Biology for Engineers

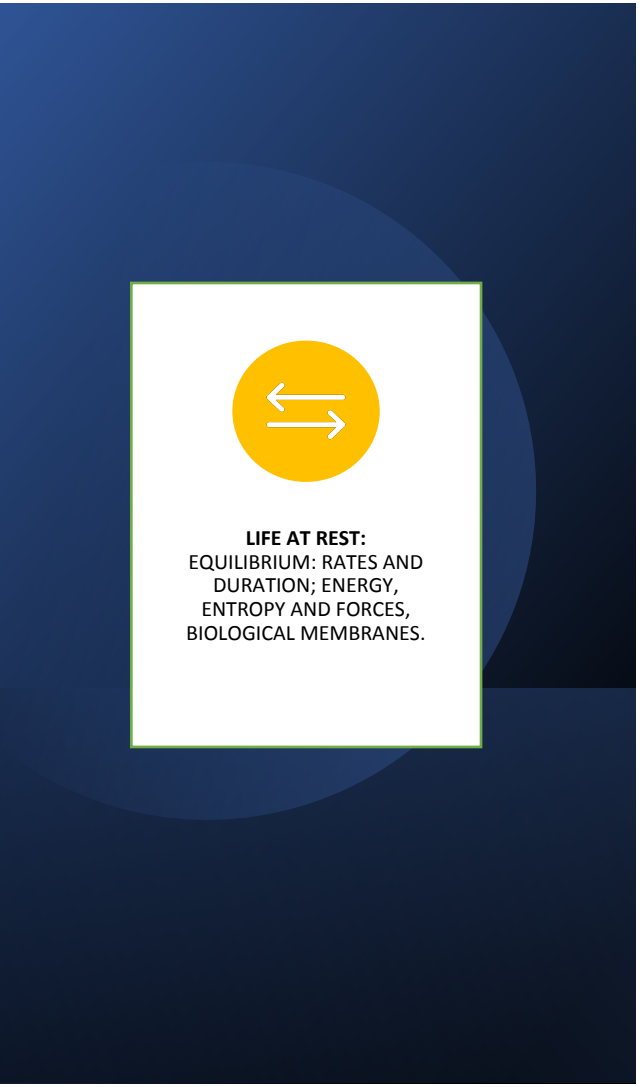
FY-BTech

Unit 2- Life at Rest

Transcription
Translation
growth rate
photosynthesis light non cyclic.

21, 25, 26
28, 29, 32
33, 34
1 Diagram ✓

Module-2: Life at rest



Thermodynamics and Static Properties of cells

Equilibrium: Mechanical and Chemical Equilibrium in the Living Cell; Cells as Chemical Factories; Chemical equilibrium, rate of reaction. The concept of steady state equilibrium.

Rates and duration: Time scales of small molecules; central dogma, Life cycle of cells.

Energy, Entropy and Forces: Thermal energy, photons and photosynthesis; energy currencies and budget.

Electrostatics

Biological Membranes: membrane permeability: pumps and channels, action potential.

RATES AND DURATIONS – INTRODUCTION

What do we learn in rates and durations section?

We explore ”how fast” processes happen in a cell?

How large the main players are (i.e. the sizes of macromolecules, organelles, cells and organisms), what concentrations they occur at and the time scales for the many processes that are carried out by living organisms?

RATES AND DURATIONS – INTRODUCTION

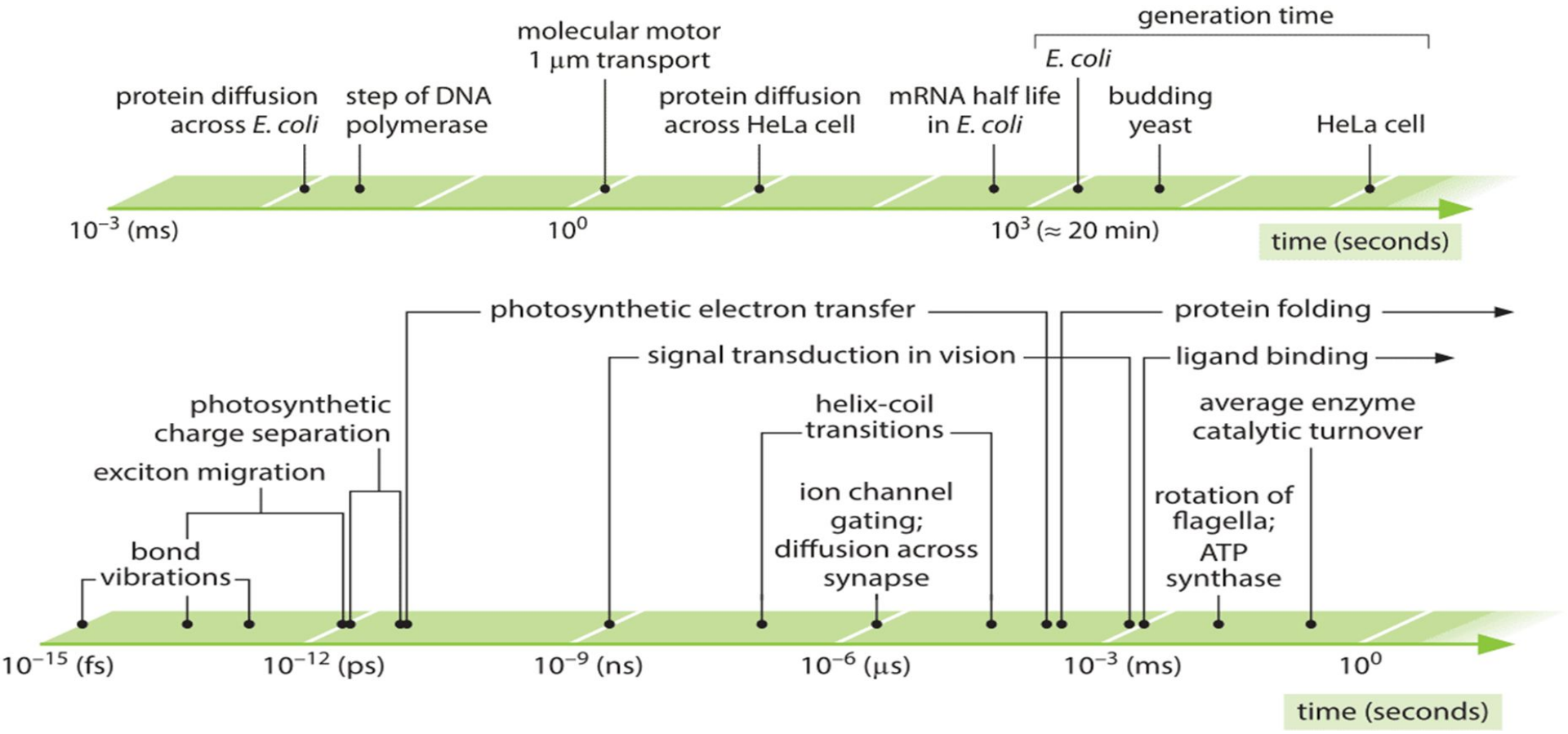


Figure 1: Range of characteristic time scales of central biological processes. Upper axis shows the longer timescales from protein diffusion across a bacterial cell to the generation time of a mammalian cell. The lower axis shows the fast timescales ranging from bond vibrations to protein folding and catalytic turnover durations.

To understand the reference of time scale—how fast a molecule will move? We use **diffusion.**

Diffusion refers to the random motions undergone by small scale objects as a result of their collisions with the molecules making up the surrounding medium.

Botanist Robert Brown in his paper "A Brief Account of Microscopical Observations Made in the Months of June, July, and August, 1827, On the Particles Contained in the Pollen of Plants, and on the General Existence of Active Molecules in Organic and Inorganic Bodies". Describes process of diffusion or random movement of particles. Brownian motion is the name given to the process in honor of Robert Brown.

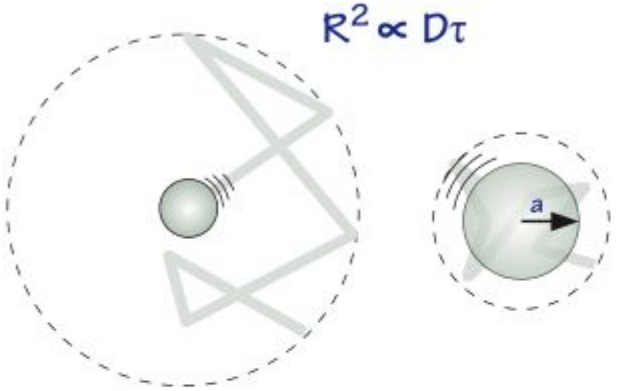
Diffusion is often the dynamical basis for a broad spectrum of different reactions.

The concentration of some diffusing species as a function of both position and time is captured mathematically using the diffusion equation.

molecule	measured context	diffusion coefficient ($\mu m^2/s$)	BNID
H_2O	water	2000	104087, 106703
H_2O	nucleus of chicken erythrocyte	200	104645
H^+ (from H_3O^+ to H_2O)	water	7000	106702
O_2	water	2000	104440
CO_2	water	2000	102625
tRNA (≈20 kDa)	water	100	107933, 107935
protein (≈30 kDa GFP)	water	100	100301
protein (≈30 kDa GFP)	eukaryotic cell (CHO) cytoplasm	30	101997
protein (≈30 kDa GFP)	rat liver mitochondria	30	100300
protein (NLS-EGFP)	cytoplasm of *D. melanogaster* embryo	20	109209
protein (≈30 kDa)	*E. coli* cytoplasm	7-8	100193, 107985
protein (≈40 kDa)	*E. coli* cytoplasm	2-4	107985
protein (≈70-250 kDa)	*E. coli* cytoplasm	0.4-2	107985
protein (≈140 kDa Tar-YFP)	*E. coli* membrane	0.2	107985
protein (≈70 kDa LacY-YFP)	*E. coli* membrane	0.03	107985
fluorescent dye (carboxy-fluorescein)	*A. thaliana* cell wall	30	105033
fluorescent dye (carboxy-fluorescein)	*A. thaliana* mature root epidermis	3	105034
transcription factor (LacI)	movement along DNA (1D, *in vitro*)	0.04 (4×10^5 bp^2s^{-1})	102036
morphogen (bicoid-GFP)	cytoplasm of *D. melanogaster* embryo	7	109199
morphogen (wingless)	wing imaginal disk of *D. melanogaster*	0.05	101072
mRNA	HeLa nucleus	0.03-0.10	107613
mRNA	various localizations and sizes	0.005-1	110667
ribosome	*E. coli*	0.04	108596

Table 1: A compilation of empirical diffusion constants showing the dependence on size and cellular context

Stokes–Einstein relation and the diffusion constant in water



$$D = \frac{k_B T}{6\pi\eta a} \approx \frac{4 \times 10^{-21}\,\mathrm{N \times m}}{6 \times 3 \times 10^{-3}\,\frac{\mathrm{N \times s}}{\mathrm{m^2}} \times \frac{a}{1\,\mathrm{nm}} \times 10^{-9}\,\mathrm{m}} \approx \frac{1}{5} \times \frac{10^{-9}\,\mathrm{m^2/s}}{\frac{a}{1\,\mathrm{nm}}} \times \frac{10^{12}\,\mu\mathrm{m^2}}{\mathrm{m^2}} = \frac{200}{\frac{a}{1\,\mathrm{nm}}}\,\frac{\mu\mathrm{m^2}}{\mathrm{s}}$$

viscosity $\approx 10^{-3}\,\frac{\mathrm{N \times s}}{\mathrm{m^2}}$

The key parameter in this equation is the diffusion constant, D, with larger diffusion constants indicating a higher rate of jiggling around. **The value of D is microscopically governed by the velocity of the molecule and the mean time between collisions.**

Time scale τ for a particle to travel a distance x is given on the average by $\tau \approx x2/D$, indicating that the dimensions of the diffusion constant are (length)(length)/time**.**

This rule of thumb shows that the diffusion time increases quadratically with the distance.

How long does it take macromolecules to traverse a given cell?

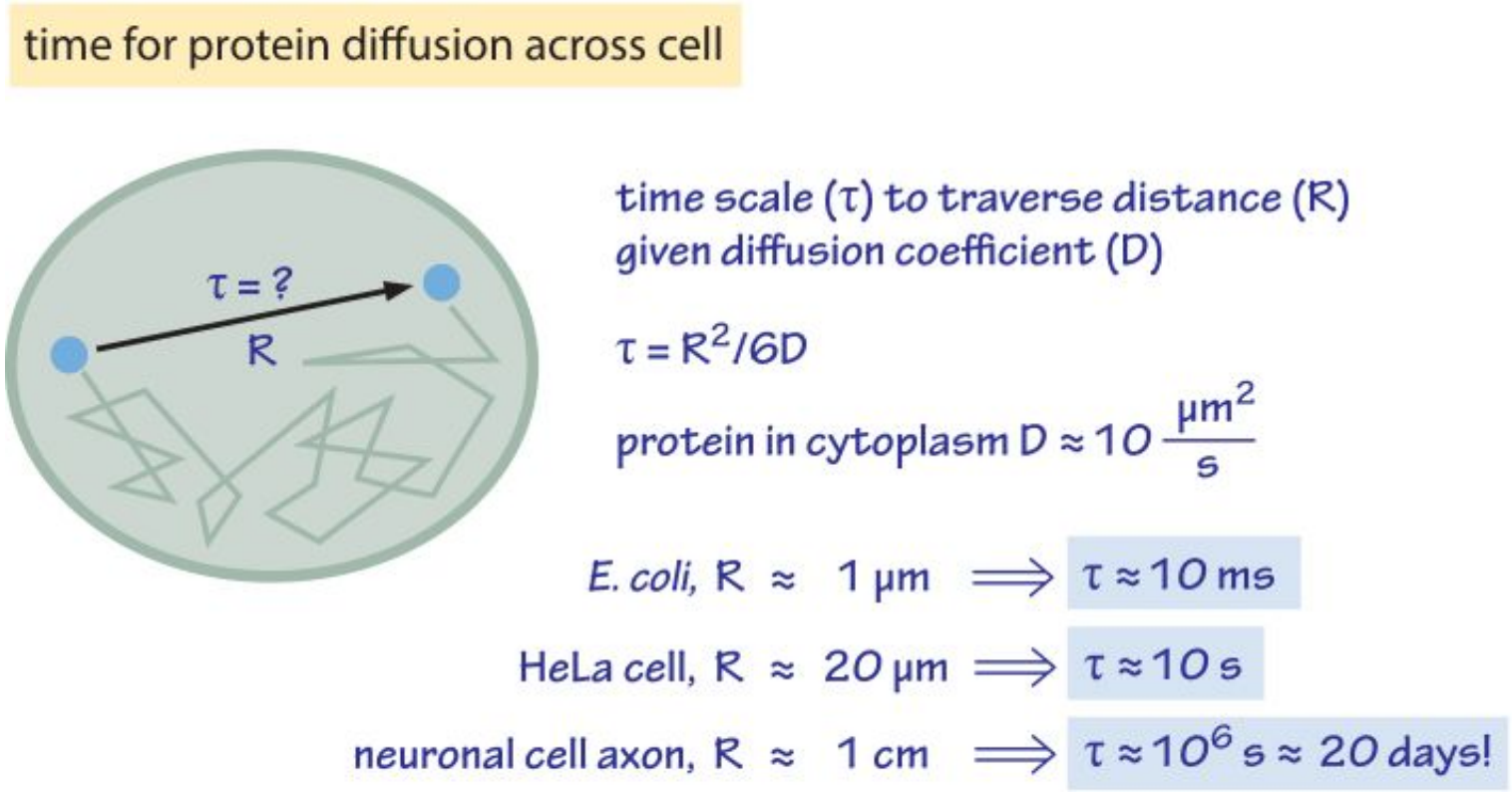


Figure 2: We assume a characteristic diffusion coefficient for a monomeric protein of 30 kDa. At higher molecular mass there is a reduction of about an order of magnitude as shown in Table 1 and the time scales will increase by the same factor. The protein diffusion constant used to estimate time scales within cells takes into account an order of magnitude reduction in the diffusion constant in the cell relative to its value in water. **The factor of 6 in the denominator of the equation for τ applies to diffusion in three dimensions.** In the two- or one-dimensional cases, it should be replaced with 4 or 2, respectively. The mammalian cell characteristic distance is taken to be 20 μm, characteristic of spreading adherent cells.

The characteristic diffusion constant for a molecule the size of a monomeric protein is ≈100 μm2/s in water and is about ten-fold smaller, ≈10 μm2/s, inside a cell with large variations depending on the cellular context as shown in Table 1 (larger proteins often show another order of magnitude decrease to ≈1 μm2/s, BNID 107985).

It takes roughly 0.01 seconds for a protein to traverse the 1 micron diameter of an E. coli cell (BNID 103801).

A similar calculation results in a value of about 10 seconds for a protein to traverse a HeLa cell (adhering HeLa cell diameter ≈20 μm, BNID 103788).

An axon 1 cm long is about 500 times longer still and from the diffusion time scaling as the square of the distance it would take 10^6 seconds or about two weeks for a molecule to travel this distance solely by diffusion.

This enormous increase in diffusive time scales as cells approach macroscopic sizes demonstrates the necessity of mechanisms other than diffusion for molecules to travel these long distances.

Using a molecular motor moving at a rate of ≈1 μm/s (BNID 105241) it will take a "physiologically reasonable" 2-3 hours to traverse this same distance.

For extremely long neurons, that can reach a meter in length in a human (or 5 meters in a giraffe), recent research raises the speculation that neighboring glia cells alleviate much of the diffusional time limits by exporting cell material to the neuron periphery from their nearby position (K. A. Nave, Nat. Rev. Neuroscience, 11:275, 2010).

This can decrease the time for transport by orders of magnitude but also requires dealing with transport across the cell membrane.

How much slower is diffusion in the cytoplasm in comparison to water and what are the underlying causes for this difference?

Cellular context affects diffusion rates by a factor that depends strongly on the compound's biophysical properties as well as size.

Small metabolites might suffer only a 4-fold decrease in their diffusive rates
DNA can exhibit a diffusive slowing down in the cell that is tens or hundreds of times slower than in water as shown in

Recent analysis (T. Ando & J. Skolnick, Proc. Natl. Acad. Sci., 107:18457, 2010) highlights the importance of hydrodynamic interactions – the effects of moving objects in a fluid on other objects similar to the effect of boats on each other via their wake.

Such interactions lead approaching bodies to repel each other whereas two bodies that are moving away are attracted.

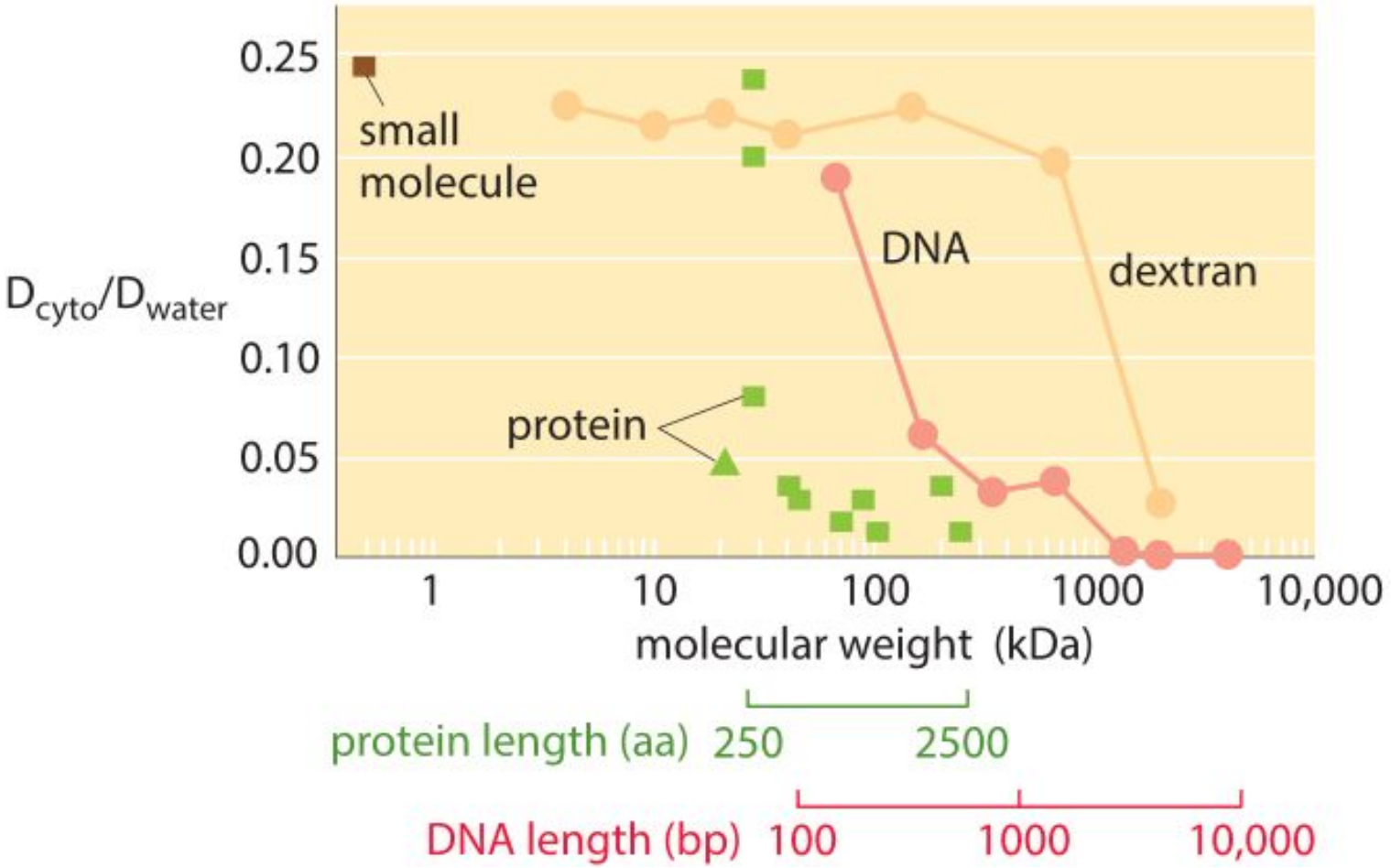


Figure 3: The decrease in the diffusion constant in the cytoplasm with respect to water as molecular weight increases. For the different proteins marked in green see Kumar et al 2010 and entries in the compilation table below. (Adapted from A. S. Verkman, Trends Biochem., 27:27, 2002; M. Kumar et al., Biophysical Journal, 98:552, 2010).

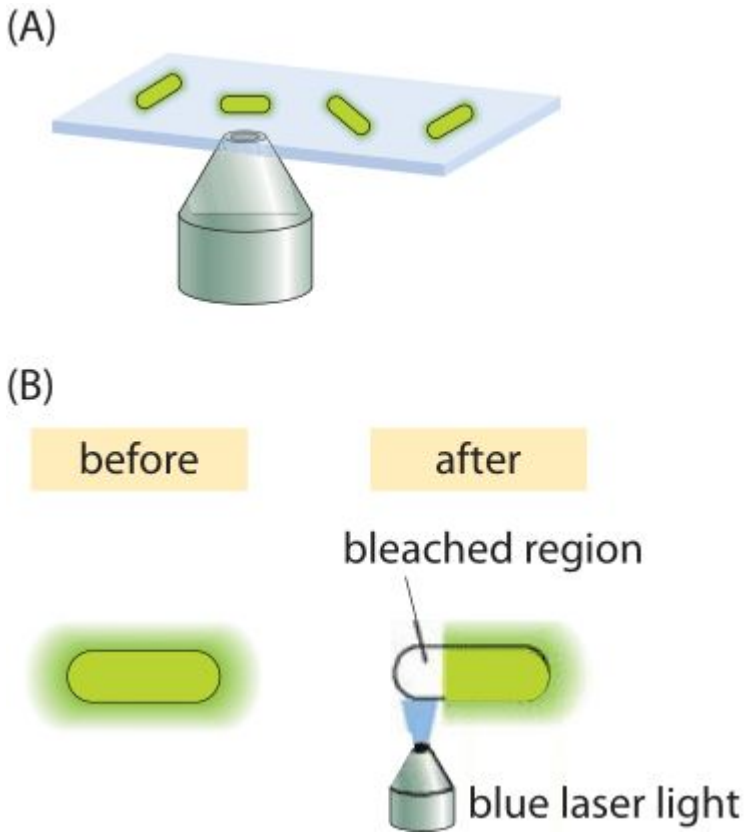


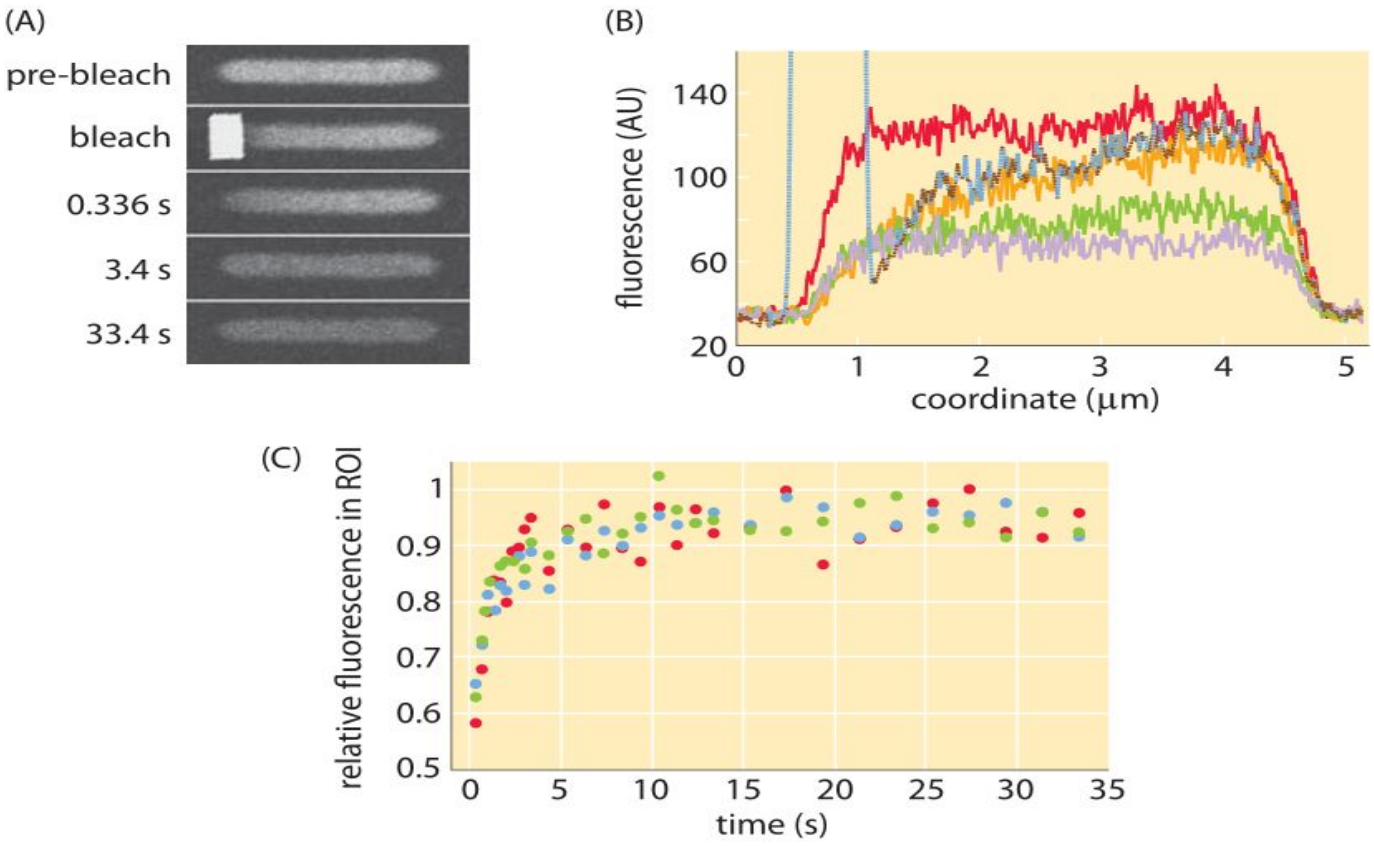
Figure 4: Fluorescence recovery after photobleaching in bacteria.

(A) Schematic of how the FRAP technique works. The laser photobleaches the fluorescent proteins in a selected region. Because of diffusion, proteins that were not bleached come into the bleached region over time.

(B) Higher resolution schematic of the photobleaching process over a selected region within the cell.

When exposed to light, fluorescent molecules lose their ability to fluoresce over time. But this becomes a convenience when the bleached region is only part of a cell. The reason is that after the bleaching event, because of the diffusion of the unbleached molecules from other regions of the cell, they will fill in the bleached region, thus increasing the fluorescence (the so called “recovery” phase in in FRAP).

Using FRAP technique, systematic studies of the dependence of the diffusion coefficient on molecular size for cytoplasmic proteins in E. coli have been undertaken



Fluorescence recovery after photobleaching in E. coli cells. (A) Images of E. coli cells before and after the bleaching process showing the spatial distribution of fluorescence. (B) Fluorescence as a function of position for different times. (C) Recovery of fluorescence over time as measured in multiple experiments. (Adapted M. Kumar et al., Biophysical Journal, 98:552, 2010)

HOW MANY REACTIONS DO ENZYMES CARRY OUT EACH SECOND?

Uncatalyzed reactions reactions taking place in cells, though thermodynamically favorable, are in most cases very slow.

The spontaneous cleavage of a peptide bond would take 400 years at room temperature and phosphomonoester hydrolysis, routinely breaking up ATP to release energy, would take about a million years in the absence of the enzymes that shuttle that reaction along (BNID 107209).

Enzymes increase rates by an astonishing 10 orders of magnitude or more (BNID 105084, 107178).

Enzymes are characterised kinetically by a catalytic rate kcat (also referred to as the turnover number).

kcat signifies how many reactions an enzyme can possibly make per unit time.

Enzyme kinetics is studied using Michaelis-Menten equations.

At very low substrate concentrations, the rate of the reaction increases linearly with substrate concentration.

At very high concentrations, the enzyme is cranking out as many product molecules as it can every second at a rate kcat and increasing the substrate concentration further will not lead to any further rate enhancement.

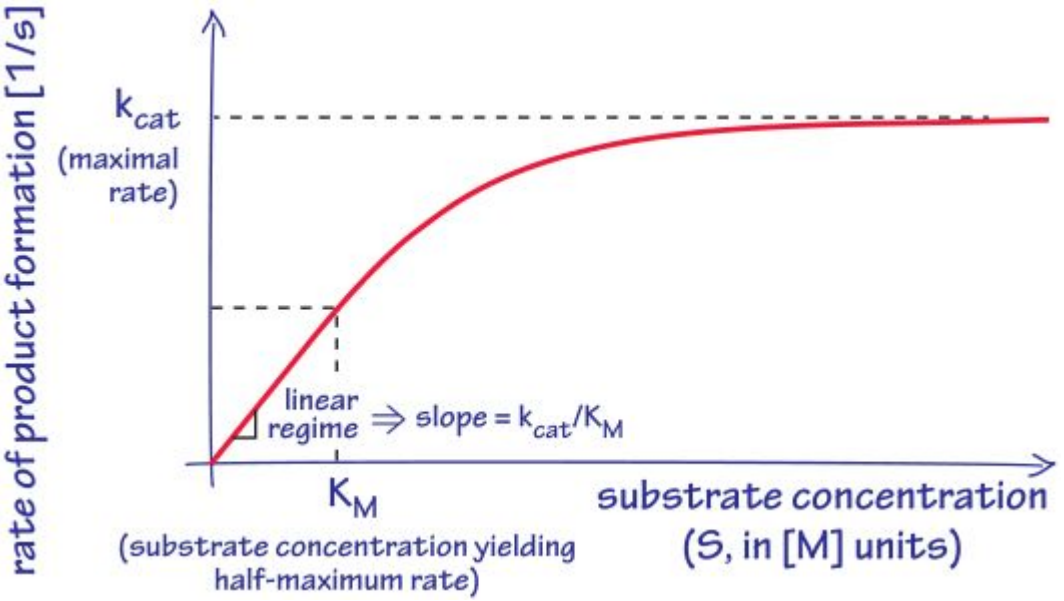


Figure 1: The characteristic dependence of enzyme catalysis rate on substrate concentration. Key defining effective parameters such as kcat, KM and their ratio, the second order rate constant that is equal to the slope at low concentrations, are denoted in the figure.

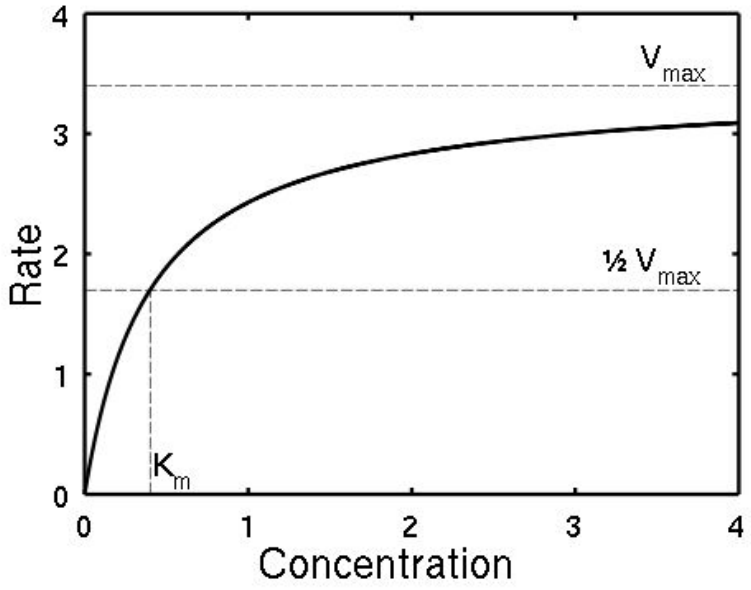
How does one know if an enzyme works close to the maximal rate?

There is a level of substrate concentration beyond which the enzyme will achieve more than half of its potential rate.

- The concentration at which the half-maximal rate is achieved is denoted KM.
- When the substrate concentration is well above KM, the reaction will proceed at close to the maximal rate kcat.
- At a substrate concentration [S]=KM the reaction will proceed at half of kcat.
- Actual rate depends upon how much substrate is present through the substrate affinity, KM.

$$Vo = \frac{V_{max}[S]}{Km + [S]}$$

V0 = Initial velocity (moles/times)
[S] = substrate concentration (molar)
V_{max}= maximum velocity
K_m = substrate concentration at half V_{max}



CO2 into bicarbonate and back (CO2+H2OHCO3–+H+) and superoxide dismutase, an enzyme that protects cells against the reactivity of superoxide by transforming it into hydrogen peroxide (2O2–+2H+H2O2+O2).

These enzymes can carry out as many as 10^6-10^7 reactions per second.

At the opposite extreme, restriction enzymes limp along while performing only ≈10^-1-10^-2 reactions per second or about one reaction per minute per enzyme (BNID 101627, 101635).

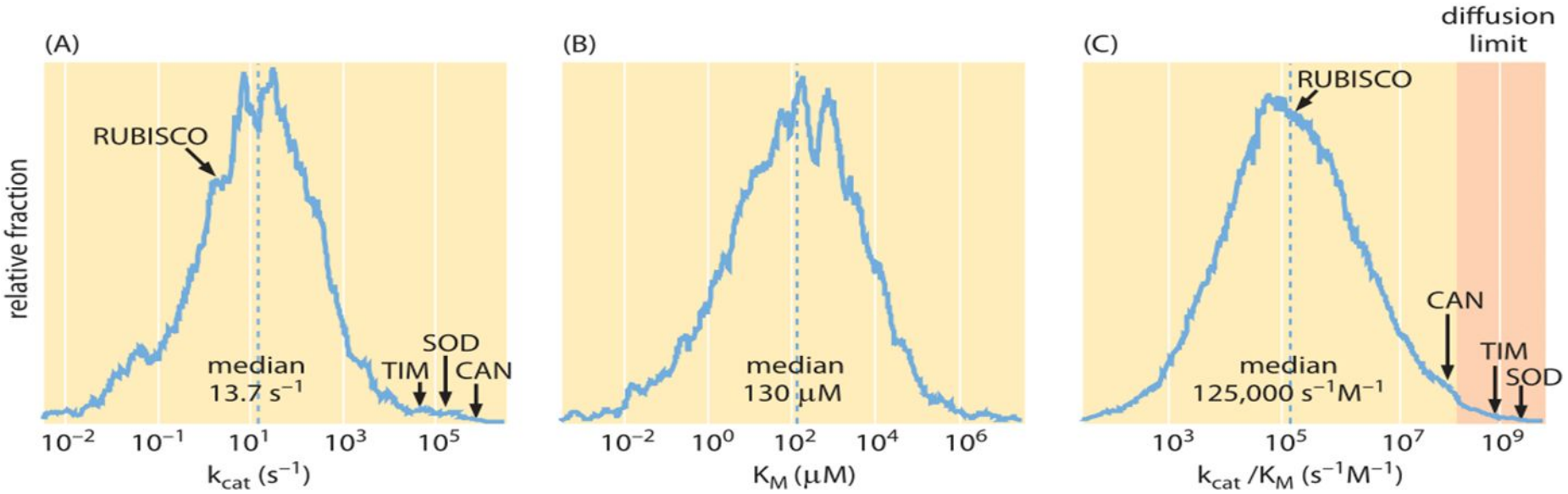


Figure 2. Distributions of enzyme kinetic parameters from the literature extracted from the BRENDA database: (A) kcat values (N = 1942), (B) kcat/KM values (N = 1882), and (C) KM values (N = 5194). Only values referring to natural substrates were included in the distributions. The location of several well-studied enzymes is highlighted: CAN, carbonic anhydrase; SOD, superoxide dismutase; TIM, triosephosphate isomerase; Rubisco, ribulose-1,5-bisphosphate carboxylase oxygenase. Adapted from Bar-Even et al, Biochemistry, 50(21):4402-4410, 2011.

What are the characteristic values of KM for enzymes in the cell?

Actual rate depends upon how much substrate is present through the substrate affinity, KM.

The median KM value is in the 0.1 mM range. From our rule of thumb (1nM is about 1 molecule per 1 E. coli volume) this is roughly equal to 100,000 substrate molecules per bacterial cell.

At low substrate concentration ([S]<<KM) we can approximate the reaction rate by [ET]*kcat*[S]/KM, which is proportional to the product [ET]*[S] that measures the collision rate of the enzyme with the substrate with a proportionality rate factor of kcat/KM.

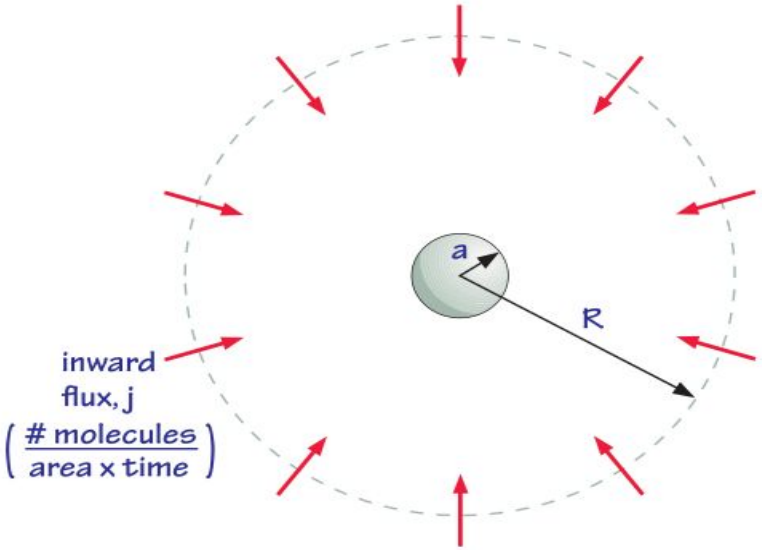
This proportionality factor, known as the second order rate constant due to the fact that it multiplies two concentration terms, is the slope.

This factor cannot be higher than the collision rate facilitated by diffusion unless electrostatic or other effects are in play.

The median value of rate of reaction is about 105 s-1M-1, about 4 orders of magnitude lower than the diffusion limit.

The rate might be compromised in many cases by the need for recognition and specificity in the interaction.

the diffusion-limited on-rate



mass conservation says $j(R) \times 4\pi R^2$ is constant for all R, hence $j(R) \propto \frac{1}{R^2}$

concentration ↓ ; constants ↓

by Fick's Law, $j \propto -\frac{\partial c}{\partial R} \Rightarrow \frac{\partial c}{\partial R} = -\frac{A}{R^2} \Rightarrow c(R) = \frac{A}{R} + B$

apply boundary conditions

1) $c(\infty) = c_\infty = B$

2) $c(a) = \frac{A}{a} + c_\infty = 0 \Rightarrow A = -c_\infty a$

$\Rightarrow c(R) = c_\infty(1 - \frac{a}{R})$

using Fick's Law, $j(a) = -D \left.\frac{\partial c}{\partial R}\right|_{R=a} = \frac{Dc_\infty}{a}$

reaction rate $\frac{dn}{dt} = j(a)\, 4\pi a^2 = 4\pi D a c_\infty = k_{on} c_\infty$

protein radius ↓

$$k_{on} = 4\pi \times 100 \frac{\mu m^2}{s} \times 2\times10^{-3}\mu m \times 6\times10^{23} \frac{molecules}{mol} \times \frac{1\,L}{10^{15}\mu m^3} \approx 10^9\, s^{-1}M^{-1}$$

↑ characteristic diffusion coefficient of metabolite in cytoplasm

The value of KM in conjunction with the diffusion-limited-on-rate can be used to estimate the off rates for bound substrate.

The goal of the simple estimate is to find the time scale over which a substrate that is bound to the enzyme will stay bound before it goes back to solution (usually without reacting), the so called ***off rate koff***.

The estimate is based upon an ideal limit in which the on-rate is controlled by diffusive encounters with the enzyme characterized by the diffusion-limited-on-rate, kon ≈109 s-1M-1.

An approximation for the koff is the product of this kon and the KM.

So for example, if KM is a characteristic 10-4 M, the product is 105 s-1, so the substrate will unbind in about 10 μs, this is the so-called ***residence time***.

For extremely strong binders where the affinity is say 1 nM=10-9 M the residence time will be 1 s.

An analogous estimate for the off-rate can be considered for interactions between signaling molecules and for transcription factors binding to DNA with characteristic time scales from milliseconds to tens of seconds or even longer.

The rate of enzyme substrate collisions is dictated by the diffusion limit which as shown above is equal to ≈10^9 s-1M^-1 times the concentrations.

In E. coli a single molecule per cell (say our substrate) has an effective concentration of about 1nM (i.e. 10-9 M).

The rate of collisions is thus 109 s-1M-1 x 10-9 M ≈ 1 s-1, i.e. they will meet within a second on average.

This allows us to estimate that every substrate molecule collides with each and every protein in the cell on average about once per second.

Think of a sugar molecule transported into the cell. Within a second it will have an opportunity to bump into all the different protein molecules in the cell.

HOW DOES TEMPERATURE AFFECT RATES AND AFFINITIES?

Catalytic rates of enzymes double when subjected to a 10oC increase in temperature

There is a free-energy barrier that the substrates have to overcome before they can be transformed to products. For a barrier of "height" Ea where Ea is the Arrhenius energy of activation, the rate scales according to the empirical Arrhenius relationship in which the rate is proportional to exp(-Ea/kBT).

If Ea is very large, the barrier is high and the exponential dependence results in a very slow rate. Many reactions have values of Ea of ≈50 kJ/mol ≈20 kBT (e.g. BNID 107803).

A 10oC (Celsius or Kelvin) change around room temperature results in ≈2 fold change in rate.

This rate factor which can be independently measured for different reactions is quantified in the literature by a quantity termed Q10 which reveals the factor by which the rate changes for a 10oC change in temperature.

The Boltzmann distribution states that the number of molecules that have energy that suffices to overcome the barrier scales as the exponent of the ratio -Ea/kBT. At higher temperatures the ratio is closer to zero and thus more molecules have the required activation energy which makes the barrier easier to overcome, resulting in an increase in the reaction rate.

change in rate for 10°C increase in temperature

$$\text{rate} \propto e^{-E_a/k_B T} \quad \text{(Arrhenius empirical relationship)}$$

$$\Downarrow$$

$$\frac{\text{rate}(T_2)}{\text{rate}(T_1)} = \frac{e^{-E_a/k_B T_2}}{e^{-E_a/k_B T_1}} = e^{-\frac{E_a}{k_B}\left(\frac{1}{T_2}-\frac{1}{T_1}\right)} = e^{-\frac{E_a}{k_B}\left(\frac{T_1-T_2}{T_1 T_2}\right)} = e^{-\frac{50\ \text{kJ/mol}}{8.3\ \text{J/mol} \times {}^\circ\text{K}} \times \frac{-10\ {}^\circ\text{K}}{(300\ {}^\circ\text{K})^2}} \approx e^{0.7} \approx 2$$

$$\Uparrow$$

$E_a \approx 50$ kJ/mol (characteristic activation energy)

$T_2 = T_1 + 10°C$

$T_1 \approx 300°$ K (room temperature)

$k_B \approx 1.38 \times 10^{-23}$ J/K ≈ 8.3 J/mol x °K

For the estimate given here, the barrier height is taken as ≈60 kJ/mol ≈20 kBT. The effect is computed for a change of temperature of 10OC.

Growth of a whole bacterium also tends to scale with temperature according to a similar functional form i.e. **log of the growth rate scaling linearly with the inverse temperature below and near the physiological temperature**.

As an example, growth of **E. coli increases by ≈2.5 fold** when moving from 17oC to 27oC and then again from 27oC to 37oC.

This is often depicted by plotting the growth rate versus 1/T as shown in Figure 3. In this range one can infer an effective value for Ea of ≈60 kJ/mol ≈25 kBT. This is termed an effective value as there is no single barrier that the bacterium has to overcome in order to grow and divide but instead the set of all barriers and processes coalesces into this one effective value.

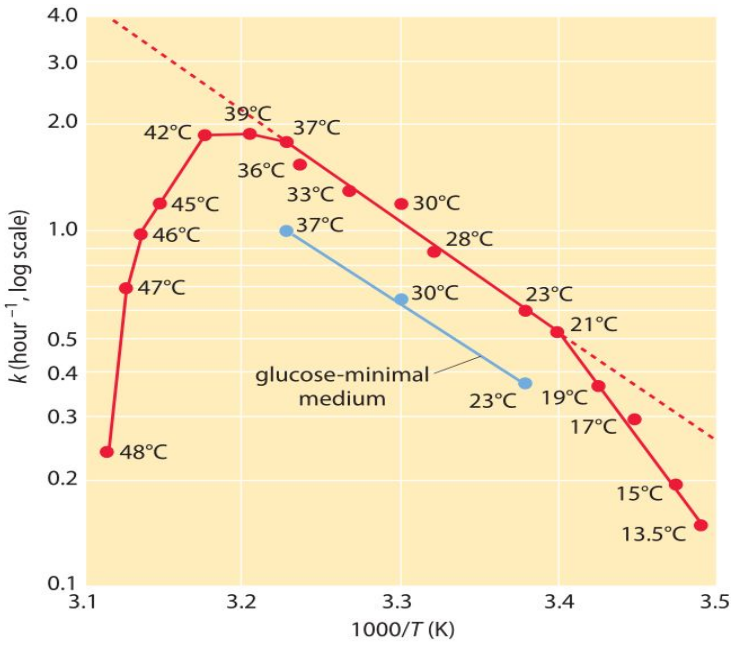


Figure 3: Dependence of the growth rate of E. coli on temperature. The growth rate is plotted versus the inverse of the temperature (an Arrhenius plot). Note the middle range where the dependence looks linear in accordance with Arrhenius rate law. (Adapted from Microbe, M. Schaechter et al., ASM press, 2006 p.63.)

WHAT ARE THE RATES OF MEMBRANE TRANSPORTERS?

Cells are buffered from the fluctuating environment that surrounds them by their plasma membranes.

Membranes control –

which molecular species are allowed to cross the membrane?

how many of them are permitted to pass to the cellular interior?

Specifically, unless a compound is simultaneously small and uncharged, passage across the plasma membrane is licensed by **molecular gatekeepers.**

Transporting molecular building blocks requires a diverse census of membrane proteins

The characteristic transport rate for sugar transporters saturated with external substrate, say a glucose transporter, is ≈100 s-1.

Many transporters are proton-coupled meaning that they use the proton motive force to drive the transport process, often against a concentration gradient of the sugar substrate. The proton concentration at pH=7 is 10-7 M and the diffusion-limited on-rate is about 109 M-1s-1. This implies that the rate at which protons hit the transporter (kon) can be roughly estimated to be ~10-7 M x 109 M-1s-1 = 102 s-1, which is the same order of magnitude as the observed turnover rate. This is effectively saying that such a proton coupled transporter works roughly as fast as it can, given the diffusion-limited rate at which protons that are serving as its energy source arrive

WHAT ARE THE RATES OF MEMBRANE TRANSPORTERS?

Capnophorin transporter

The fastest transporter is capnophorin, literally meaning “smoke carrier”, a transporter in red blood cells whose physiological role is to transport CO2 from the lungs, the “smoke” of metabolism.

This chloride-bicarbonate transporter was suggested to reach turnover rates on the order of 100,000 s-1.

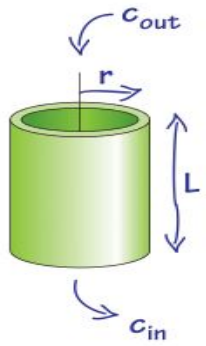
Higher Concentration of substrates (mM) leads to 1000-fold increase in rate over the proton-coupled transporters

Lactose transporter in E.coli

The surface area of an E. coli membrane dividing every half an hour is ≈6 µm^2. The structurally determined lactose transporter has an oval shape normal to the membrane with dimensions (long and short axis) of 6 nm x 3 nm (BNID 102929). Assuming a similar size for the glucose transporter, the area it occupies on the membrane is ≈10-20 nm2 (though a value about 4 fold larger for the glucose like PTS transport system is reported in another species of bacterium). For importing the ≈2×10 ^ 9 sugar molecules needed solely to build the cell mass (each consisting of six carbon atoms) within a conservative cell cycle duration of ≈2000 seconds, the fraction of the membrane area required is already ≈2% as estimated in Figure 1.

WHAT ARE THE RATES OF MEMBRANE TRANSPORTERS?

Estimating the characteristic current flowing through an H^+-dependent channel



We use Fick's Law for the flux: $J_z = -D\frac{\partial c}{\partial z} \approx D\frac{\Delta c}{L}$

A linear profile of concentration satisfies the steady-state diffusion equation:

$$c(z) = c_{out} - \frac{(c_{out} - c_{in})}{L} z$$

Units of flux are $\frac{\text{number}}{\text{area} \times s}$; current is $J \times A = J \times \pi r^2 = D\frac{\Delta c}{L}\pi r^2$

$D \approx 1000 \frac{\mu m^2}{s}$ for ions

Membrane thickness, $L \approx 4nm$

Channel radius, $r \approx 1nm$

For H^+-dependent transporters:

$pH=7 \Rightarrow$ conc. of $10^{-7}M \Rightarrow 100/\mu m^3 \approx \Delta c = \frac{100}{\mu m^3}$

$$J \times A \approx \underbrace{1000 \frac{\mu m^2}{s}}_{D} \times \underbrace{100 \mu m^{-3}}_{\Delta c} \times \underbrace{3 \times 10^{-6} \mu m^2}_{\pi r^2} / \underbrace{4 \times 10^{-3} \mu m}_{L} \approx 100 s^{-1}$$

Calculation of the fraction of membrane that needs to be occupied by a sugar transporter (glucose) to enable a bacterium (e.g E. coli) to divide once every half hour.

Sugar transporter in yeast

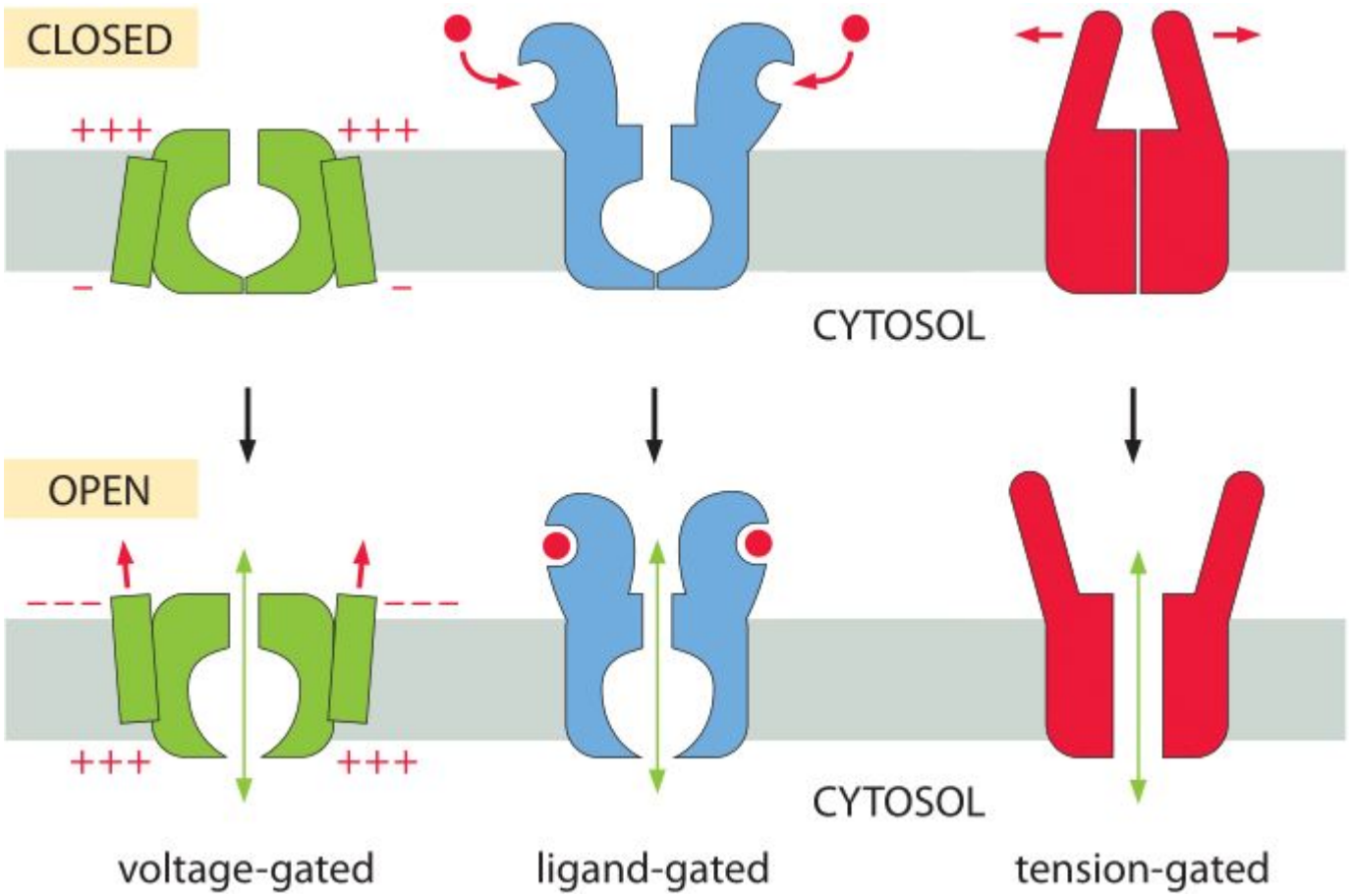
The volume and thus the number of carbons required is ≈50 times (BNID 100427) larger than in E. coli, whereas the surface area is ≈10 times larger and the fastest generation time is ≈5 times longer at ≈6000 seconds (BNID 100270).

Thus, the areal fraction required for the transport of carbon building blocks is suggested to be similar. Notice though that under maximal growth rate conditions, yeast performs fermentation to supply its energy needs, which dictates a significant additional transport of sugars.

A measurement shows that under growth rates up to one division per 140 min, approximately half the carbon is lost in fermentation (with an even higher proportion at faster growth rates) (BNID 102324).

Thus, the required surface fraction covered by transporters is suggested to be at least double that found in the bacterial setting, resulting in ≈4% areal coverage.

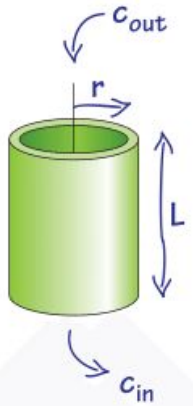
HOW MANY IONS PASS THROUGH AN ION CHANNEL PER SECOND?



Different mechanisms of ion channel gating. The green channel is gated by a transmembrane voltage. The blue channels are gated by ligands that bind the protein and induce a conformational change. The red channel is gated by mechanical forces.

HOW MANY IONS PASS THROUGH AN ION CHANNEL PER SECOND?

Estimating the characteristic current flowing through an ion channel



We use Fick's Law for the flux: $J_z = -D\frac{\partial c}{\partial z} \approx D\frac{\Delta c}{L}$

A linear profile of concentration satisfies the steady-state diffusion equation:

$$c(z) = c_{out} - \frac{(c_{out} - c_{in})}{L} z$$

Units of flux are $\frac{\text{number}}{\text{area x s}}$; current is JxA $= J \times \pi r^2 = D\frac{\Delta c}{L}\pi r^2$

$D \approx 1000\ \frac{\mu m^2}{s}$ for ions

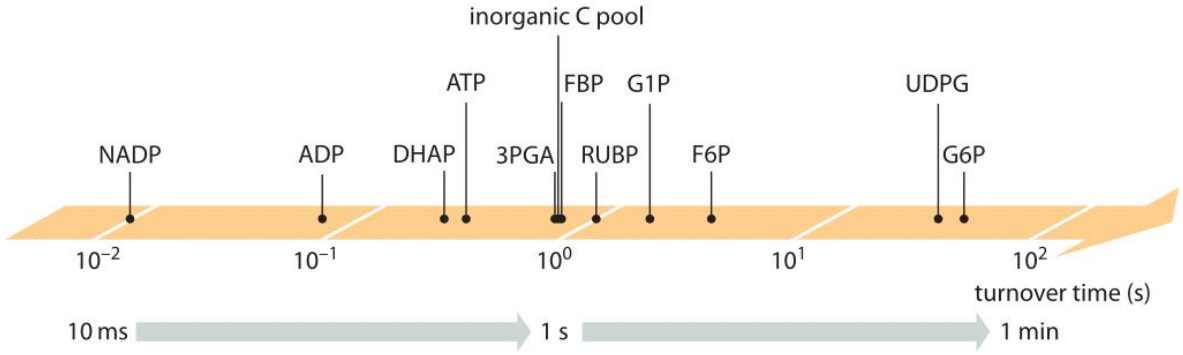
Membrane thickness, $L \approx 4nm$

Channel radius, $r \approx 1nm$

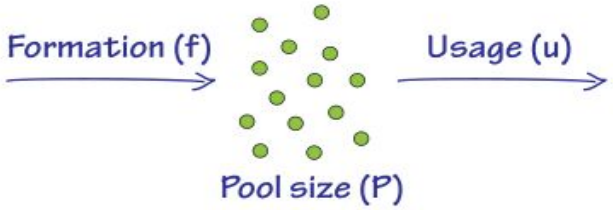
For ions characteristic $\Delta c \approx 10mM \approx 10^7/\mu m^3$

$$JxA \approx \underbrace{1000\ \frac{\mu m^2}{s}}_{D} \times \underbrace{10^7 \mu m^{-3}}_{\Delta c} \times \underbrace{3\times10^{-6}\mu m^2}_{\pi r^2} / \underbrace{4\times10^{-3}\mu m}_{L} \approx 10^7 s^{-1}$$

WHAT IS THE TURNOVER TIME OF METABOLITES?



defining the turnover time



$$\frac{dP}{dt} = f - u = 0 \Rightarrow f = u \equiv v$$

at steady state — the flow rate

turnover time or residence time is defined as $\tau \equiv \frac{P}{v}$

the ratio of pool size to flow rate

e.g. $P = 10\text{mM};\ v = 2\ \text{mM/s} \Rightarrow \tau = \frac{10\ \text{mM}}{2\ \text{mM/s}} = 5\ \text{s}$

metabolite	turnover time (s)		
	Arabidopsis	*S. cerevisiae*	*E. coli*
NADP	0.01	-	-
ADP	0.07	0.3	0.8
Calvin-Benson cycle intermediates (R5P, S6P, X5P, Ru5P, SBP, RuBP)	0.1-1	-	-
DHAP/G3P	0.2	-	-
ATP	0.3	1.4	2
3PGA	0.7	7	3
inorganic C	0.8	-	-
FBP	0.8	7	1.2
pyruvate	-	1.7	1.5
F6P	3	7	1.2
AMP	-	3	9
UDPG	40	-	-
G6P	40	17	4
glycerol-3-phosphate	-	60	13
TCA cycle (Suc, Fum, Mal)	-	4-30	0.7-9

Energy, Entropy and Forces: Thermal energy, photons and photosynthesis; energy currencies and budget.

Enzymes speed up metabolic reactions by lowering energy barriers

- A **catalyst** is a chemical agent that speeds up a reaction without being consumed by the reaction
- An **enzyme** is a catalytic protein
- Hydrolysis of sucrose by the enzyme sucrase is an example of an enzyme-catalyzed reaction

The Activation Energy Barrier

- Every chemical reaction between molecules involves bond breaking and bond forming
- The initial energy needed to start a chemical reaction is called the free energy of activation, or **activation energy (E_A)**
- Activation energy is often supplied in the form of thermal energy that the reactant molecules absorb from their surroundings

Figure 8.13

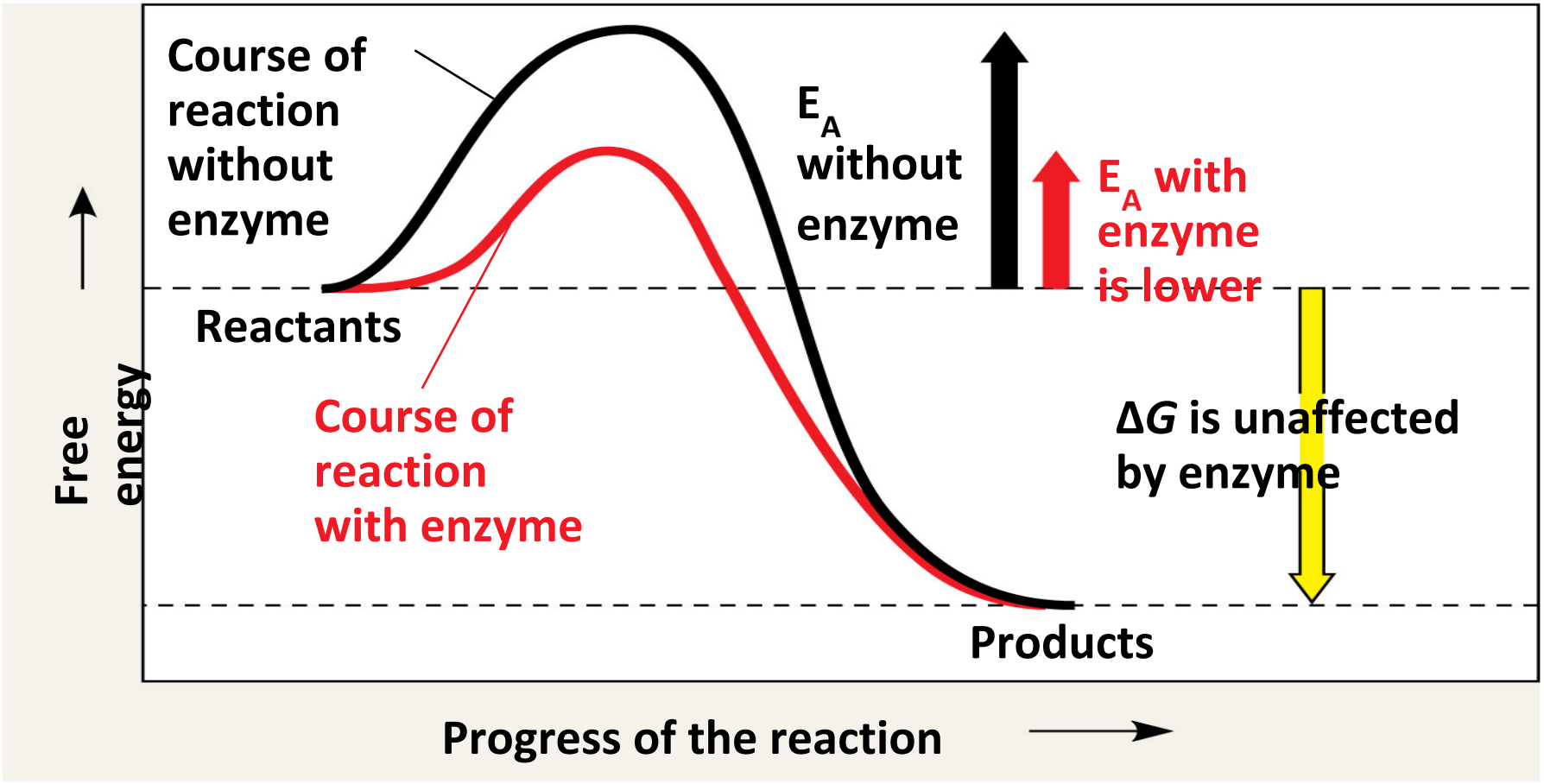
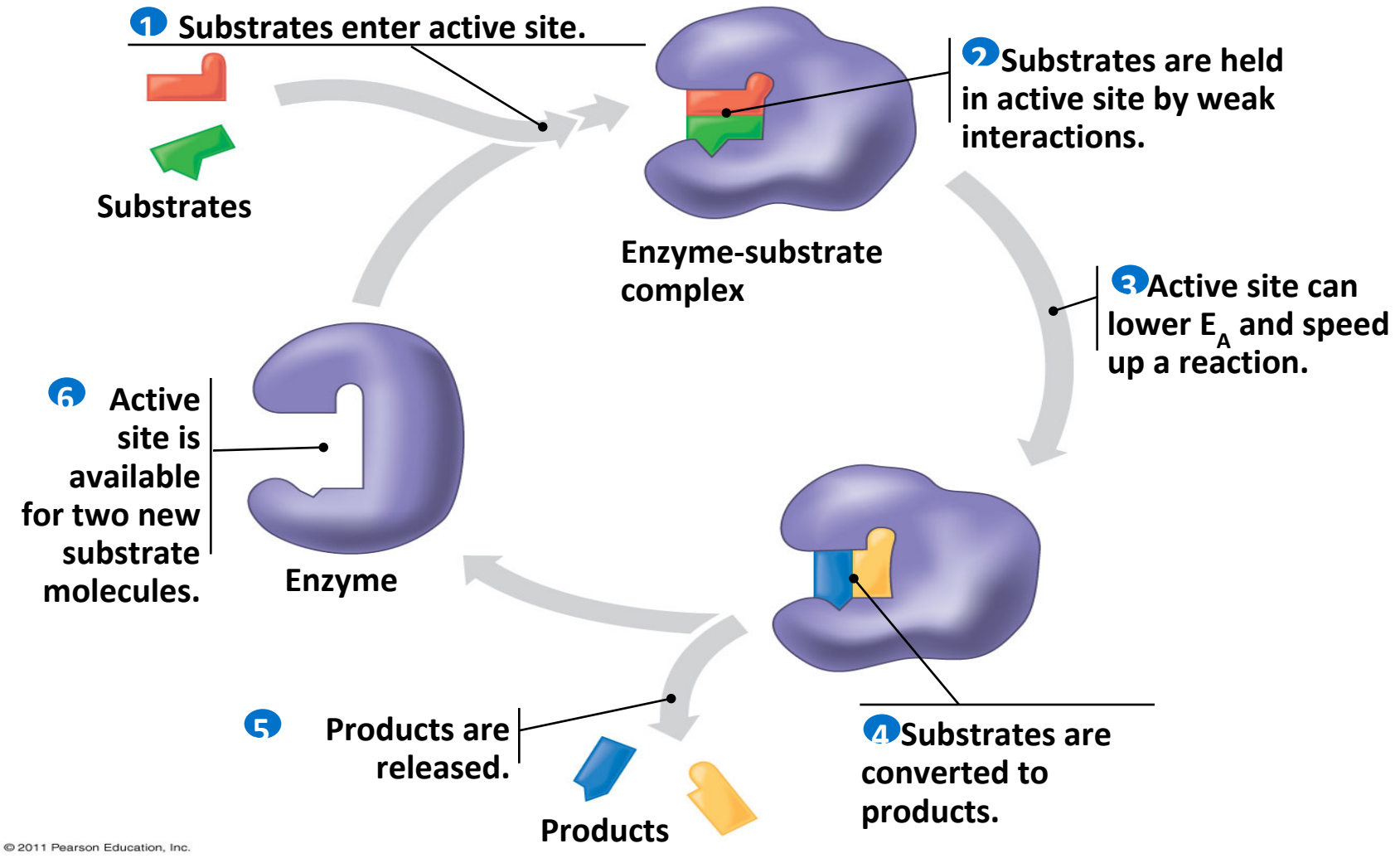
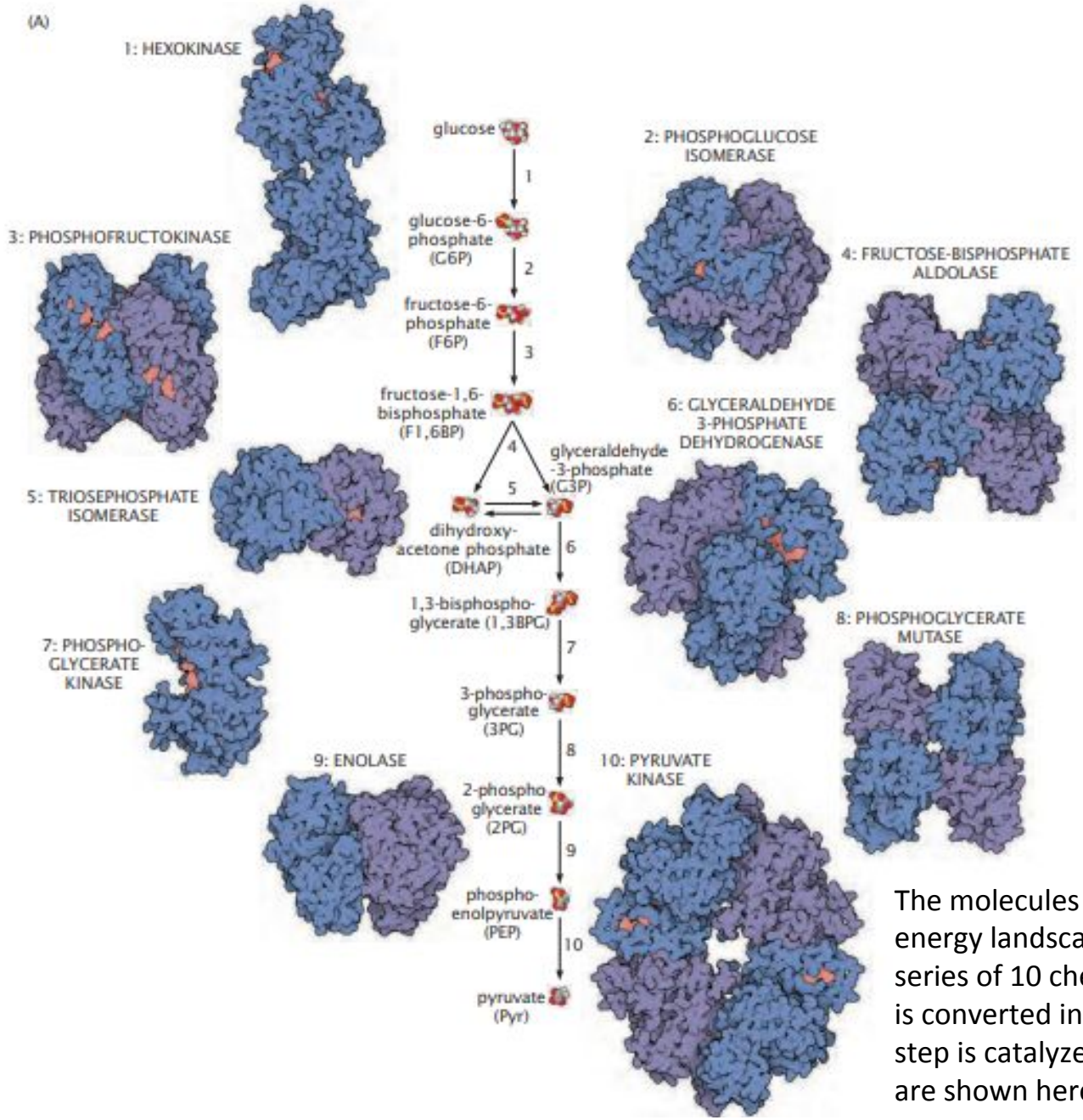
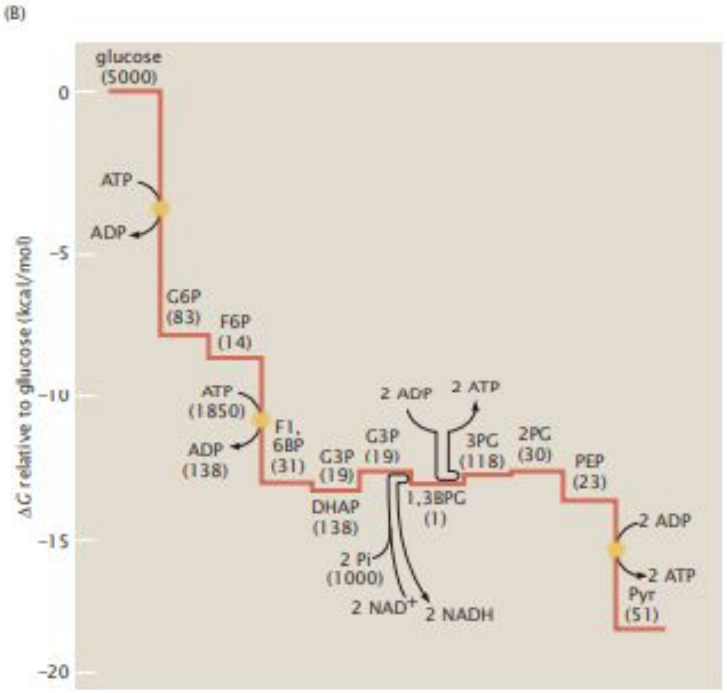


Figure 8.15-3



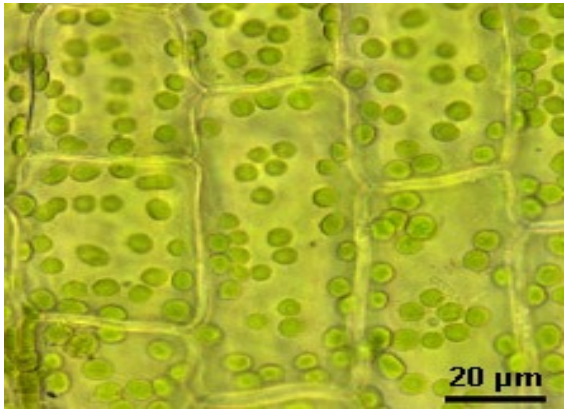


The molecules of the glycolytic pathway and the energy landscape for their transformations. (A) By a series of 10 chemical steps, one molecule of glucose is converted into two molecules of pyruvate. Each step is catalyzed by a specific enzyme, all of which are shown here as space-filling models. The enzymes are substantially larger than the small-molecule substrates on which they act.



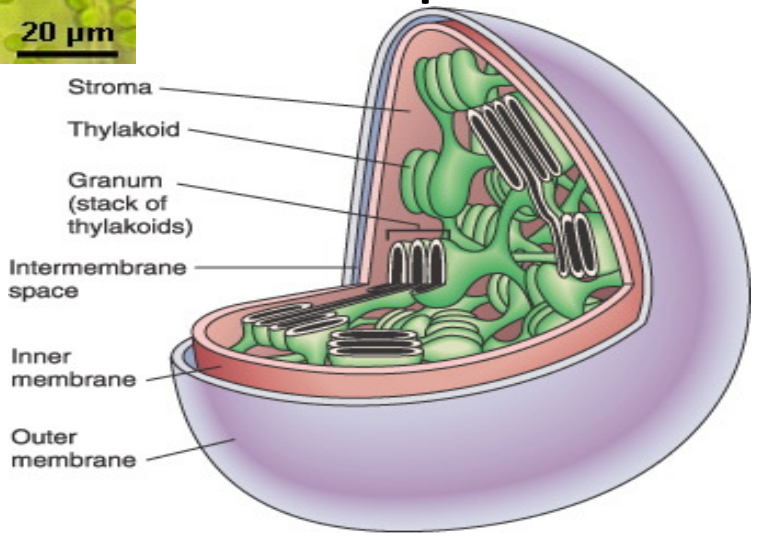
The downward energetic progression of the glycolytic pathway is illustrated graphically, where each horizontal bar represents the relative energy level of one of the glycolytic intermediates. The approximate concentration of each intermediate in micromolar units (μM) is shown in parentheses. Overall, the transformation of glucose to pyruvate is extremely energetically favorable. Some of the energy liberated during each of these transformation steps is captured by the high-energy carrier molecules, ATP and NADH. Three of the steps in glycolysis have such large negative energy changes associated with them that they are considered irreversible: phosphorylation of glucose to glucose 6-phosphate, phosphorylation of fructose 6-phosphate to fructose 1,6-bisphosphate, and conversion of phosphoenolpyruvate to pyruvate with the concomitant synthesis of ATP. Many of the other steps take place with little net energy change

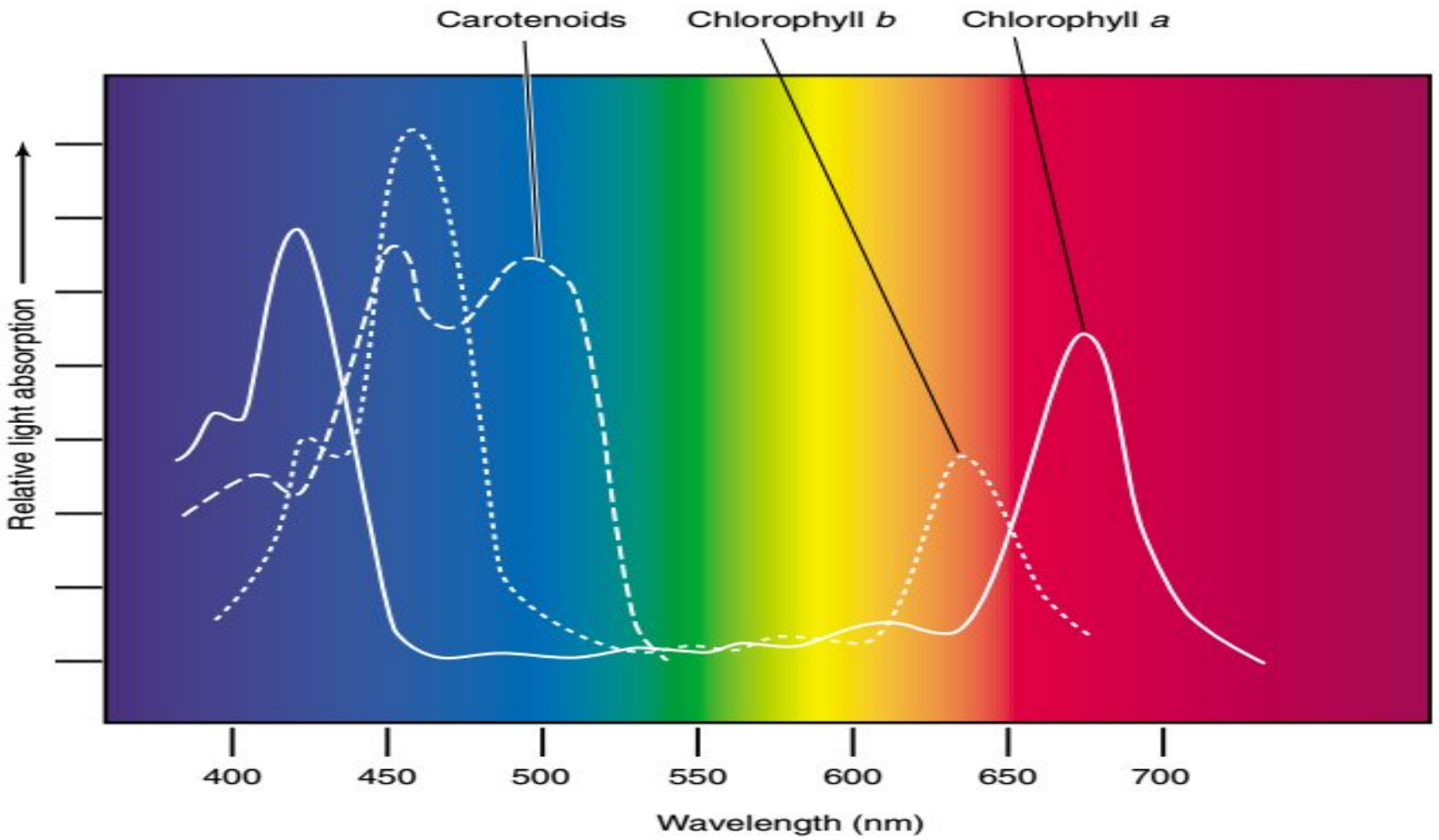
WHY ARE PLANTS GREEN?



Plant Cells have Green Chloroplasts

The thylakoid membrane of the chloroplast is impregnated with photosynthetic pigments (i.e., chlorophylls, carotenoids).

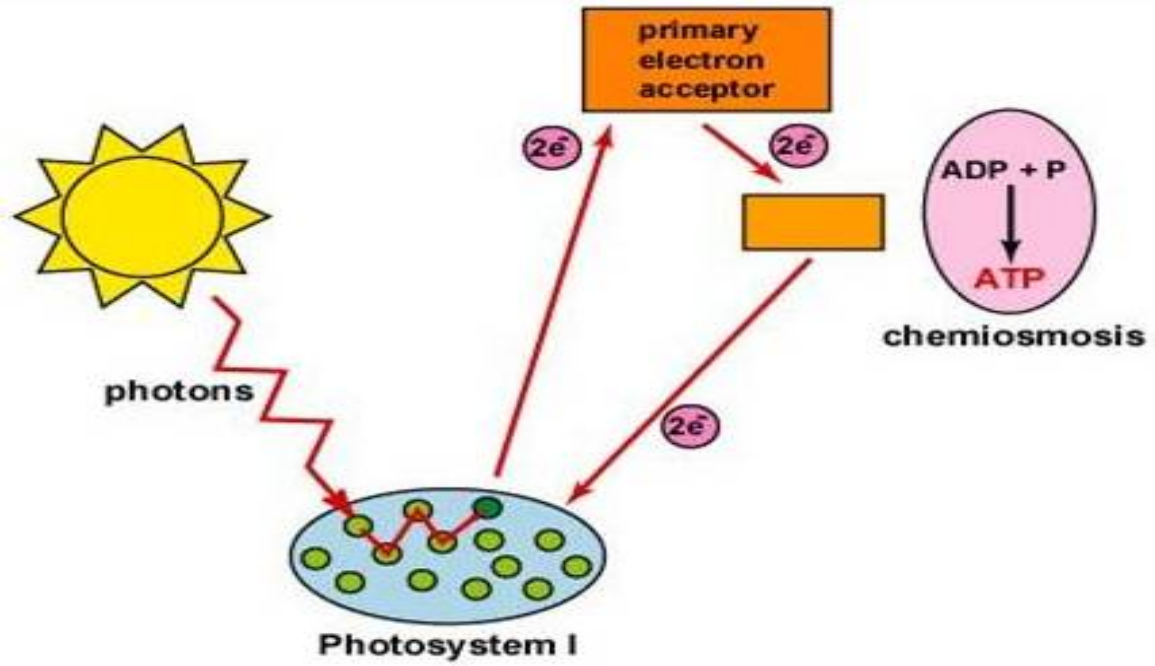


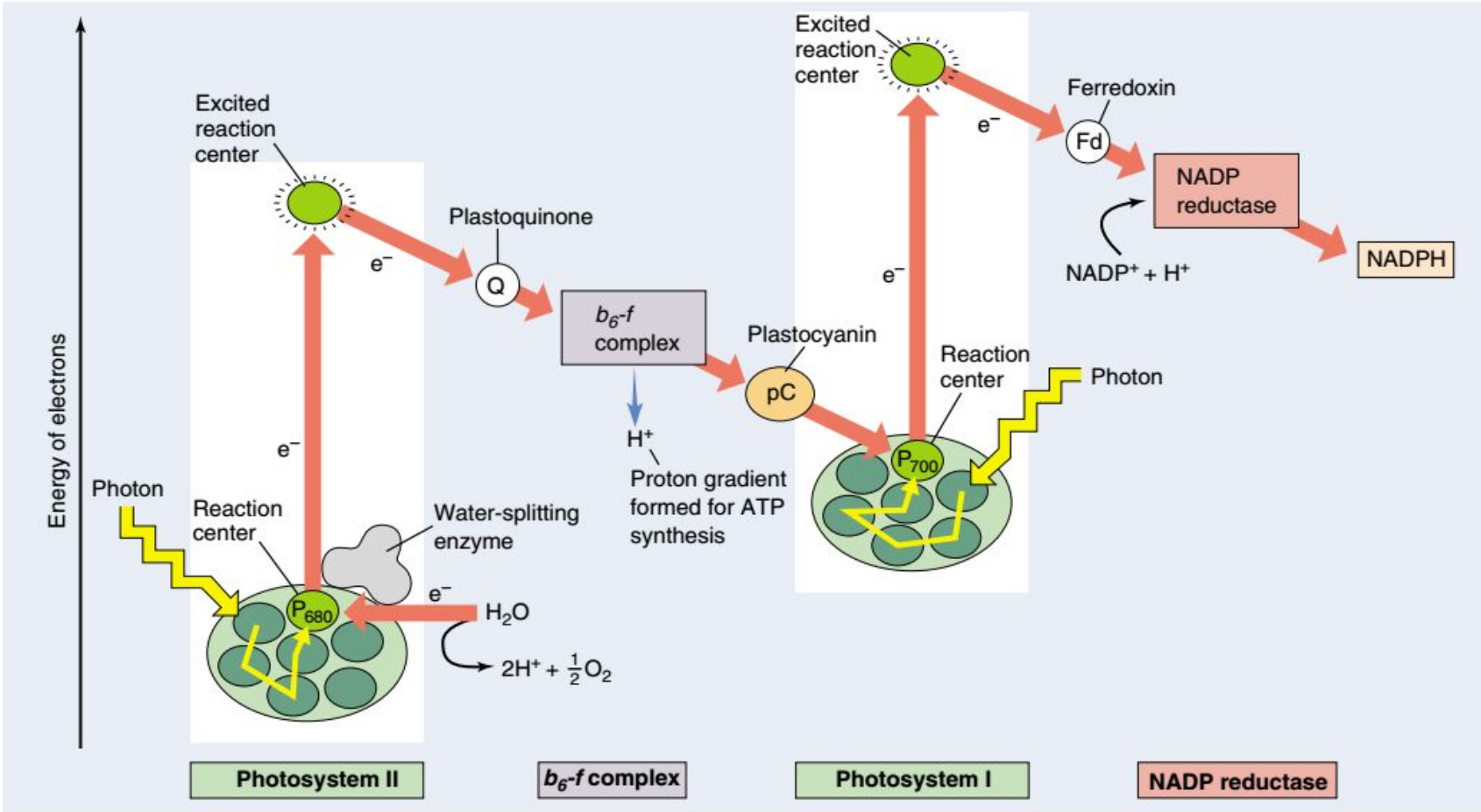


In photosynthesis, photons of light are absorbed by pigments; the wavelength of light absorbed depends upon the specific pigment.

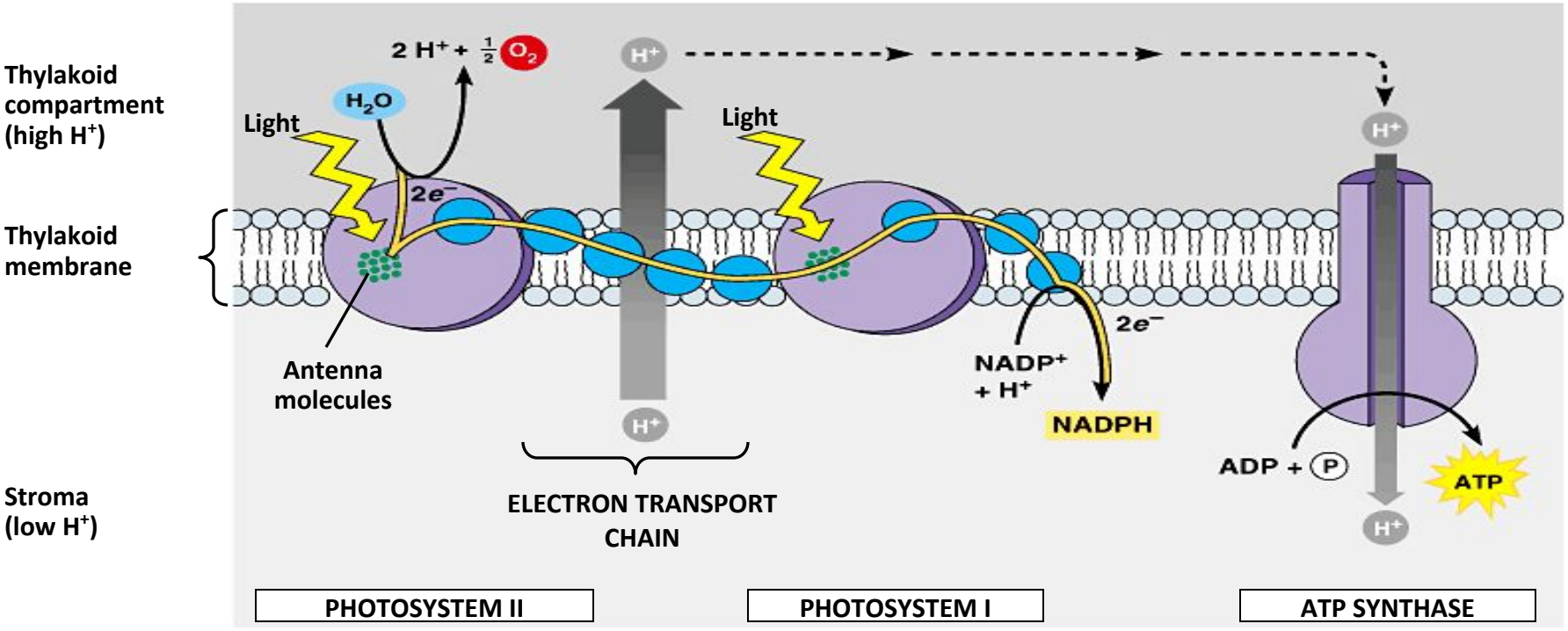
Cyclic Photophosphorylation

- Process for ATP generation associated with some Photosynthetic Bacteria
- Reac




Energy of electrons
Excited reaction center
Plastoquinone
e⁻
Q
b6-f complex
Plastocyanin
pC
Excited reaction center
Ferredoxin
Fd
NADP reductase
NADPH
NADP⁺ + H⁺
e⁻
Reaction center
Photon
P700
H⁺
Proton gradient formed for ATP synthesis
Photon
Reaction center
Water-splitting enzyme
e⁻
H2O
P680
2H⁺ + ½O2
Photosystem II
b6-f complex
Photosystem I
NADP reductase

- The production of ATP by chemiosmosis in photosynthesis



Photosynthesis as energy efficient model

- The photosynthetic process serves as an excellent model for highly efficient engineering design.
- Plants convert readily available resources (water, sunlight and carbon dioxide) into plant fuel (glucose).
- The only byproduct of the process is oxygen, which is an environmentally friendly product that is consumable by other organisms.
- Engineers who are working to optimize fuel efficiency and minimize hazardous emissions can look to the effective process of photosynthesis as an example.