larger than water molecules- how can water move particles?
  - The speed of water molecules is 10^3m/s and there would be about 10^{12} collisions/sec. Too fast for the eye to see
- How to resolve this???

Einstein strikes again

- Clarified the stochastic nature of molecular motion- there are many events happening very rapidly
- If you take the look at the probabilities, then with that many collisions with water molecules with a range of velocities, then periodically you will get a displacement of the particle by many more collisions on one side than another
- The process will lead to a 3D random walk of the particle: Diffusion

The Diffusion Law

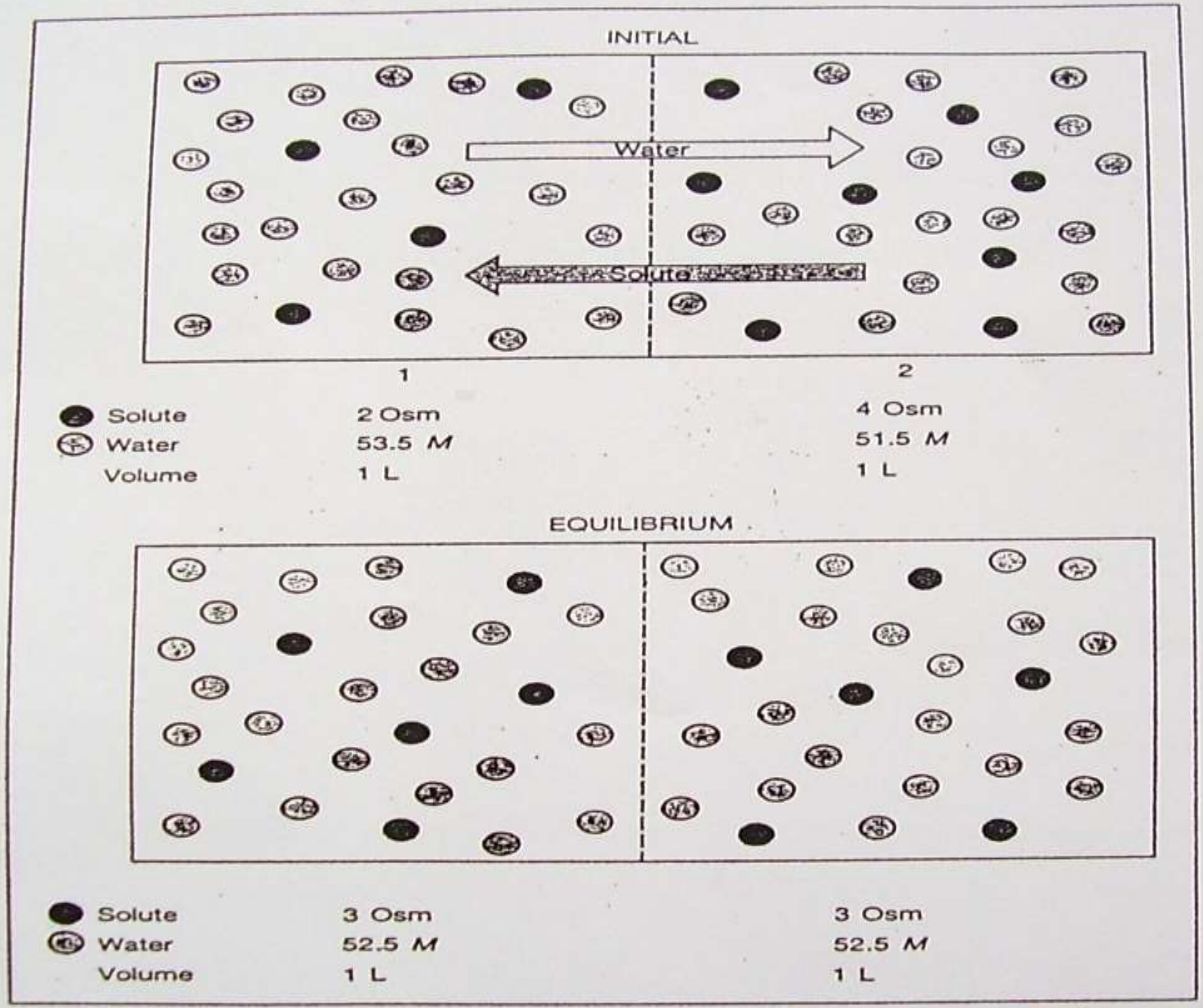
- mean square displacement $x^2=6Dt$
- This is stochastic, not the behavior of a individual molecule
  - Any molecule might not move at all
  - Others may move a great distance
- There is no “rate” of diffusion
- $x/t=v=6D/x$ or the rate gets slower the farther you are away
  - So if you follow a certain concentration of molecules, that concentration will move rapidly away from a source, and the farther you get from the source, the slower that concentration will move
  - If the source only produces a limited number of molecules, then at some distance, you will never reach that concentration

Diffusion of Biological Molecules

Substance	M	D (cm2/sec)	time to diffuse 1μ	diffuse 10μm
bacterium	5x10-9	1 sec	100sec	
albumin	7x104	6x10-7	10 msec	1 sec
sucrose	3x102	5x10-6	1msec	100msec

2D random walk, 18050 steps

Simple Diffusion through cell membrane



INITIAL

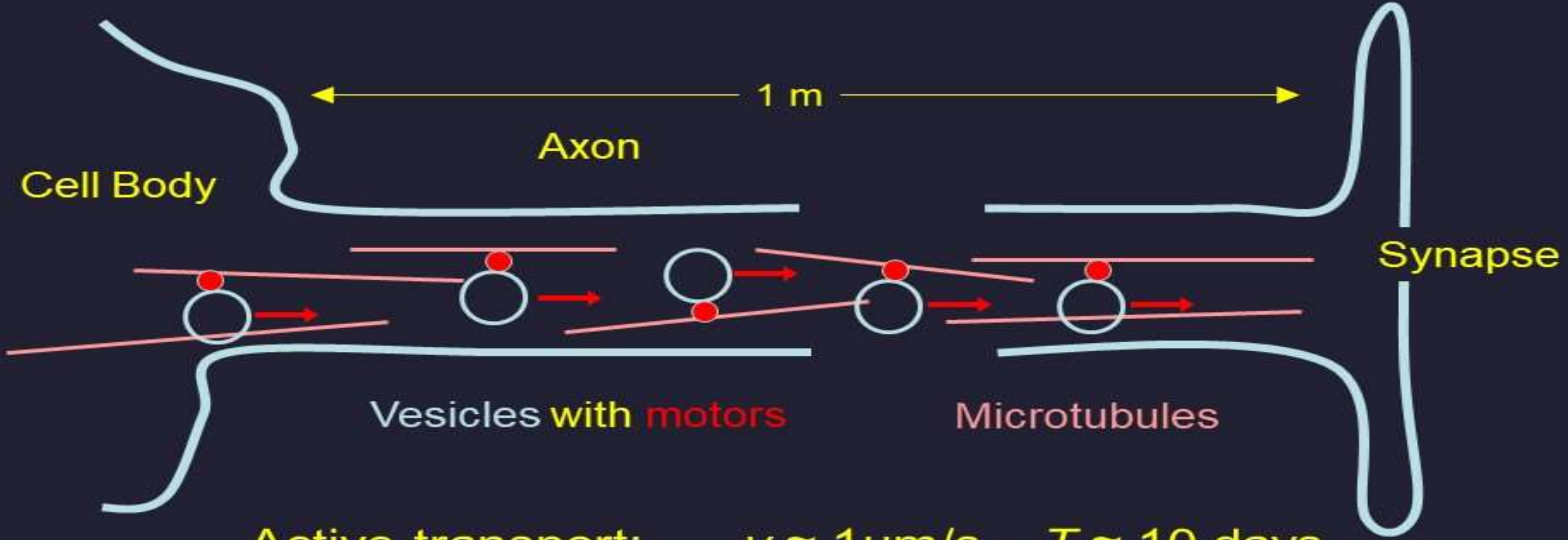
	1	2
● Solute	2 Osm	4 Osm
⊛ Water	53.5 *M*	51.5 *M*
Volume	1 L	1 L

EQUILIBRIUM

	1	2
● Solute	3 Osm	3 Osm
⊛ Water	52.5 *M*	52.5 *M*
Volume	1 L	1 L

FIGURE 6-20 The net diffusion of water and solute in opposite directions across membrane permeable to both leads to diffusion equilibrium with no change in the volume of either compartment.

Intracellular Transport on Cytoskeletal Tracks



Active transport: $v \approx 1 \mu m/s$, $T \approx 10$ days

Diffusion: $T = x^2/6D \approx 26{,}000$ years

BIOPHYSICAL METHODS

- Analysis of Bio molecules
- UV and Visible Light
- Spectroscopy NMR and ESR
- Circular dichorism
- X ray diffraction
- Mass Spectroscopy
- Surface plasmon Resonance

Photosynthetic studies – cont.

1845 that Julius Robert von Mayer, a German physician and physicist, proposed that photosynthetic organisms convert light energy into chemical energy.

Middle of 19th century: A chemical reaction was proposed,

$$CO_2 + 2H_2O + \text{Light Energy} \rightarrow [CH_2O] + O_2 + H_2O$$

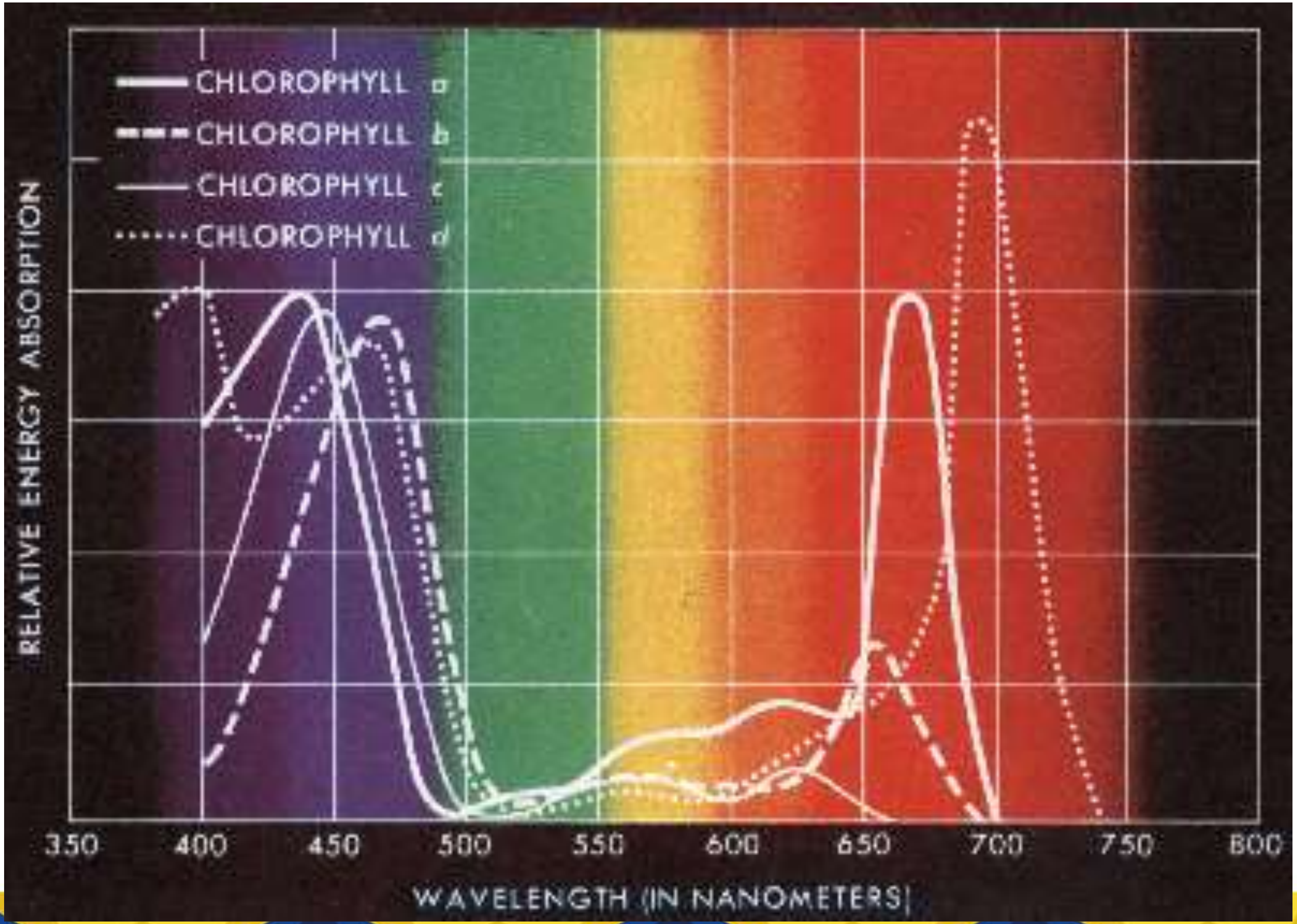
Where does O_2 comes from, CO_2 or H_2O?

Hill and Scarisbrick (1940) demonstrated oxygen evolution in the absence of CO_2 in illuminated chloroplasts and by Ruben et al. (1941) who used ^{18}O enriched water

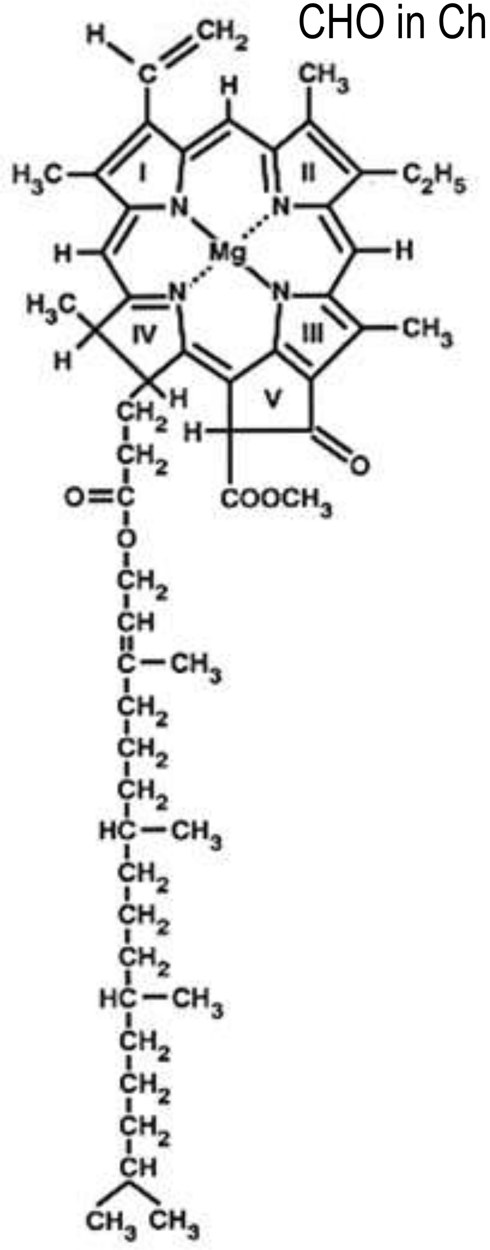
Photosynthetic studies – cont.

Carbon reduction can occur in the dark and involves a series of biochemical reactions that were elucidated by Melvin Calvin, Andrew Benson and James Bassham in the late 1940s and 1950s. Using the radioisotope ^{14}C, most of the intermediate steps that result in the production of carbohydrate were identified. Calvin was awarded the Nobel Prize for Chemistry in 1961 for this work.

Plant pigments and light absorption



Ch



Chlorophyll *a*

CHO in Chlorophyll b

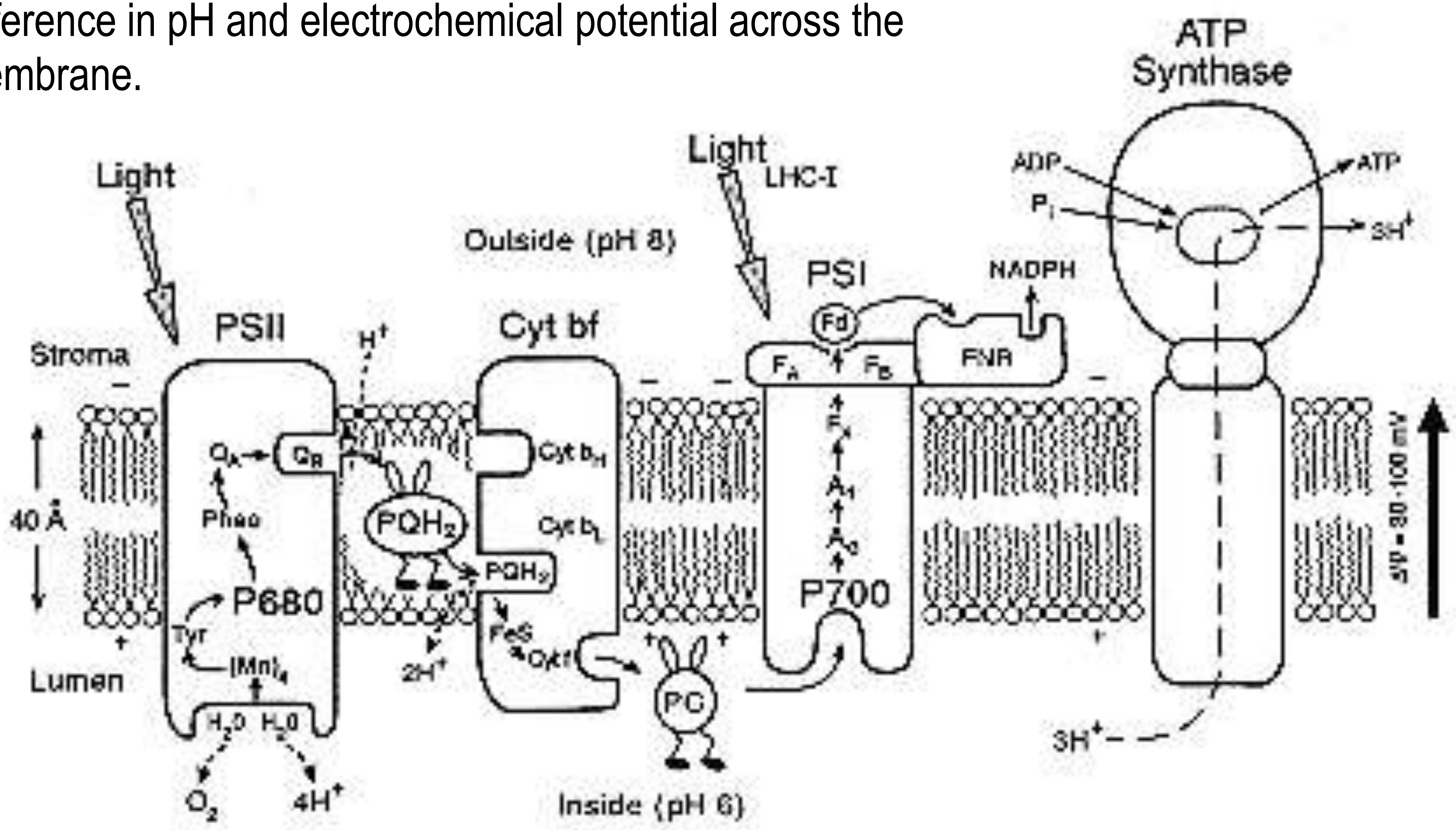
Chlorophyll, a pigment, absorbs sun light.

Antenna contains chlorophyll molecules to collect light.

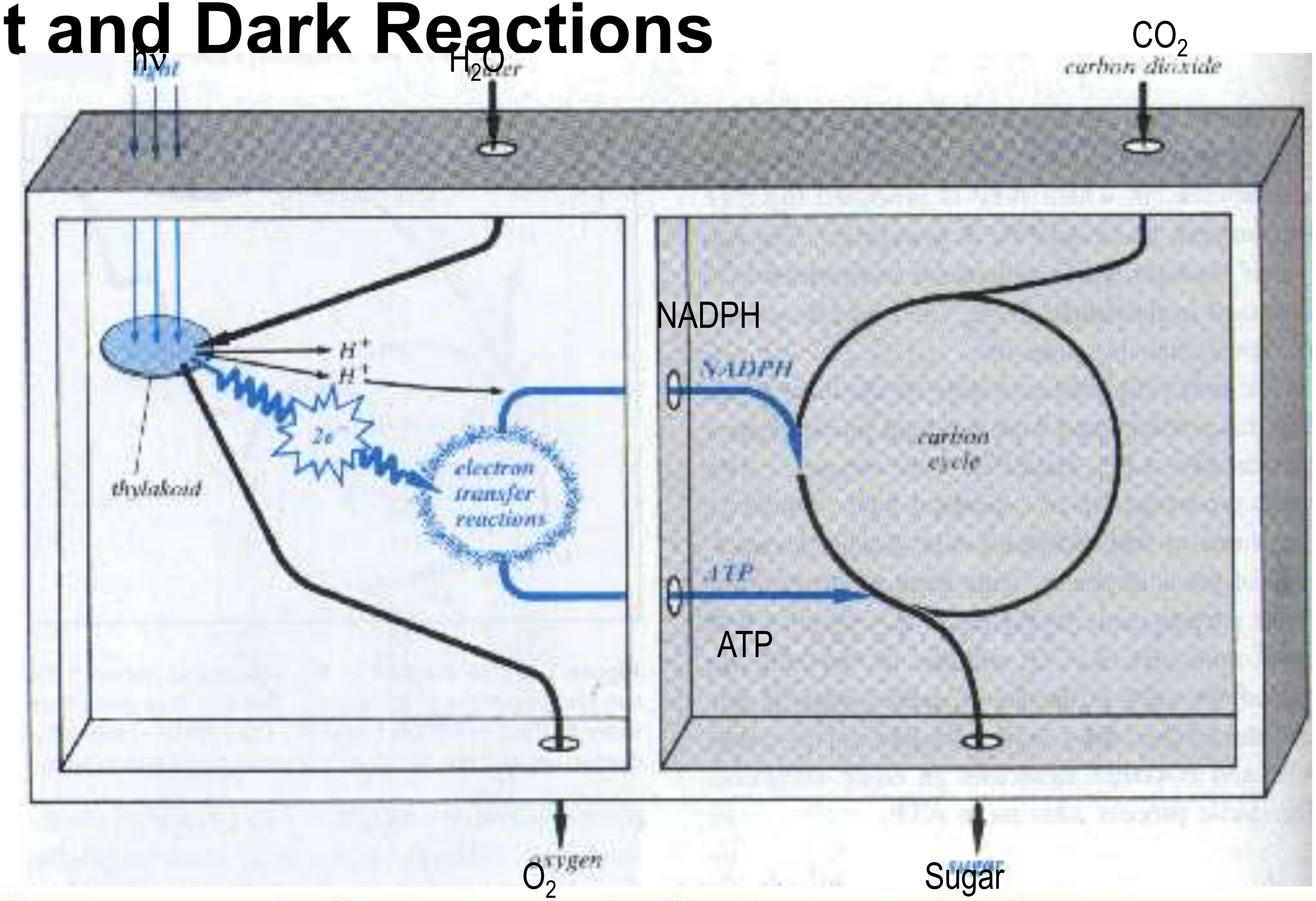
Antenna absorb quanta and transfer the reaction center.

Photosynthesis

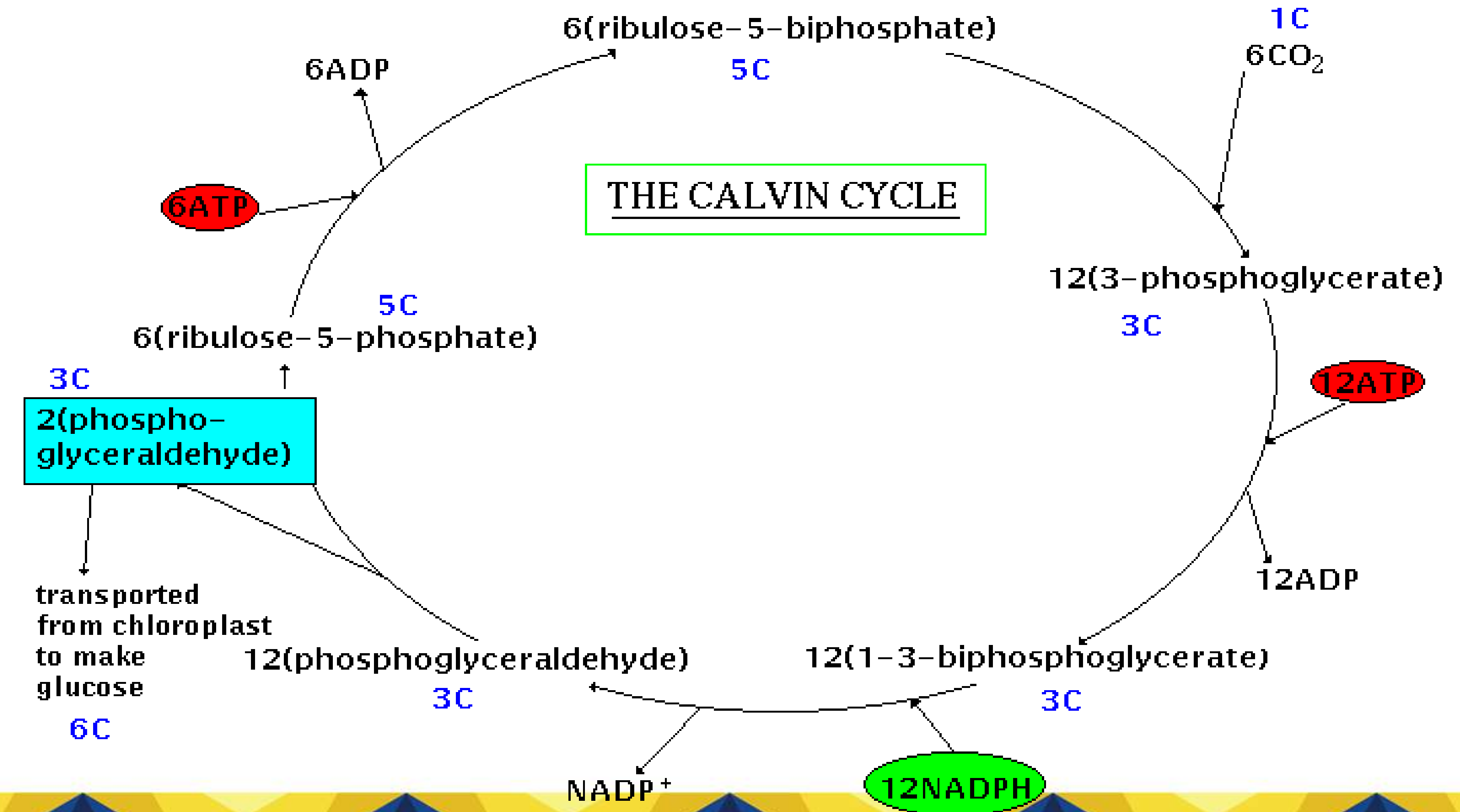
The protons released into the inner aqueous solution results in a difference in pH and electrochemical potential across the membrane.



Light and Dark Reactions



The Calvin Cycle for Dark Reactions



A computer simulation is a simulation, run on a single computer, or a network of computers, to reproduce behavior of a system. The simulation uses an abstract model to simulate the system.

The abstract model (or interaction potential) for protein:

Quantum mechanics:

atoms, electrons, …

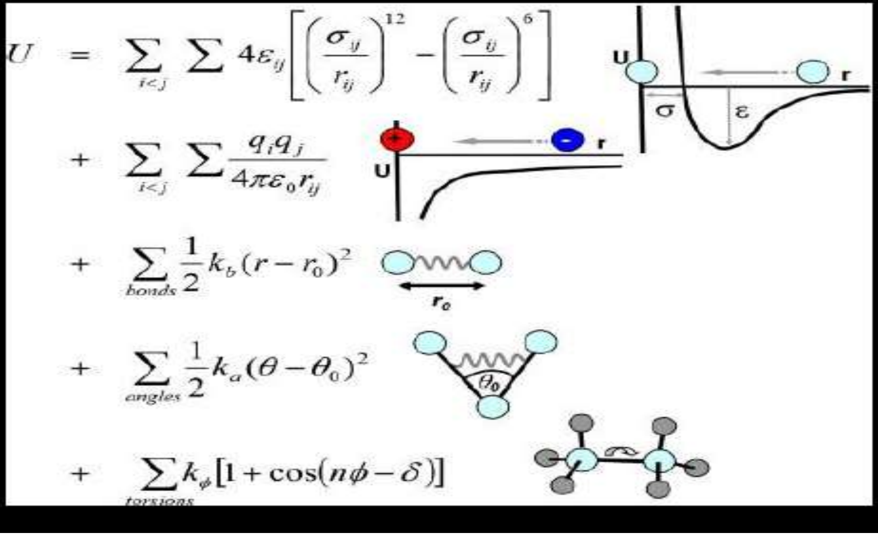
$$\hat{H}\psi = E\psi$$

The Schrodinger equation was discovered in 1926 by Erwin Schrodinger, an Austrian theoretical physicist.
It is an important equation that is fundamental to quantum mechanics.

Molecular mechanics:

atoms, bonds, angles, torsions, …

The first protein simulations appeared in 1977 with the simulation of the bovine pancreatic trypsin inhibitor (BPTI) .
McCammon, J. A., Gelin, B. R., and Karplus, M. *Nature* 267, 585 (1977)
Simulation time: 8.8 psec (1 psec = 10^{-12} sec)
Now a 10^{-3} sec simulation is possible



$$U = \sum_{i<j}\sum 4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \sum_{i<j}\sum \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}} + \sum_{bonds}\frac{1}{2}k_b(r-r_0)^2 + \sum_{angles}\frac{1}{2}k_a(\theta-\theta_0)^2 + \sum_{torsions}k_\phi[1+\cos(n\phi-\delta)]$$

MD: The Verlet Method

Molecular dynamics simulations calculate the motion of the atoms in a molecular assembly using Newtonian dynamics to determine the net force and acceleration experienced by each atom. Each atom ***i*** at position r_i, is treated as a point with a mass m_i and a fixed charge q_i.

Energy function: $U(\vec{r}_1, \vec{r}_2, \cdots \vec{r}_N) = U(\vec{R})$

used to determine the force on each atom:

$$m_i \frac{d^2\vec{r}_i}{dt^2} = \vec{F}_i = -\vec{\nabla} U(\vec{R})$$

Newton's equation represents a set of N second order differential equations which are solved numerically at discrete time steps to determine the trajectory of each atom.

Deriving the Verlet algorithm

- Uses positions and accelerations at time t and the positions from time t-δt to calculate new positions at time t+ δ t.
- Uses no explicit velocities.

$$\mathbf{r}(t+\delta t) \approx \mathbf{r}(t) + \mathbf{v}(t)\delta t + \frac{1}{2}\mathbf{a}(t)\delta t^2$$

+

$$\mathbf{r}(t-\delta t) \approx \mathbf{r}(t) - \mathbf{v}(t)\delta t + \frac{1}{2}\mathbf{a}(t)\delta t^2$$

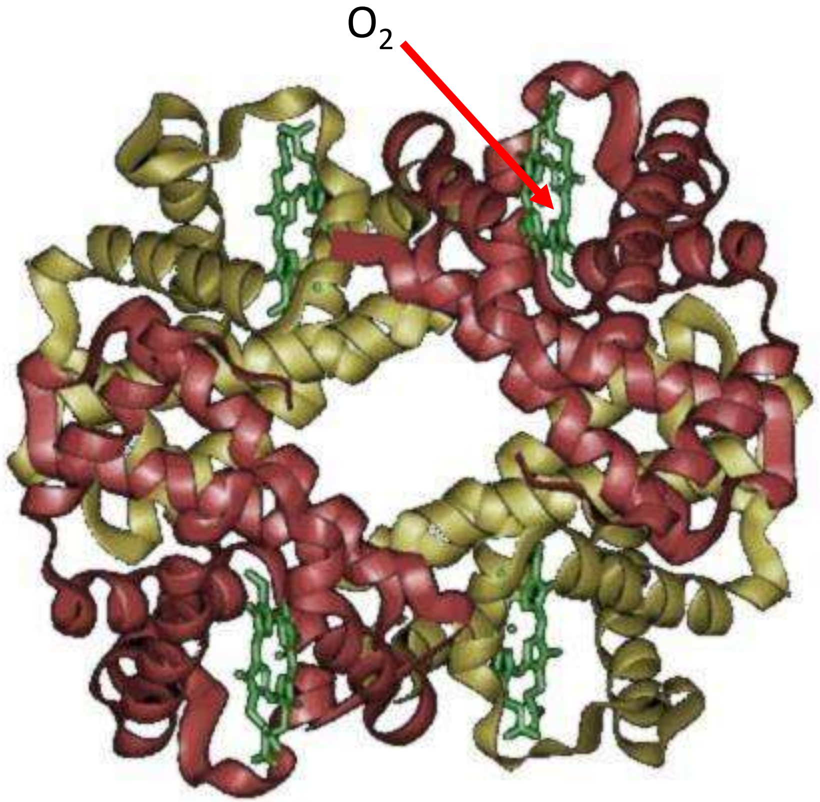
⬇

$$-\vec{\nabla}U(\vec{R})/m_i$$

$$\boxed{\mathbf{r}(t+\delta t) \approx 2\mathbf{r}(t) - \mathbf{r}(t-\delta t) + \mathbf{a}(t)\delta t^2}$$

Experiments that show protein dynamics

Hemoglobin



The oxygen would need seconds to diffuse through the protein matrix to the hem groups in rigid protein. However, the time scale of oxygen uptake is ms!

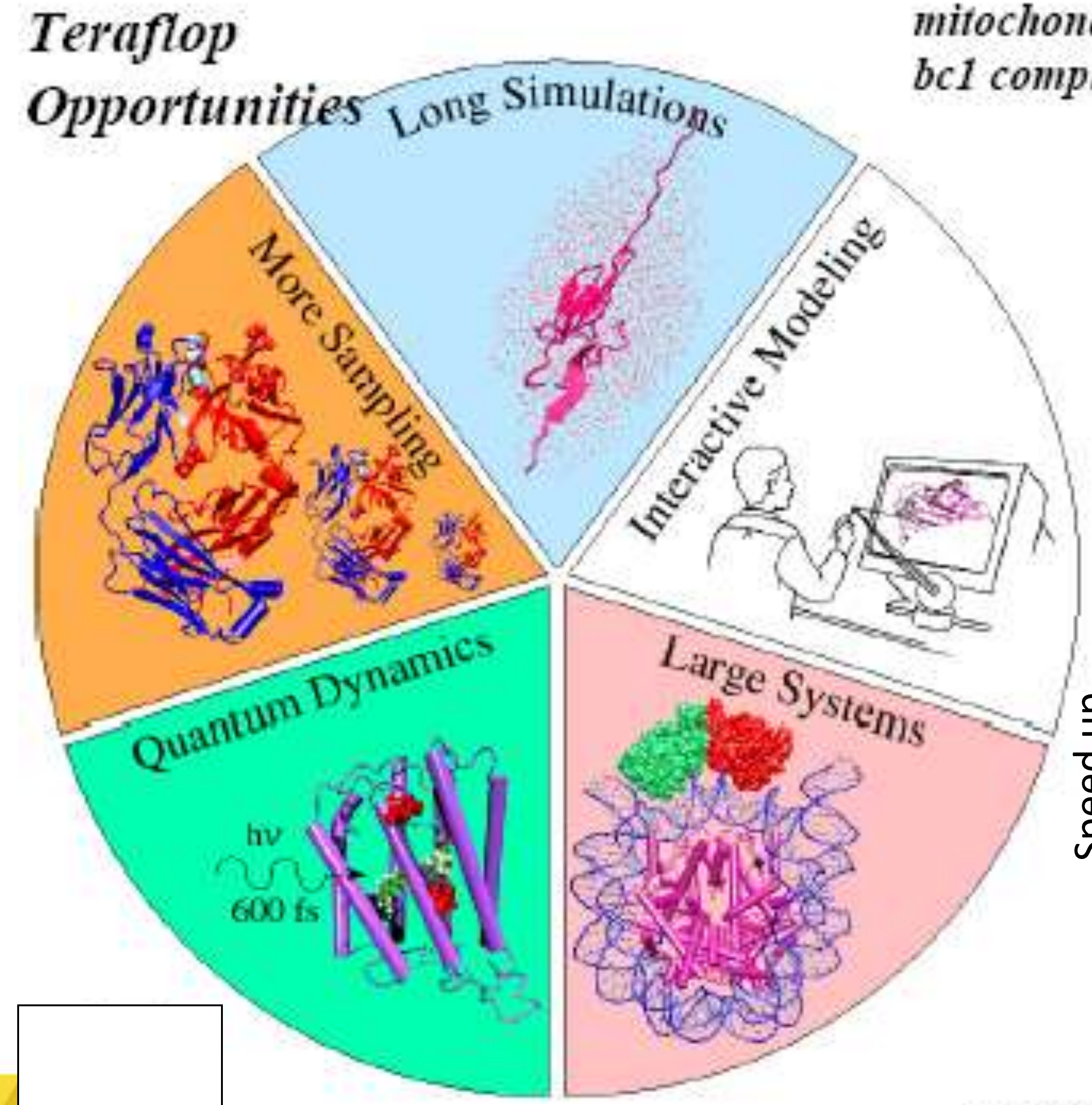
Hans Frauenfelder, PNAS 1979

Bacterial Reaction Center

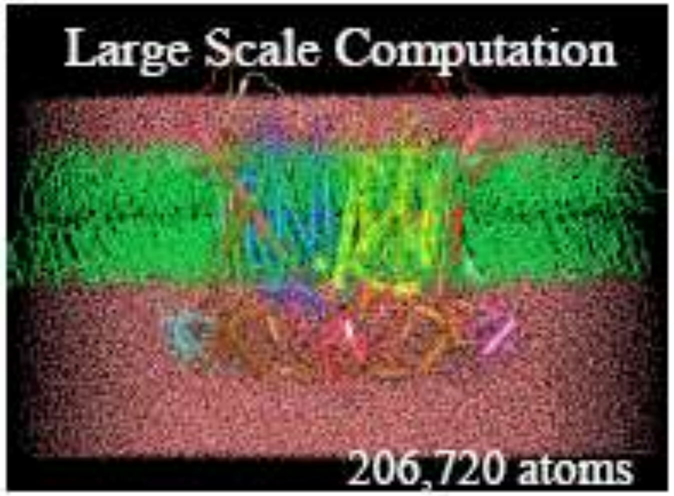
The rate of proton uptake from the aqueous bulk phase is governed by the dynamics of exposure of the protonatable group of the protein.

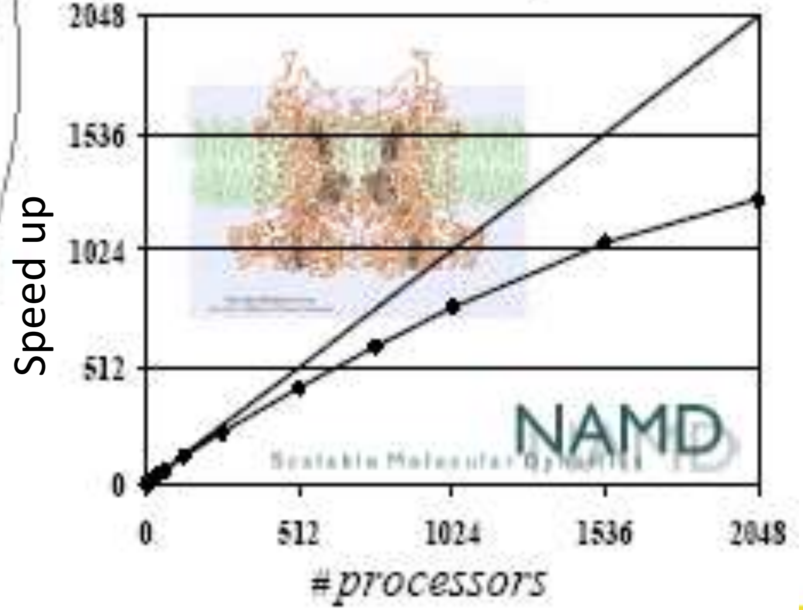
P. Maróti and C.A: Wraight, Biophys. J. 1997

Use of Molecular Dynamics in Biophysics



mitochondrial
bc1 complex

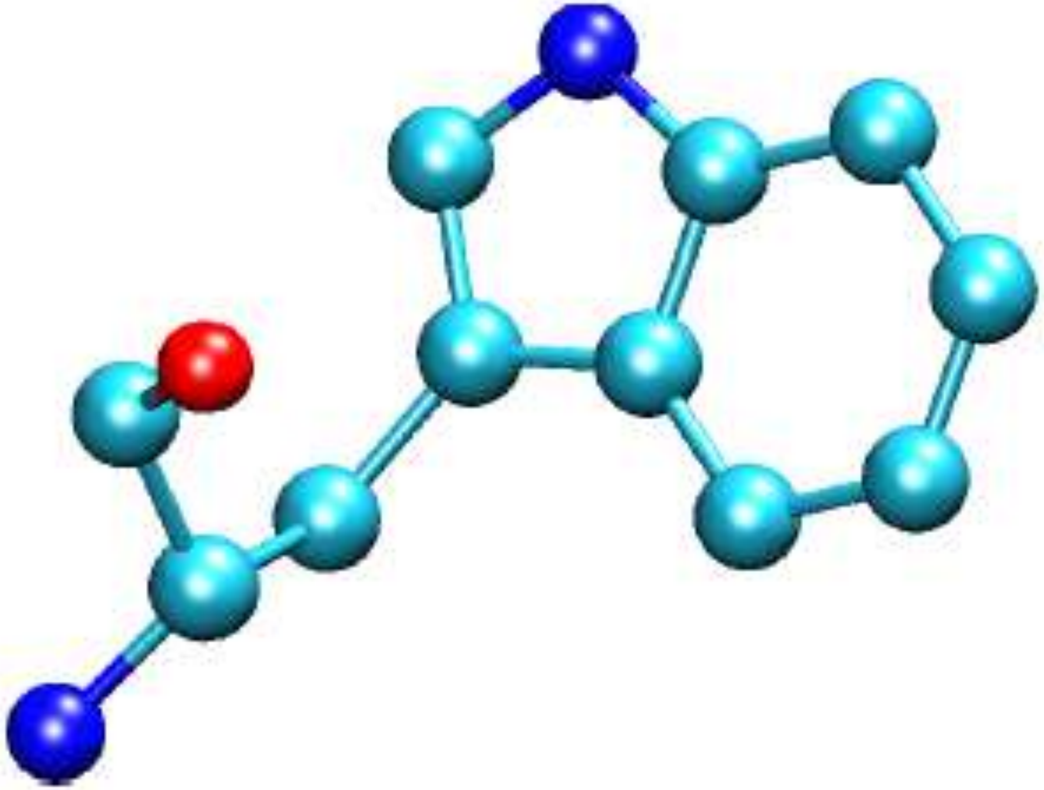




Brunner *et al.*, SC2000, finalist for Gordon Bell award.

What is the Force Field $-\vec{\nabla}U(\vec{R})$?

In molecular dynamics a molecule is described as a series of charged points (atoms) linked by springs (bonds).



To describe the time evolution of bond lengths, bond angles and torsions, also the non-bonding van der Waals and elecrostatic interactions between atoms, one uses a forcefield.

The forcefield is a collection of equations and associated constants designed to reproduce molecular geometry and selected properties of tested structures.

Energy Terms Described in the CHARMm Force Field

Bond

Angle

Dihedral

Double V-shape

Improper

Energy Functions

$$
\begin{aligned}
U(\vec{R}) \; = \; & \underbrace{\sum_{bonds} k_i^{bond}(r_i - r_0)^2}_{U_{bond}} + \underbrace{\sum_{angles} k_i^{angle}(\theta_i - \theta_0)^2}_{U_{angle}} + \\
& \underbrace{\sum_{dihedrals} k_i^{dihe}[1 + \cos(n_i \phi_i + \delta_i)]}_{U_{dihedral}} + \\
& \underbrace{\sum_i \sum_{j \neq i} 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^{6} \right] + \sum_i \sum_{j \neq i} \frac{q_i q_j}{\epsilon r_{ij}}}_{U_{nonbond}}
\end{aligned}
$$

U_{bond} = oscillations about the equilibrium bond length
U_{angle} = oscillations of 3 atoms about an equilibrium angle
$U_{dihedral}$ = torsional rotation of 4 atoms about a central bond
$U_{nonbond}$ = non-bonded energy terms (electrostatics and Lenard-Jones)

Time scales

☐• Time scale of biological events

Motion	Time Scale (sec)
Bond stretching	10^{-14} to 10^{-13}
Elastic vibrations	10^{-12} to 10^{-11}
Rotations of surface sidechains	10^{-11} to 10^{-10}
Hinge bending	10^{-11} to 10^{-7}
Rotation of buried side chains	10^{-4} to 1 sec
Allosteric transistions	10^{-5} to 1 sec
Local denaturations	10^{-5} to 10 sec

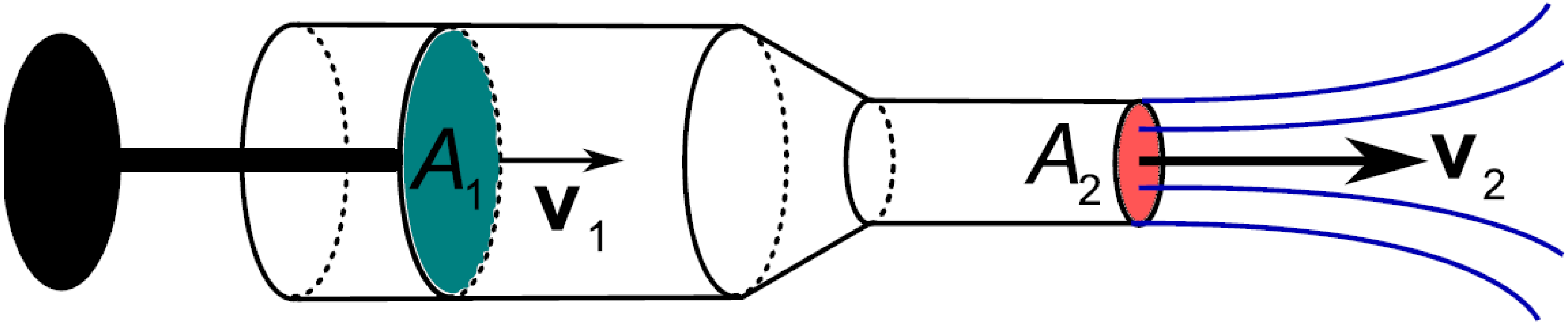
Equation of continuity

- the fluid is incompressible, so
  - the density is the same between (1) and (1') and (2) and (2'): $\rho_1 = \rho_2 = \rho$
  - the mass flowing in at (1) is equal to the mass flowing out at (2): $\Delta m_1 = \Delta m_2 = \Delta m$
  - $\Delta m = \rho \Delta V_1 = \rho \Delta V_2 \rightarrow$
  - the volume flowing in at (1) is equal to the volume flowing out at (2): $\Delta V_1 = \Delta V_2 = \Delta V$
- $\Delta V_1 = A_1 s_1 = A_1 v_1 \Delta t$
- $\Delta V_2 = A_2 s_2 = A_2 v_2 \Delta t$
- $\Delta V_1 = \Delta V_2 \Rightarrow A_1 v_1 \Delta t = A_2 v_2 \Delta t$

$$A_1 v_1 = A_2 v_2$$

- since (1) and (2) were chosen arbitrarily, this must hold to any two cross-sections along the flow: $\boxed{A \cdot v = \text{const}}$
- this is the **equation of continuity**
- since $Av = I$, this means that the **volume current is constant along the tube**

Example: a syringe



$$A_1 v_1 = A_2 v_2$$

$$A_1 \gg A_2 \Rightarrow v_2 \gg v_1$$

Example: flow speed in blood vessels

Blood vessel	**cross-section area [cm^2]**	**velocity [cm/s]**
Aorta	4.5	40
Arteries	20	9
Arterioles	400	0.45
Capillaries	4500	0.04
Veins	40	4.5
Vena cava	18	10

Homework: what is common to all the rows?

Bernoulli's equation

- conservation of mechanical energy: $W = \Delta E = \Delta E_{\mathrm{P}} + \Delta E_{\mathrm{K}}$

$$\frac{\Delta m}{\rho}(p_1 - p_2) = \Delta m g(h_2 - h_1) + \frac{1}{2}\Delta m(v_2^2 - v_1^2) \qquad // \cdot \frac{\rho}{\Delta m}$$

$$p_1 - p_2 = \rho g h_2 - \rho g h_1 + \frac{1}{2}\rho v_2^2 - \frac{1}{2}\rho v_1^2$$

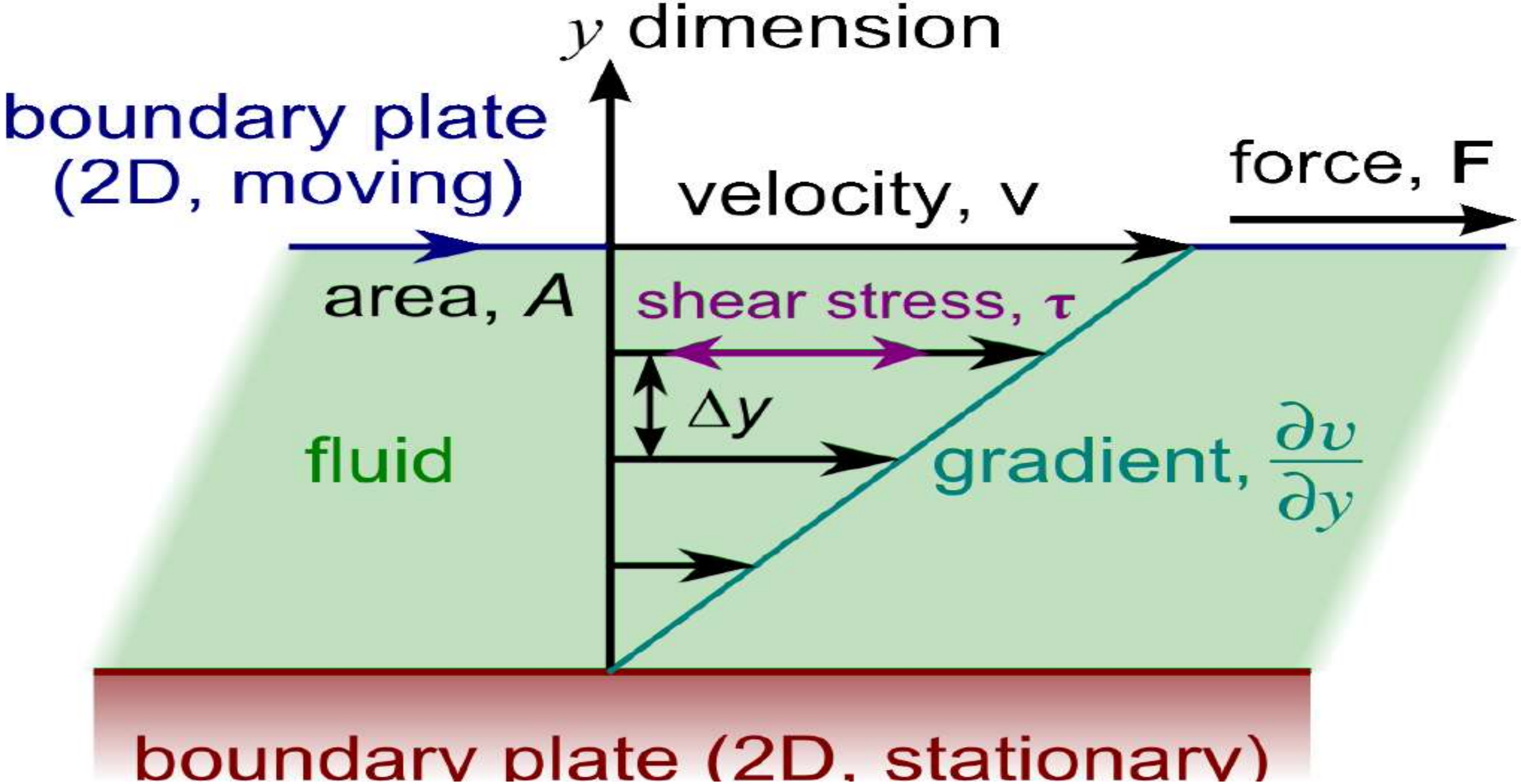
$$p_1 + \rho g h_1 + \frac{1}{2}\rho v_1^2 = p_2 + \rho g h_2 + \frac{1}{2}\rho v_2^2$$

- fluid discs (1) and (2) were chosen arbitrarily, so this must hold to any two cross-sections along the flow: $p + \rho g h + \frac{1}{2}\rho v^2 = \mathrm{const}$
- this is **Bernoulli's law**

What is viscosity?

- fluids (by definition) cannot *support* shearing stress
- but they *do resist* shearing motion
- interactions between the particles of the fluid ⇒ friction
- force is needed to make fluid layers slide upon each other
- viscosity: the resistance of a fluid to shearing motion due to internal friction
- everyday term for viscosity: ‘thickness’ (riddle: which English saying involves viscosity?)
- etymology: < Latin *viscum* ‘mistletoe’ (mistletoe glue was used to catch birds)

Illustration



What happens in a viscous fluid?

- two parallel solid plates with surface area A with viscous fluid between them
- lower plate: fixed
- upper plate: pulled sideways with force $\mathbf{F}$
- bottom layers of fluid: stick to the lower plate due to adhesion, velocity: $v = 0$
- top layers of fluid: stick to the upper plate due to adhesion, velocity: $v \neq 0$
- we imagine fluid flow as fluid layers sliding upon each other
- particles within the same layer move together with the same velocity: $\mathbf{v}(y)$

What happens in a viscous fluid?

- thickness of layers: Δy
- speed difference between neighbouring layers: Δv
- instead of the force, it is more practical to use the shear stress τ

$$\tau := \frac{F}{A}$$

- how much the velocity changes across layers — *velocity gradient:*

$$\frac{\Delta v}{\Delta y}$$

- in reality, there are no homogeneous layers, the velocity changes continuously across the cross-section of the tube
- $\Rightarrow$ layer thickness Δy should be made infinitely small
- thus the velocity gradient (also called the **shear rate**):

$$\lim_{\Delta y \to 0} \frac{\Delta v}{\Delta y} = \frac{\mathrm{d}v}{\mathrm{d}y}$$

Newton's law of friction

- the stronger the internal friction, the more the layers move together ⇒ the less the velocity difference between layers (shear rate)
- non-viscous fluid (eg, water): we can slide a solid plate on top of it without making the whole bulk of fluid moving
- viscous fluid (eg, honey): sliding a solid plate on its surface makes the whole bulk of fluid move
- in many fluids, shear rate $\frac{dv}{dy}$ is proportional to the shear stress τ
- the constant of proportionality is called the **viscosity** η
- **Newton's law of friction:**

$$\tau = \frac{F}{A} = \eta \frac{dv}{dy}$$

- **Newtonian fluids:** fluids which obey Newton's law of friction

Viscosity

- using Newton's law of friction, we can define viscosity:

$$\eta := \tau \left(\frac{\mathrm{d}v}{\mathrm{d}y} \right)^{-1}$$

- the unit of viscosity:

$$[\eta] = 1\,\mathrm{Pa} \cdot \mathrm{s} \qquad \left(\Leftarrow 1\,\frac{\mathrm{N}}{\mathrm{m}^2} \div \frac{\mathrm{m/s}}{\mathrm{m}} = 1\,\frac{\mathrm{Pa}}{1/\mathrm{s}} \right)$$

Fluid	glycerine	blood	water	air
Viscosity [Pa · s]	0.83	0.02–0.04	0.001	0.00001

Table 1: Typical viscosity values

Things get weird when viscosity increases

- Consider a cylinder containing corn syrup
- Add a dot of dye in corn syrup
- Stir the syrup/dye in one direction
- Reverse the direction of stirring
- The dot reforms
- Viscous fluids do not flow or mix
- No turbulence, no inertia

Now consider density and viscosity

Fluid	Density	Viscosity
Air	1	$2x10^{-5}$
Water	1000	.0009
Olive oil	900	.08
Glycerine	1300	1
Corn syrup	1000	5

Viscosity as a diagnostic tool

- blood viscosity measurement has a great potential as a diagnostic tool
- viscosity changes in conditions of
  - myocardial infarction
  - coronary occlusion
  - arteriosclerosis
  - diabetes, *&c*
- it is not yet known whether viscosity changes are just symptoms or themselves contribute to the disorders they accompany

Molecular origin of viscosity in gases

- in ideal gases, molecules only interact through collisions
- source of friction: *momentum exchange between layers*
- molecules in gas flow:
    - ordered motion — due to pressure difference
    - disordered motion — due to temperature (usually with much greater speed than ordered motion)
- disordered motion ⇒ molecules may enter other layers, and through collisions, change the momentum of the layer
- momentum: $\mathbf{p} := m\mathbf{v}$; Newton's 2nd law: $\mathbf{F} = m\mathbf{a} = \frac{\mathrm{d}\mathbf{p}}{\mathrm{d}t}$
- momentum exchange ⇒ force of friction between layers
- force of friction ⇒ viscosity

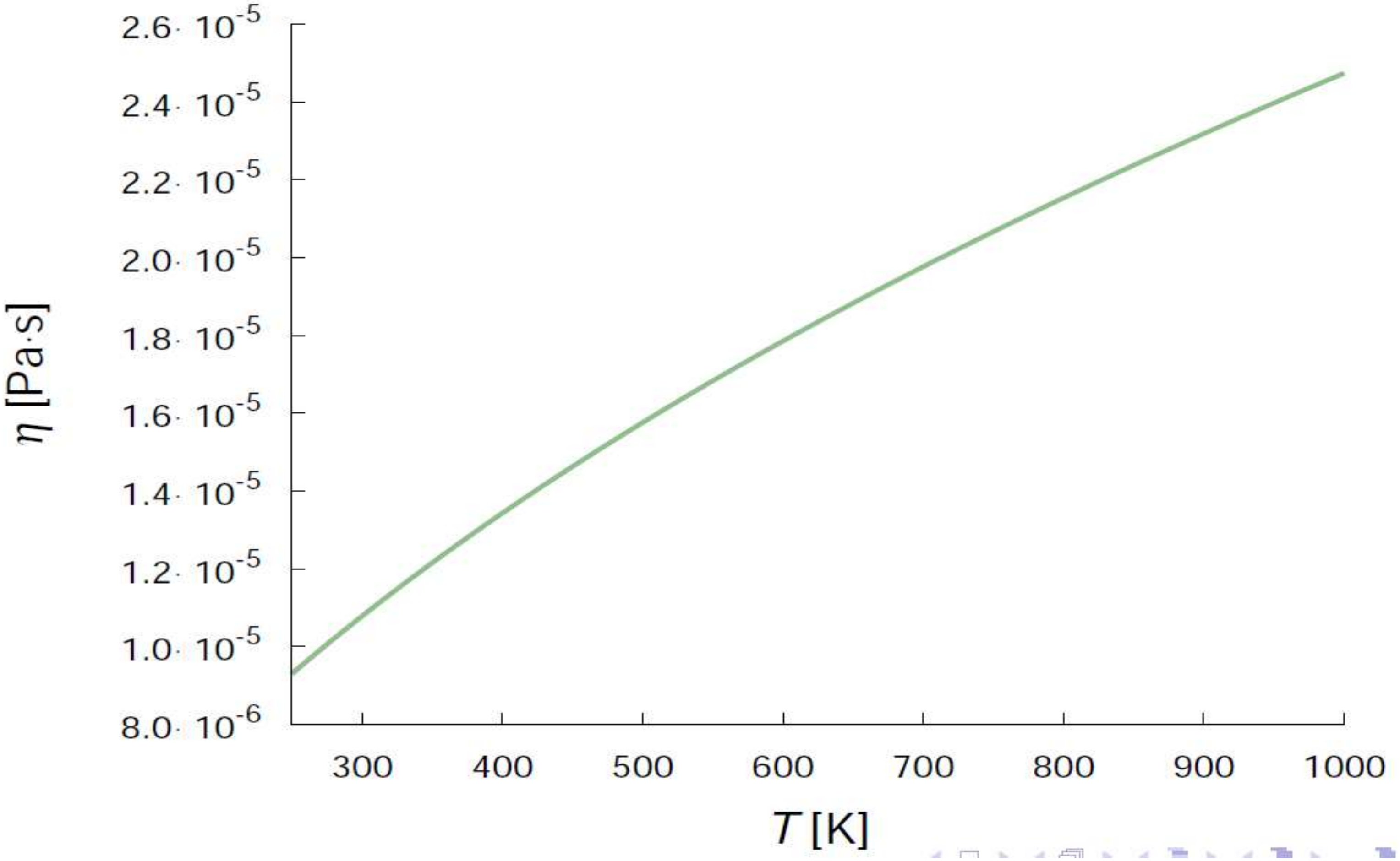
Temperature dependence of viscosity in gases

- equipartition theory for ideal gases: $\frac{1}{2}mv^2 = \frac{f}{2}kT$, where v is the average speed of gas molecules, k is Boltzmann's constant, T is the thermodynamic temperature (in Kelvins) and f denotes the degrees of freedom
- higher temperature ⇒ faster disordered motion
- faster disordered motion ⇒ more collisions in unit time ⇒ stronger force of friction
- **the viscosity of gases increases with temperature**

$$\eta = \eta_0 \sqrt{\frac{T}{T_0}} \cdot \frac{1 + \frac{C}{T_0}}{1 + \frac{C}{T}},$$

where η_0 is the viscosity of the gas at absolute temperature T_0 and C is called the Sutherland constant

Temperature dependence of viscosity in gases



Molecular origin of viscosity in liquids

- in liquids, there are strong interactions between molecules
- attractive forces ⇒ internal friction
- flow requires free space in order for the molecules to move and change places
- *How can liquids flow at all when there is not enough free space within them?*

Frenkel's theory

- thermal motion results in occasional molecular gaps in the liquid
- it provides room for liquid molecules to move ⇒ fluid flow
- the higher the concentration of the gaps, the more easily liquid molecules can move ⇒ lower viscosity

Temperature dependence of viscosity in liquids

- liquid molecules possess potential energy due to interactions with neighbouring molecules
- to create a gap, a molecule must be freed ⇒ some activation energy E must be invested
- source of activation energy: kinetic energy of liquid molecules
- *How many molecules have kinetic energy greater than or equal to E?*
- Boltzmann distribution ⇒

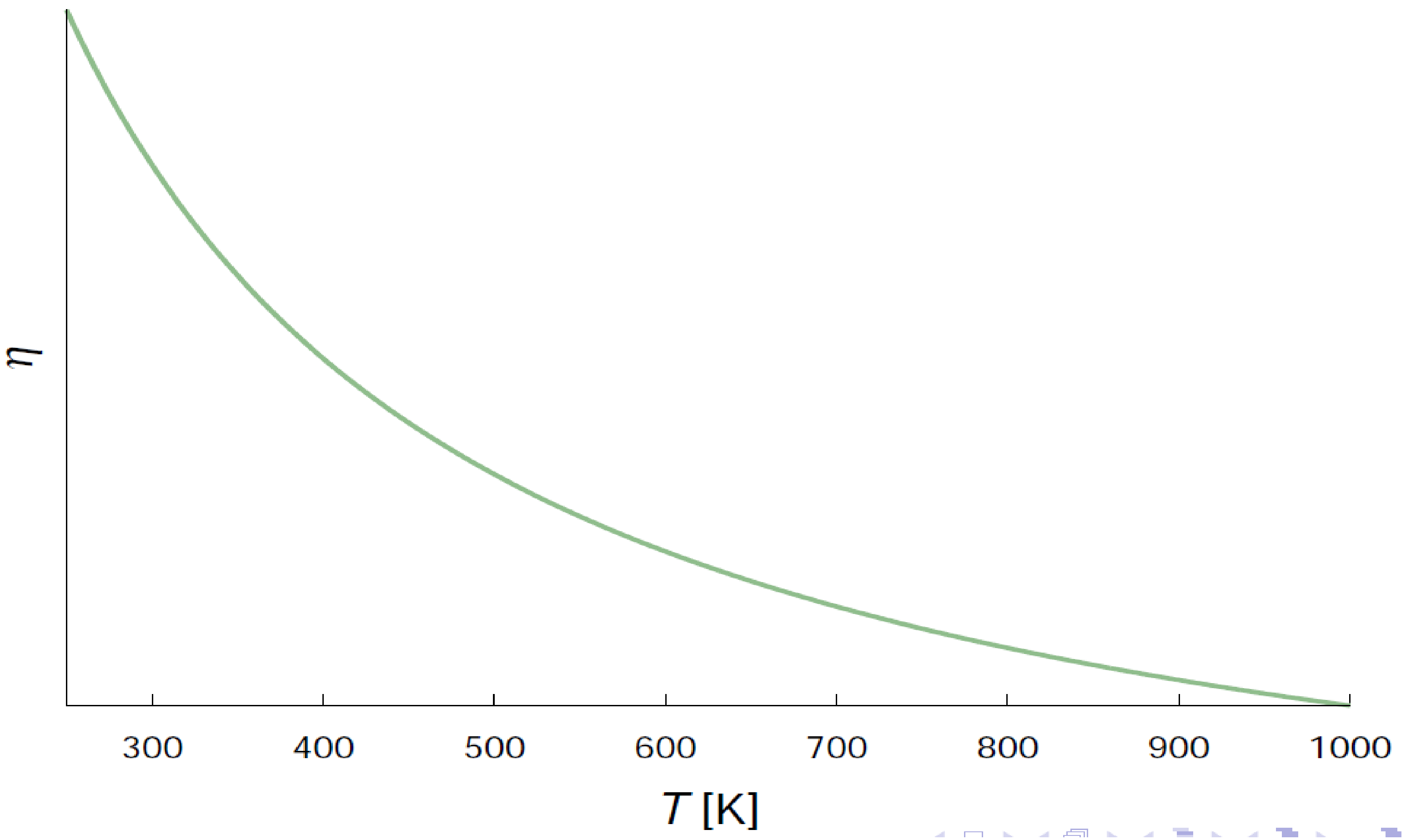
  $$N \propto T \cdot e^{-\frac{E}{kT}},$$

  where N is the number of molecules above the activation energy E, k is the Boltzmann constant and T is the absolute temperature
- the higher the concentration of the gaps, the lower the viscosity ⇒ $\eta \propto \frac{1}{N}$:

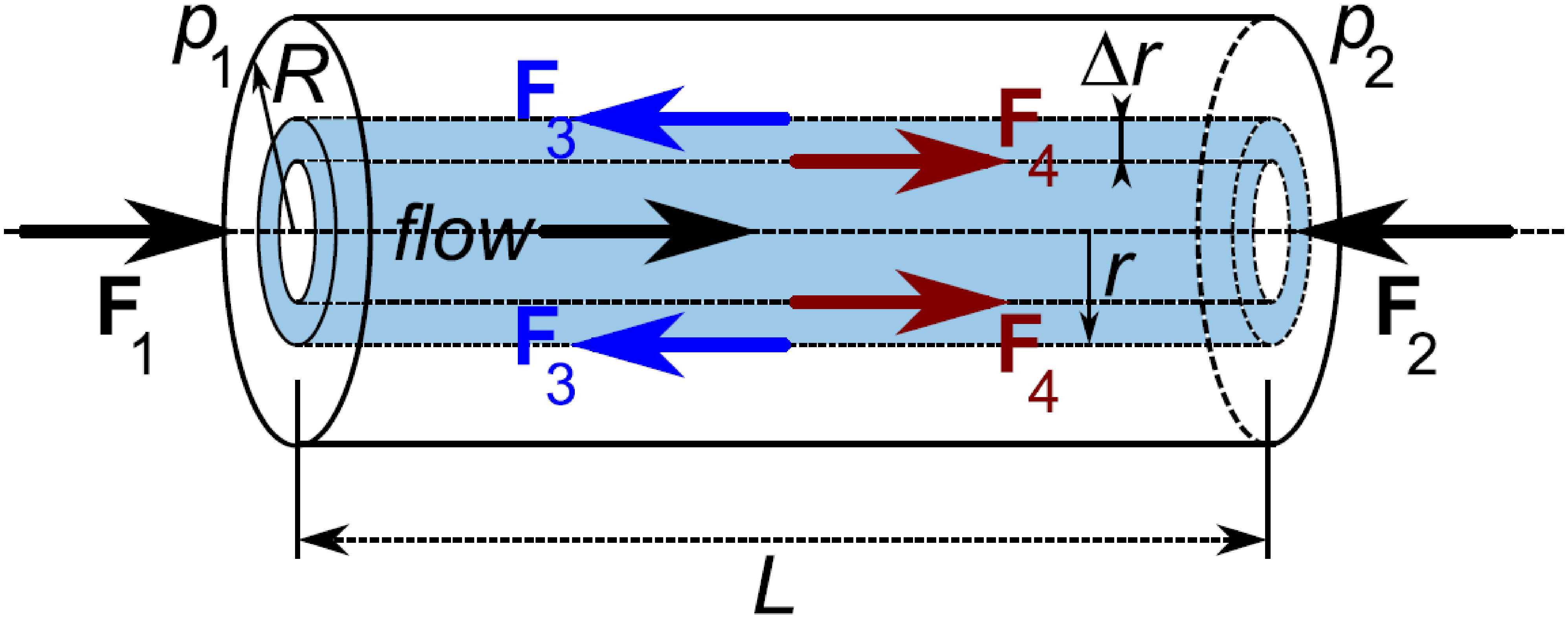
  $$\eta \propto \frac{1}{T} e^{\frac{E}{kT}}$$

- **the viscosity of liquids decreases with temperature**

Temperature dependence of viscosity in liquids



Hagen–Poiseuille law: illustration



Hagen–Poiseuille equation

- exact solution obtained through integration

$$I = \lim_{\Delta r \to 0} \sum_{k=0}^{N-1} 2 r_k \pi \cdot v(r_k) \cdot \Delta r = \int_0^R 2 r \pi \cdot v(r)\,\mathrm{d}r$$

$$I = \int_0^R 2r\pi \cdot v(r)\,\mathrm{d}r = \int_0^R 2r\pi \cdot \frac{\Delta p}{4\eta L}\left(R^2 - r^2\right)\,\mathrm{d}r = \frac{\pi}{2\eta L} \cdot \Delta p \cdot \int_0^R \left(rR^2 - r^3\right)\,\mathrm{d}r$$

$$I = \frac{\pi}{2\eta L} \cdot \Delta p \cdot \left(R^2 \int_0^R r\,\mathrm{d}r - \int_0^R r^3\,\mathrm{d}r\right) = \frac{\pi}{2\eta L} \cdot \Delta p \cdot \left(R^2 \left[\frac{r^2}{2}\right]_0^R - \left[\frac{r^4}{4}\right]_0^R\right)$$

$$I = \frac{\pi}{2\eta L} \cdot \Delta p \cdot \left\{R^2 \left(\frac{R^2}{2} - 0\right) - \left(\frac{R^4}{4} - 0\right)\right\} = \frac{\pi}{2\eta L} \cdot \Delta p \frac{R^4}{4}$$

$$\boxed{I = \frac{\pi}{8\eta L} \cdot \Delta p \cdot R^4}$$

- this is the **Hagen–Poiseuille equation**

Medical examples

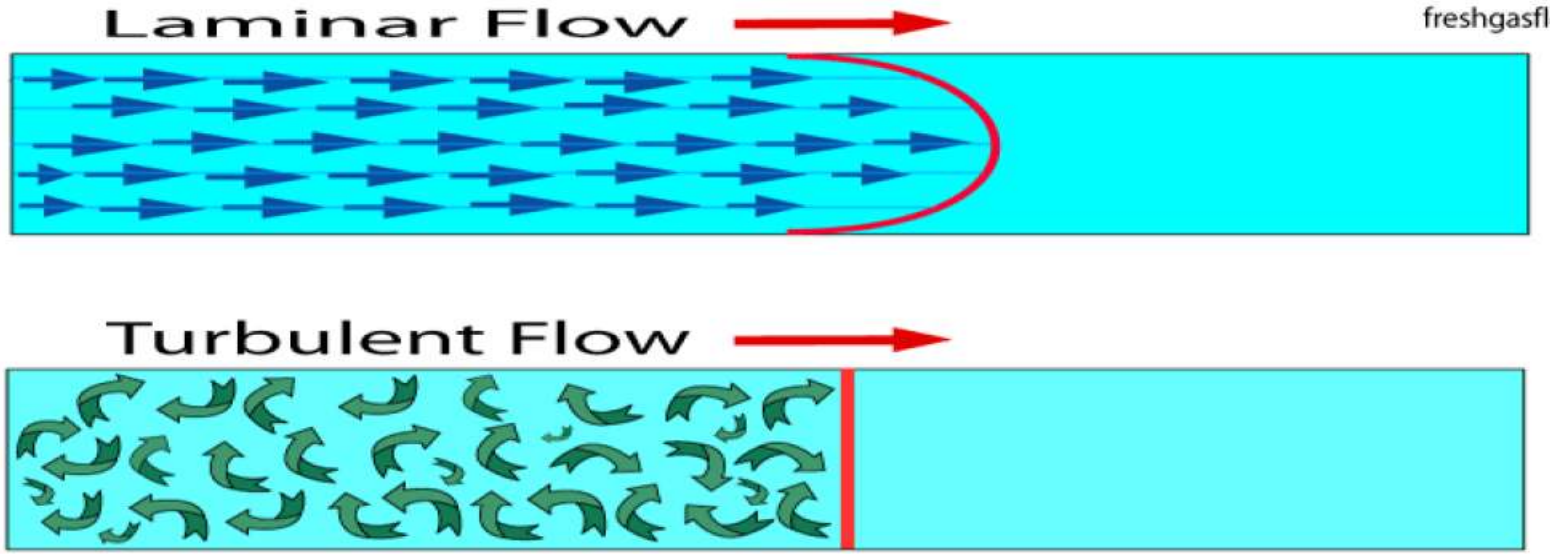
Muscles in use (eg, sports)

- oxygen demand increases
- more blood (higher current) needed to supply this oxygen
- blood vessels dilate (become wider)
- $I \propto R^4$
- the current through the dilated blood vessels increases drastically

Arteriosclerosis

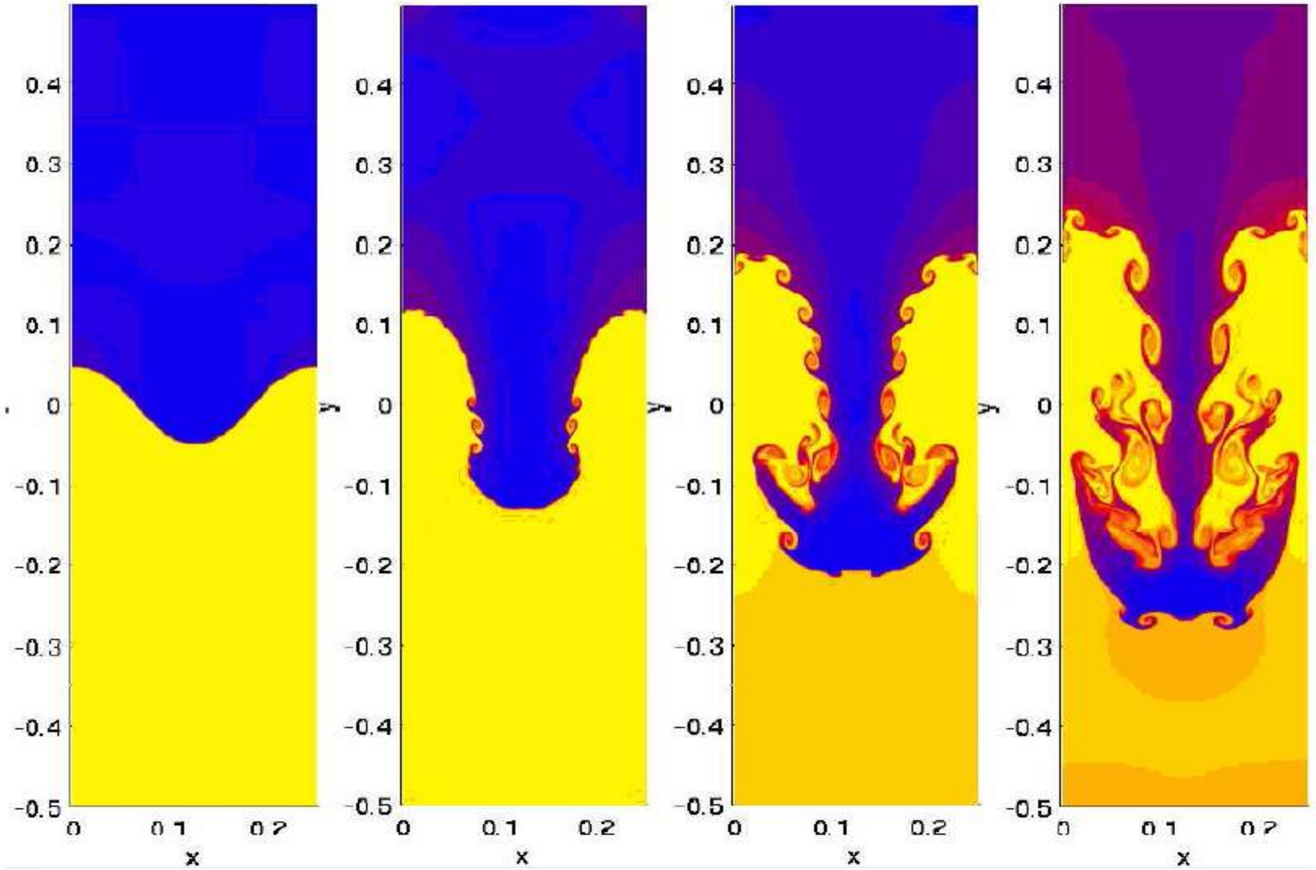
- blood vessels become rigid and *narrow*
- narrower tubes $\Rightarrow$ R drops
- $I \propto R^4 \Rightarrow I$ drops drastically
- much higher pressure needed to maintain the same current
- the heart may not sustain the increased load

Laminar and turbulent flow



freshgasflow.com

Laminar and turbulent flow



Reynolds number

- Is the flow laminar or turbulent? $\Leftarrow$ *Reynolds number*

$$\boxed{\mathrm{Re} = \frac{\rho v L}{\eta}}$$

- ρ: density of the fluid
- v: velocity of the flow
- L: characteristic length (eg, radius of the tube)
- η: viscosity of the fluid

- Re: dimensionless empirical number
- How is it used to predict turbulence? $\Rightarrow$ *transition Reynolds numbers*
  - $\mathrm{Re}_{\mathrm{flow}} < \mathrm{Re}_1$: laminar flow
  - $\mathrm{Re}_1 \leq \mathrm{Re}_{\mathrm{flow}} < \mathrm{Re}_2$: transition region — both laminar and turbulent flow are possible
  - $\mathrm{Re}_2 \leq \mathrm{Re}_{\mathrm{flow}}$: turbulent flow
- transition Reynolds numbers are determined experimentally (eg, wind tunnels)
- transition Reynolds number values are similar for different fluids, they mostly depend on flow geometry

What does it mean?

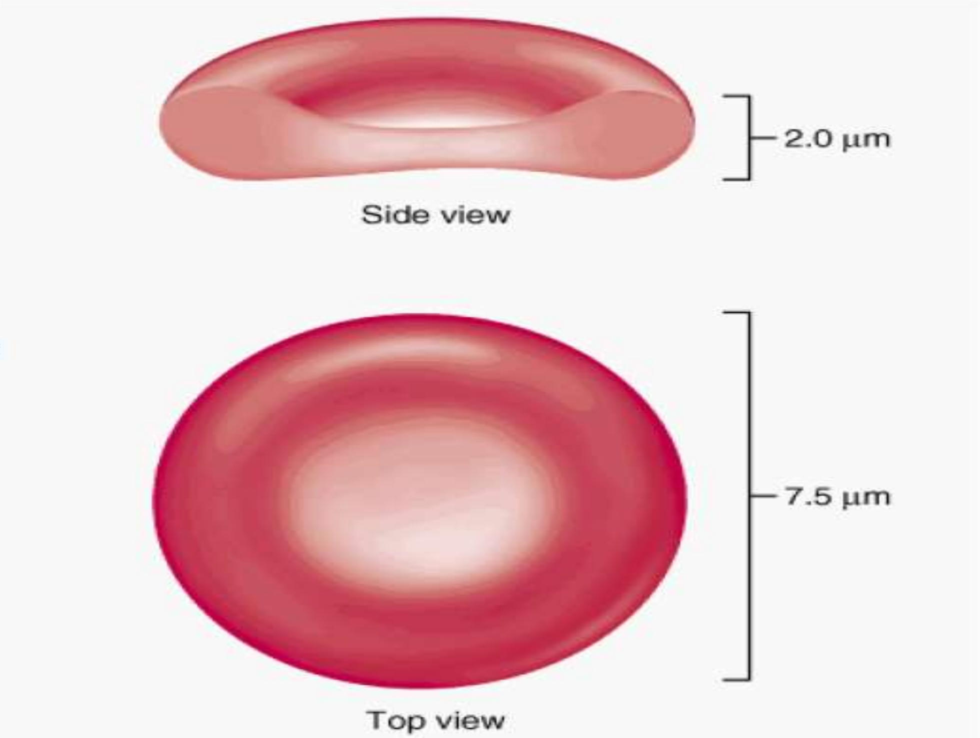
- As size goes down, Re goes down
- As viscosity goes up, Re goes down
- At high Reynold’s numbers- inertial forces dominate
- At low Reynold’s numbers- viscous forces dominate
- Small objects in fluids are affected by the frictional drag of the media to a great extent

Sample Reynolds' numbers

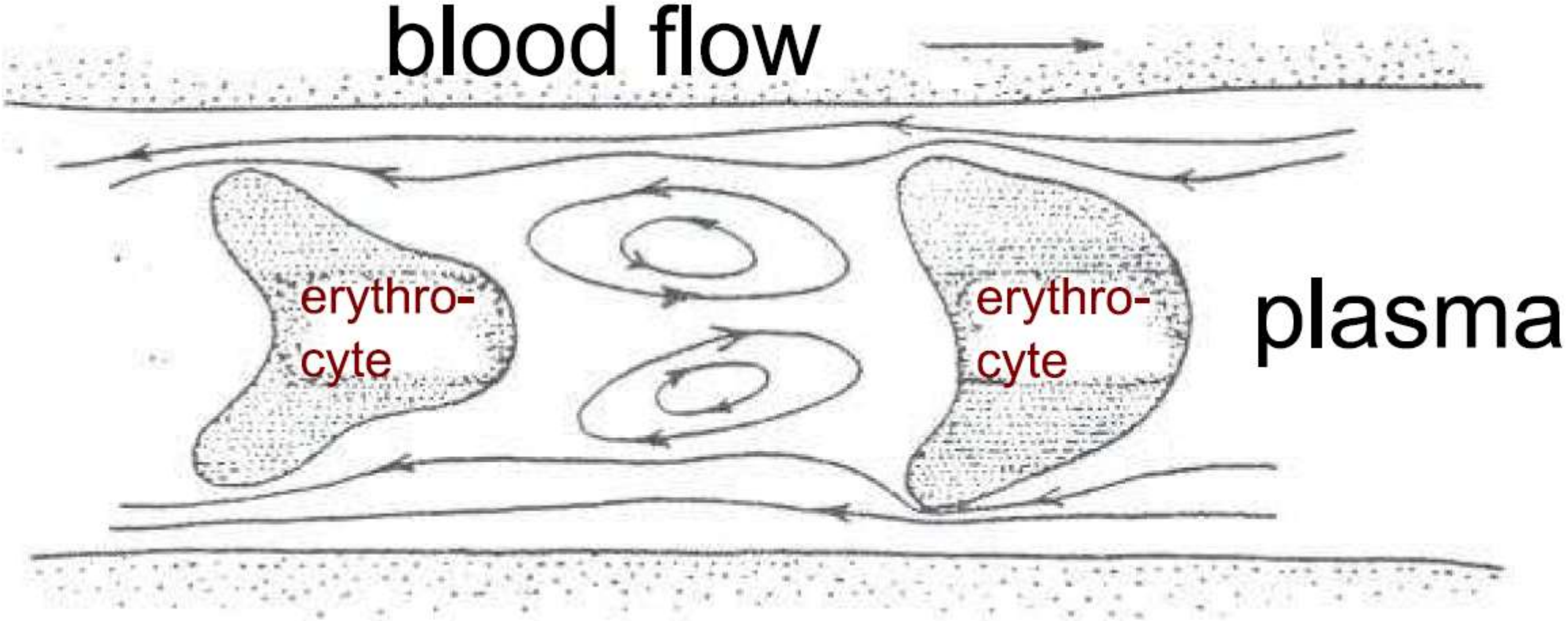
Bacterium swimming (organelle)	10^{-6}
Sperm swimming	10^{-2}
Fruit fly in flight	100
Small bird flying	10^{5}
Whale swimming	2×10^{8}

Flow properties of blood

- volume of blood: 5–6 litres
- cellular components of blood:
  - erythrocytes (red blood cells)
  - leukocytes (white blood cells)
  - platelets
- the diameter of erythrocytes is greater than that of capillaries ⇒ erythrocytes can only squeeze through capillaries due to their elasticity
- **bolus flow**: erythrocytes block normal flow, blood plasma between them is forced to rotate ⇒ better circulation
- anomalies: sickle anaemia — reduced membrane elasticity of erythrocytes ⇒ being trapped (ageing of erythrocytes also reduces elasticity)



Bolus flow



"INSANITY
IS DOING THE
SAME THING OVER
AND OVER AND
EXPECTING A
DIFFERENT RESULT."

--ALBERT EINSTEIN