Biology

UOB1001A

Module 1

Characteristics and purposes of Science and Engineering

Biology

Revision-01

1. Characteristics and purposes of Science and Engineering
2. Use of the principles of Physics, Chemistry and Mathematics learnt so far in understanding particular biological responses.

Science and Engineering

- Science: understanding phenomenon, processes
- Engineering: pursuit of science

Three different attributes

1. Phylogeny
2. Motivation
3. Methods

What is Science?

Study of the physical and natural world using theoretical models and data from experiments or observation

Ability to produce solutions in some problem domain

Research into questions posed by scientific theories and hypotheses

Models, Experiments, Observations, Research, Theory, Hypothesis

What is Science?

Concept: An abstract or general idea inferred or derived from specific instances

Hypothesis: A concept that is not yet verified but that if true would explain certain facts or phenomena

Theory: An organized system of accepted knowledge that applies in a variety of circumstances to explain a specific set of phenomena

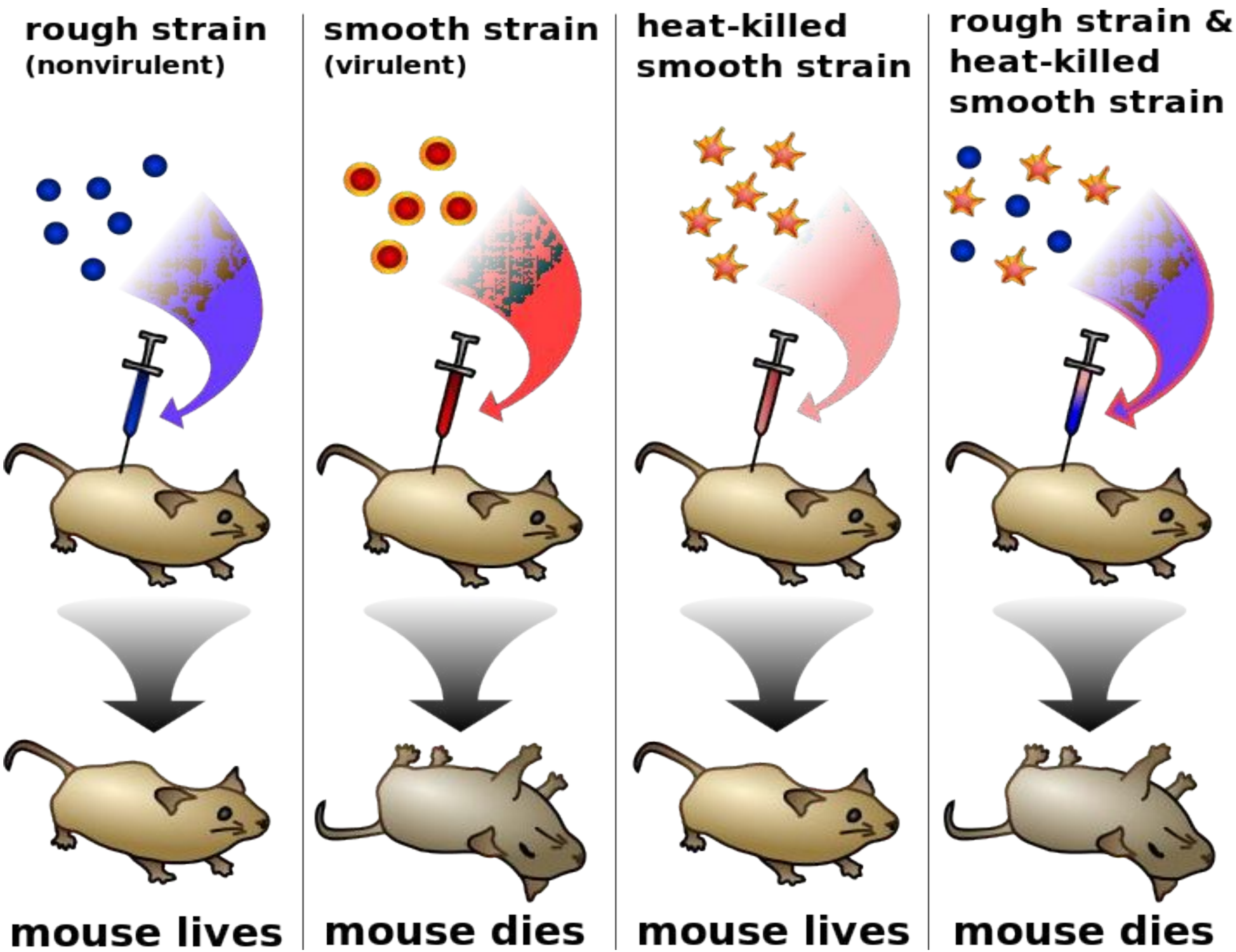
Law: A generalization that describes recurring facts or events in nature

Concept	• Apples/fruit fall on the ground
Hypothesis	• Earth attracts apple
Theory	• Newton's theory of gravity
Law	• Newton's Law of Gravity

Do you do Science?

Why do you do Science?

To understand the world better!


rough strain
(nonvirulent)
smooth strain
(virulent)
heat-killed
smooth strain
rough strain &
heat-killed
smooth strain
mouse lives
mouse dies
mouse lives
mouse dies

Griffith experiment

- In 1928, British bacteriologist Frederick Griffith conducted a series of experiments using *Streptococcus pneumoniae* bacteria and mice.

- **R strain.** R bacteria formed colonies that had a rough appearance and were nonvirulent, (did not cause disease)

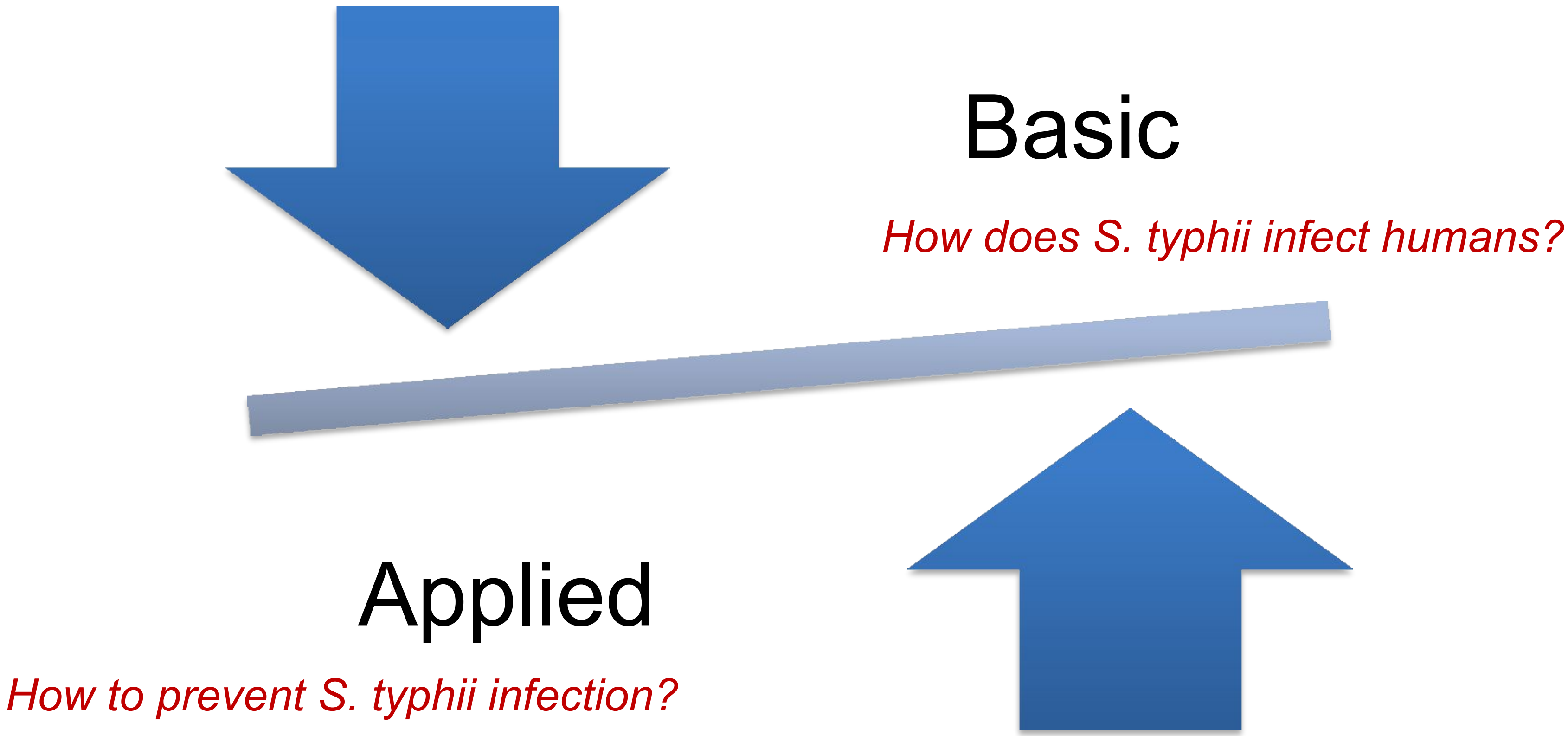
- **S strain.** S bacteria formed colonies that were rounded and smooth were virulent (capable of causing disease). Mice injected with live S bacteria developed pneumonia and died.

- As part of his experiments, Griffith tried injecting mice with heat-killed S bacteria (that is, S bacteria that had been heated to high temperatures, causing the cells to die). Unsurprisingly, the heat-killed S bacteria did not cause disease in mice.

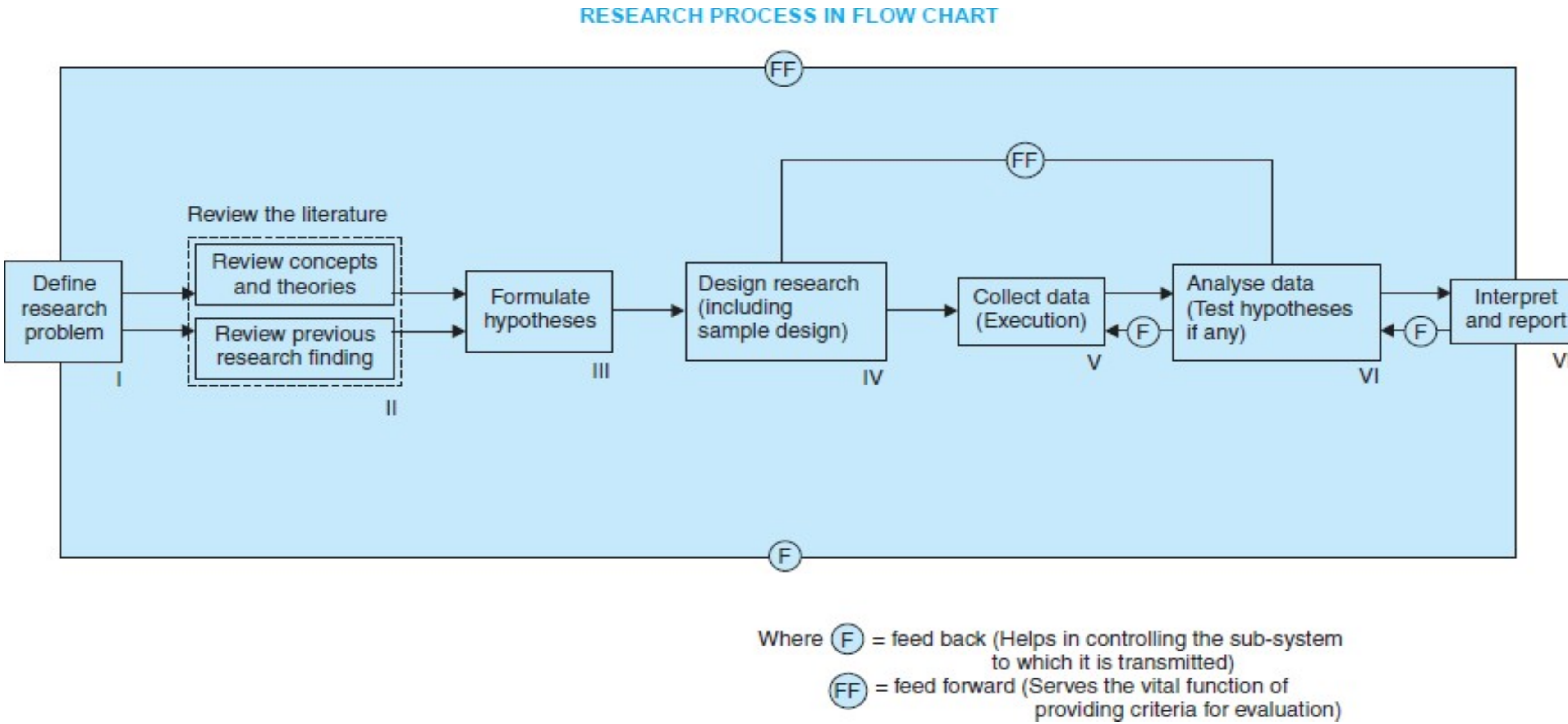
- When harmless R bacteria were combined with harmless heat-killed S bacteria and injected into a mouse. Not only did the mouse develop pnenumonia and die, but when Griffith took a blood sample from the dead mouse, he found that it contained living S bacteria!

- Griffith concluded that the R-strain bacteria must have taken up what he called a "***transforming principle***" from the heat-killed S bacteria, which allowed them to "transform" into smooth-coated bacteria and become virulent.

Research

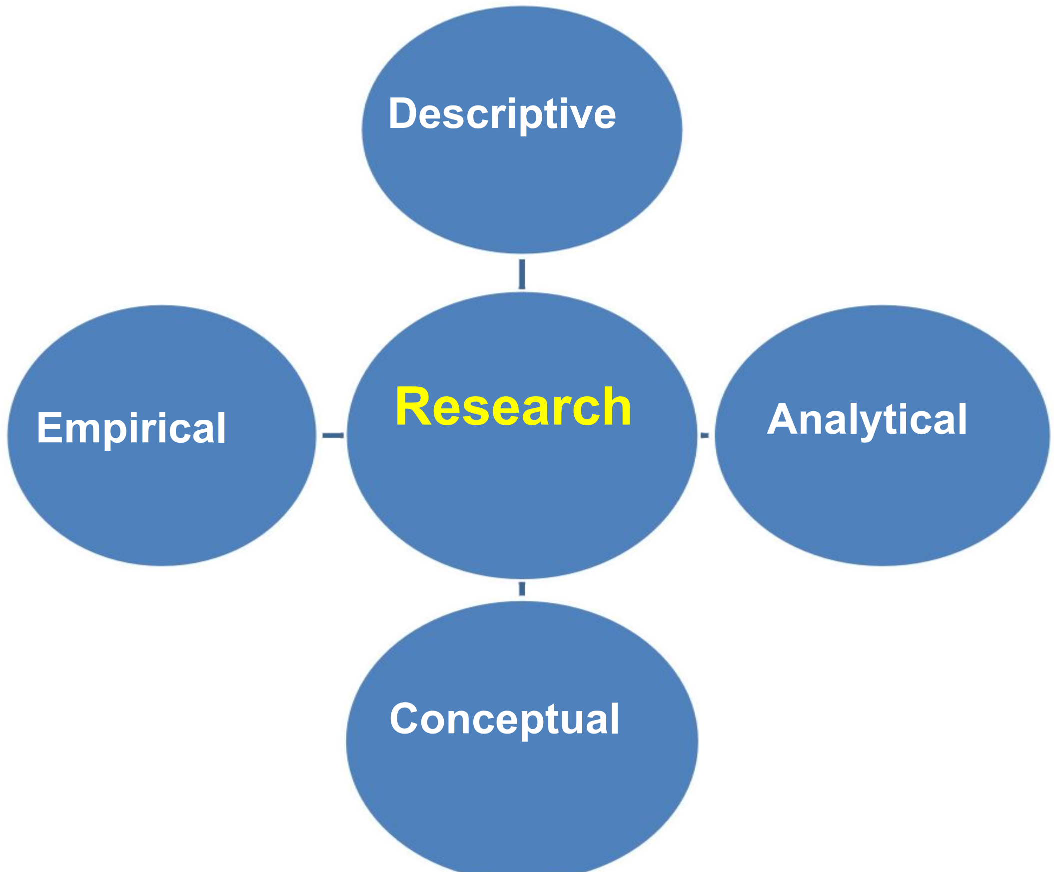

Basic
How does S. typhii infect humans?
Applied
How to prevent S. typhii infection?

Research



Systematized effort to gain new knowledge

Research



Phylogeny

The evolution of technology usually occurs with at least four distinct phases: 1) A random phase where events occur by chance and observation occurs

A random phase: events occur by chance and observation occurs haphazardly. Electricity – Ben Franklin

1. Outcome: make the observers aware of the phenomenon being observed.
2. **Descriptive phase:** Genetics – Gregor Mendel,
3. **Quantitative phase:** Mechanics – Aristotle
4. **Control phase:** where modeling and predictive equations lead to knowledge of useful substance amounts

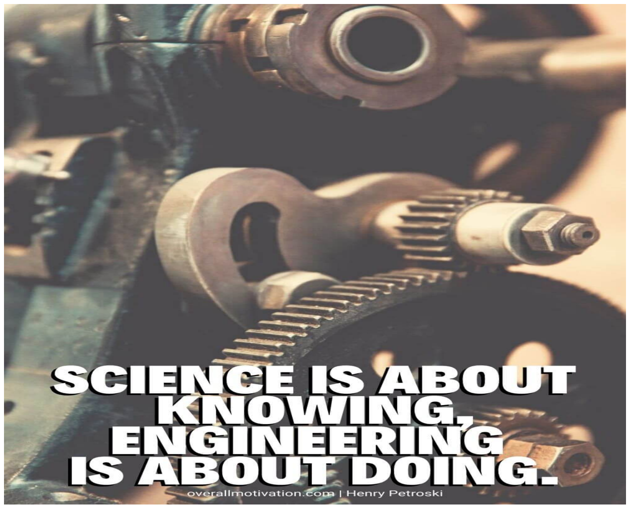
The Four Phases of Technology

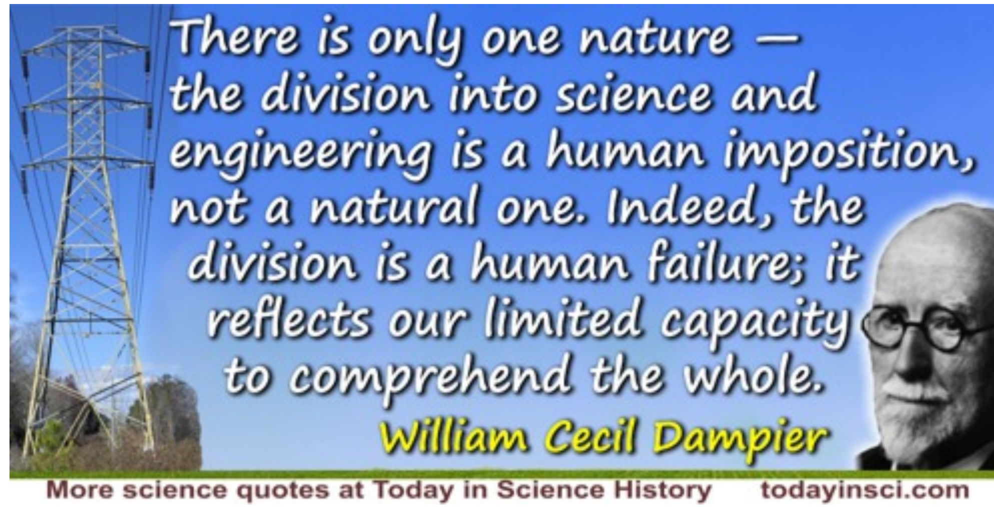
Phase	Description	Physical Example	Biological Example
Random	Phenomena are encountered haphazardly	Heavenly bodies are observed to move	Differences and similarities are noted in animals and plants
Descriptive	Cause-and-effect relationships are established	Apparent heavenly movement appears to be related to seasonal changes	Genetic material is discovered and transgenic organisms are developed
Quantitative	Measurements are refined and dependencies are given numerical values	Kepler's laws describe planetary motion	Optimal microbial growth environments are determined
Control	Modeling and predictive equations lead to knowledge of useful substance amounts, design of systems, and applications to achieve desired ends	Satellites are orbited around the Earth, moon, and other planets	Transgenic microbial production of biochemicals becomes reality

Source: Johnson, A.T. and Davis, D.C., *Eng. Educ.*, 80, 15, January/February 1990. With permission.

Motivation

- Motivation for Scientists and Engineeres

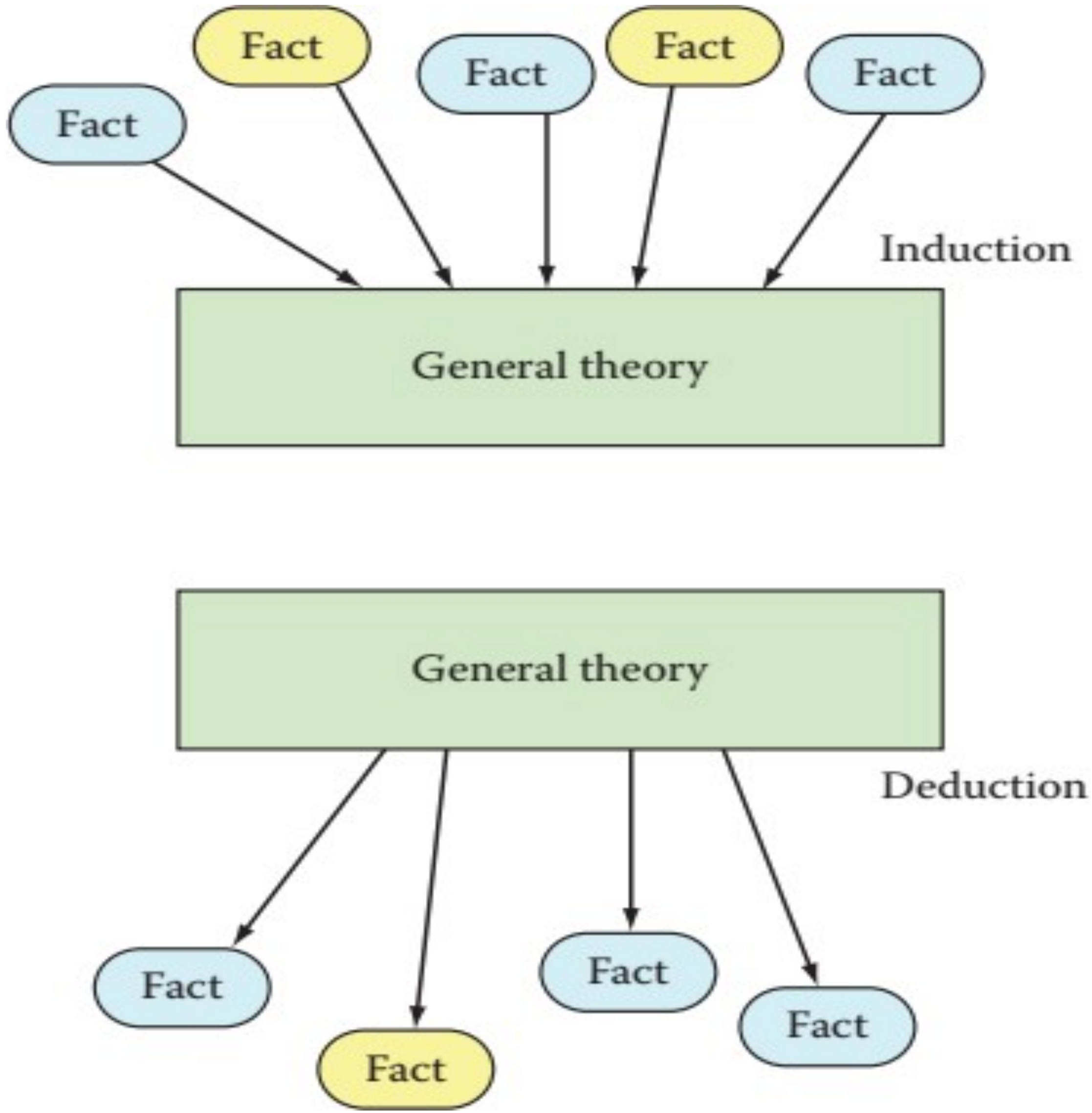




The major source of motivation and satisfaction for engineers comes in the final products or processes as a result of their efforts. Biologists, generally more removed from the ultimate applications of their work than are engineers, are often motivated by the subjects of their study

Methods

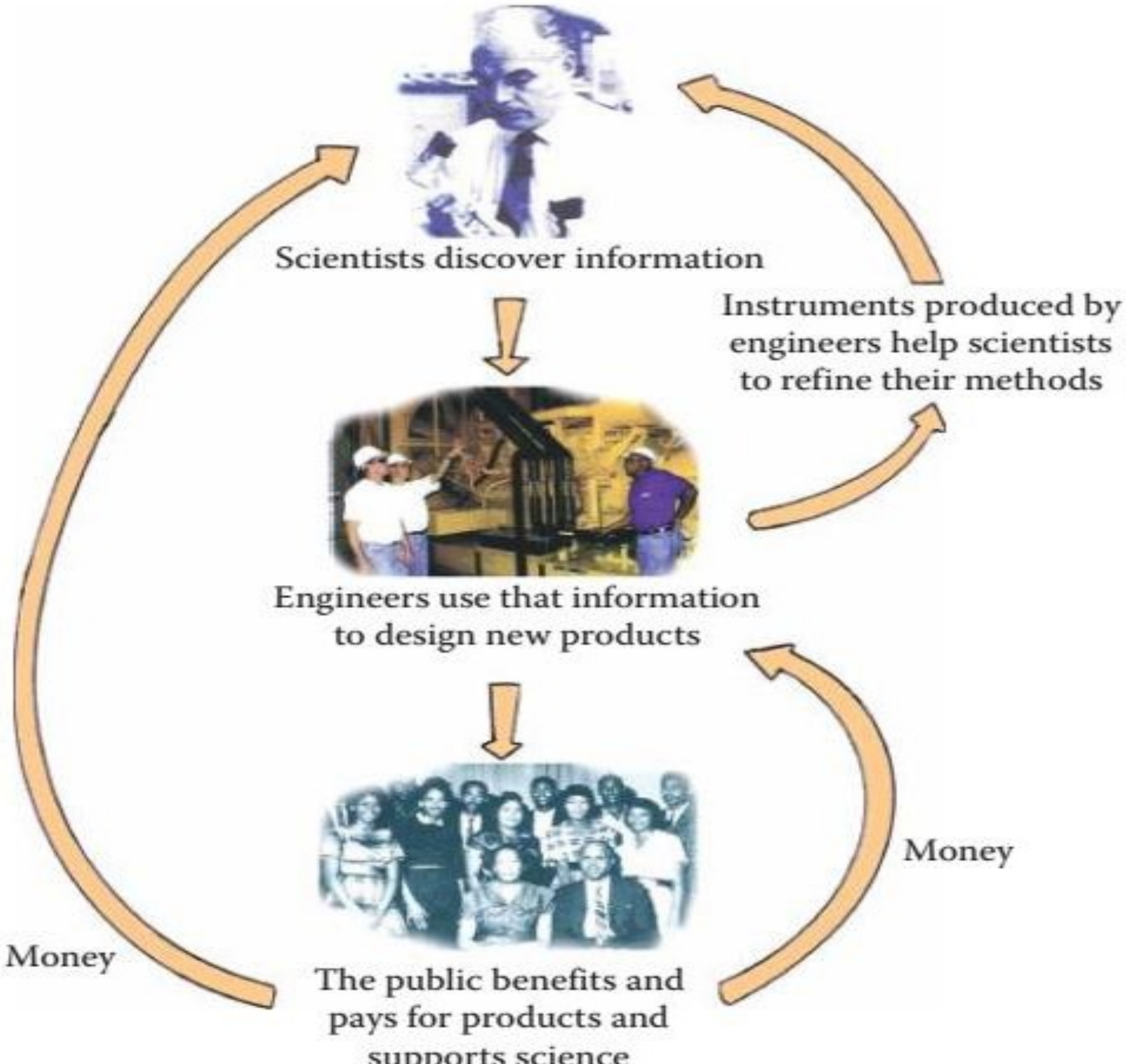
Scientist	Engineers
Perform experiments to ascertain facts Experiments determined by observed facts	Attempt to predict or control the outcome

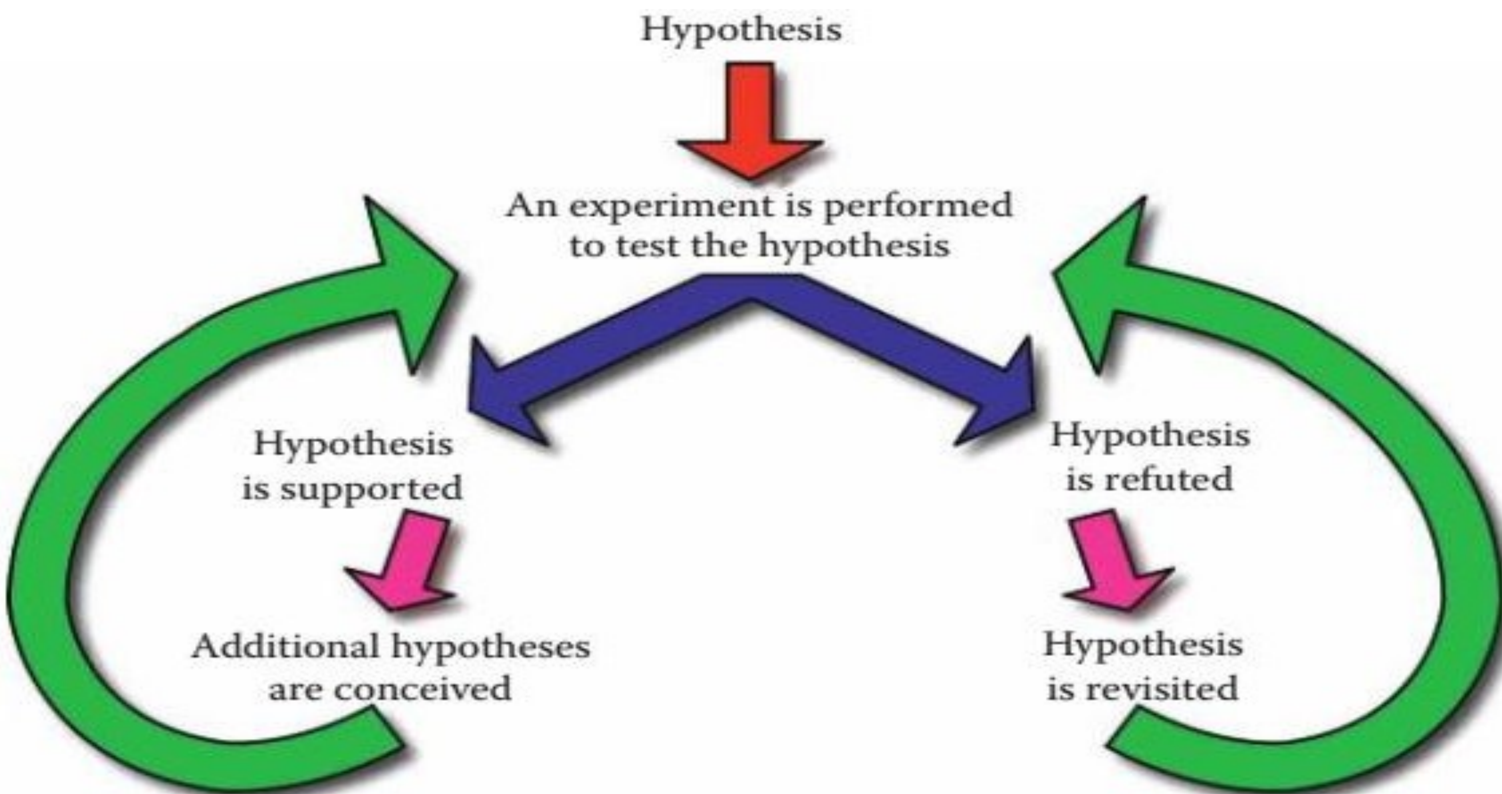

Fact
Fact
Fact
Fact
Fact
Induction
General theory
General theory
Deduction
Fact
Fact
Fact
Fact
Fact

Contrast between Science & Engineering

	Science	Engineering
Phylogeny	Random phase through quantitative phase	Quantitative phase and control phase
Motivation	Objects of study	Objects of creativity
Methods	Inductive: large numbers of facts suggest a unifying concept	Deductive: a small set of basic principles leads to specifics
Literature	Incremental	Conceptual
Synthesis	Scientists need engineers to show eventual applications	Engineers need scientists to identify basic facts

Source: Johnson, A.T. and Phillips, W.M., *J. Eng. Educ.*, 84, 311, 1995. With permission.


Scientists discover information
Instruments produced by engineers help scientists to refine their methods
Engineers use that information to design new products
Money
Money
The public benefits and pays for products and supports science


Hypothesis
An experiment is performed to test the hypothesis
Hypothesis is supported
Additional hypotheses are conceived
Hypothesis is refuted
Hypothesis is revisited

Boeing's "Desired Attributes of an Engineer"

- A good understanding of engineering science fundamentals
  - Mathematics
  - Physical and life sciences
  - Information technology (far more than "computer literacy")
- A good understanding of design and manufacturing processes (i.e., understands engineering)
- A multidisciplinary, systems perspective
- A basic understanding of the context in which engineering is practiced
  - Economics (including business practice)
  - History
  - The environment
  - Customer and societal needs
- Good communication skills
  - Written
  - Oral
  - Graphic
  - Listening
- High ethical standards
- An ability to think both critically and creatively—independently and cooperatively
- Flexibility—the ability and self-confidence to adapt to rapid or major change
- Curiosity and a desire to learn for life
- A profound understanding of the importance of teamwork
- DIVERSITY—wanted and needed!

• This is a list, begun in 1994, of basic durable attributes into which can be mapped specific skills reflecting the diversity of the overall engineering environment in which we in professional practice operate. • This current version of the list can be viewed on the Boeing web site as a basic message to those seeking advice from the company on the topic.

Interdisciplinary nature of Bioengineering

- Bioengineering is defined as the application of engineering principles to understand, modify, or control living systems.

- Bioengineers need to have a solid education in engineering and a working knowledge of biology, physiology, and medicine.

- What do bioengineers do?

Understand and model physiological and biological functions

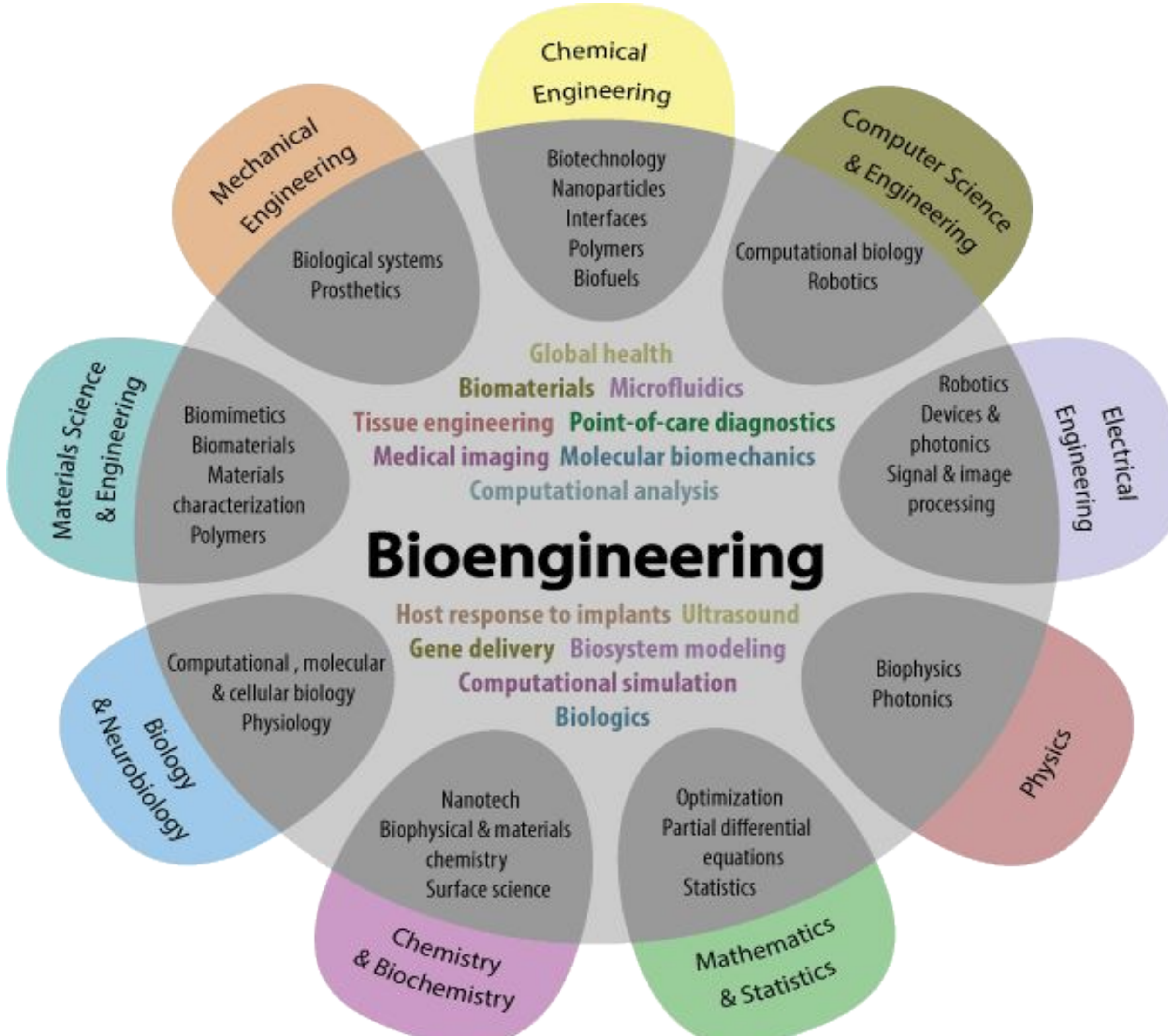
- -gain a comprehensive and integrated understanding of the function of living organisms.
- -Develop mathematical descriptions of physiological events

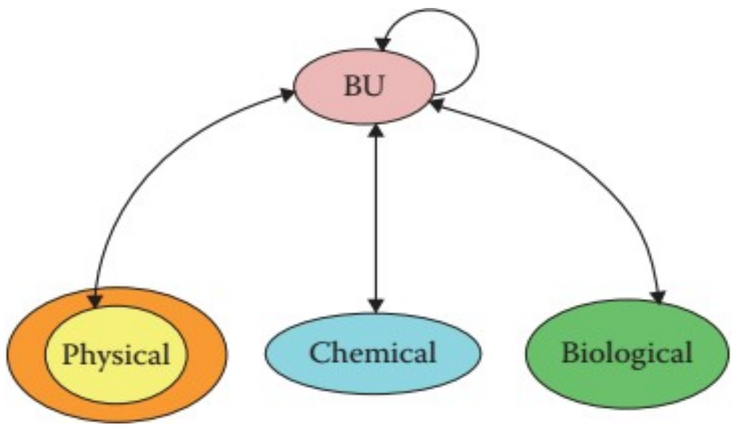
Improve existing devices/processes

- -Diagnostics
- -Surgical Instruments
- -Imaging

Develop new Materials/methods

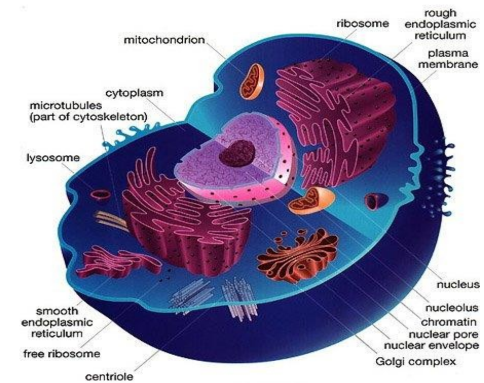
- -Drug Delivery
- -Biosensors
- -Tissue Engineering
- -Macromolecular Engineering (Protein/DNA)


Chemical Engineering
Biotechnology
Nanoparticles
Interfaces
Polymers
Biofuels
Computer Science & Engineering
Computational biology
Robotics
Electrical Engineering
Robotics
Devices & photonics
Signal & image processing
Physics
Biophysics
Photonics
Mathematics & Statistics
Optimization
Partial differential equations
Statistics
Chemistry & Biochemistry
Nanotech
Biophysical & materials chemistry
Surface science
Biology & Neurobiology
Computational , molecular & cellular biology
Physiology
Materials Science & Engineering
Biomimetics
Biomaterials
Materials characterization
Polymers
Mechanical Engineering
Biological systems
Prosthetics
Global health
Biomaterials
Microfluidics
Tissue engineering
Point-of-care diagnostics
Medical imaging
Molecular biomechanics
Computational analysis
Bioengineering
Host response to implants
Ultrasound
Gene delivery
Biosystem modeling
Computational simulation
Biologics



The biological unit (BU) is affected by interactions with its physical, chemical, and biological environment. Likewise, environmental elements are affected by the BU. Self-adjustment is also a possibility.

What is life?



Unit of life is a ***cell***. Processes of living.

(according to F. Harold, "The Way of the Cell," 2001)

- *Flux of matter and energy*

  Chemical activities: absorb nutrients, produce biomass, eliminate waste products

- *Adaptation*

  Structure and function evolve to promote organism survival

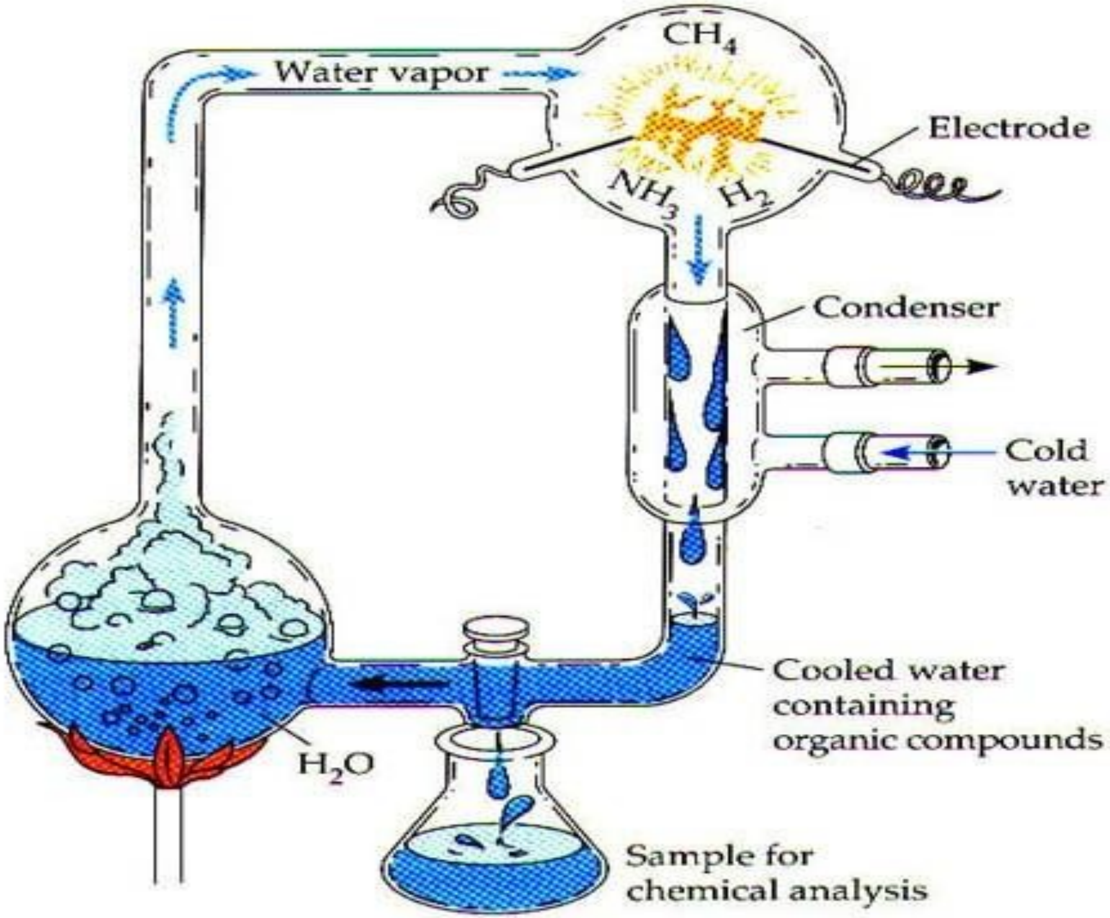
- *Organization*

  A bacterial cell consists of 300 million molecules, assembled non-randomly

  DNA RNA Protein is strategically planned and executed

- *Self-reproduction*

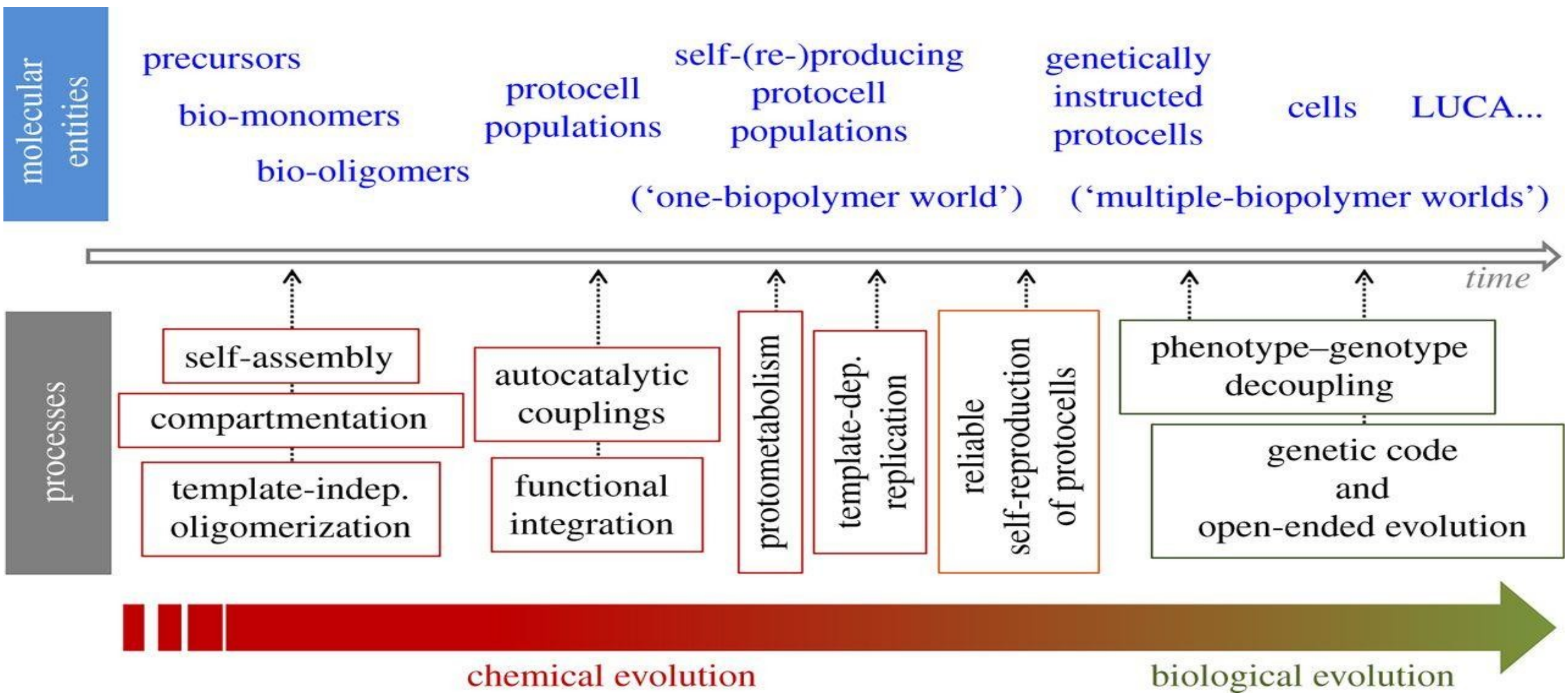
Chemical Evolution



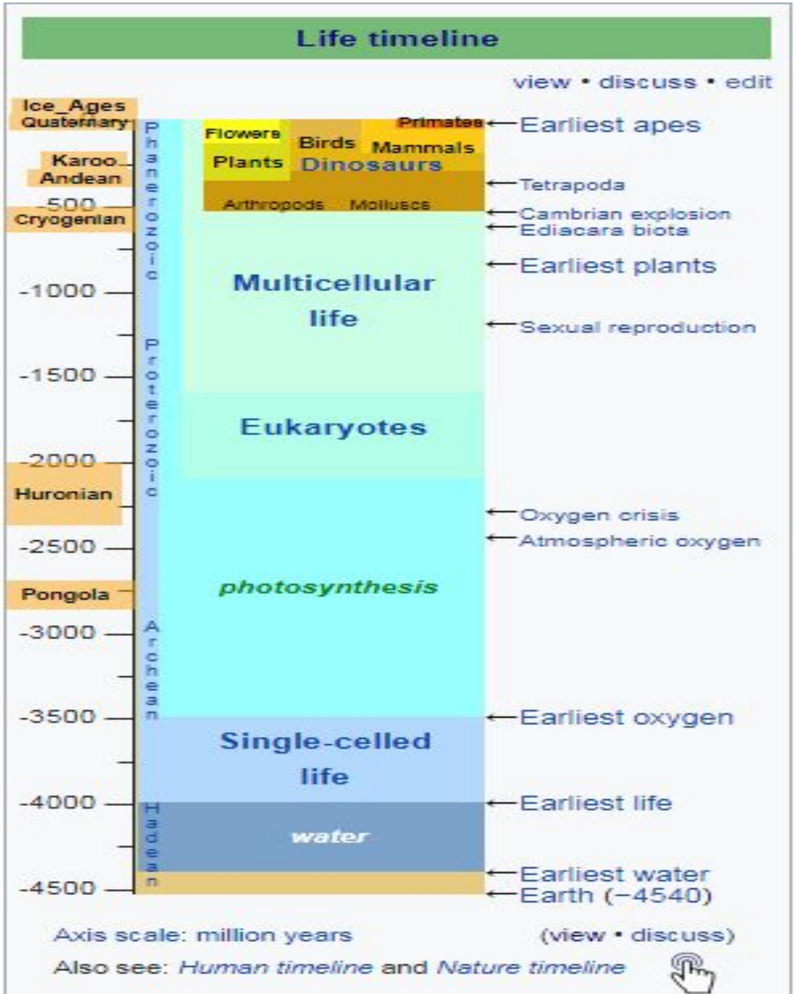
Miller-Urey Experiment 1953

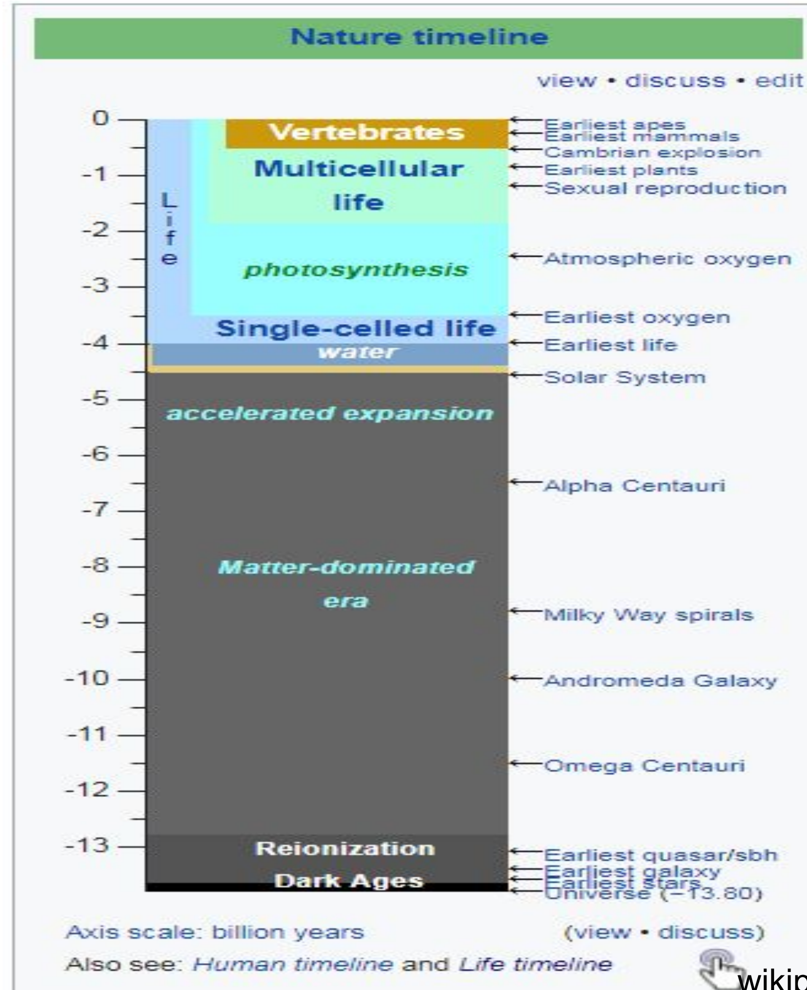
Stanley Miller and Harold C. Urey in 1953 set up an experiment with an air-tight apparatus in which four gases (NH4, CH4, H2 and H2O) were subjected to an electric discharge for one week. On analyzing the liquid, they found a variety of organic substances in it, such as amino acids, urea, acetic acid, and lactic acid

Chemical Evolution



Chemical Evolution





wikipedia

Chemical evolution

The earth originated about 5 billion years ago.

It was initially made up of hot gases and vapours of various chemicals.

Gradually it cooled down and a solid crust was formed.

The early atmosphere contained ammonia (NH_3), water vapour (H_2O), hydrogen (H_2), methane (CH_4). At that time there was no free oxygen.

This sort of atmosphere (with methane, ammonia and hydrogen) is still found on Jupiter and Saturn Heavy rains fell on the hot surface of earth, and over a very very long period the water bodies appeared that still contained hot water.

Chemical Evolution

- Methane and ammonia from the atmosphere dissolved in the water of the seas.

- In this water, chemical reactions occurred and gave rise to amino acids, nitrogenous bases, sugars and fatty acids which further reacted and combined to give rise to biomolecules of life such as proteins and nucleic acids

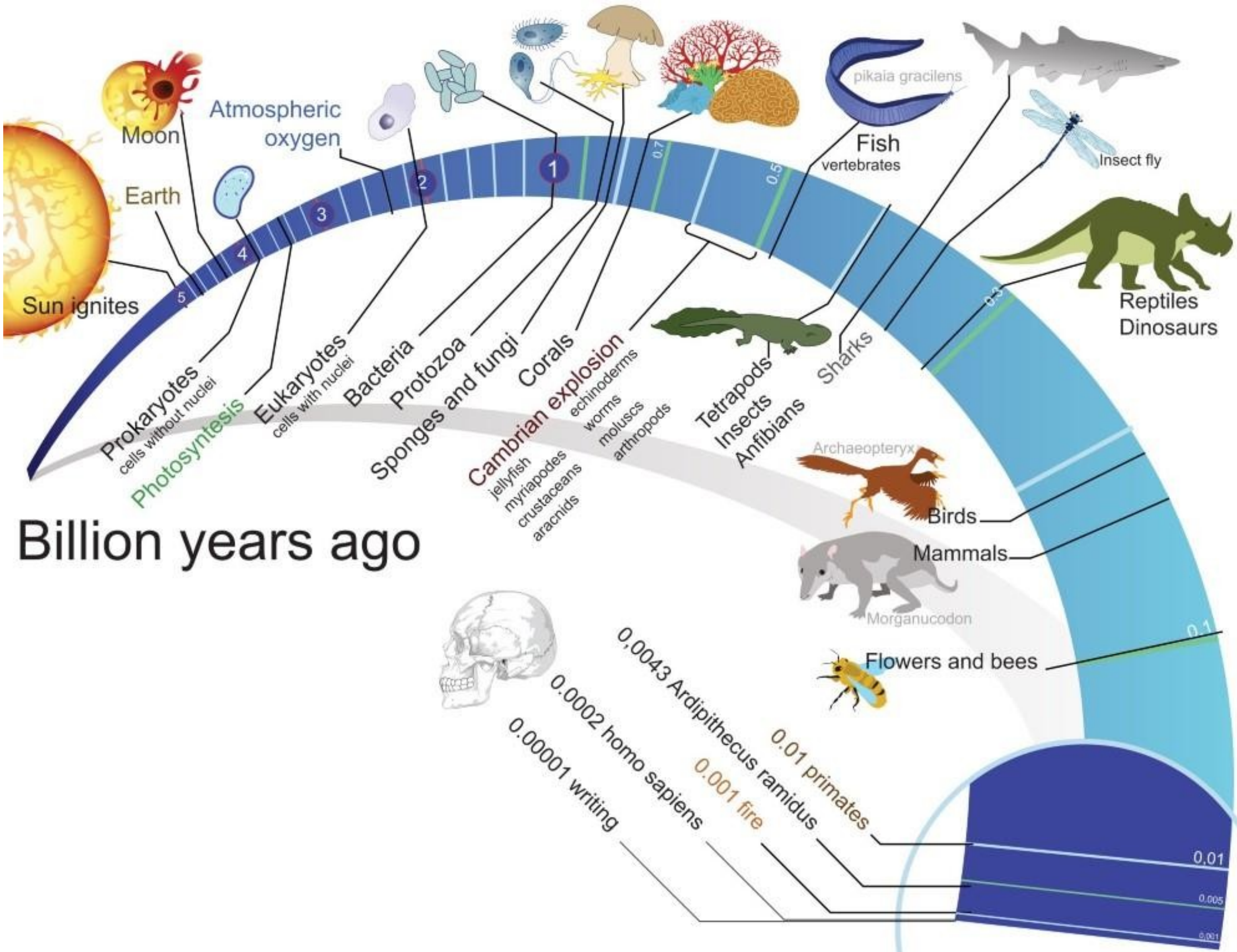
- Simple organic molecules combined to form large molecules which included peptides (leading to the formation of proteins), sugars, starch and fat molecules.

- The large molecules of different kinds combined together to form multi-molecular heaps or complexes.

- Some simple fat molecules arranged themselves around this molecular complex in a sort of membrane. It was observed in the laboratory experiments that when such complexes
- reached a certain size they separated from the surrounding solution in the form of what were termed “coacervate drops” of microscopic size.

Chemical Evolution

- Now, some sort of “metabolism” could occur within these coacervates with synthesis of certain substances and breakdown of others.
- The latter (i.e. breakdown reactions) could provide energy. Some of the earliest formed proteins might have acted like enzymes and would have affected the rates of reactions.
- It is also believed that RNA molecules might have shown enzymatic activity in the “primordial soup” of chemical compounds. Such molecules have been termed ribozymes.
- Some sort of nucleoproteins or nucleic acids may have evolved by random combinations which have provided two more properties to coacervate–like bodies.
-
- These include : (i) chemical reactions from the nucleic acids, and (ii) the capacity to reproduce through duplication of the nucleic acids
- Thus, cells were produced that could be called the simplest primordial life



Moon
Atmospheric oxygen
Earth
Sun ignites
Fish
vertebrates
pikaia gracilens
Insect fly
Reptiles Dinosaurs
Prokaryotes
cells without nuclei
Photosyntesis
Eukaryotes
cells with nuclei
Bacteria
Protozoa
Sponges and fungi
Corals
Cambrian explosion
jellyfish
myriapodes
crustaceans
aracnids
echinoderms
worms
moluscs
arthropods
Tetrapods
Insects
Anfibians
Sharks
Archaeopteryx
Birds
Mammals
Morganucodon
Flowers and bees
Billion years ago
0,0043 Ardipithecus ramidus
0.0002 homo sapiens
0.00001 writing
0.01 primates
0.001 fire
5
4
3
2
1
0.7
0.5
0.3
0.1
0,01
0,005
0,001

Evolution

- Evolution is the gradual unfolding of living forms from the earlier simpler forms into the complex ones. It was in operation in the past, it is operating at present and will continue do so in the future.
- Chief evidences in favour of organic evolution come from comparative anatomy, embryology, palaeontology and molecular biology
- Darwin's theory of 'Origin of Species' by natural selection', explains the process of evolution through useful variation and natural selection.
- Neo-Darwinism is the modern interpretation of Darwinism based on natural selection, mutation and reproductive isolation. This is also called the modern synthetic theory.

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Evolution

- Sources of variation are mutation, recombination, geneflow and genetic drift.
- Natural selection acts upon variation through “differential reproduction” which means greater reproduction of favourable genes.
- Isolation helps in formation of new species and also in keeping species distinct.
- The reproductive isolating mechanisms are ecological isolation, seasonal, ethological, mechanical and physiological isolation, zygote inviability, hybrid sterility and F2 breakdown.
- Evolution of new species is termed speciation.
- Speciation occurs through (a) geographical isolation, or (b) polyploidy

Biology

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Module 2

Chemistry in Biology (Part 1)

Elements & Biomolecules

Chemical Basis of Life

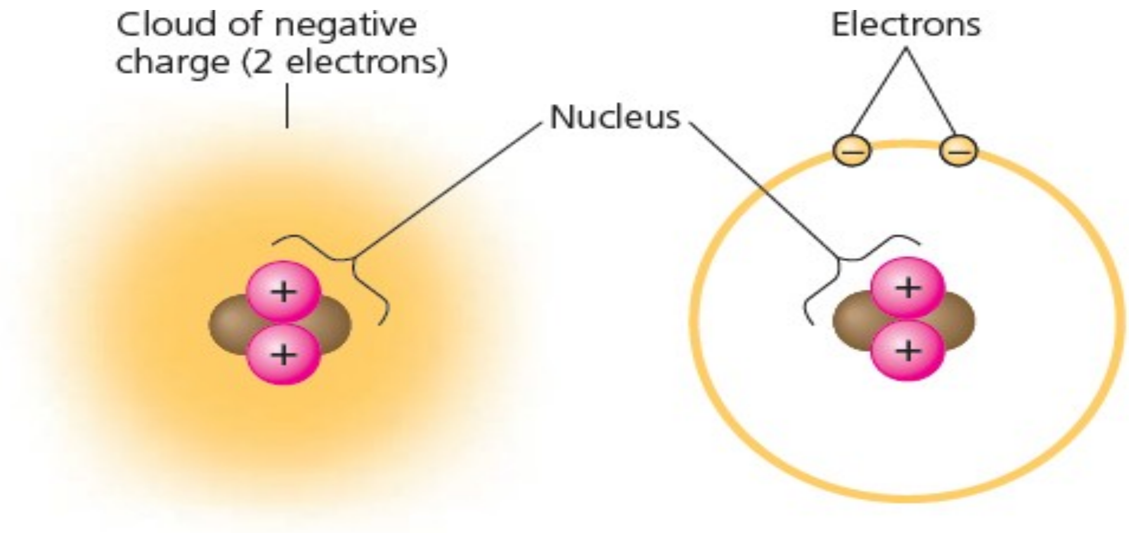
Table 2.1 Elements in the Human Body

Element	Symbol	Percentage of Body Mass (including water)	
Oxygen	O	65.0%	96.3%
Carbon	C	18.5%	
Hydrogen	H	9.5%	
Nitrogen	N	3.3%	
Calcium	Ca	1.5%	3.7%
Phosphorus	P	1.0%	
Potassium	K	0.4%	
Sulfur	S	0.3%	
Sodium	Na	0.2%	
Chlorine	Cl	0.2%	
Magnesium	Mg	0.1%	

Trace elements (less than 0.01% of mass): Boron (B), chromium (Cr), cobalt (Co), copper (Cu), fluorine (F), iodine (I), iron (Fe), manganese (Mn), molybdenum (Mo), selenium (Se), silicon (Si), tin (Sn), vanadium (V), zinc (Zn)

- Essential Elements
  - Trace Elements
- CHON makes 96% of living matter
- Some elements are toxic - Arsenic

Chemical Basis of Life

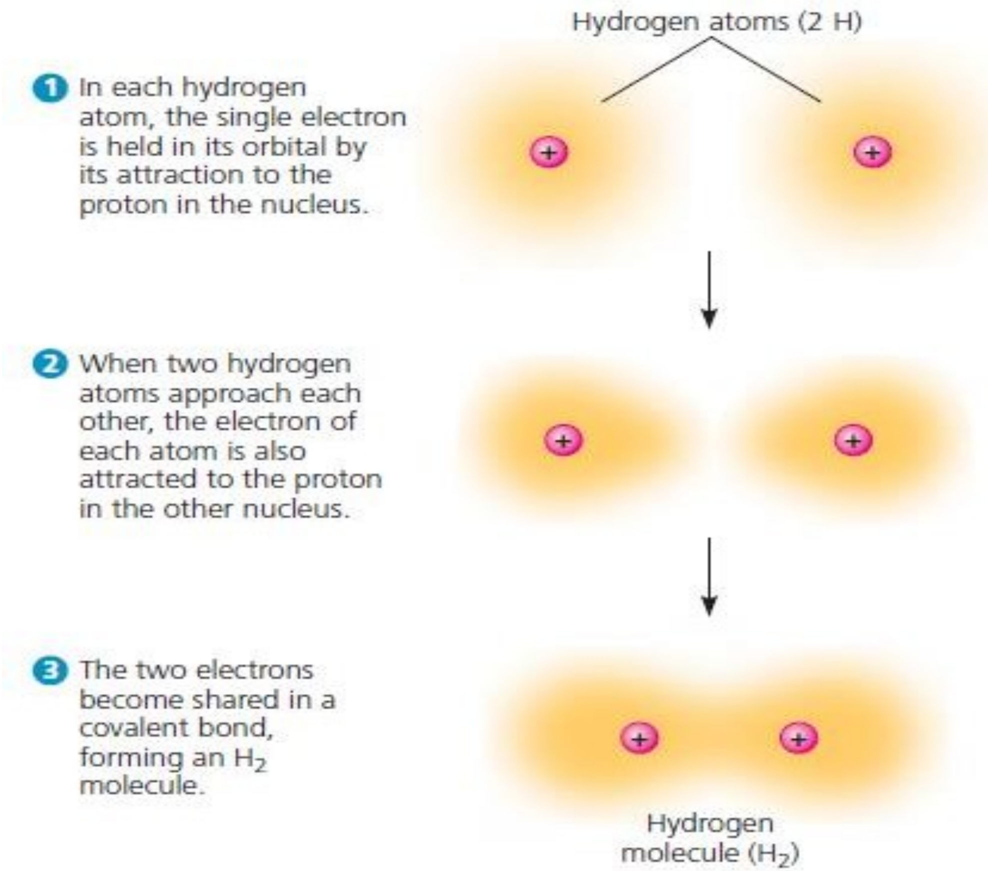


(a) This model represents the two electrons as a cloud of negative charge.

(b) In this more simplified model, the electrons are shown as two small yellow spheres on a circle around the nucleus.

▲ **Figure 2.4 Simplified models of a helium (He) atom.** The helium nucleus consists of 2 neutrons (brown) and 2 protons (pink). Two electrons (yellow) exist outside the nucleus. These models are not to scale; they greatly overestimate the size of the nucleus in relation to the electron cloud.

Chemical Basis of Life



▲ **Figure 2.11 Formation of a covalent bond.**

The formation and function of molecules depend on chemical bonding between atoms

Strong Interactions

- **Covalent bonds**
- **Ionic bonds**

Review of Covalent Bonding

The most abundant elements in cells are H>O>C>N>P>S. The number of covalent bonds formed by these elements is shown in Table 2.1. Note that oxygen and nitrogen have unshared pairs of electrons in bonding orbitals. The most common bonding orbitals for carbon (sp^3, tetrahedral; sp^2, trigonal planar) are shown in Fig. 2.3 (right). When 4 different substituents are bonded to sp^3 carbon, the carbon is asymmetrical. These carbons are chiral and optically active.

TABLE 2-1 Bonding Properties of Atoms Most Abundant in Biomolecules

ATOM AND OUTER ELECTRONS	USUAL NUMBER OF COVALENT BONDS	TYPICAL BOND GEOMETRY
H·	1	H
·Ö·	2	O
·S̈·	2, 4, or 6	S
·N̈·	3 or 4	N
·P̈·	5	P
·Ċ·	4	C

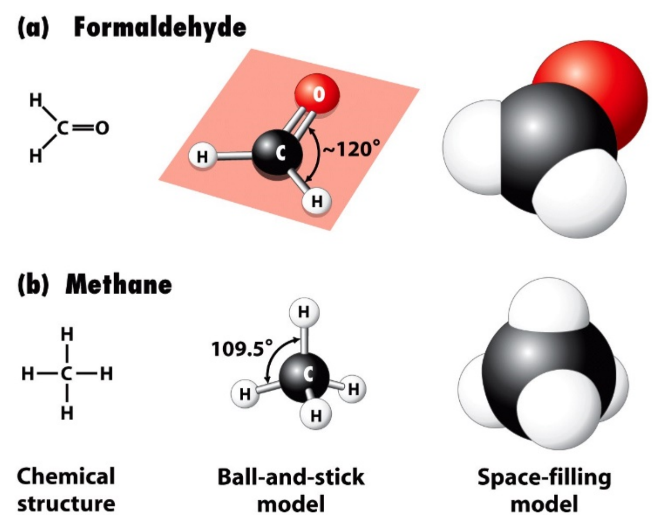
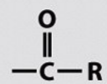
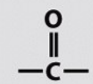
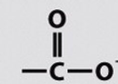
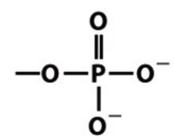
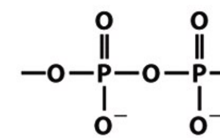
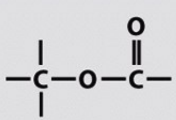
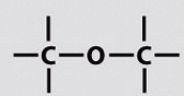
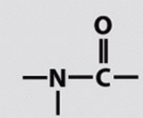


TABLE 2-2 Common Functional Groups and Linkages in Biomolecules

FUNCTIONAL GROUPS

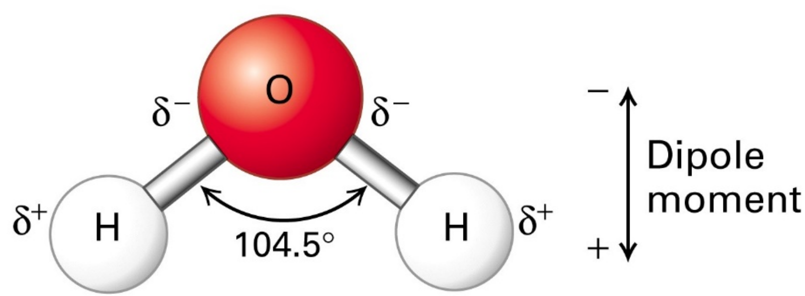
—OH **Hydroxyl** **(alcohol)**	 **Acyl** **(triacylglycerol)**	 **Carbonyl** **(ketone)**	 **Carboxyl** **(carboxylic acid)**
—SH **Sulfhydryl** **(Thiol)**	$—NH_2$ or $—NH_3$ **Amino** **(amines)**	 **Phosphate** **(phosphorylated molecule)**	 **Pyrophosphate** **(diphosphate)**

LINKAGES

 **Ester**	 **Ether**	 **Amide**

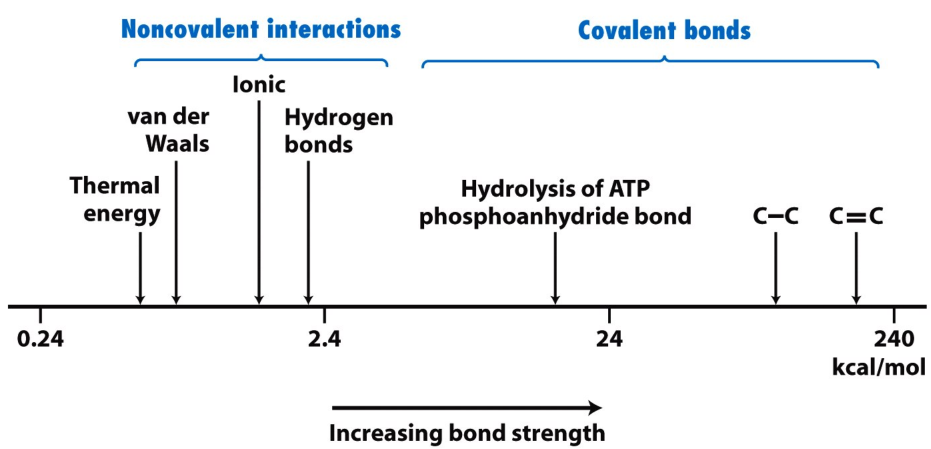
Properties of Water Molecules

Water is a polar solvent. It readily dissolves polar and ionic compounds, but not nonpolar hydrocarbons. Water molecules are polar because hydrogen and oxygen atoms have substantially different electronegativities (affinities for electrons) (Fig. 2.5). Because electrons are shared unequally, the -O-H bonds are dipolar and partial positive and negative charges occur on H and O. This feature plus the fact that 2 unshared pairs of electrons are located at the top of these sp^3 hybridized molecules creates a net dipole moment. Water dipoles interact well with dissolved polar and ionic solutes.



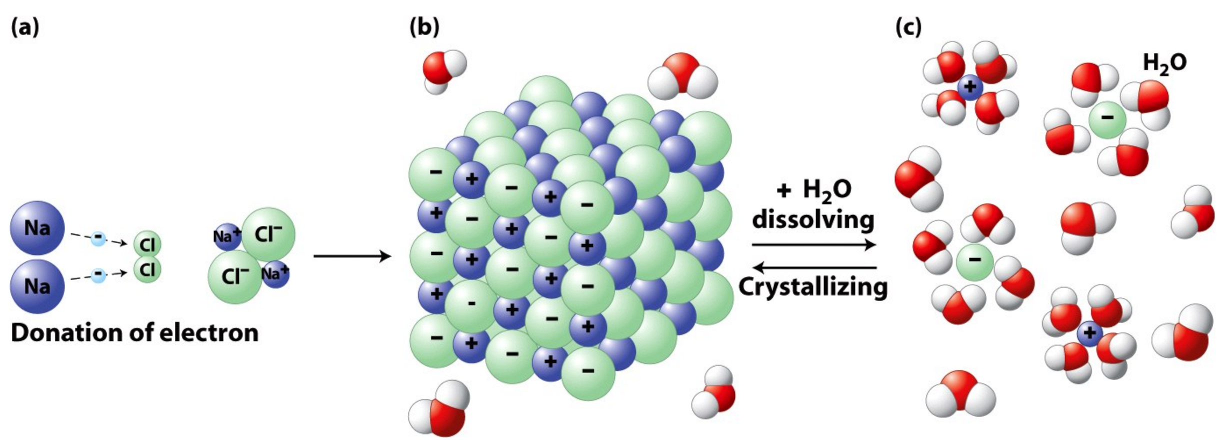
Noncovalent Interactions (Bonding)

Noncovalent interactions are weak electrical bonds between molecules. Types of noncovalent interactions are 1) ionic (electrostatic) bonds, 2) H-bonds, and 3) van der Waals interactions. Noncovalent interactions (1-5 kcal/mol) are typically ~100-fold weaker than covalent bonds (Fig. 2.6). Their stability is only slightly greater than thermal energy in biological systems. Nonetheless, noncovalent interactions play important roles in protein and nucleic acid stabilization because they are "collectively strong." Note that the hydrophobic effect drives molecular interactions, but is not a noncovalent bond per se.



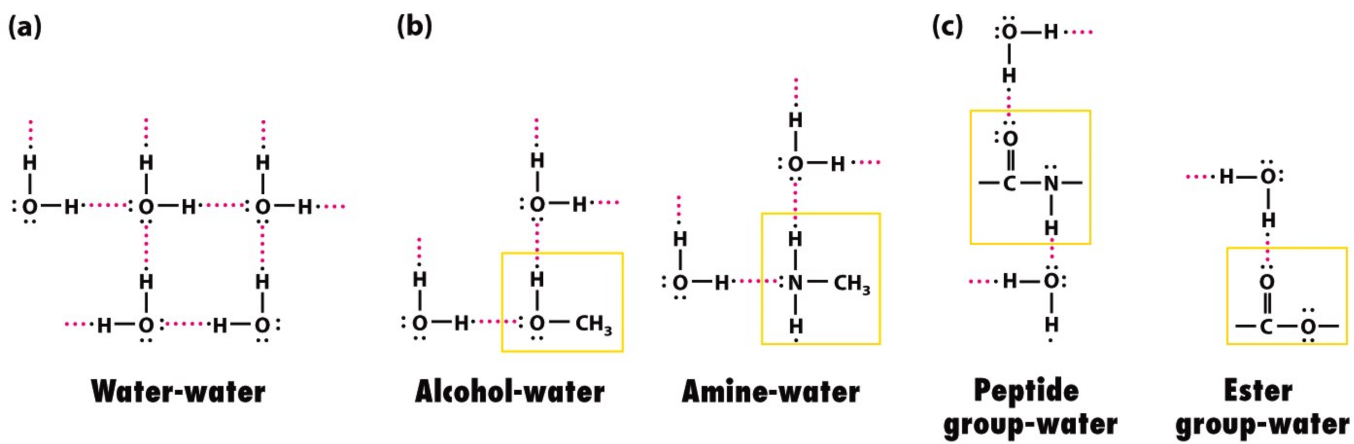
Ionic Interactions

<u>Ionic interactions</u> occur between cations and anions. These bonds are non-directional, and strength depends on the distance of separation (r) according to $1/r^2$. Strength also depends on the medium (<u>dielectric constant</u>), and is less in polar than nonpolar solvents. Ionic compounds such as NaCl are readily dissolved n water (Fig. 2.7). Solvation spheres of water molecules surround ions in solutions. Water molecules orient so that the negative ends of their dipoles contact cations and the positive ends contact anions in solution.



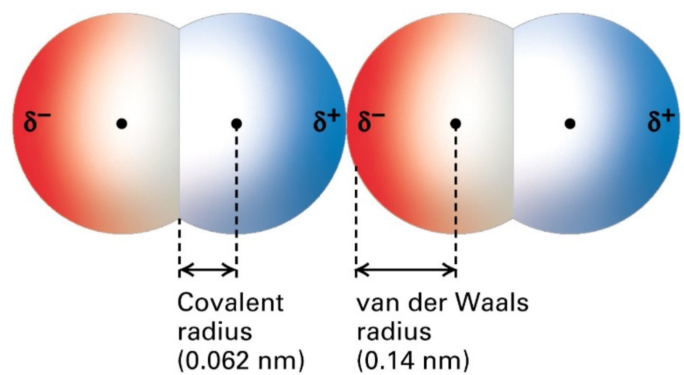
H-bonds

H-bonds are noncovalent interactions occurring between the H atom of a dipolar molecule such as water, and the unshared electron pair of another atom (i.e., O or N). These bonds represent the primary way in which water molecules interact with themselves and many types of biomolecules (Fig. 2.8). H-bonds are highly <u>directional</u> in that strength depends on the proper alignment of the interacting atoms. Directionality confers bonding <u>specificity</u> as with the Watson-Crick H-bonds between the bases of double helical DNA.



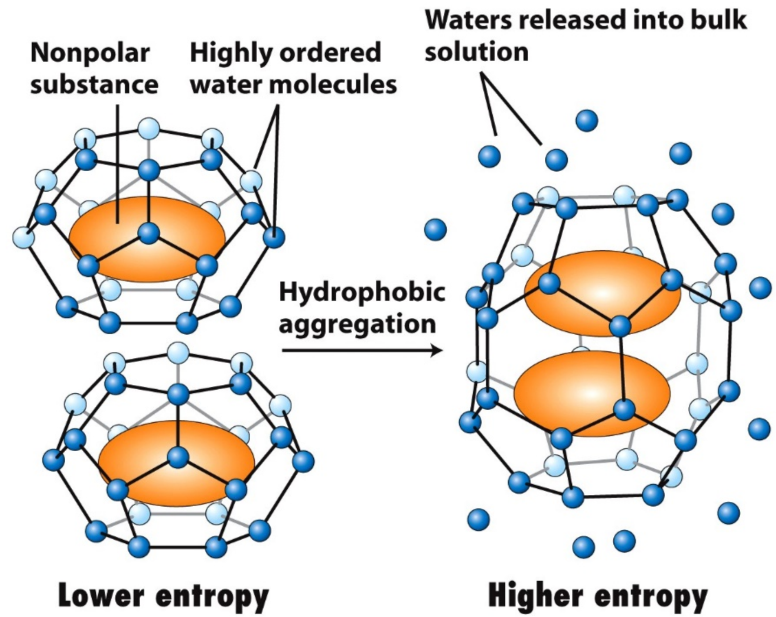
van der Waals Interactions

van der Waals interactions are bonds between fluctuating, induced dipoles within the electron clouds of interacting molecules. These bonds can occur between nonpolar or polar molecules. van der Waals bonds are extremely dependent on the distance of separation between molecules, and are significant only when the electron clouds of the molecules are just touching. van der Waals interactions are demonstrated for two O_2 molecules in Fig. 2.10. The covalent and van der Waals radii are shown.



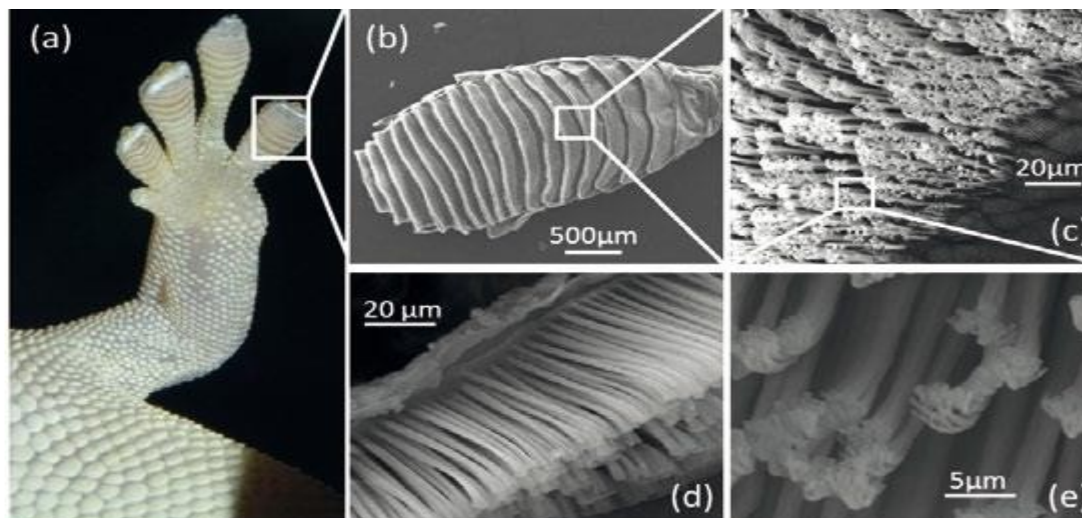
The Hydrophobic Effect

The hydrophobic effect refers to the <u>entropy-driven aggregation</u> of nonpolar molecules in aqueous solution that occurs to minimize the ordering of water molecules with which they are in contact. This is not an attractive force, but rather a thermodynamically driven process. Fig. 2.11 shows the cage-like structures formed by water molecules surrounding a nonpolar solute. The hydrophobic effect drives the formation of membranes and contributes to the folding of proteins and the formation of double helical DNA.



Chemical Basis of Life

Weak Interactions
- **Hydrogen bond**
- **Van der Waals**



Geckos' secret revealed

- Geckos and lizards employ dry adhesion system using a combination of microscopic hairs (setae) on their toe pads as well as other aspects of internal anatomy to climb on vertical walls and run on ceilings

- Though adult geckos can weigh as much as 300 g, the ease with they climb vertical walls remains the same.

- Geckos and lizards employ a mechanical principle called contact splitting. Each of the microscopic hairs found on their feet split up into hundreds of flat tips.

- The ends temporarily rearrange electrons on the walking surface, creating an van der Waals' attraction.

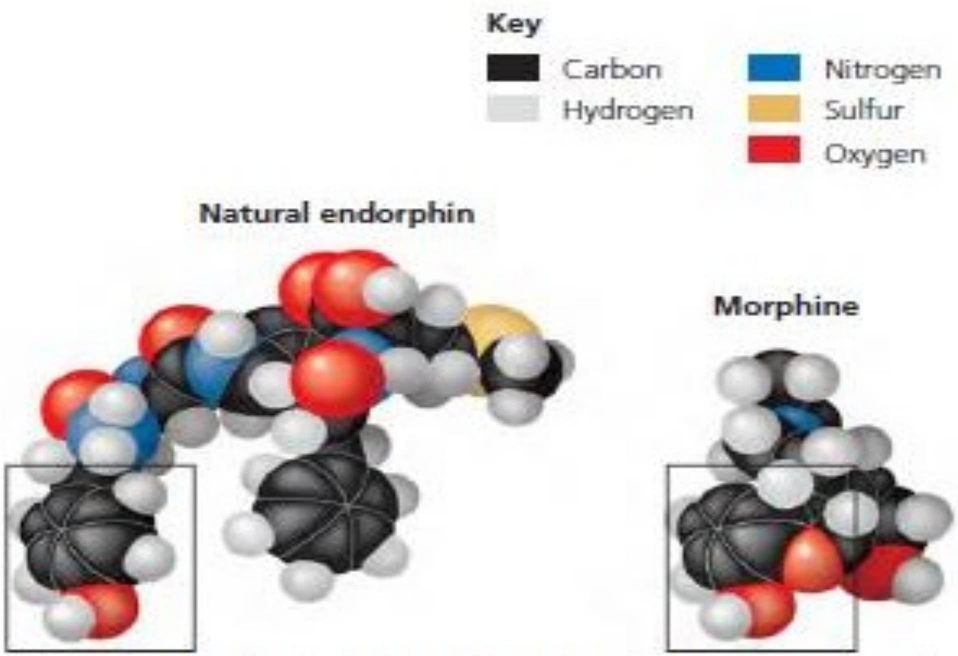
Molecular Shape and Function

- Molecular shape is crucial in biology because it determines how biological molecules recognize and respond to one another with specificity

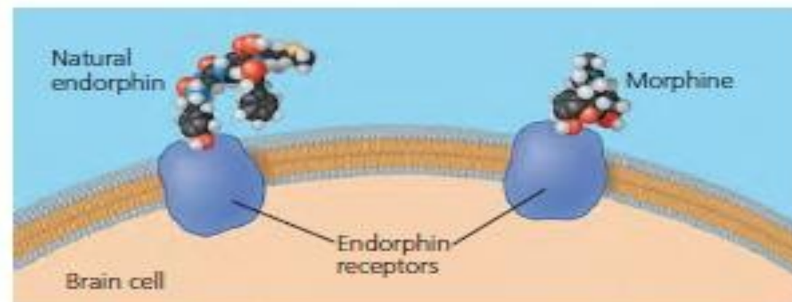
- Why would brain cells carry receptors for opiates, compounds that are not made by our bodies?

"Bugger the sweeties old lady. Got any meth-amphetamine tablets?"

Molecular Shape and Function



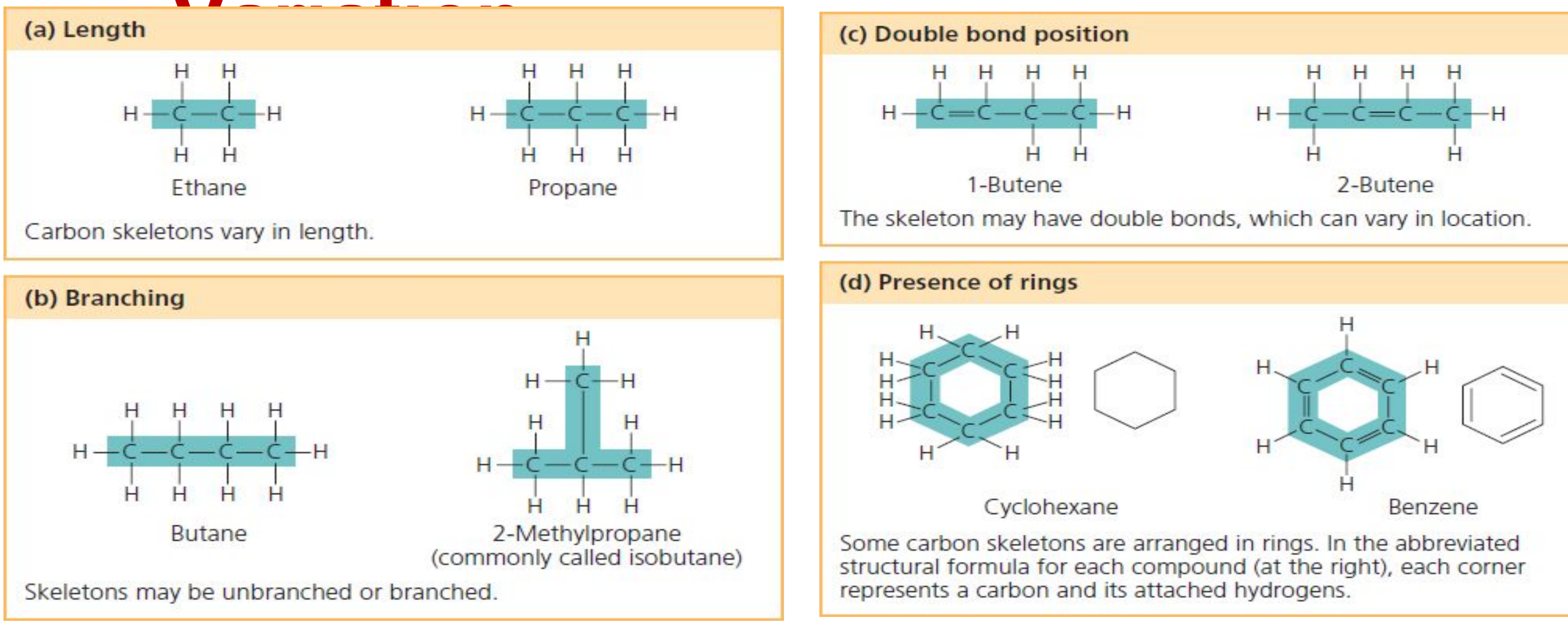
(a) Structures of endorphin and morphine. The boxed portion of the endorphin molecule (left) binds to receptor molecules on target cells in the brain. The boxed portion of the morphine molecule (right) is a close match.



(b) Binding to endorphin receptors. Both endorphin and morphine can bind to endorphin receptors on the surface of a brain cell.

▲ **Figure 2.18 A molecular mimic.** Morphine affects pain perception and emotional state by mimicking the brain's natural endorphins.

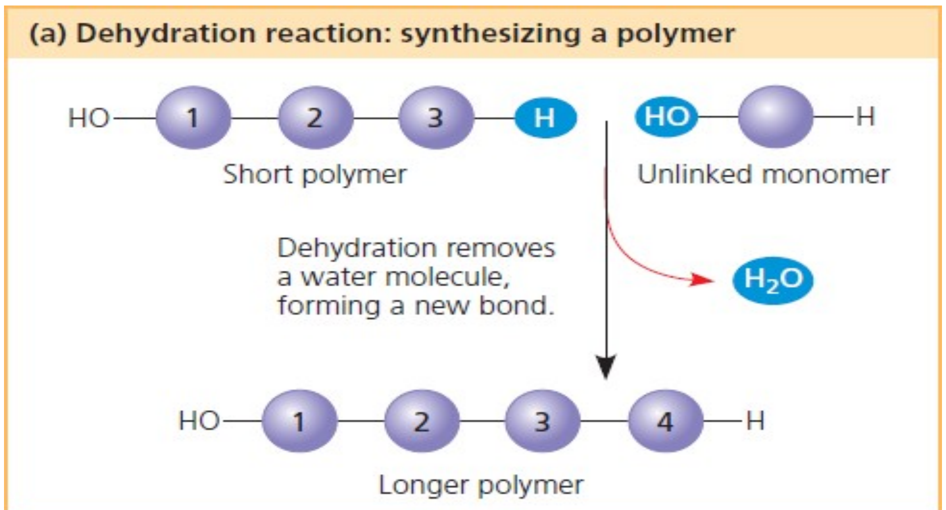
Molecular Diversity Arising from Carbon Skeleton Variation

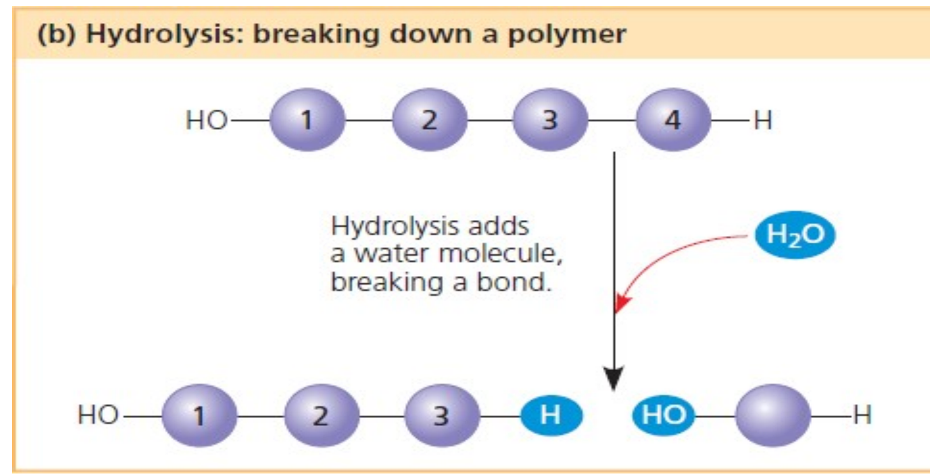


Hydrocarbons and Isomers

Large Biological Molecules

Macromolecules are polymers, built from monomers





Diversity of Biological Molecules

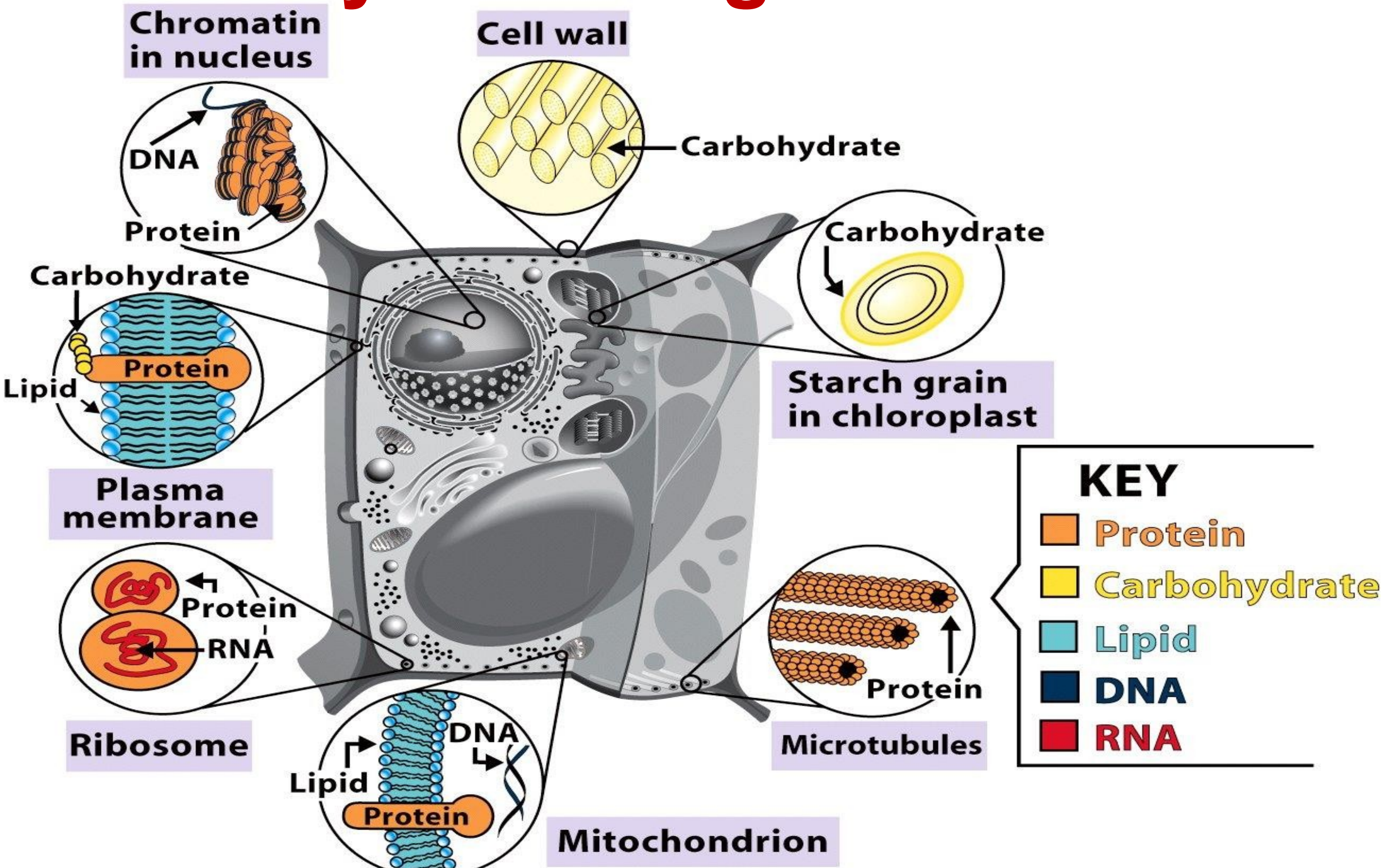


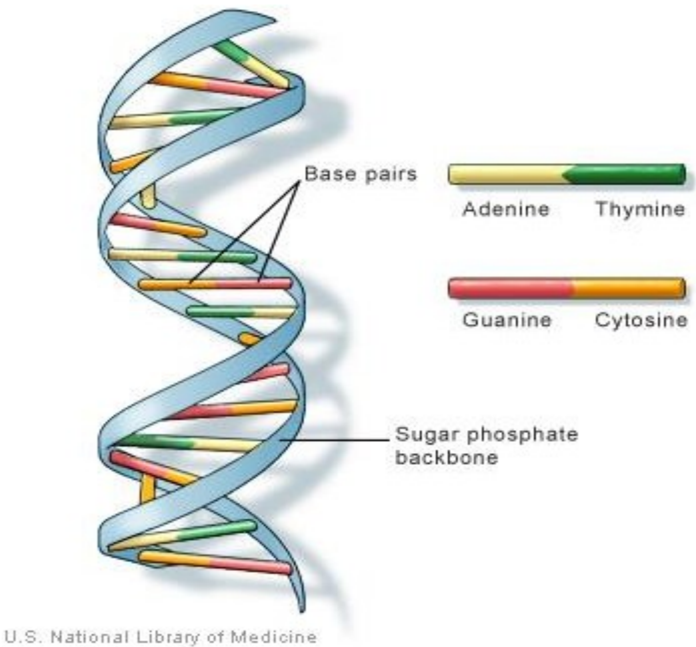
Figure 2-11 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

Basic Functions

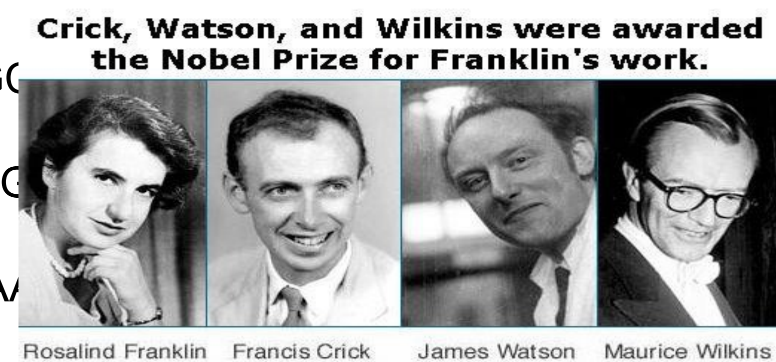
	Carbs	Lipids	Nucleic Acids	Proteins
Functions	• Energy • Storage • Structure	• Long term storage • Insulation • Protection	• Inheritance • Blueprint for metabolism	• Catalysts • Hormones • Structure
Forms	• Starch • Glycogen • Glucose • Sucrose • Cellulose	• Lipid • Fats • Oils • Waxes	• DNA • RNA • ATP	• Proteins • Enzymes

DNA (Deoxyribonucleic acid)

DNA as a CPU of the cell



GTACCTTGATTTCGTATTCTGAGAGGCTGCTGCT
T
AGCGGTAGCCCCTTGGTTTCCGTGGCAACGGAA
A
AGCGCGGGAATTACAGATAAATTAAAACTGCGA
CT
GCGCGGCGTGAGCTCGCTGAGACTTCCTGGAC
GG
GGGACAGGCTGTGGGGTTTCTCAGATAACTGGG
C
CCCTGCGC
G
GGTAAAGG
GG
GGGCCCAA
GG
AGAGTGGATTTCCGAAGCTGACAGATGGGTATT



Building Blocks of Nucleic acid

Nucleotides = Base + Sugar + Phosphate

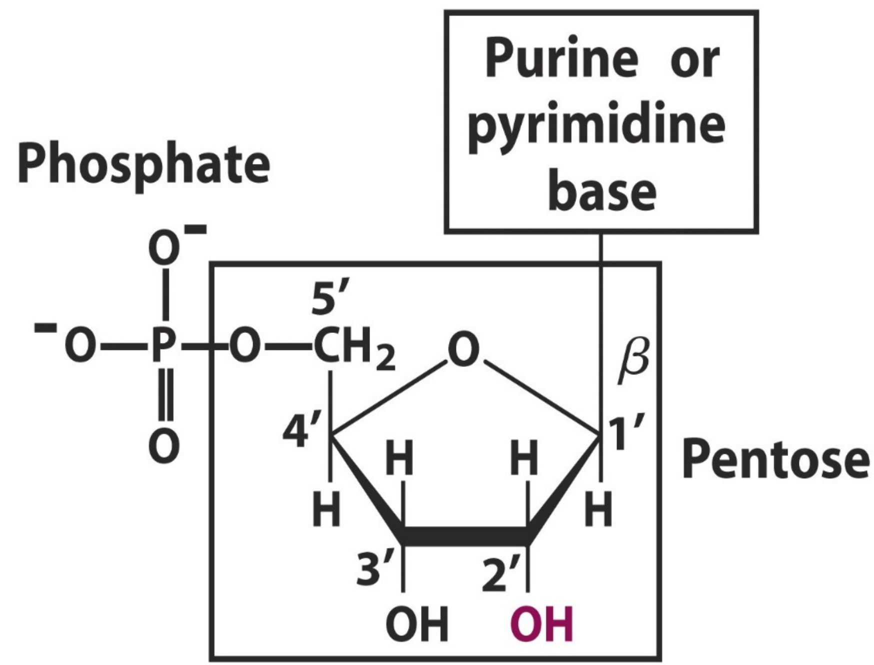
Nucleosides = Base + Sugar

Nitrogen Bases

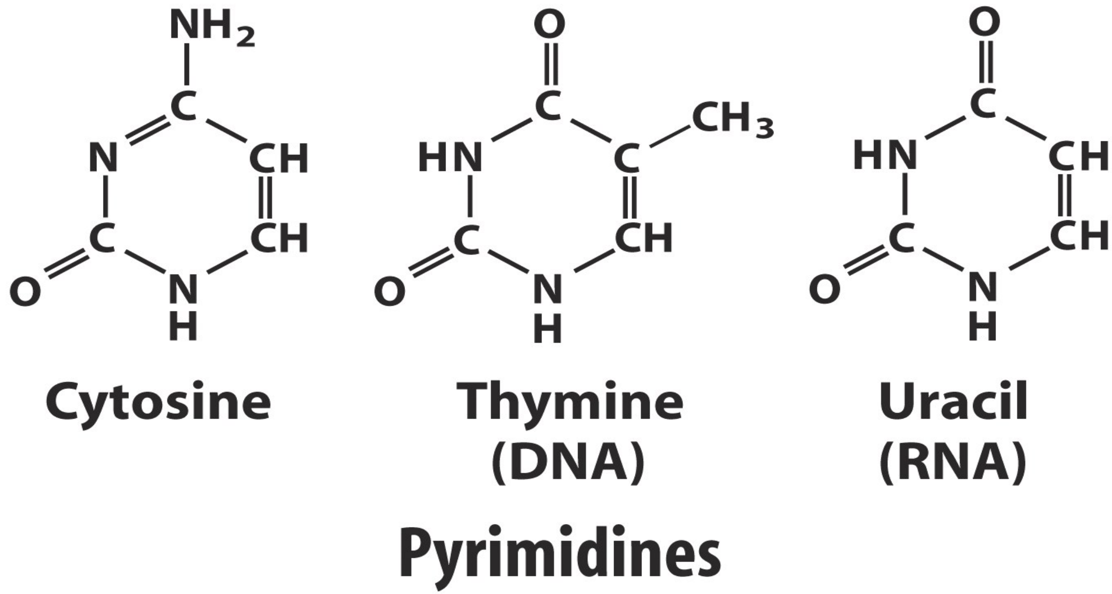
- Purines
  - Adenine and Guanine
- Pyrimidines
  - Thymine, Cytosine and Uracil

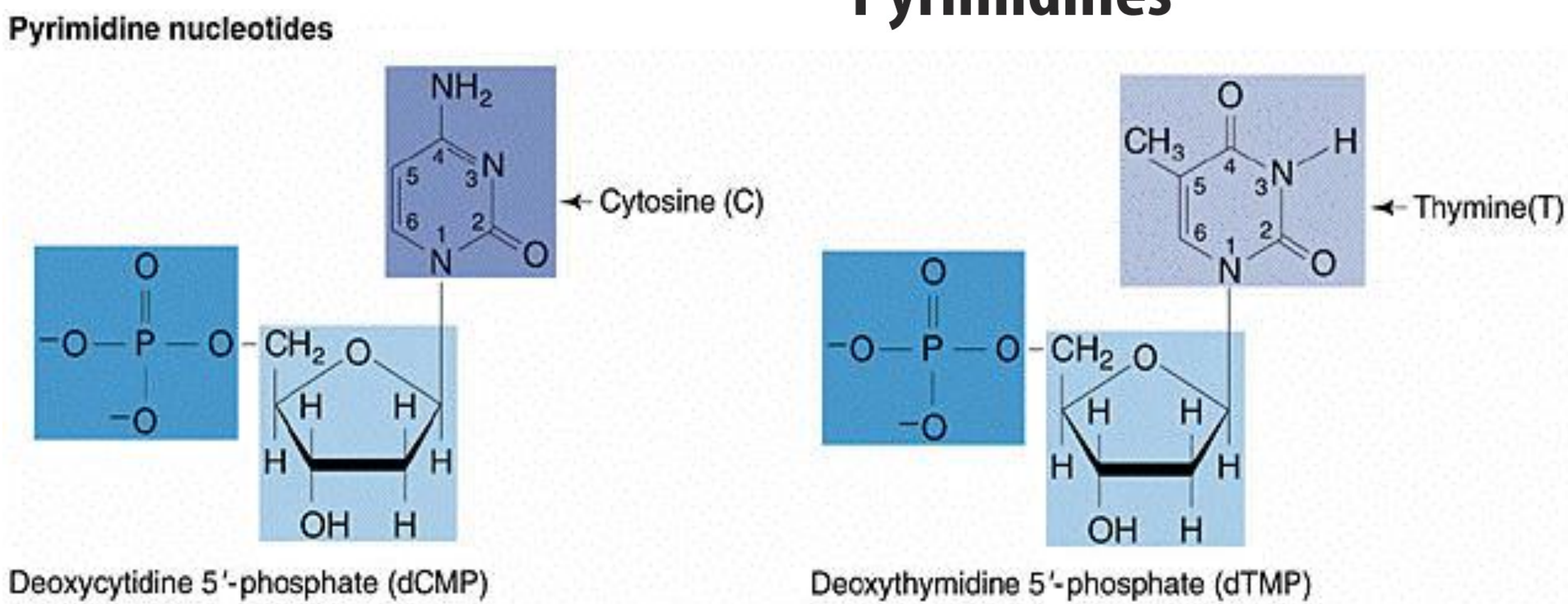
Pentose Sugars

- Ribose
- Deoxyribose



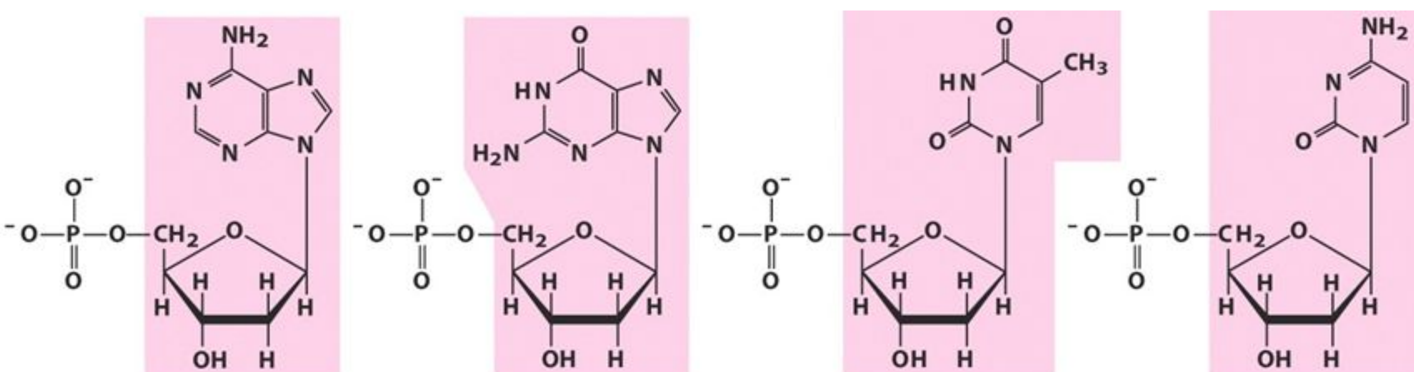
Pyrimidine N





Nucleosides and Nucleotides

- Base is linked via β-N-Glycosidic bond
- Named by adding -idine to the root name of a pyrimidine or -osine to the root name of a purine



Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

Characteristic features of DNA

- DNA is a long spirally coiled double stranded macromolecule
- Acts as genetic material in most of the organisms
- DNA controls all the chemical changes which take place in cells
- In Prokaryotes – lies naked and vigorously coiled in cytoplasm
- In Eukaryotes – mainly in nucleus and associated with histone proteins to form chromatin fibers or chromosomes

Other Functions of Nucleotides

- Nucleoside 5'-triphosphates are carriers of energy

- Bases serve as recognition units

- Cyclic nucleotides are signal molecules and regulators of cellular metabolism and reproduction

- ATP is central to energy metabolism
- GTP drives protein synthesis
- CTP drives lipid synthesis
- UTP drives carbohydrate metabolism

Characteristic features of DNA Double Helical Structure

- Double helical model of DNA was given by Watson and Crick in 1953
- Composed of 2 complementary chains of dNTPs units which are spirally twisted around each other to form double helix (or a ladder like structure)
- Sides of the ladder are made up of alternating molecules of phosphate and deoxyribose sugar (sugar phosphate backbone)
- Bases make up the rungs of the ladder which projects inwards to helix at about 90 along axis of helix

Characteristic features of DNA Double Helical Structure

- Base pairing between bases of 2 opposite strand is specific i.e. A=T and C=G

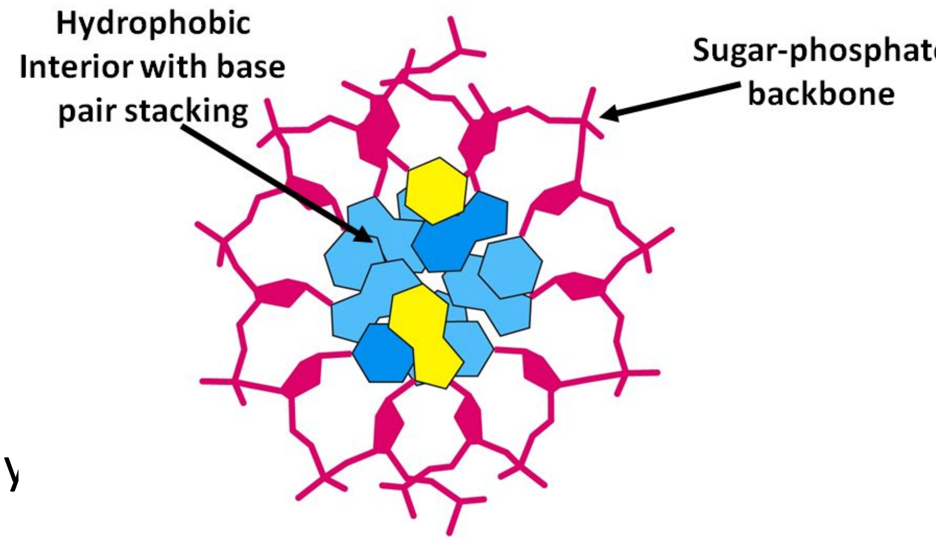
- Bases that make up the rungs of the ladder are attracted by hydrogen bonds (weak chemical bonds)

- Two strands of a DNA are anti-parallel are complementary but not identical

- Distance between the 2 sugar-phosphate backbones is always the same, give DNA molecule a regular shape

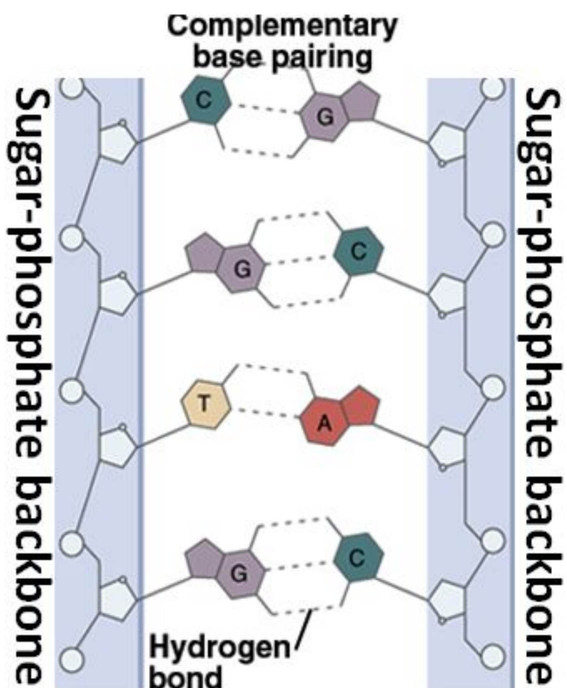
Characteristic features of DNA Double Helical Structure

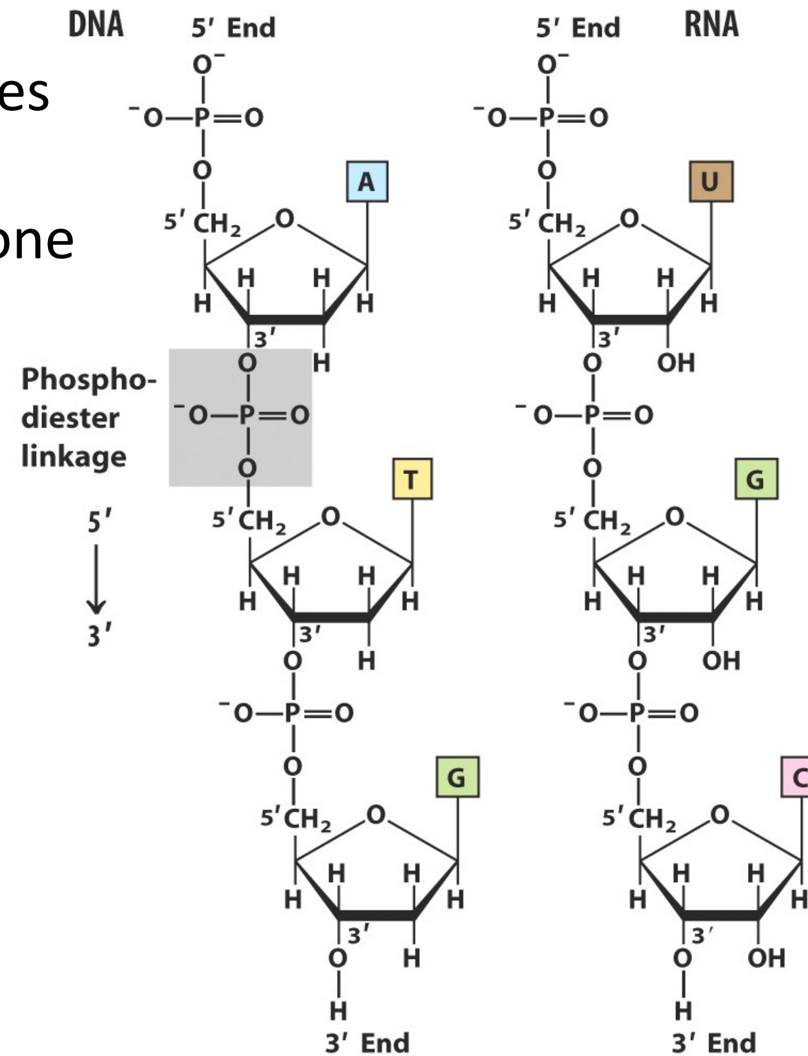
- Hydrophillic sugar phosphate backbone winds around outside of helix
- Noncovalent interactions between upper and lower surfaces of base-pairs (stacking) forms a closely packed hydrophobic interior



Phosphodiester bond

- Links successive nucleotides in nucleic acids (DNA and RNA) and form the backbone of the macromolecule



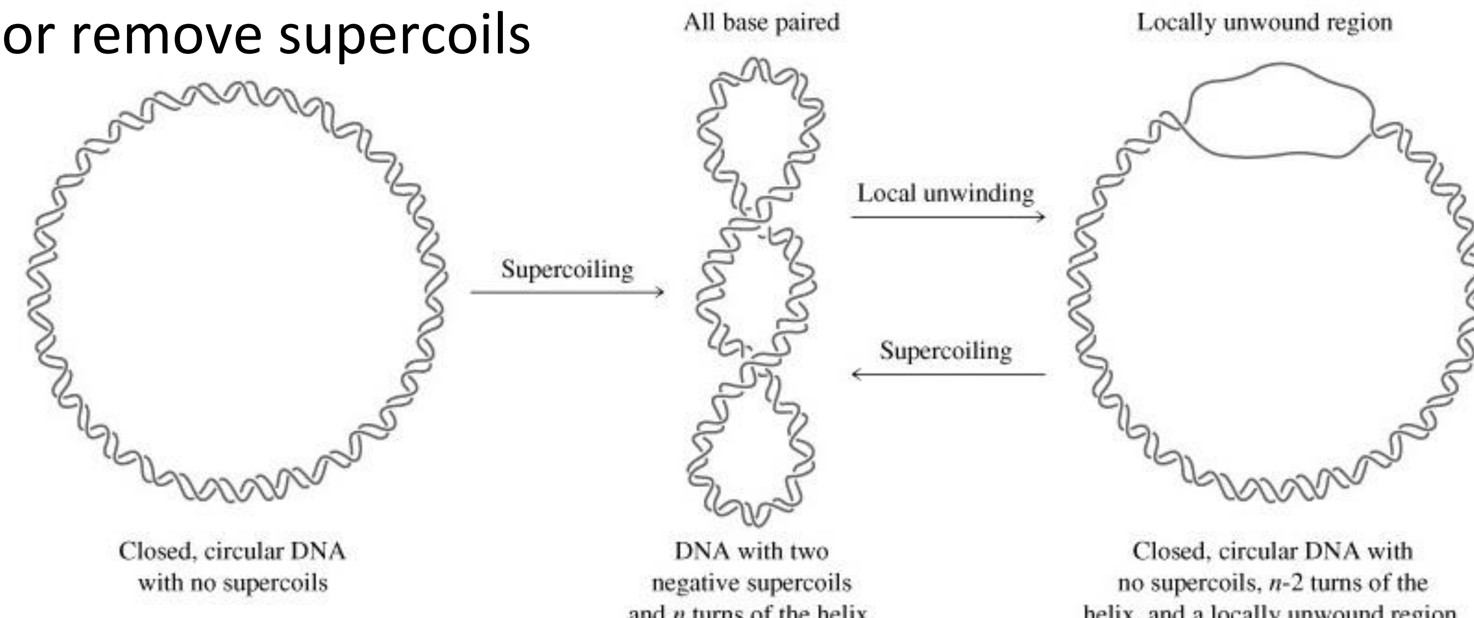


Structure of DNA

- 1^{o} Structure – Linear array of nucleotides
  - Can determine the sequence of DNA bp in any DNA molecule
  - Chain-termination method developed by Sanger
- 2^{o} Structure – Double helix
  - DNA is double stranded with antiparallel strands
  - Three different helical forms (A, B and Z DNA
- 3^{o} Structure – Super-coiling, stem-loop formation
  - In duplex DNA, ten bp per turn of helix (relaxed form)
  - DNA helix can be over-wound.
  - Over winding of DNA helix can be compensated by supercoiling
- 4^{o} Structure – Packaging into chromatin
  - In chromosomes, DNA is tightly associated with proteins

Supercoiling of DNA (3° Structure)

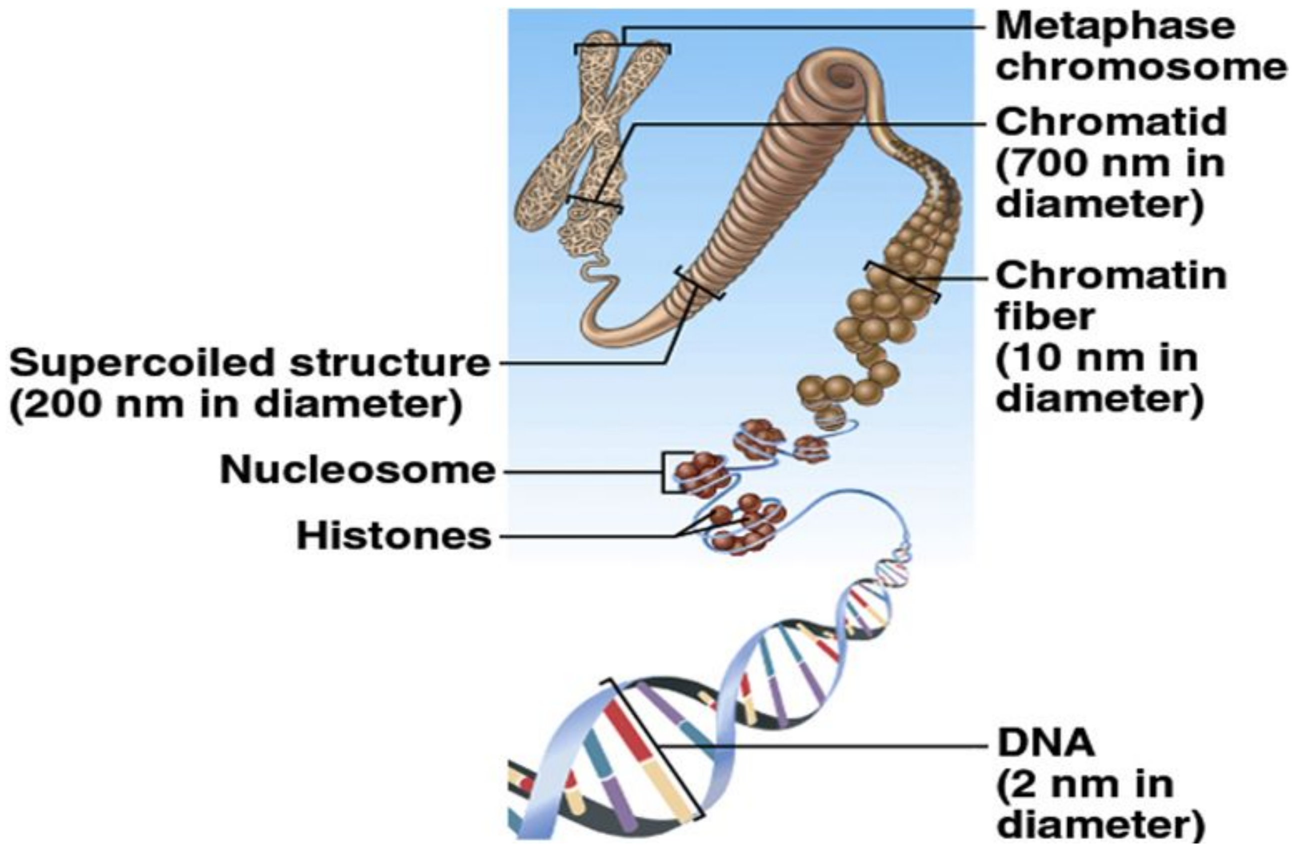
- Each super coil compensates for one + or – turn of the double helix
- Supercoiling prevalent in circular DNA molecules and within local regions of long linear DNA strands
- Enzymes called topoisomerases or gyrases can introduce or remove supercoils



Chromosome Structure (4^o Str of DNA)

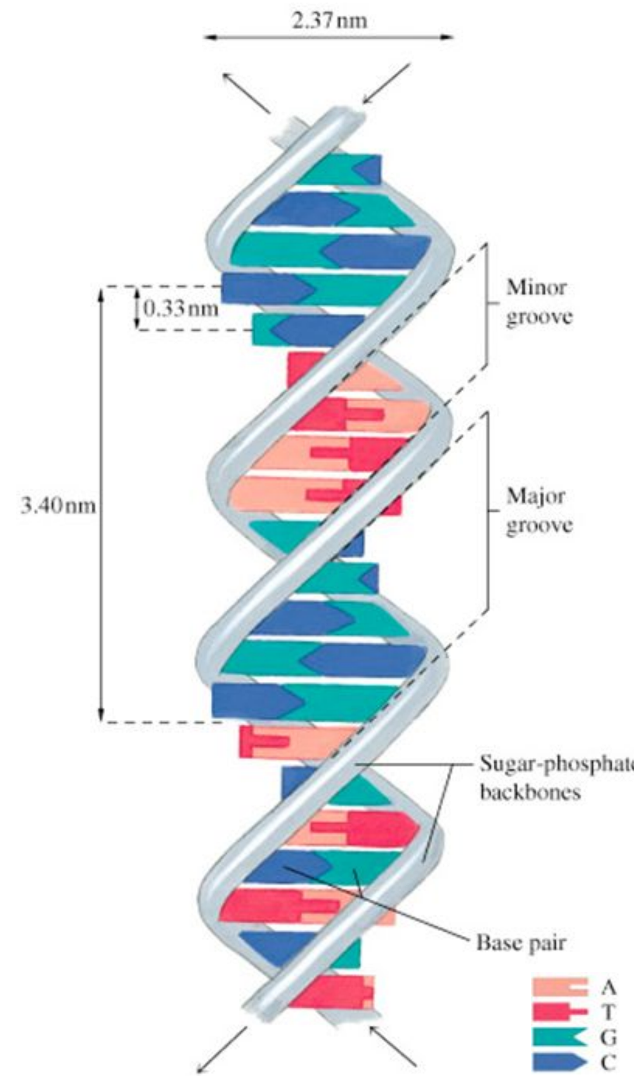
- Human DNA’s total length is ~2 meters!
- This must be packaged into a nucleus that is about 5 micrometers in diameter
- Compression of the magnitude (100,000!), is possible by wrapping the DNA around histone and non-histone proteins (Chromatin, the nucleoprotein complex)
- Major histone proteins: H1, H2A, H2B, H3 and H4
  - 4 major histone (H2A, H2B, H3, H4) proteins form octomer
    - 200 base pair long DNA strand winds around the octomer
  - H1 protein involved in higher-order chromatin structure
    - 146 base pair DNA "spacer" separates individual nucleosomes
  - Without H1, chromatin looks like beads on string

Chromatin Structure

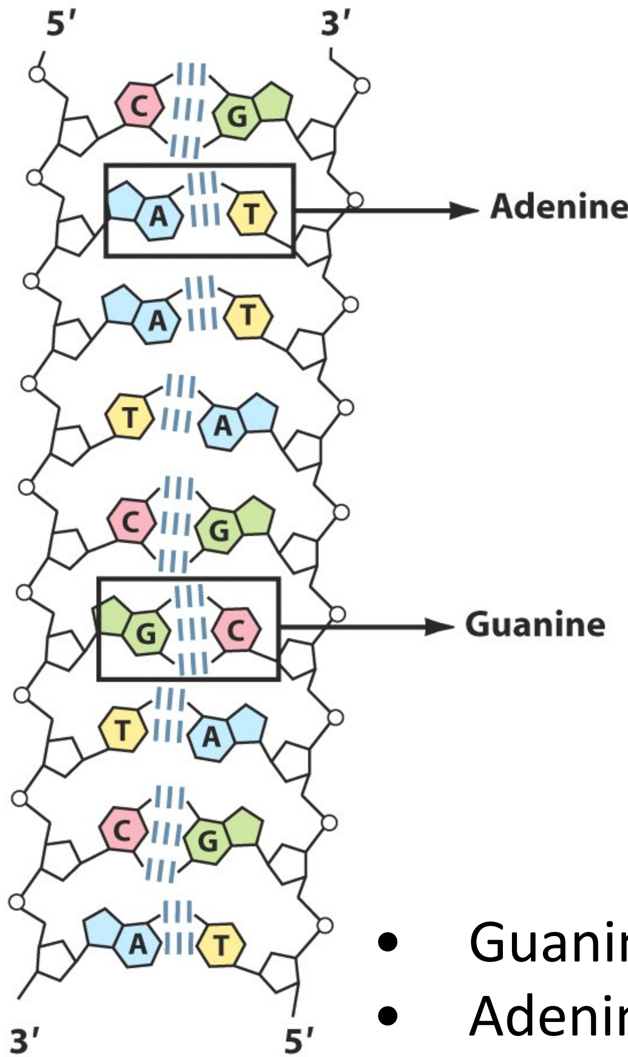


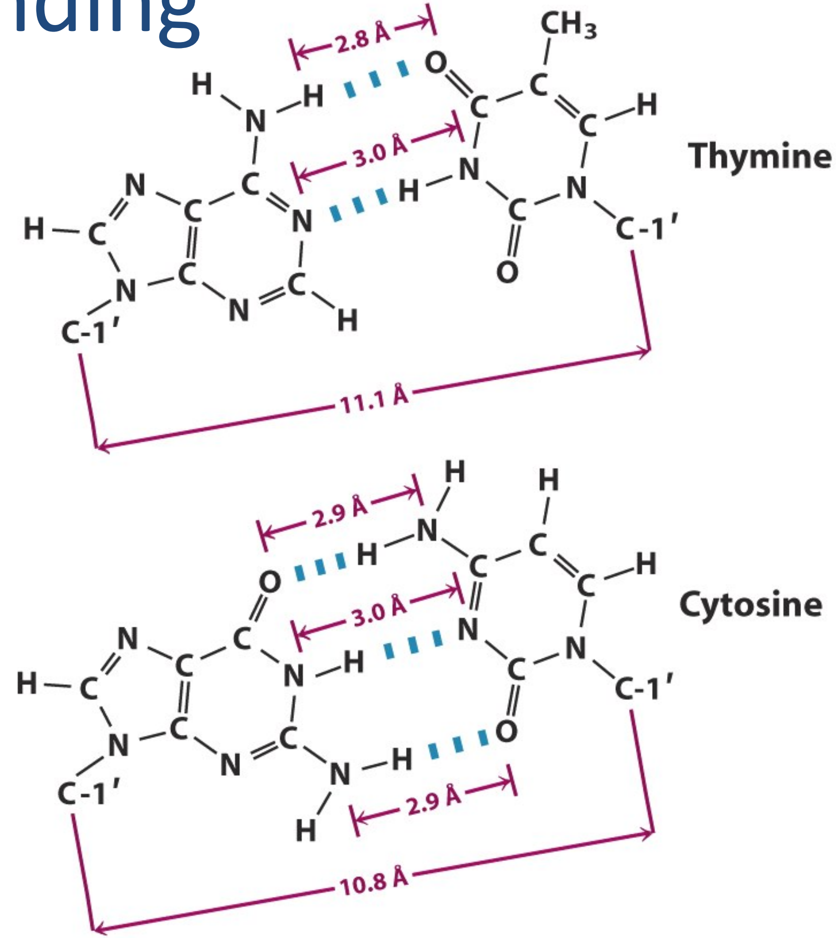
Structure of DNA Double Helix

- Right handed helix
- Rise = 0.33 nm/nucleotide
- Pitch = 3.4 nm / turn
- 10.4 nucleotides per turn
- Two groves – major and minor



Hydrogen bonding

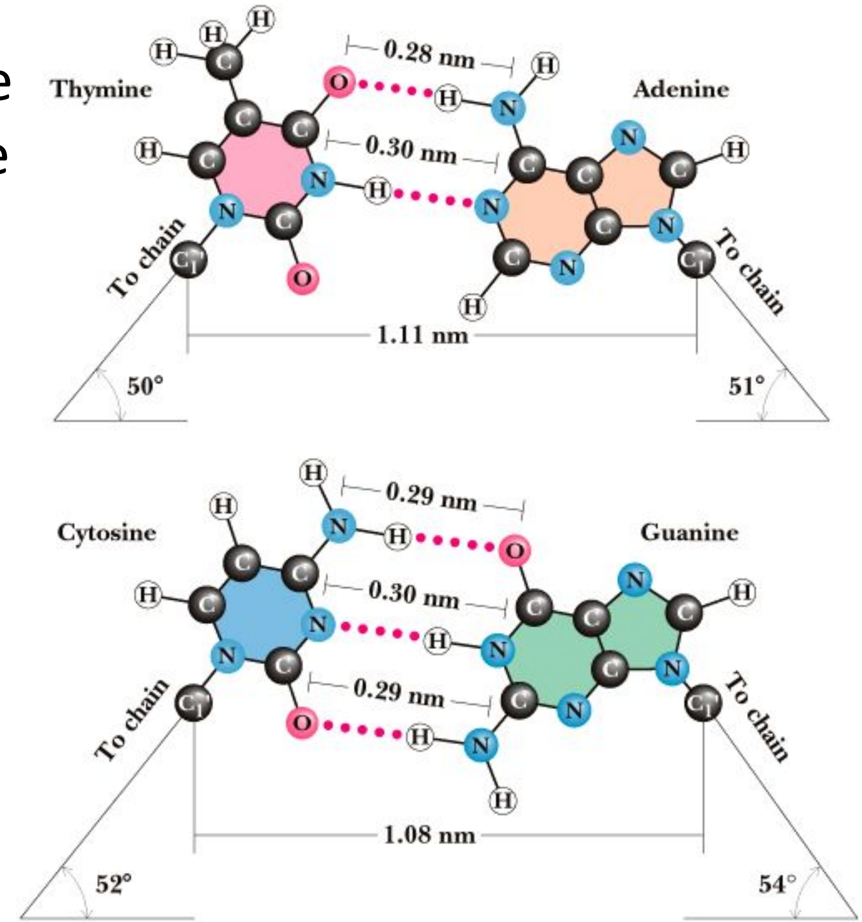




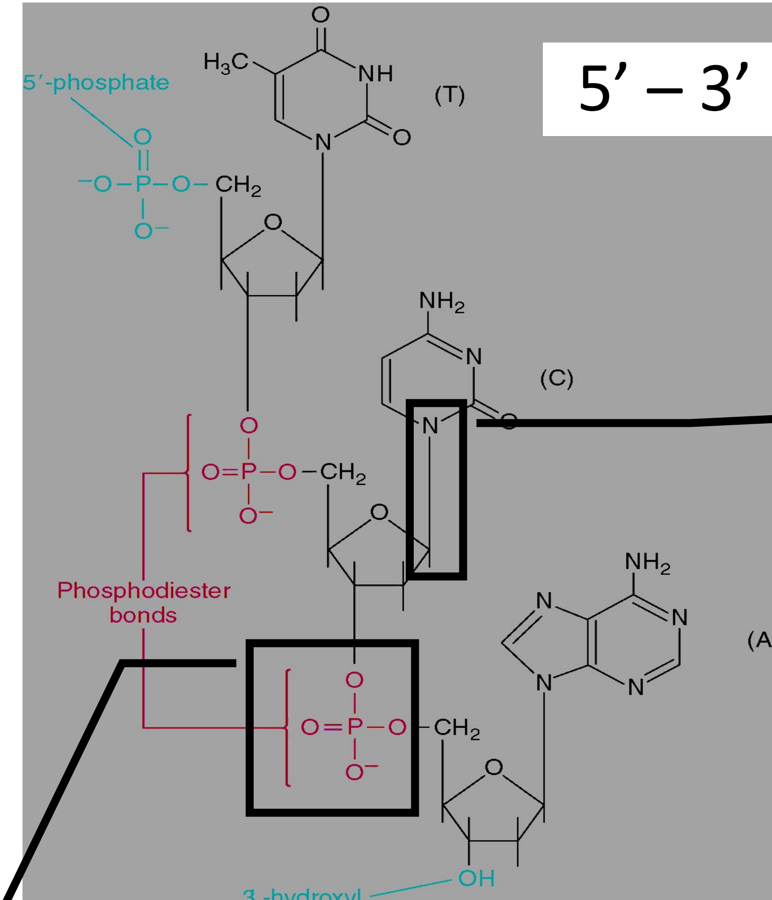
- Guanine pairs with cytosine
- Adenine pairs with thymine

Hydrogen bonding

- Guanine pairs with cytosine
- Adenine pairs with thymine



5’ – 3’ polynucleotide *linkages*



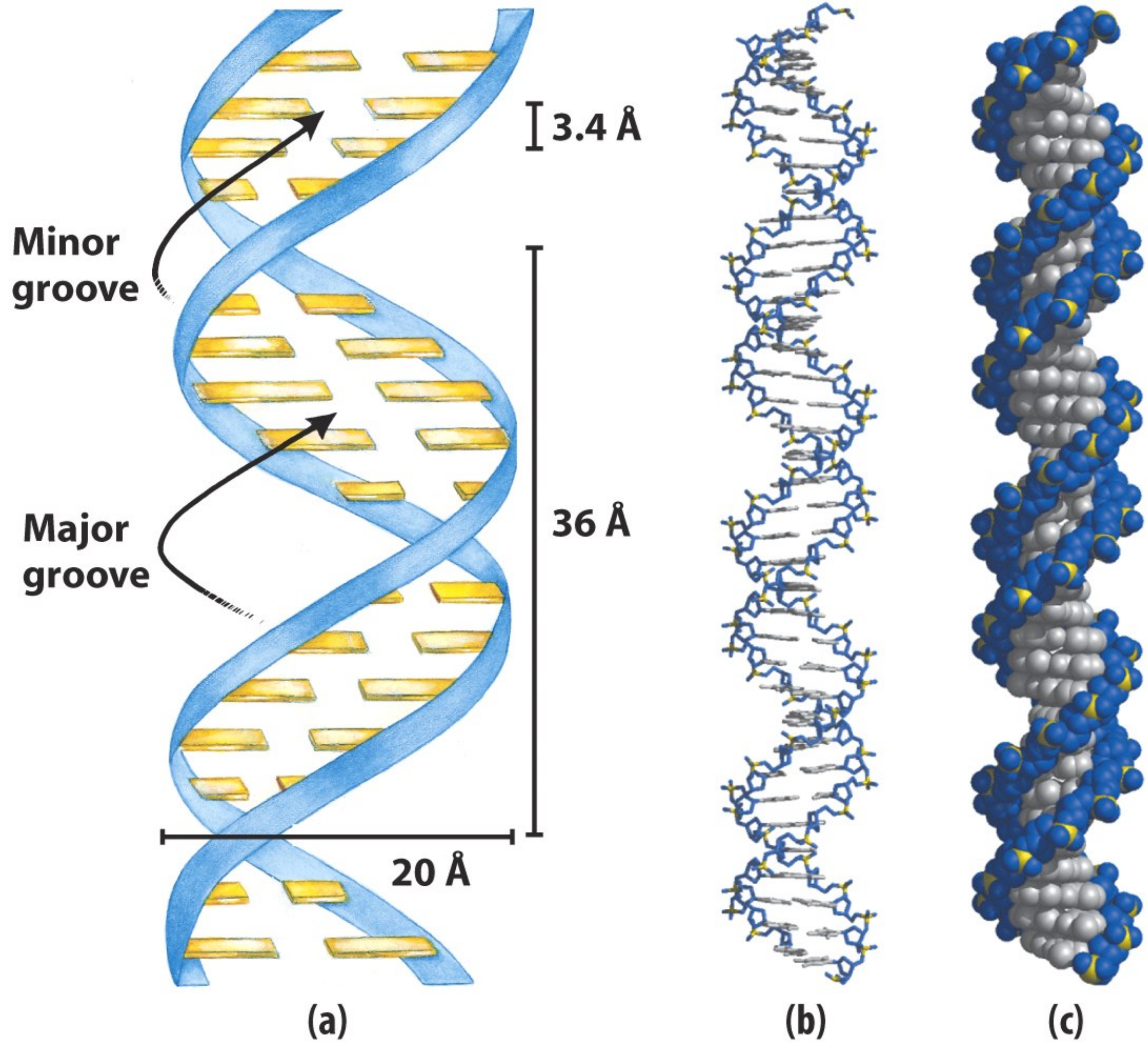
2) N-glycosidic bonds

Links nitrogenous base to C1’ pentose in beta configuration

1) Phosphodiester bonds

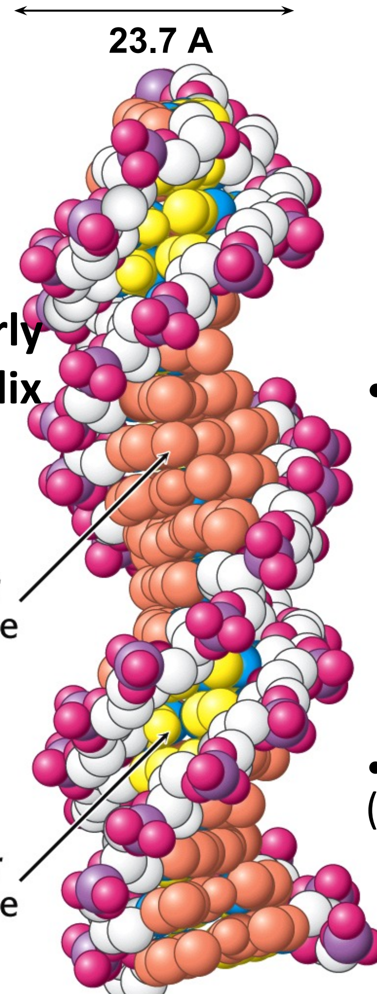
5’ and 3’ links to pentose sugar

B-DNA

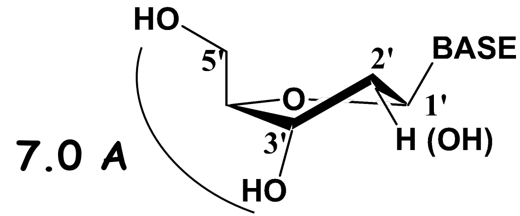


Essential Features of B-DNA

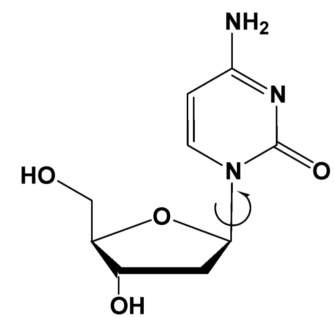
- right handed helix
- helical axis passes through base pairs
- planes of bases are nearly perpendicular to the helix axis.
- 3.4 A rise between base pairs



- Sugars are in the 2' endo conformation.



- Bases are the *anti* conformation.



- Bases have a helical twist of 36º (10.4 bases per helix turn)

TABLE 27.1 Comparison of A-, B-, and Z-DNA

	Helix type		
	A	**B**	**Z**
Shape	Broadest	Intermediate	Narrowest
Rise per base pair	2.3 Å	3.4 Å	3.8 Å
Helix diameter	25.5 Å	23.7 Å	18.4 Å
Screw sense	Right-handed	Right-handed	Left-handed
Glycosidic bond	*anti*	*anti*	alternating *anti and syn*
Base pairs per turn of helix	11	10.4	12
Pitch per turn of helix	25.3 Å	35.4 Å	45.6 Å
Tilt of base pairs from normal to helix axis	19°	1°	9°
Major groove	Narrow and very deep	Wide and quite deep	Flat
Minor groove	Very broad and shallow	Narrow and quite deep	Very narrow and deep

Functional Role of DNA

Storage of genetic information

Genetic material (carries all the hereditary information)

Self-duplication & inheritance

Transfer of genetic information from one generation to another due to its unique property of replication

Crossing over of chromosomes (during meiosis) creates genetic variation in populations

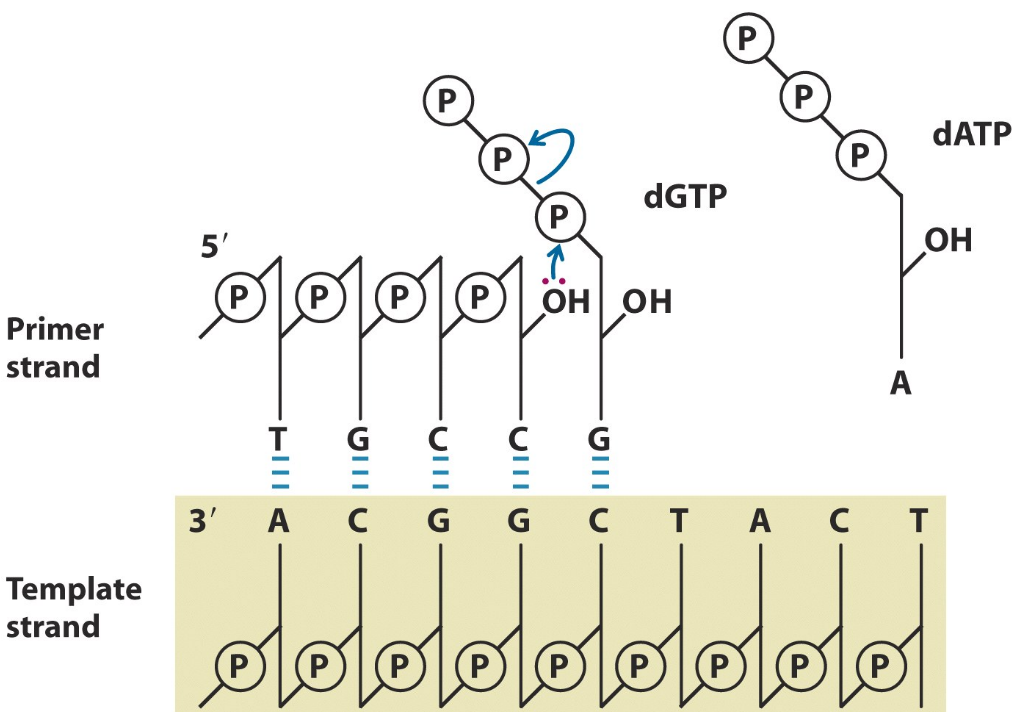
DNA Mutation contributes evolution in organisms

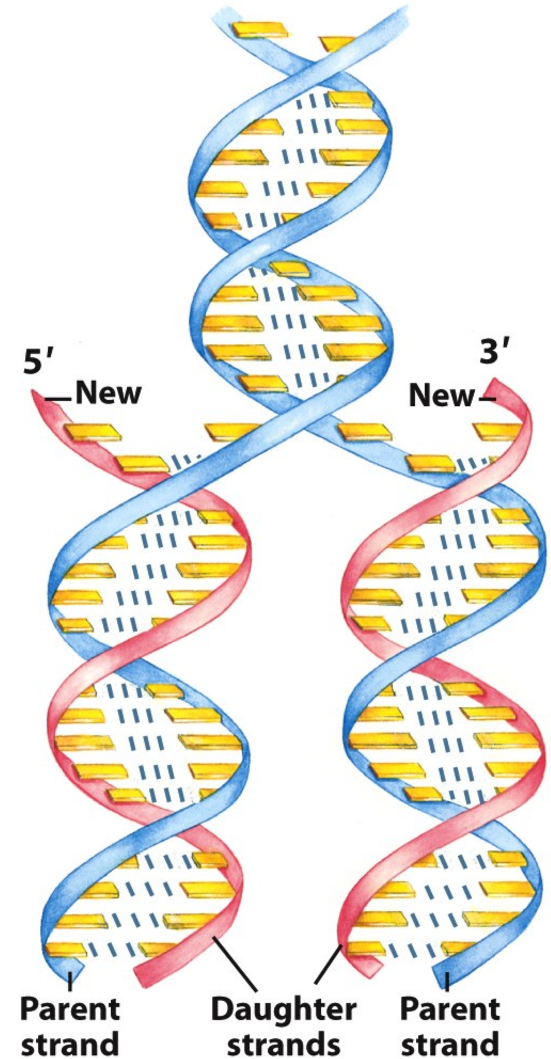
Expression of the genetic message

Controls the metabolic reactions of cells (Blueprint of making proteins)

Differential gene expression brings about differentiation during growth and development of cells

Semi-conservative Replication

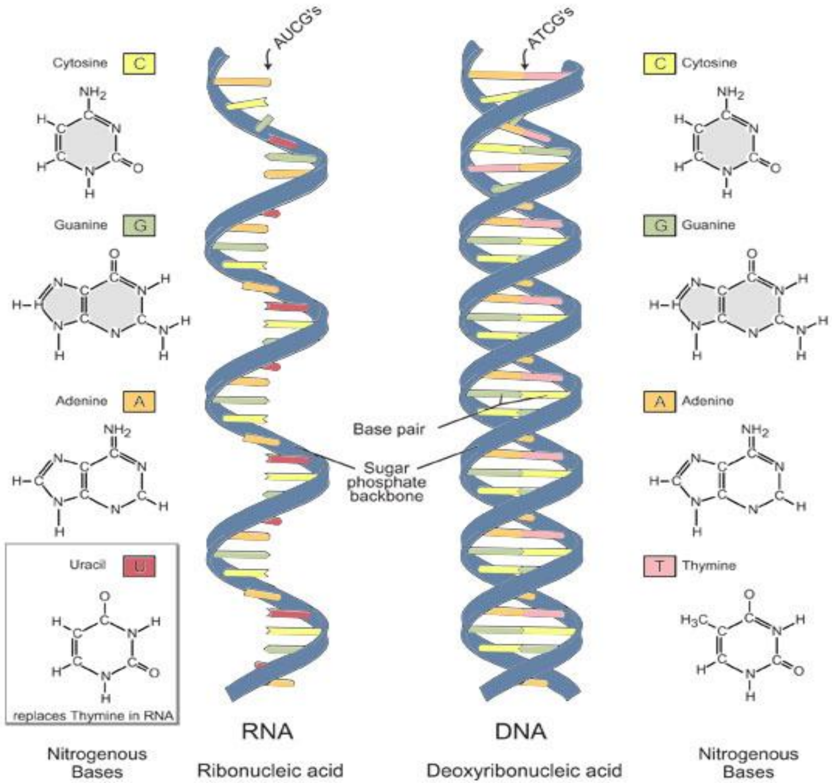


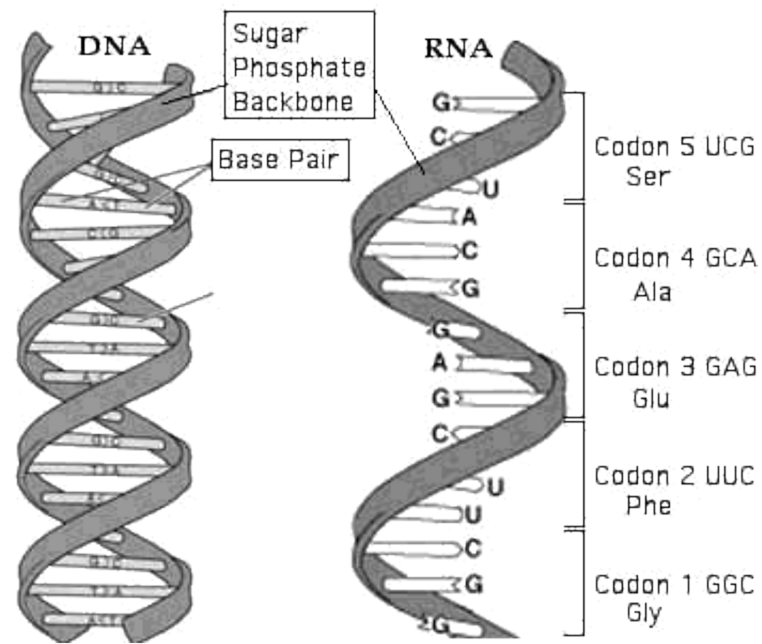


Ribonucleic acid (RNA)

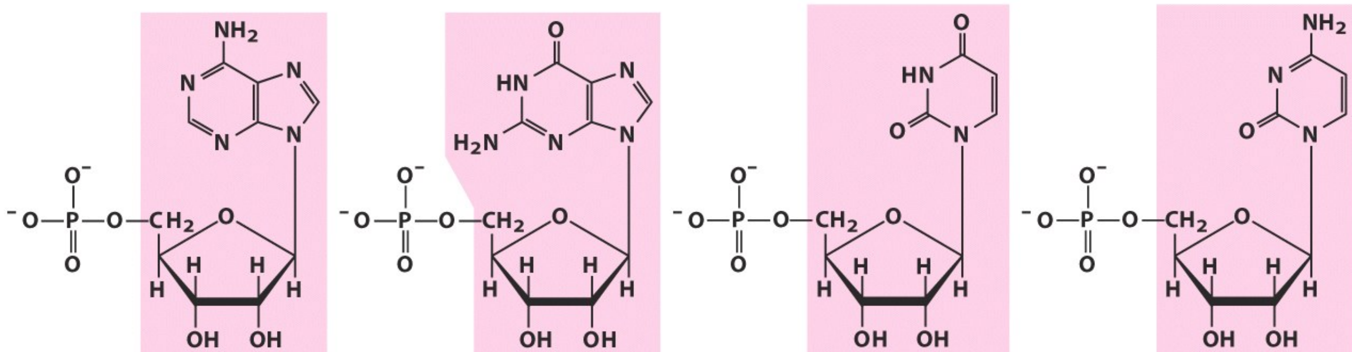
- Single stranded chain formed by polymerization of large number of ribonucleotides
- Ribonucleotide:
  - Ribose sugar, Nitrogenous Base (A,U,C,G) & Phosphate group
- Presence of Sugar-Phosphate backbone as in DNA
- Base sequence of RNA is complementary to DNA template sequence
- Chemically less stable than DNA
  - Presence of 2'-OH makes RNA more susceptible to hydrolytic attack
- Has secondary structure, can form intra-chain base pairing (i.e. cruciform structures)

Comparison between RNA and DNA



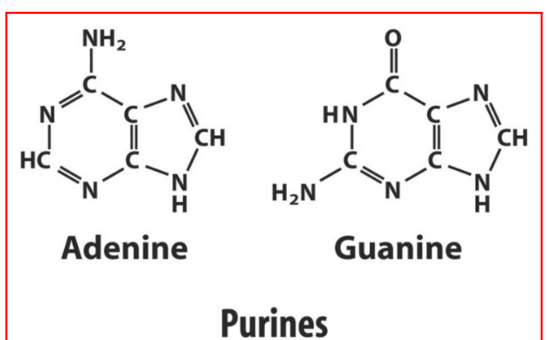


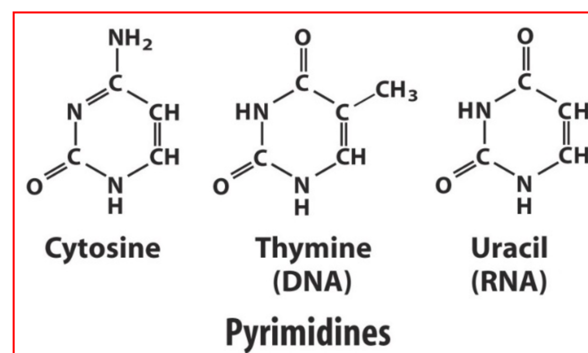
Ribonucleotides of nucleic acids



Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

(b) Ribonucleotides





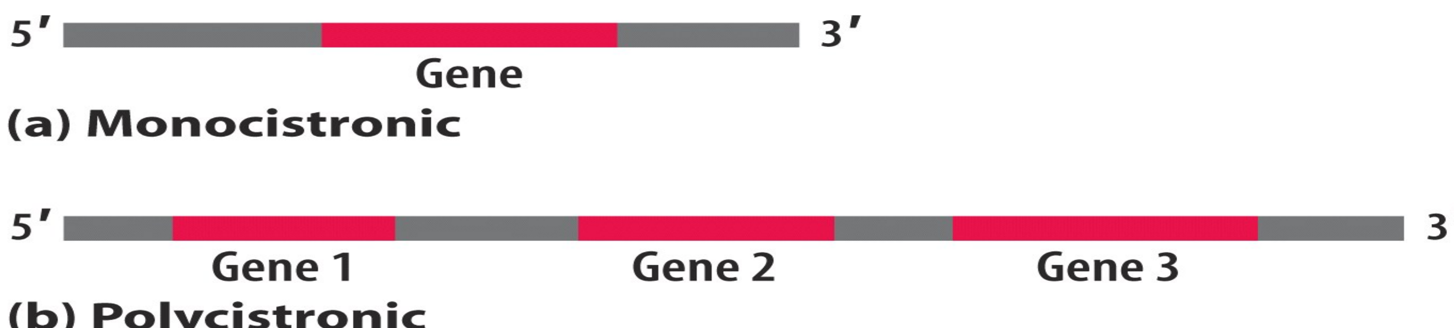
Types of RNA

- Ribosomal RNA (rRNA)
  - integral part of ribosomes (very abundant)
- Transfer RNA (tRNA)
  - carries activated amino acids to ribosomes.
- Messenger RNA (mRNA)
  - Endcodes sequences of amino acids in proteins.
- All play an important role in protein synthesis

- Catalytic RNA (Ribozymes)
  - Catalyze cleavage of specific RNA species

Messenger RNA (mRNA)

- longest among all RNA types
- Only 5% of total RNA population in a cell
- Linear molecule (limited random coiling but no base pairing)
- Acts as a messenger – brings information from DNA for formation of particular polypeptide
- monocistronic mRNA- one gene codes for single mRNA strand
- polycistronic mRNA- several adjacent genes transcribe into single mRNA strand



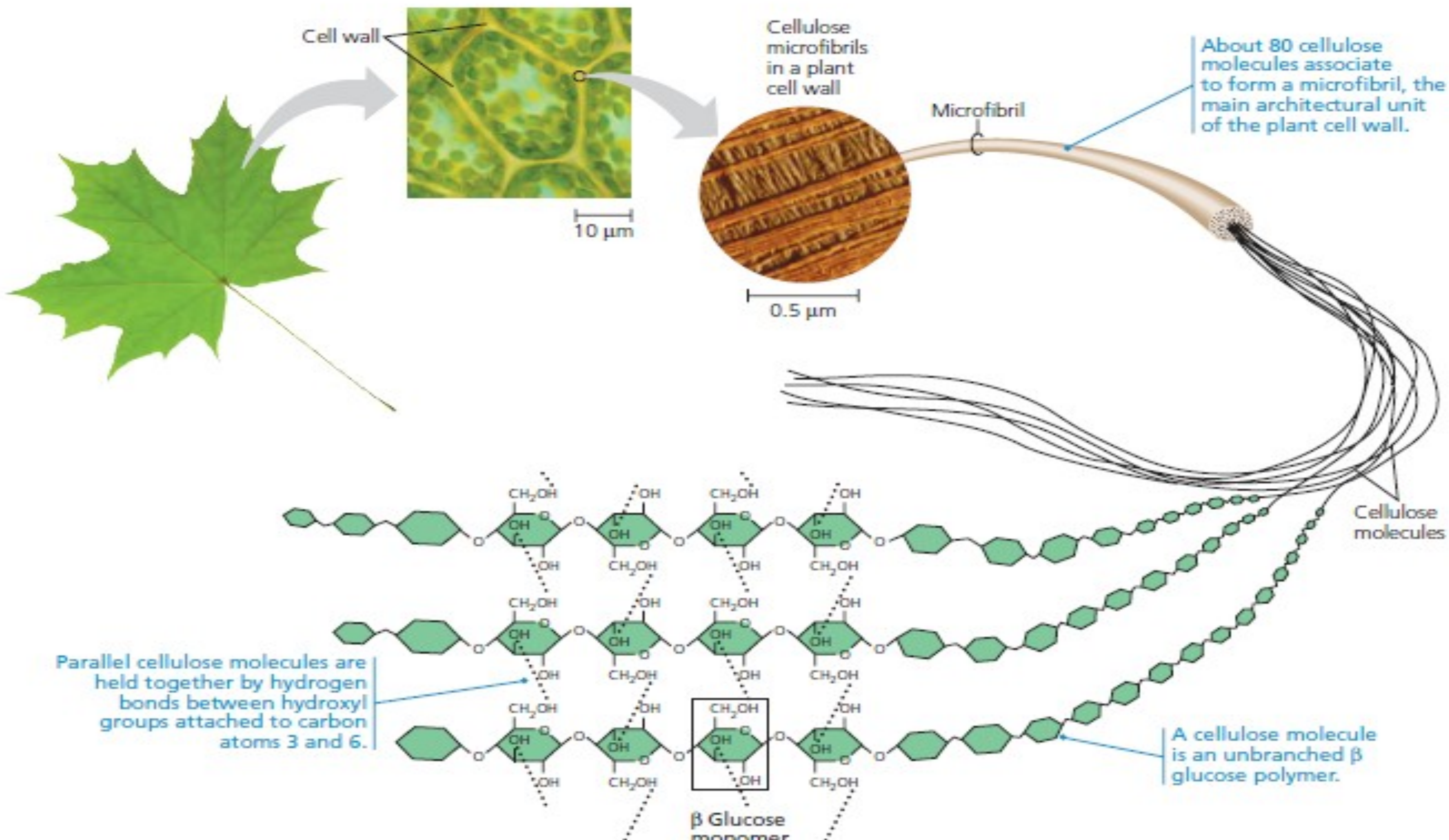
Functional Role of RNA

mRNA carries the information of DNA for protein synthesis

tRNA carries amino-acid to mRNA-ribosome complex during protein synthesis

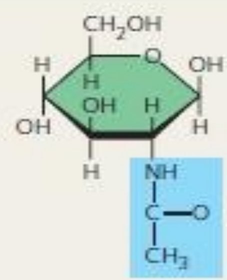
rRNA with help of ribosomal proteins consitute ribosomes which in turn are called protein factories

Carbohydrates



▲ **Figure 5.8 The arrangement of cellulose in plant cell walls.**

Carbohydrates



◀ The structure of the chitin monomer

◀ Chitin forms the exoskeleton of arthropods. This cicada is molting, shedding its old exoskeleton and emerging in adult form.

▲ Chitin is used to make a strong and flexible surgical thread that decomposes after the wound or incision heals.

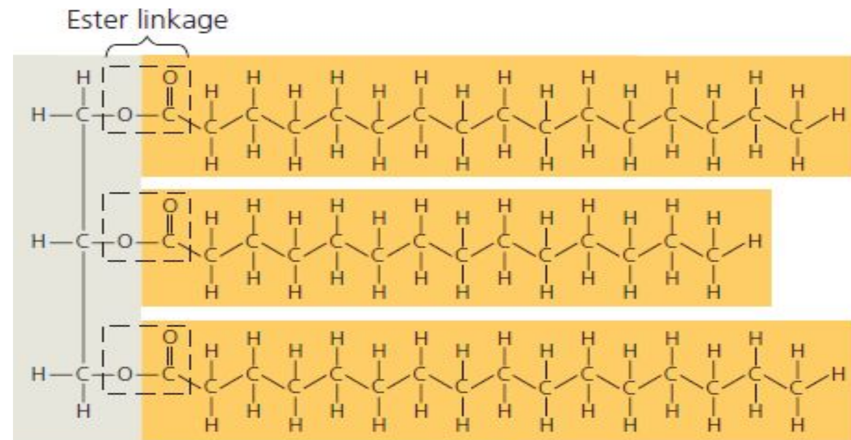
▲ **Figure 5.9 Chitin, a structural polysaccharide.**

Several functions

- **Cellulose**
- **Chitin**
- **Starch**

Lipids

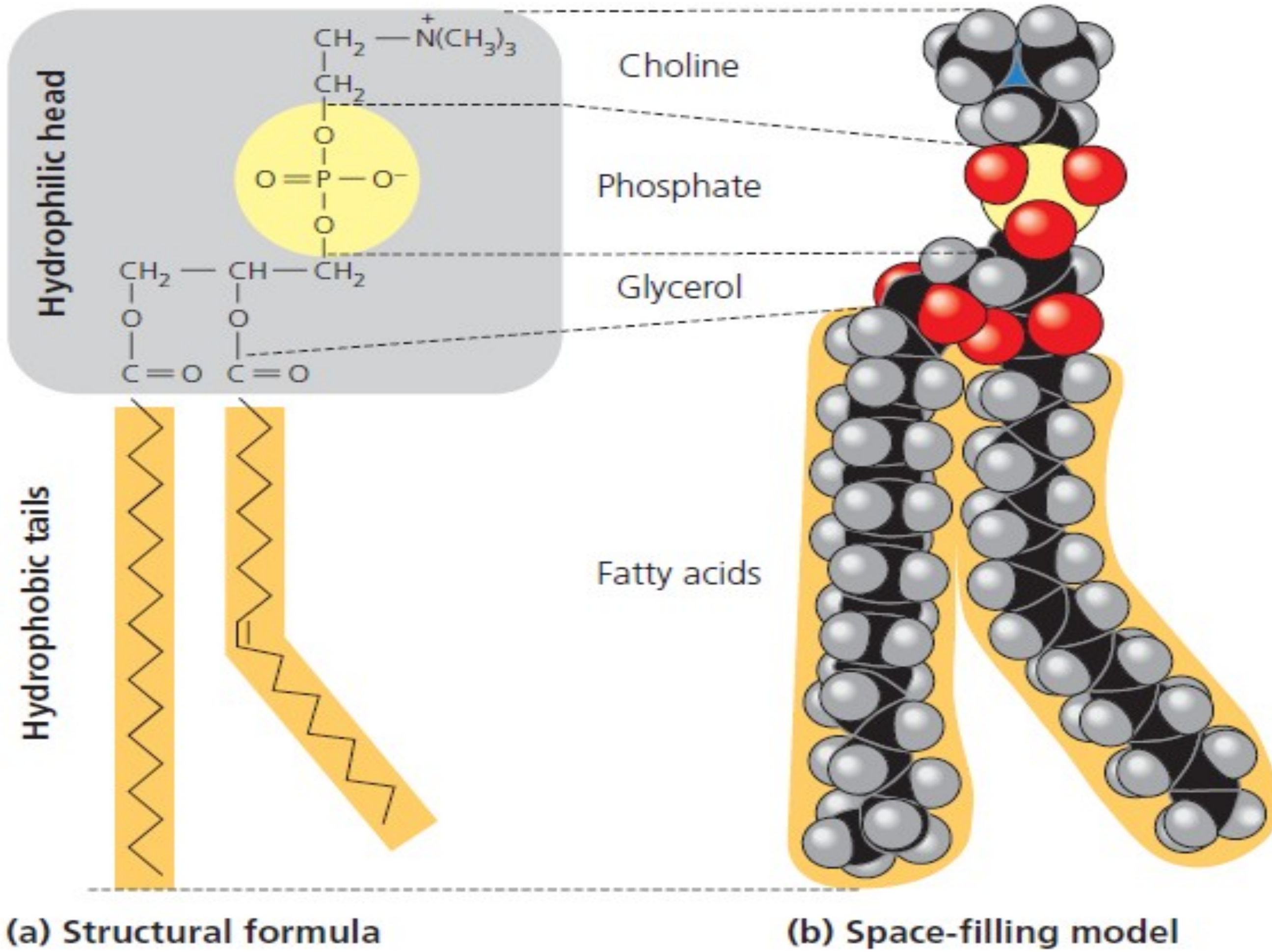
Fats in Practice



Fat in Theory

Fatty acids, oils, phospholipids, and steroids

Phospholipids



Phospholipids – Lipid Bilayer

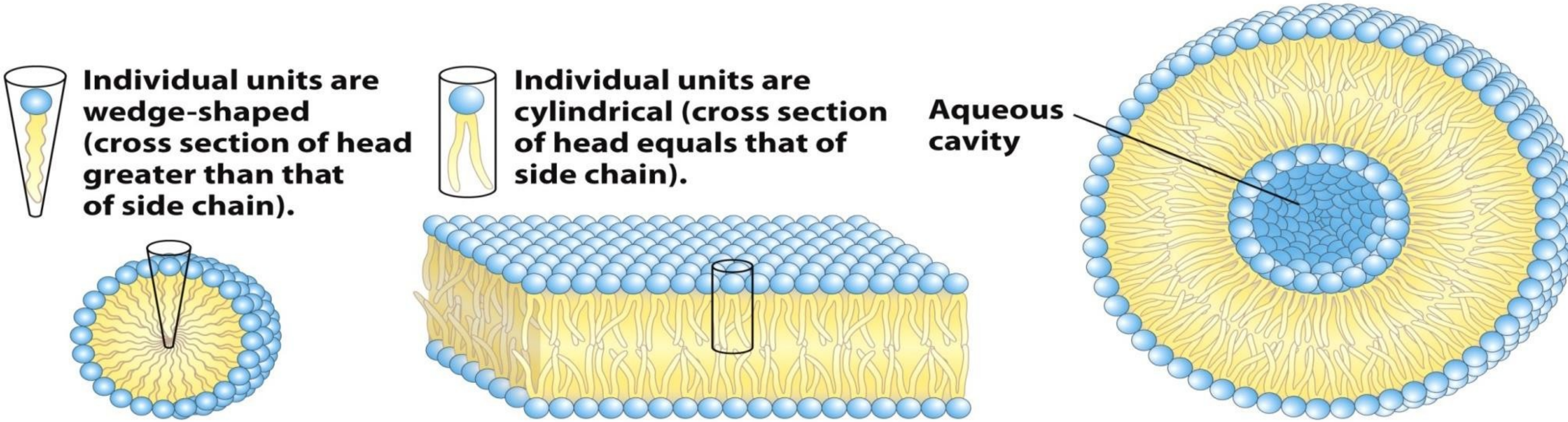
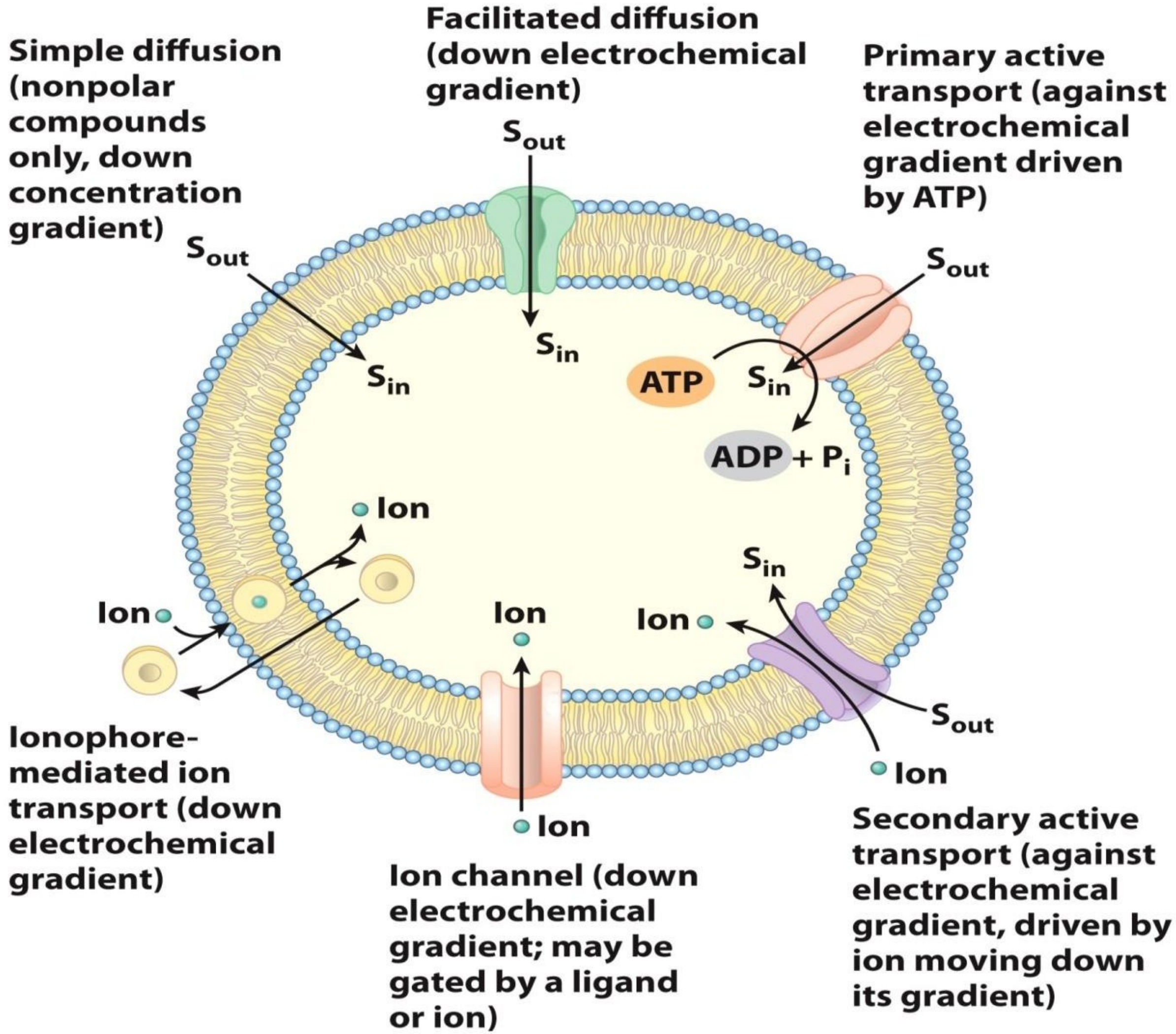


Figure 11-4
Lehninger Principles of Biochemistry, Sixth Edition



Cell Membrane

Figure 11-26
Lehninger Principles of Biochemistry, Sixth Edition

Proteins

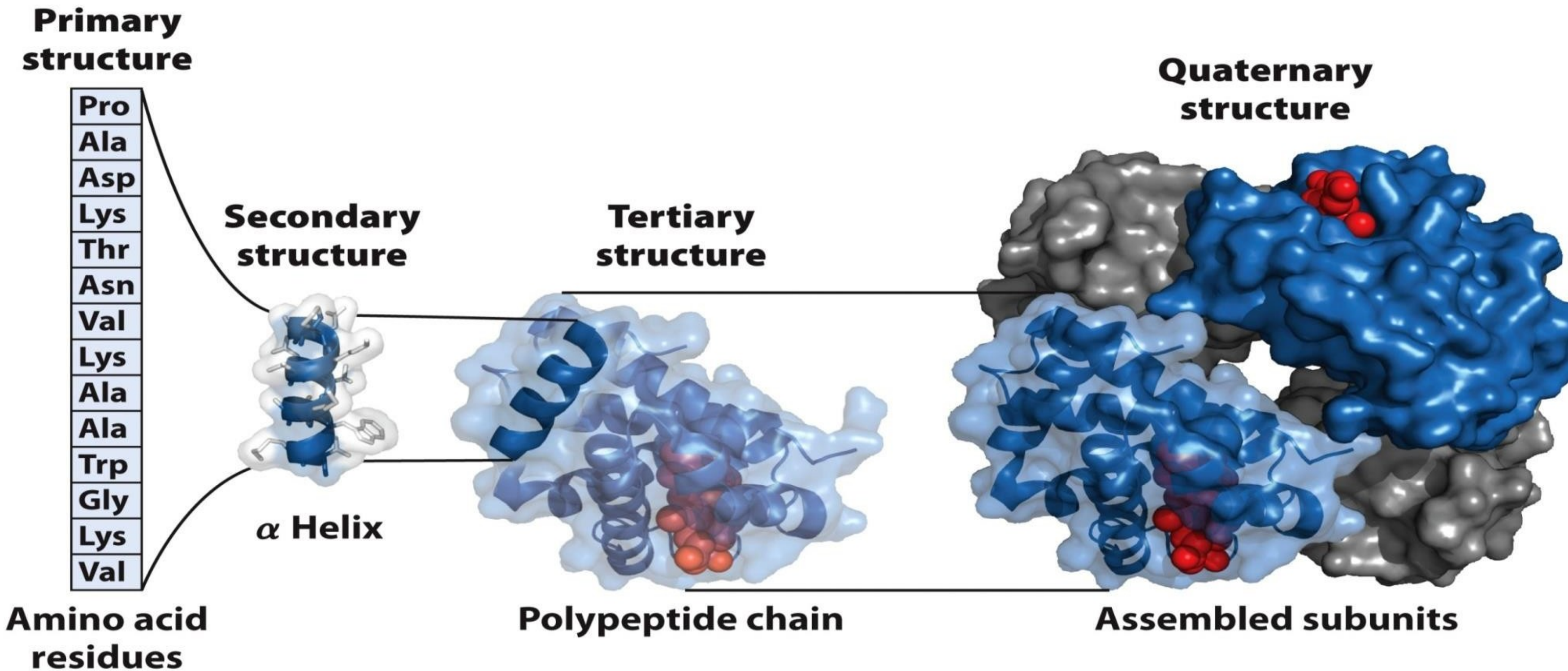


Figure 3-23
Lehninger Principles of Biochemistry, Sixth Edition

Proteins are made up of Amino Acids (building blocks for proteins)

Amino Acids

- Proteins make up more than 50 % of the dry mass of animals and bacteria, and perform important functions in living organisms.

- Essential amino acids: can not be synthesized by animals, so must be taken in diet. In humans such amino acids are 8, in other animals are 7.

- Non Essential Amino acids: Can be synthesized by animals, so may not be taken in diet

Structural Organization of Proteins

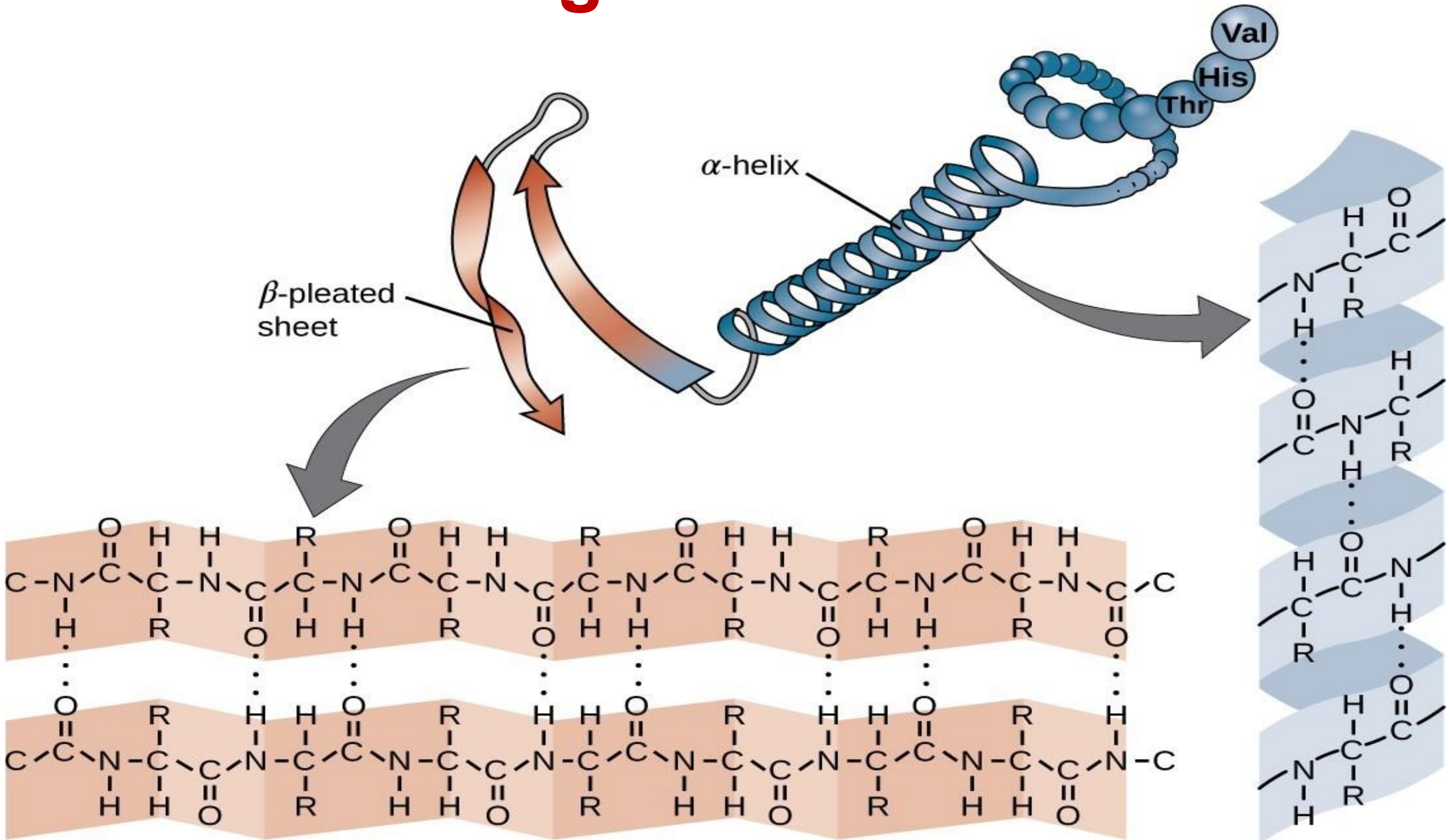
- **Primary Structure:** two dimensional, simple chain of AA with
  peptide (covalent) bond e.g. Insulin

- **Secondary Structure:** Various functional groups exposed on outer surface interact with hydrogen bonds
  α-helix – e.g. keratin, hair, fur, clans, hooves
  β-pleated – B. keratin of feathers, silk fibroin
  Collagen Helix: 3 α-helices coiled around one another

- **Tertiary Structure:** Additional bonds between functional groups, twisting of secondary structure, weak covalent and high energy disulphide bonds are formed e.g. Myoglobin

- **Quaternary Structure:** Formed as a result of 2-more polypeptide chain and have specific orientation

Structural Organization of Proteins



Different Types of Proteins

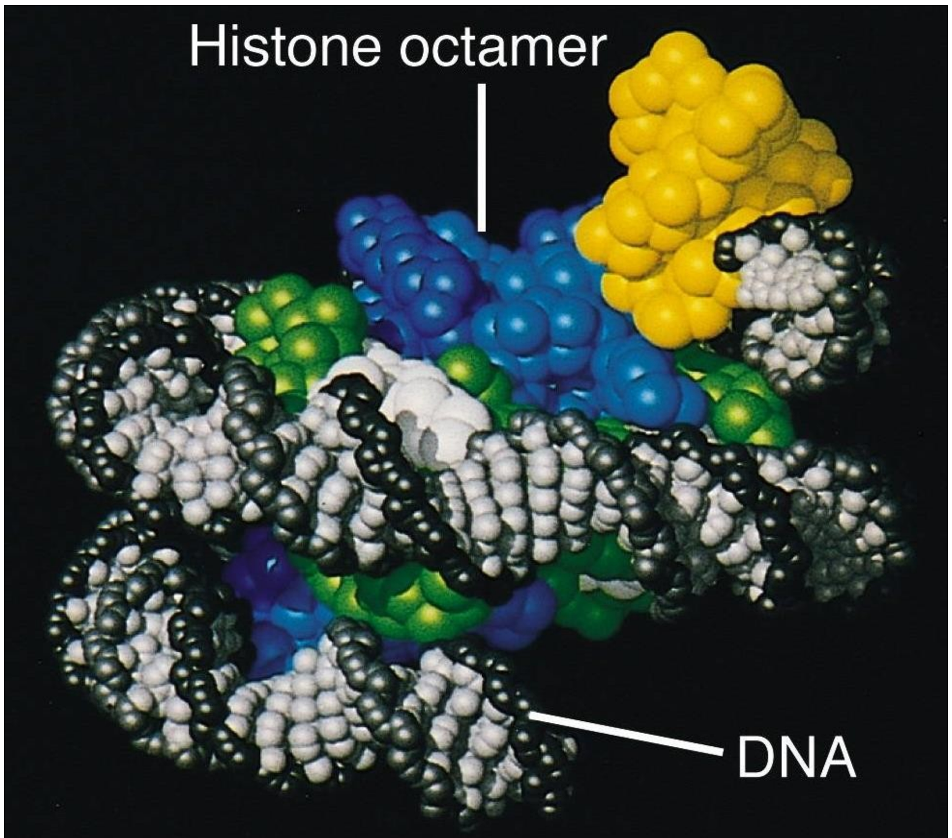
Types of proteins according to structure

1. **Fibrous** – collagen fibres, keratin, elastin, fibrin, fibroin, actin, myosin
2. **Globular** – glutelin, protemine, globulin, albumin, orygemin. glutenin,
3. **Intermediate** – myosin, fibrinogen

Types of proteins according to chemical nature

1. **Simple** – only AA. Albumin, globulin, protanine, fish, prolamine (corn, pl, wheat), histone (corn, wheat), glutelin (glutenin), keratin.
2. **Conjugated** – protein + non protein (prosthetic group) e.g. **Nucleoprotein** (nucleic acid), **chromoprotein** (Hb, cytochrome), **metallo** (with metals Zn, Fe), **lipoprotein**, **glycoprotein** etc.

Structural Proteins



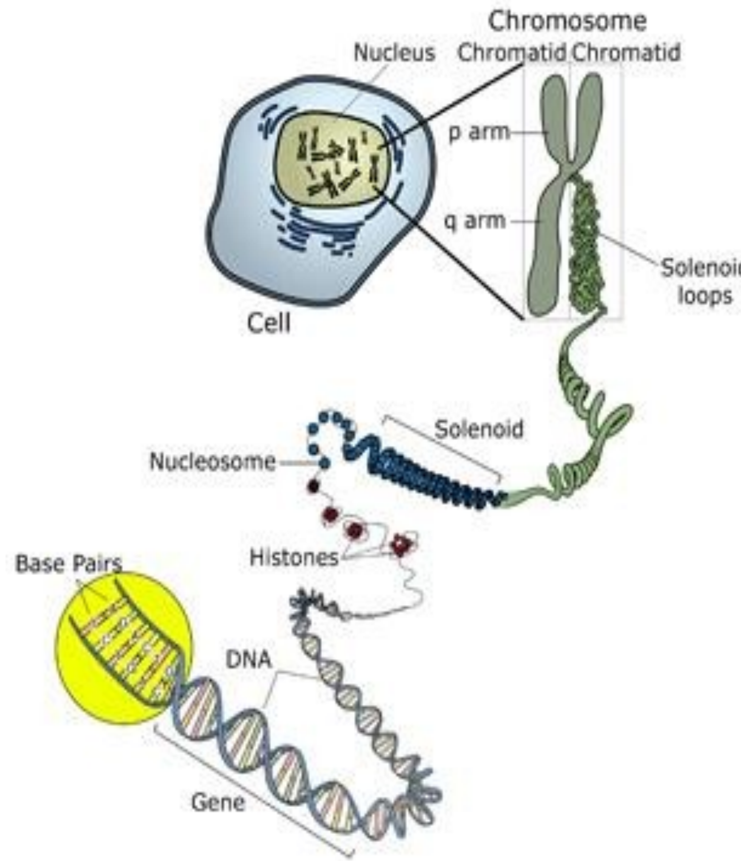
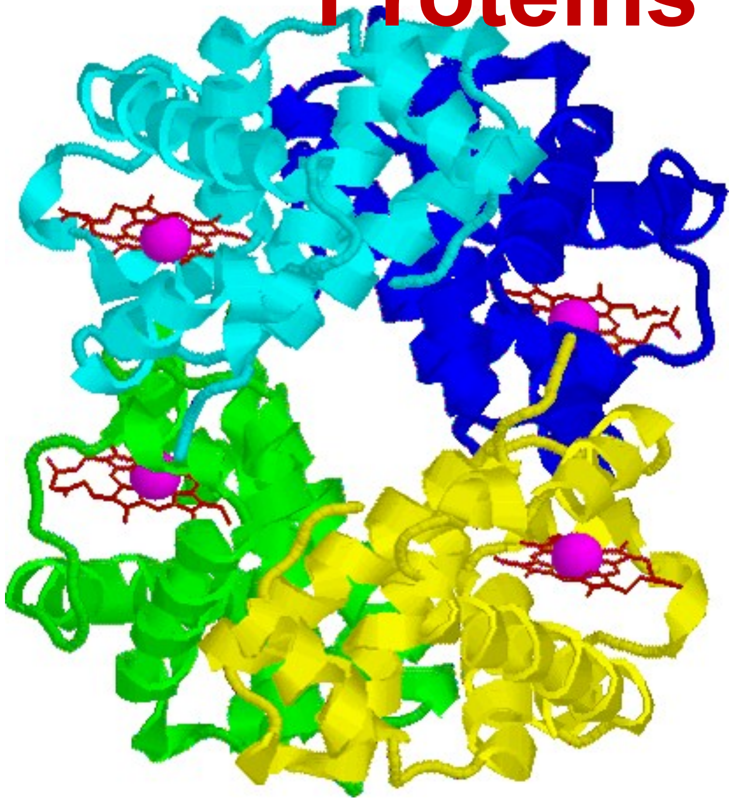
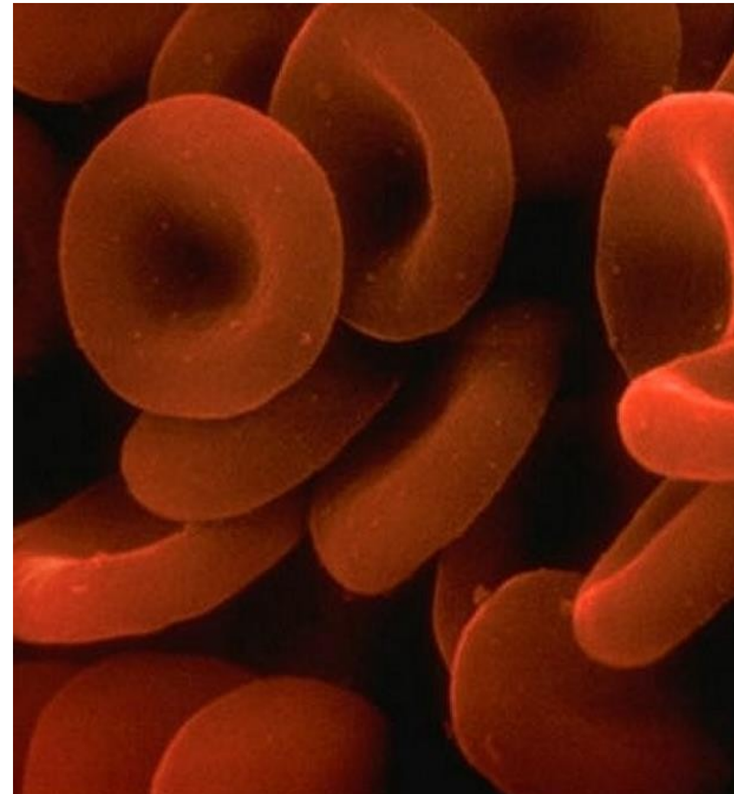


Image adapted from: National Human Genome Research Institute.

Transport Proteins

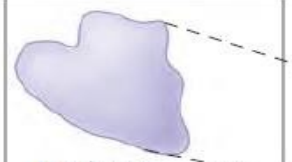
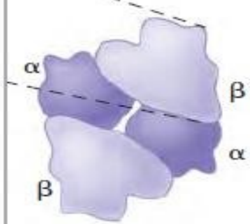
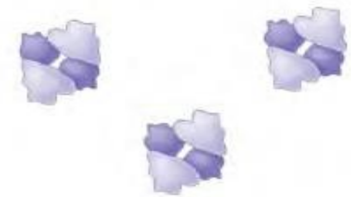
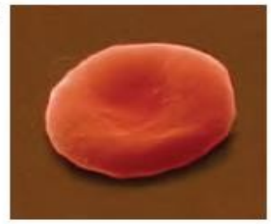
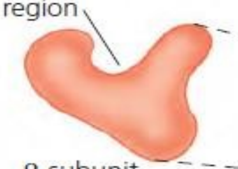
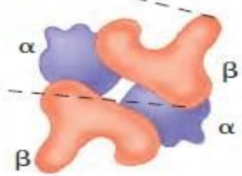
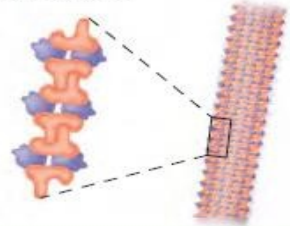


Hemoglobin



Red Blood Cell

Sickle-cell Anemia

	Primary Structure	Secondary and Tertiary Structures	Quaternary Structure	Function	Red Blood Cell Shape
Normal hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Glu 7 Glu	 	Normal hemoglobin  	Molecules do not associate with one another; each carries oxygen. 	Normal red blood cells are full of individual hemoglobin molecules, each carrying oxygen. 
Sickle-cell hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Val 7 Glu	Exposed hydrophobic region  	Sickle-cell hemoglobin  	Molecules interact with one another and crystallize into a fiber; capacity to carry oxygen is greatly reduced. 	Fibers of abnormal hemoglobin deform red blood cell into sickle shape. 

Sickle cell anemia

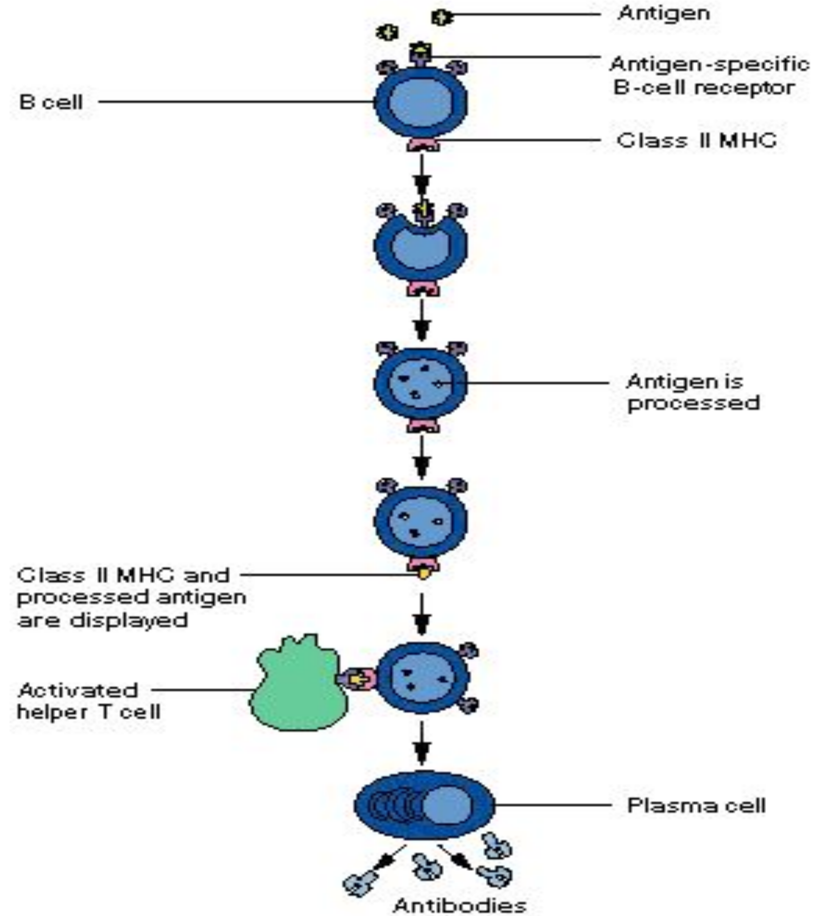
- Hemoglobin consists of four protein subunits, two subunits called alpha-globin and two subunits called beta-globin.
- .Various versions of beta-globin result from different mutations in the *HBB* gene. *HBB* gene mutations can also result in an unusually low level of beta-globin; this abnormality is called beta thalassemia.
- In people with sickle cell disease, at least one of the beta-globin subunits in hemoglobin is replaced with hemoglobin S.
- In sickle cell anemia (also called homozygous sickle cell disease), which is the most common form of sickle cell disease, hemoglobin S replaces both beta-globin subunits in hemoglobin.
- Abnormal versions of beta-globin can distort red blood cells into a sickle shape. The sickle-shaped red blood cells die prematurely, which can lead to anemia.
- Sometimes the inflexible, sickle-shaped cells get stuck in small blood vessels and can cause serious medical complications

Humoral immune response

1. B lymphocytes recognize specific antigens proliferate and differentiate into antibody-secreting plasma cells

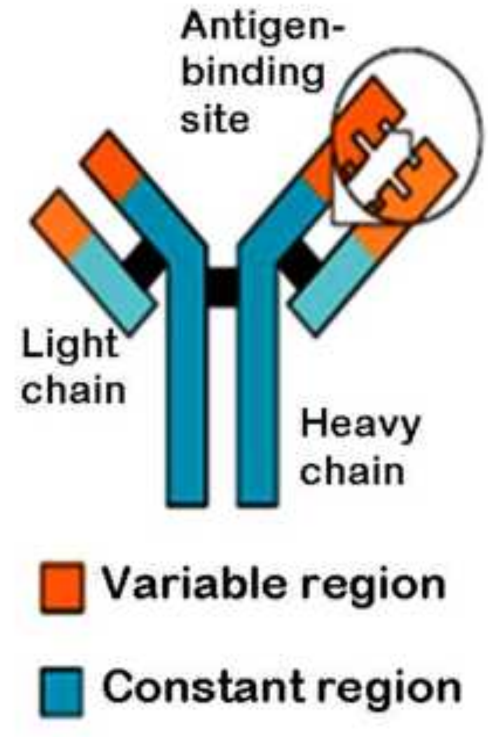
2. Antibodies bind to specific antigens on microbes; destroy microbes via specific mechanisms

3. Some B lymphocytes evolve into the resting state - memory cells

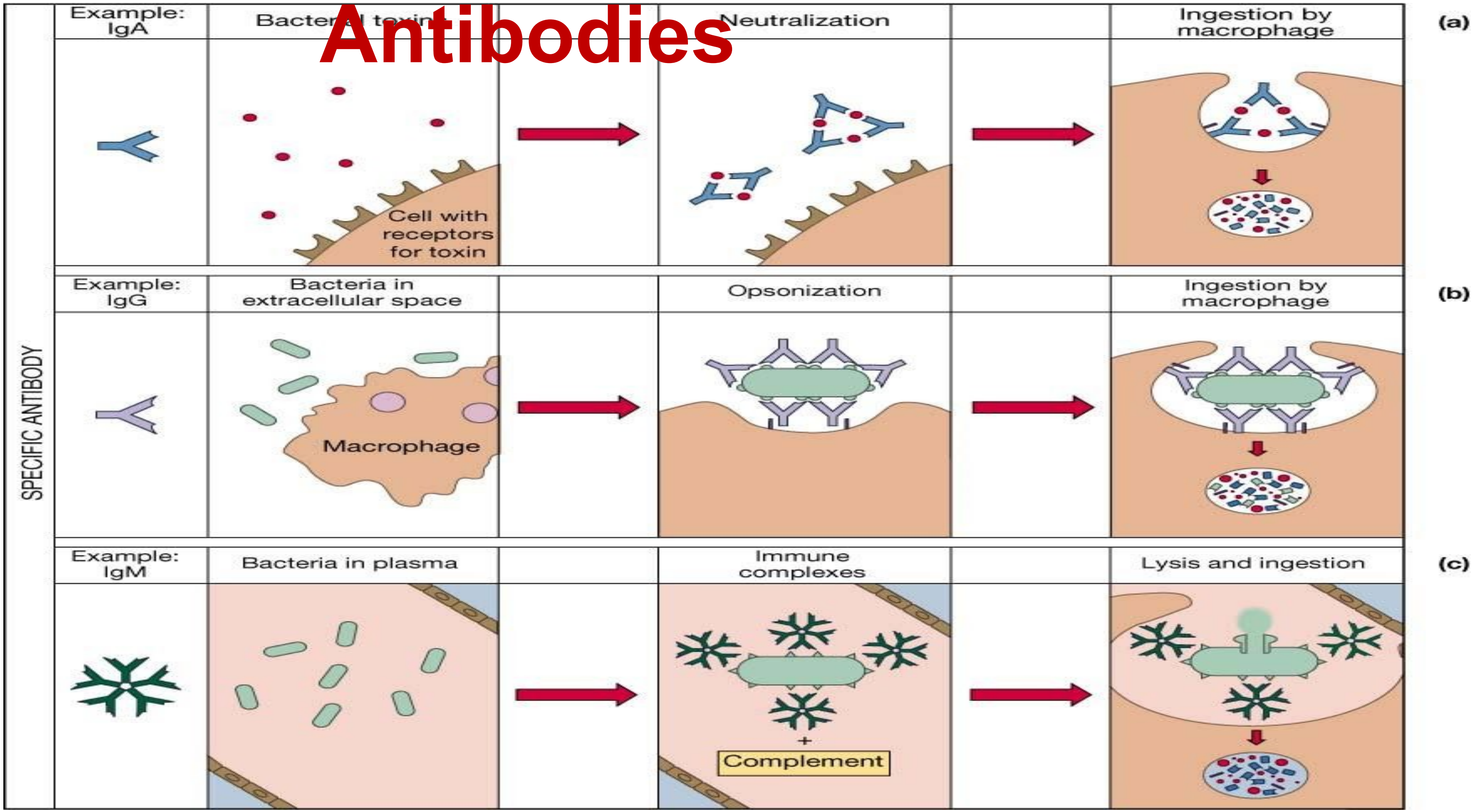


Antibodies (immunoglobulins)

- Belong to the gamma-globulin fraction of serum proteins
- Y-shaped or T-shaped polypeptides
  - 2 identical heavy chains
  - 2 identical light chains
- All immunoglobulins are not antibodies
- Five kinds of antibodies
  - IgG, IgM, IgA, IgD, IgE



Immunity: Antibodies



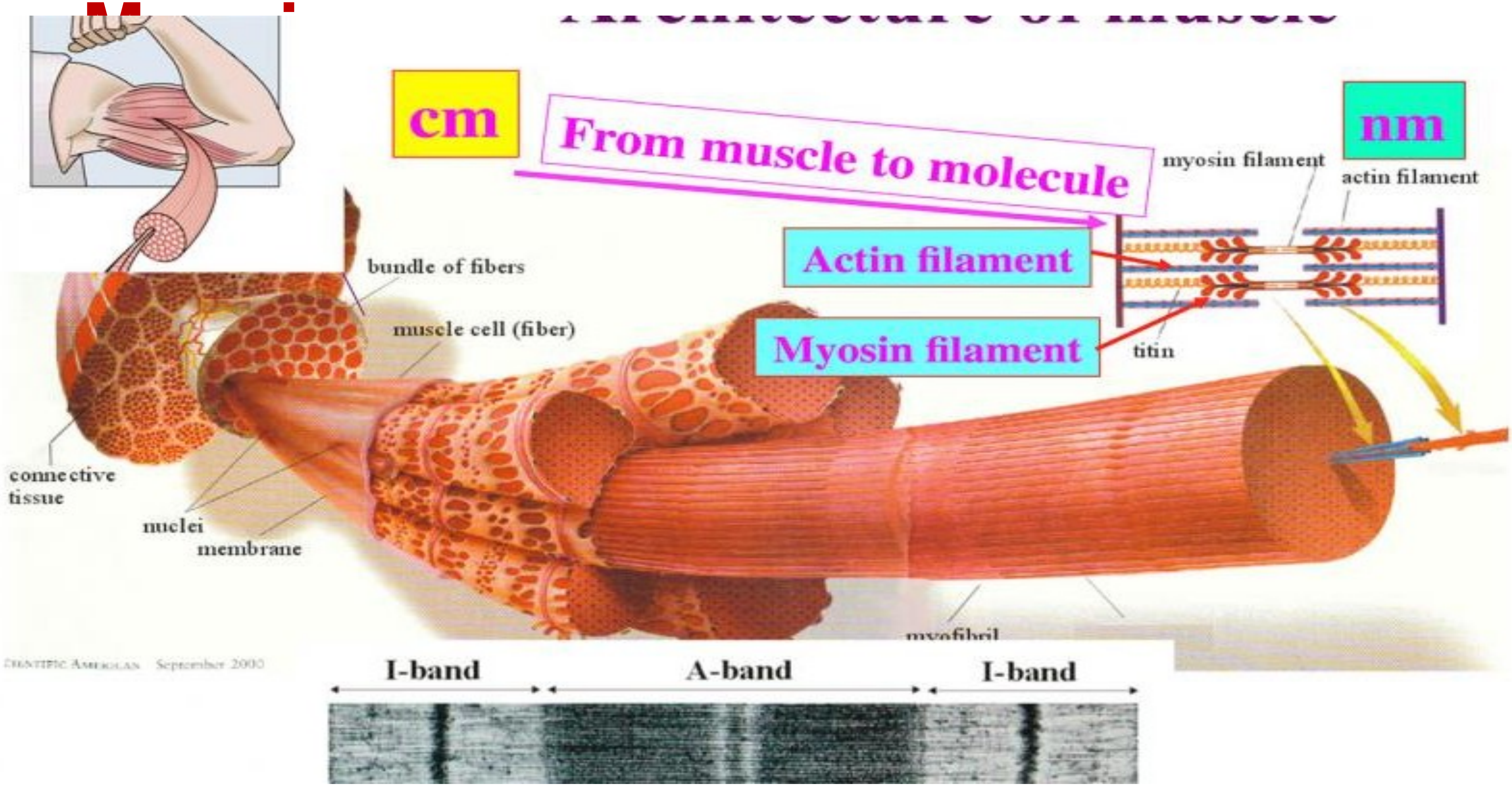
Major antibody types

- **IgA** protects the host by diversifying the microbiota, neutralizing toxins and viruses, blocking colonization and penetration of pathogenic bacteria

- **IgG**. Immunoglobulin G is the predominant Ig in the serum; Its concentration in tissue fluids is increased during inflammation. It is particularly effective at the neutralization of bacterial exotoxins and viruses. It also has opsonizing ability and complement-fixing ability. IgG crosses the placental barrier, and thereby provides passive immunity to the fetus and infant for the first six months of life.

- **IgM** is the first immunoglobulin to be synthesized by infants and the first to appear in the blood stream during the course of an infection. IgM is arranged to resemble a pentamer of five immunoglobulin molecules (mw = 900kDa) tethered together at by their Fc domains

Contractile Function: Actin & Myosin



Muscle structure

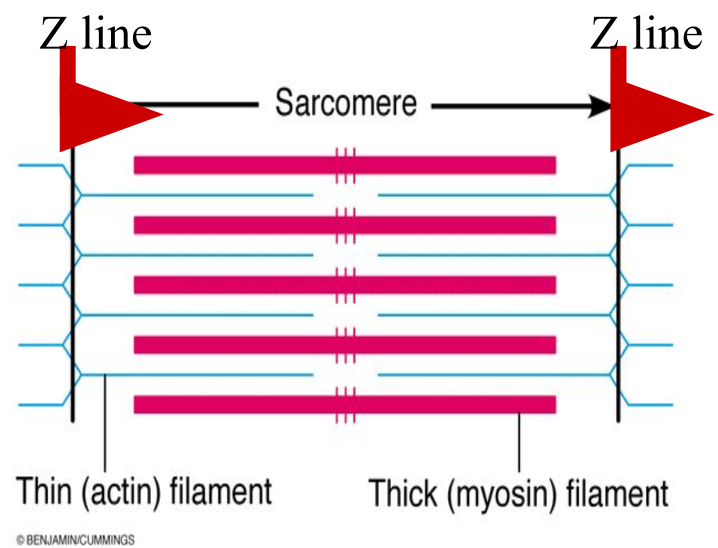
- Mitochondria are abundant in muscle tissue

Myofibrils: contractile element of the skeletal muscle fibers.

  -2 µm in diameter
  -have prominent striations (stripes
  -composed of filaments.

The diameter of the THIN FILAMENTS is about 8 nm (thin filaments) and the THICK FILAMENTS 16 nm

-Filaments are arranged in small compartments known as sarcomeres.



Sarcomeres are the basic functional unit of the microfibril.

-Z discs are narrow plate-shaped regions of dense material that separate sarcomeres from each other.

Mechanism of muscle contraction

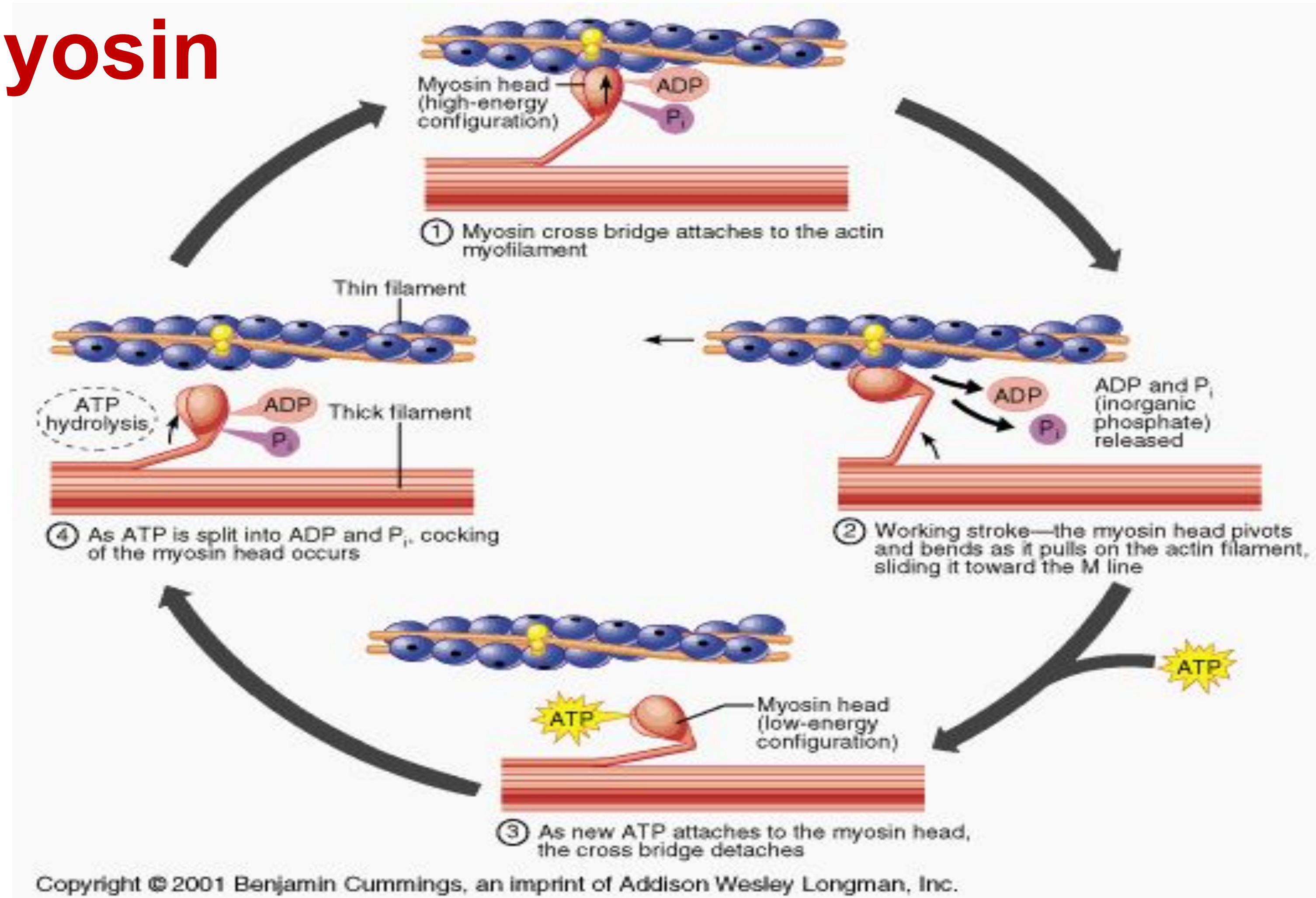
-Thick and thin filaments overlap one another to varying degrees.

-This is dependent on whether the muscle is contracted, relaxed or stretched.

-The pattern of this overlap, that consists of a variety of zones and bands creates the striations that are characteristic of skeletal muscle.

-Elastic component in muscles include titin molecules, connective tissue around muscle fibers (endomysium, perimysium and epimysium, as well as tendons.

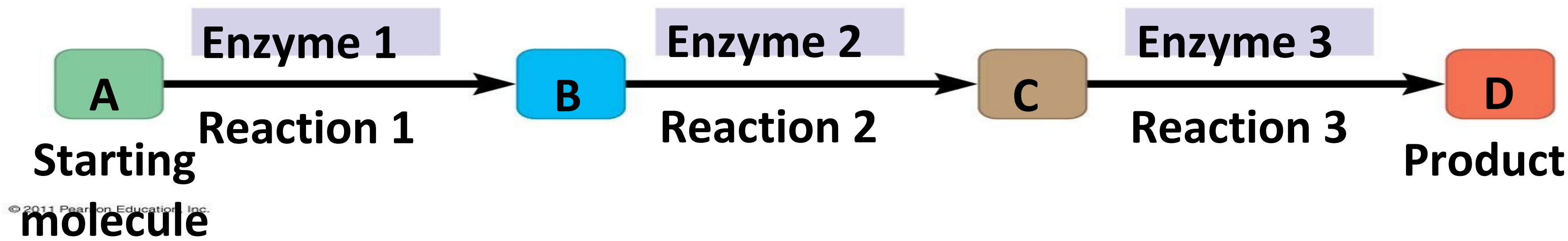
Contractile Function: Actin & Myosin



Metabolism

- **Metabolism** is the totality of an organism's chemical reactions
- Metabolism is an emergent property of life that arises from interactions between molecules within the cell
- An organism's metabolism transforms matter and energy, subject to the laws of thermodynamics

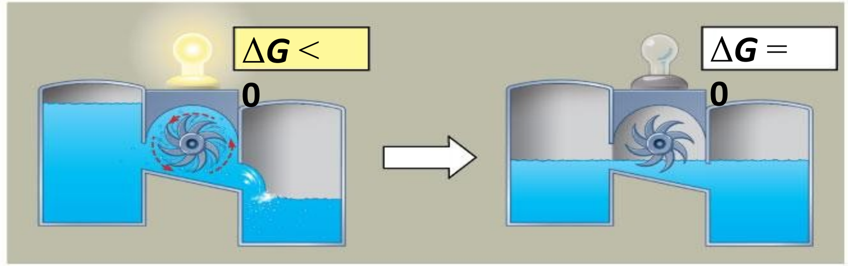
Metabolism



- A **metabolic pathway** begins with a specific molecule and ends with a product

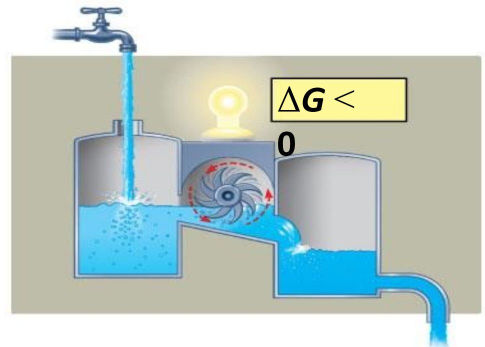
  - All metabolic pathways occur step-wise manner

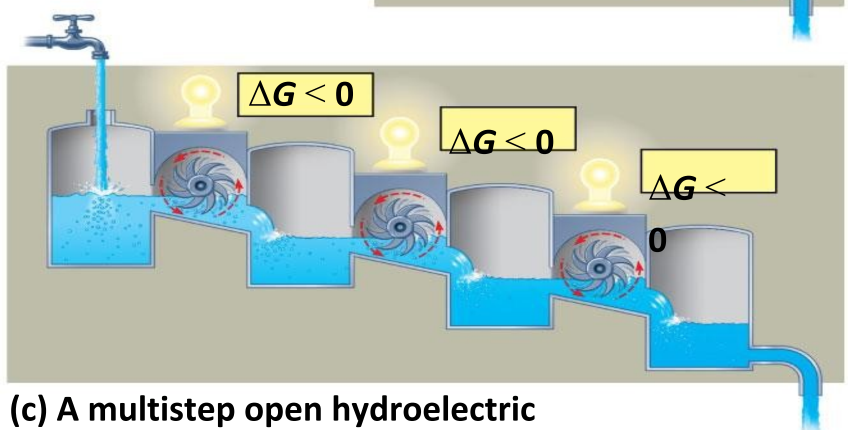
  - Each step is catalyzed by a specific enzyme



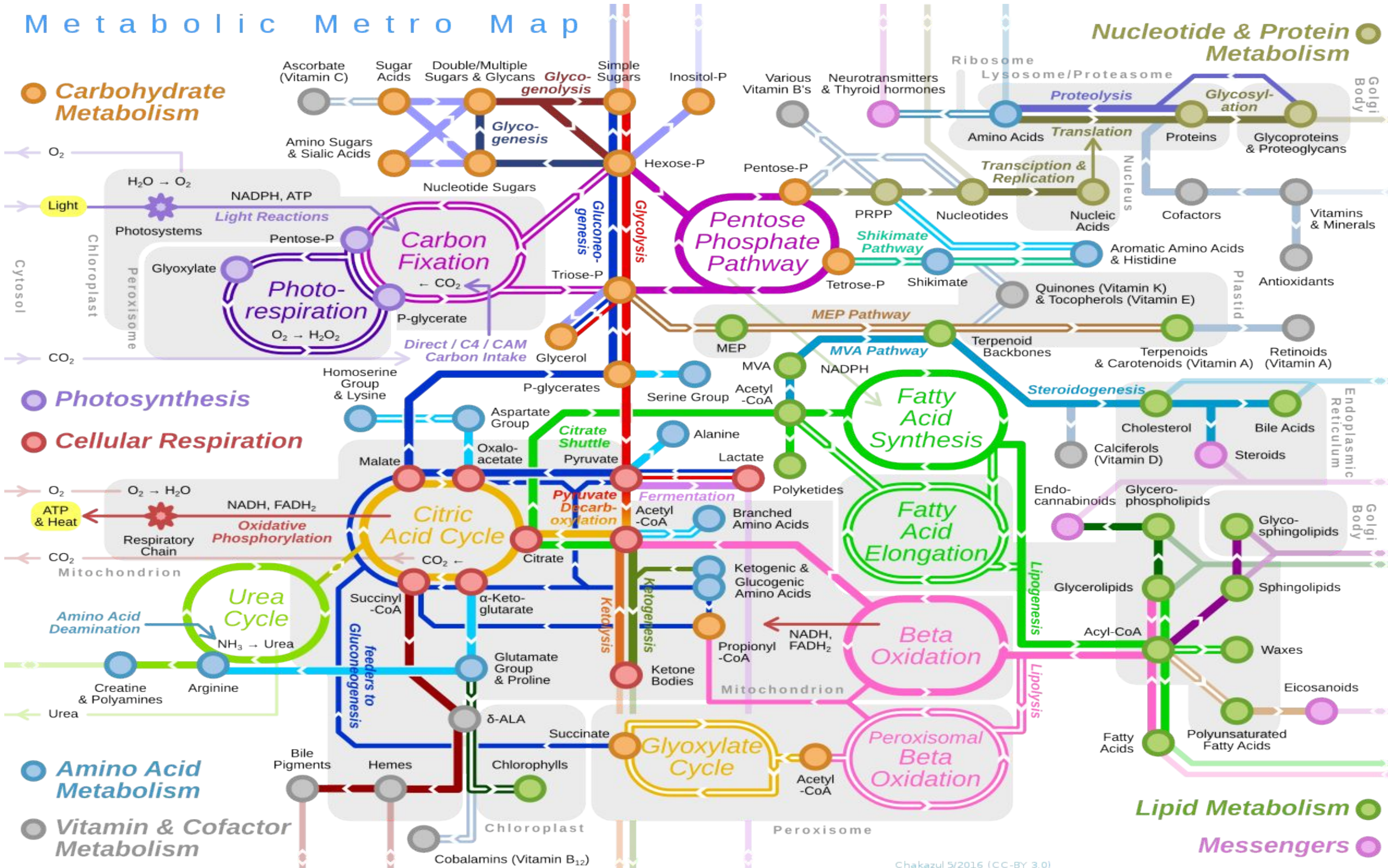
(a) An isolated hydroelectric system

(b) An open hydro- electric system

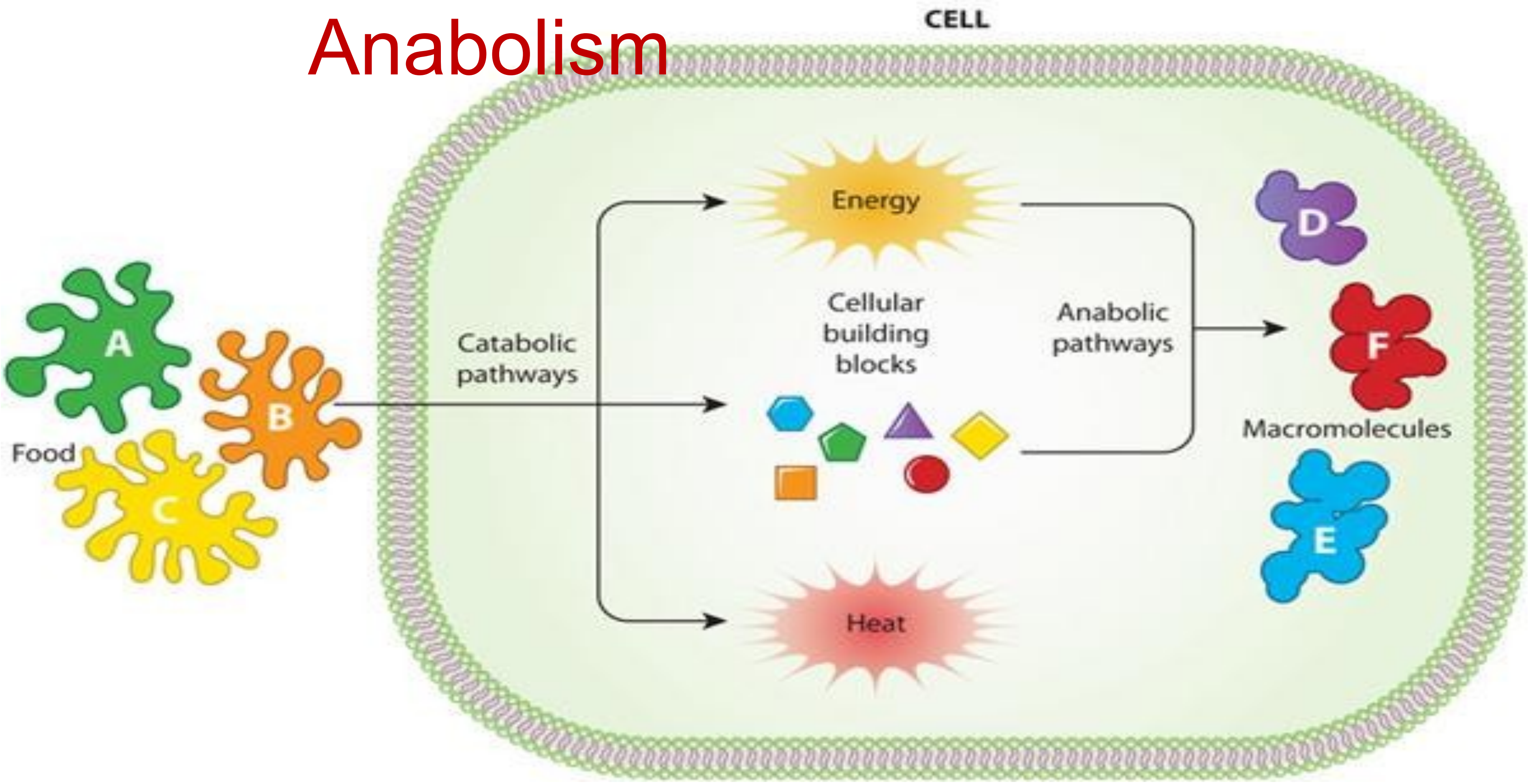




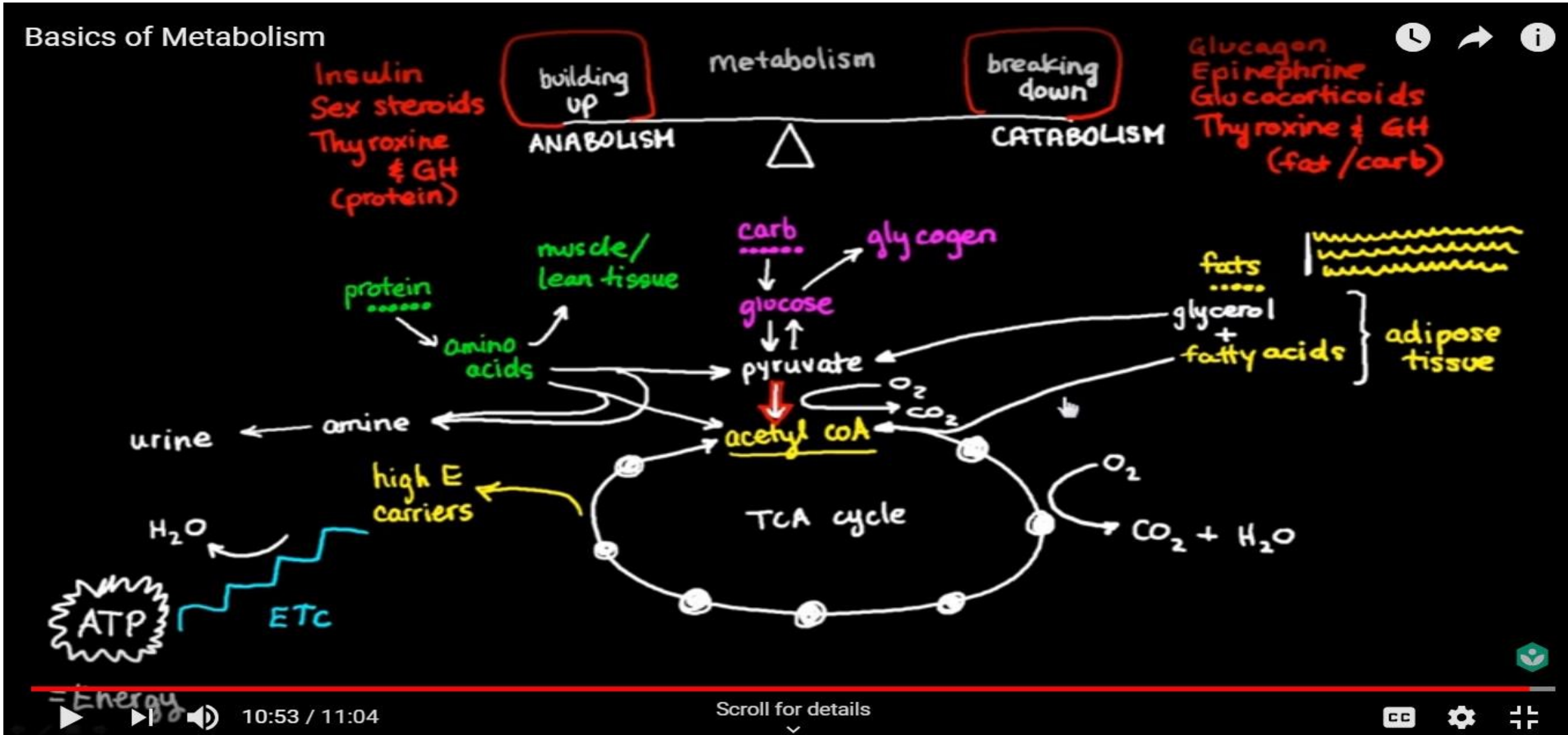
(c) A multistep open hydroelectric system


Metabolic Metro Map
Carbohydrate Metabolism
Photosynthesis
Cellular Respiration
Amino Acid Metabolism
Vitamin & Cofactor Metabolism
Nucleotide & Protein Metabolism
Lipid Metabolism
Messengers
Ascorbate (Vitamin C)
Sugar Acids
Double/Multiple Sugars & Glycans
Glyco-genolysis
Simple Sugars
Inositol-P
Amino Sugars & Sialic Acids
Glyco-genesis
Nucleotide Sugars
Hexose-P
O_2
$H_2O \rightarrow O_2$
Light
NADPH, ATP
Photosystems
Light Reactions
Pentose-P
Carbon Fixation
Glyoxylate
Photo-respiration
$\leftarrow CO_2$
P-glycerate
$O_2 \rightarrow H_2O_2$
Cytosol
Chloroplast
Peroxisome
CO_2
Direct / C4 / CAM Carbon Intake
Glycerol
Triose-P
Gluconeo-genesis
Glycolysis
Pentose Phosphate Pathway
Pentose-P
PRPP
Nucleotides
Nucleic Acids
Transciption & Replication
Various Vitamin B's
Neurotransmitters & Thyroid hormones
Ribosome
Lysosome/Proteasome
Proteolysis
Glycosyl-ation
Golgi Body
Amino Acids
Translation
Proteins
Glycoproteins & Proteoglycans
Nucleus
Cofactors
Vitamins & Minerals
Antioxidants
Shikimate Pathway
Aromatic Amino Acids & Histidine
Tetrose-P
Shikimate
Quinones (Vitamin K) & Tocopherols (Vitamin E)
Plastid
MEP Pathway
MEP
Terpenoid Backbones
Terpenoids & Carotenoids (Vitamin A)
Retinoids (Vitamin A)
MVA
MVA Pathway
NADPH
Homoserine Group & Lysine
P-glycerates
Serine Group
Acetyl -CoA
Fatty Acid Synthesis
Steroidogenesis
Cholesterol
Bile Acids
Calciferols (Vitamin D)
Steroids
Endoplasmic Reticulum
Aspartate Group
Citrate Shuttle
Alanine
Malate
Oxalo-acetate
Pyruvate
Lactate
Polyketides
Pyruvate Decarb-oxylation
Fermentation
Acetyl -CoA
Branched Amino Acids
Fatty Acid Elongation
Endo-cannabinoids
Glycero-phospholipids
Glyco-sphingolipids
Golgi Body
O_2
$O_2 \rightarrow H_2O$
NADH, $FADH_2$
ATP & Heat
Respiratory Chain
Oxidative Phosphorylation
Citric Acid Cycle
Citrate
CO_2
$CO_2 \leftarrow$
Mitochondrion
Urea Cycle
Amino Acid Deamination
$NH_3 \rightarrow$ Urea
Succinyl -CoA
α-Keto-glutarate
Ketolysis
Ketogenesis
Ketogenic & Glucogenic Amino Acids
Lipogenesis
Glycerolipids
Sphingolipids
Propionyl -CoA
NADH, $FADH_2$
Beta Oxidation
Acyl-CoA
Waxes
Creatine & Polyamines
Arginine
Glutamate Group & Proline
Ketone Bodies
Mitochondrion
Lipolysis
Eicosanoids
feeders to Gluconeogenesis
Urea
δ-ALA
Succinate
Glyoxylate Cycle
Acetyl -CoA
Peroxisomal Beta Oxidation
Fatty Acids
Polyunsaturated Fatty Acids
Bile Pigments
Hemes
Chlorophylls
Chloroplast
Peroxisome
Cobalamins (Vitamin B_{12})
Chakazul 5/2016 (CC-BY 3.0)

Catabolism and Anabolism



Metabolism in



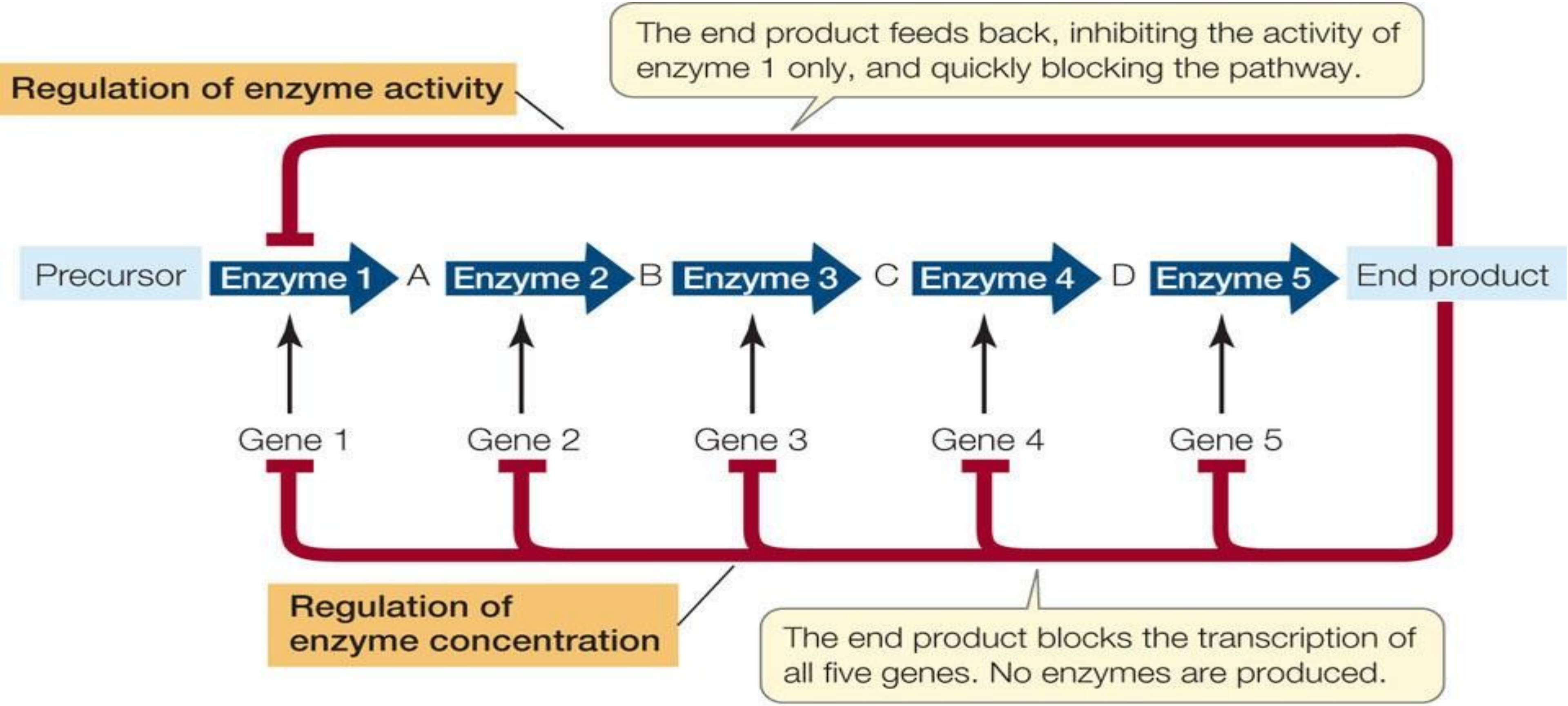
https://www.youtube.com/watch?v=wQ1QGZ6gJ8w

Regulation of Metabolism

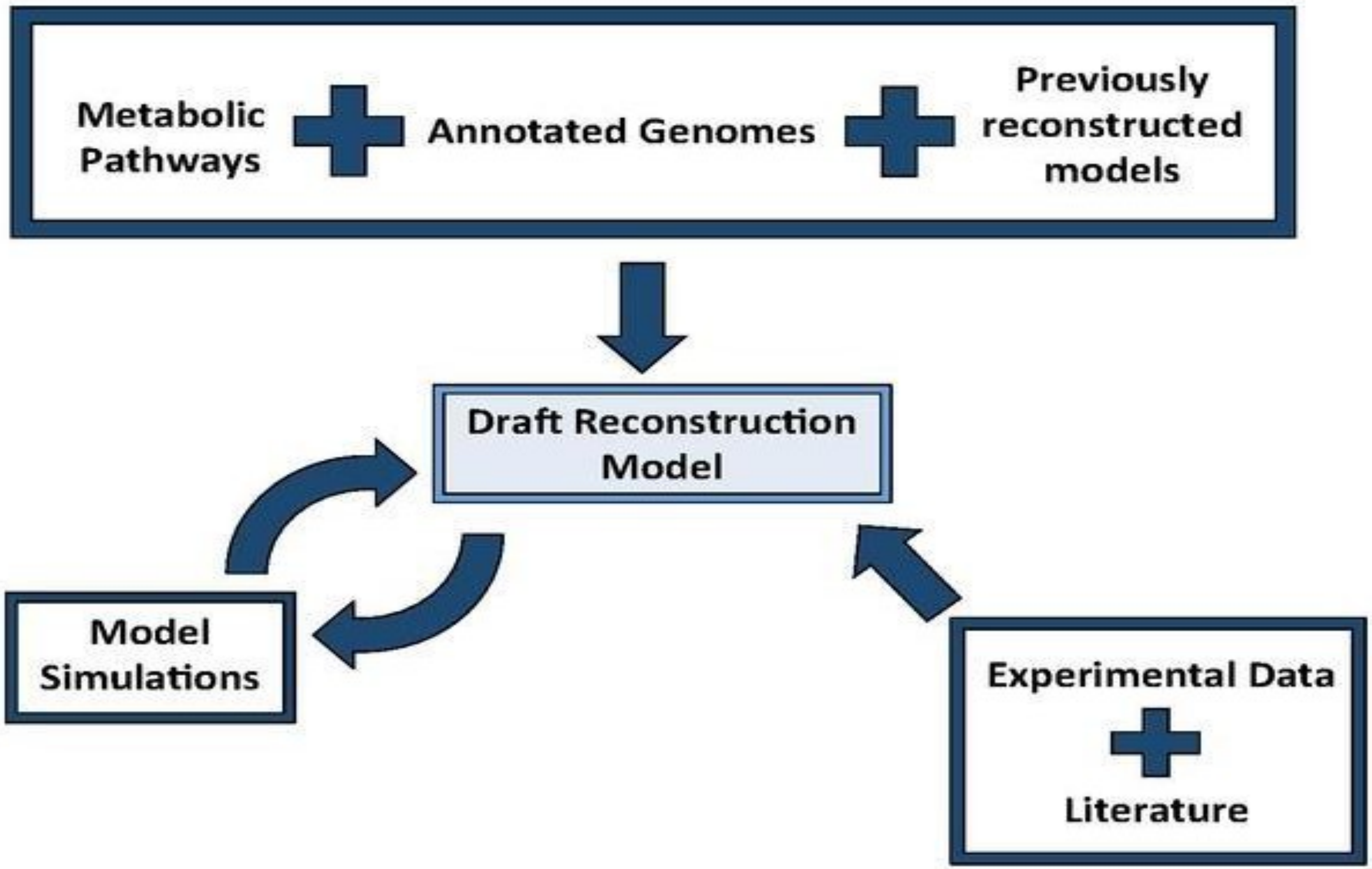
- **Rate Limiting Step: Slowest step; beginning of the pathway**
  - **Covalent and Non-covalent modifications**
- **Metabolic flux is regulated by** the Stoichiometric Reaction Model*, the utilization rate of metabolites, and the translocation pace of molecules across the lipid bilayer

*Law of conservation of mass = Matter is not created or destroyed in a chemical reaction

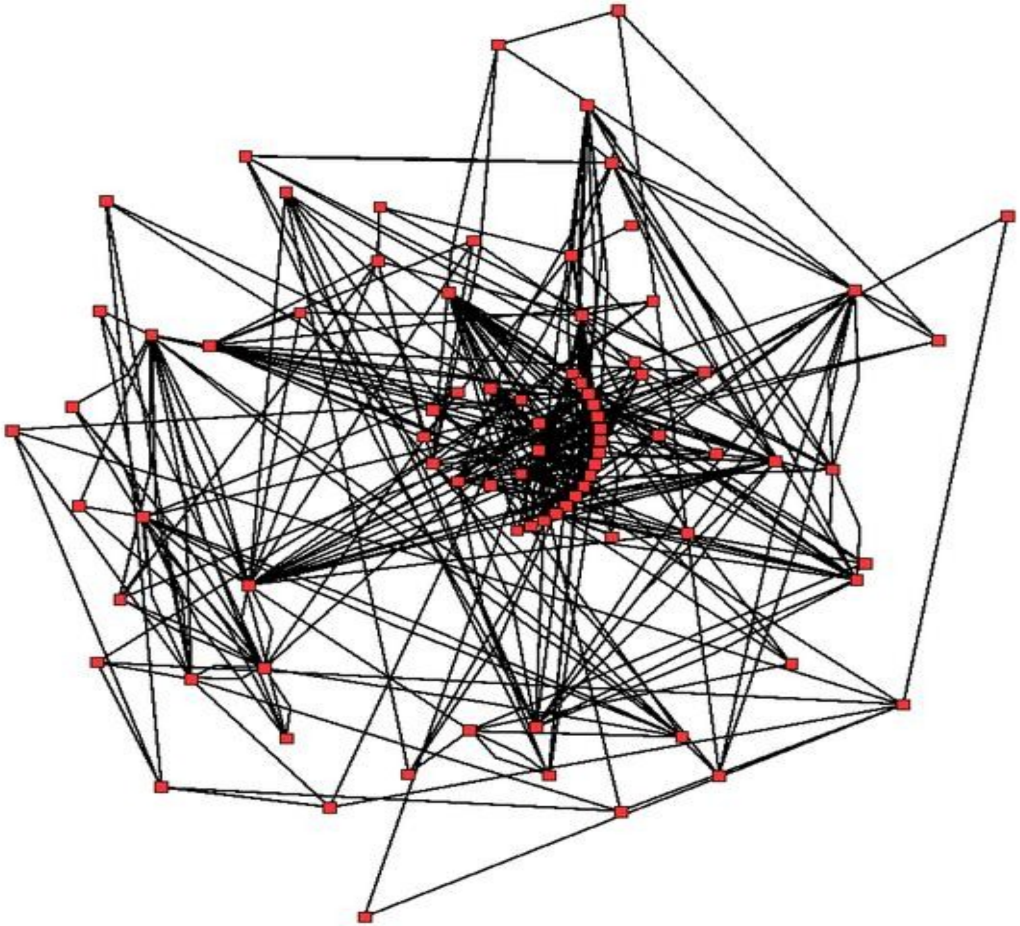
Regulation of Metabolism

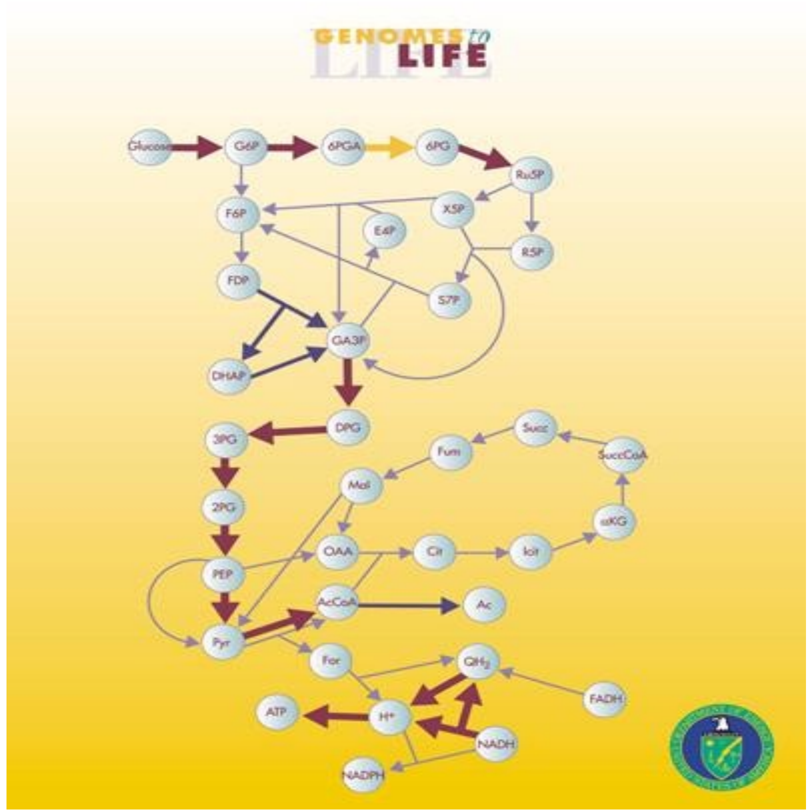


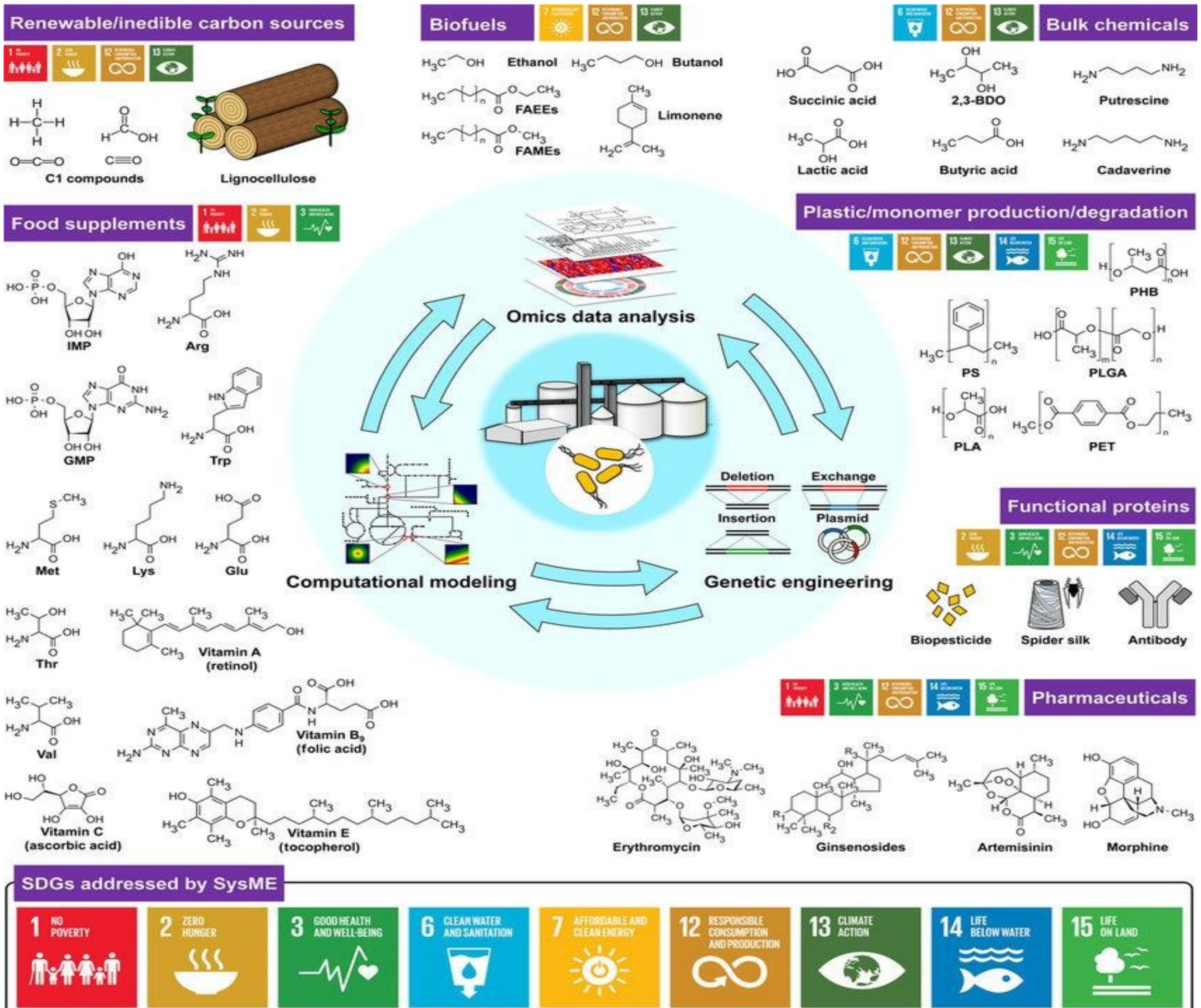
Metabolic Network Modeling



Metabolic Network Modeling







Metabolic Engineering

Biology

UOB1001A

Module 2

Physics in Biology (Part 1)

Thermodynamics

IMPORTANT PHYSICAL PRINCIPLES

1. There are places with higher potential and places with lower potential. Things move from higher to lower potential. "Potential" is a word used to describe the tendency of something to move

2. *The maintenance of order requires energy*. Living things are highly ordered instead of random. As a consequence, living things require constant expenditure of energy.

3. *What goes in but doesn't come out is stored inside*.

4. *Different forms of energy can be used to perform mechanical work*.

5. The transfer of something from one place to another depends directly on the surface area and is inversely proportional to the distance between the two places. No matter whether the "something" is heat, mass, electrical current, or something else, BU must deal with the constraints imposed by geometry

IMPORTANT PHYSICAL PRINCIPLES

6 *Mechanical strength depends on geometrical configuration, the amount of material present, and the properties of the material*.

7. *Unbalanced mechanical forces cause acceleration*. If there are no net forces, then a body in motion continues to remain in motion and a body at rest stays at rest.

8. *Heat is the ultimate nonspecific form of energy*. Low grade waste heat is useless to perform any kind of work

9. *Hydrostatic pressures are equal in all directions*. Strong walls are unnecessary if hydrostatic pressures are equal on both sides. Pressure can distort objects or may support them.

10. *Flowing fluids require energy to overcome resistance*. Fluid movement is important in biological systems to supply oxygen, nutrients, and control chemicals, and to remove wastes. The capacity of the heart to move these fluids depends mostly on the ability to overcome resistance.

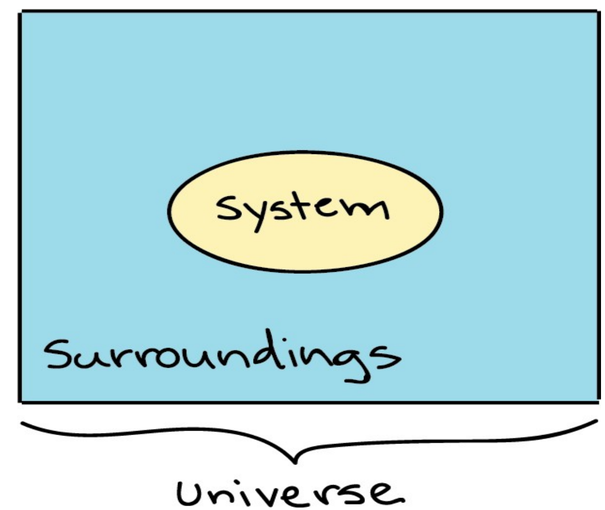
The Laws of Energy Transformation

- Thermodynamics is the study of energy transformations

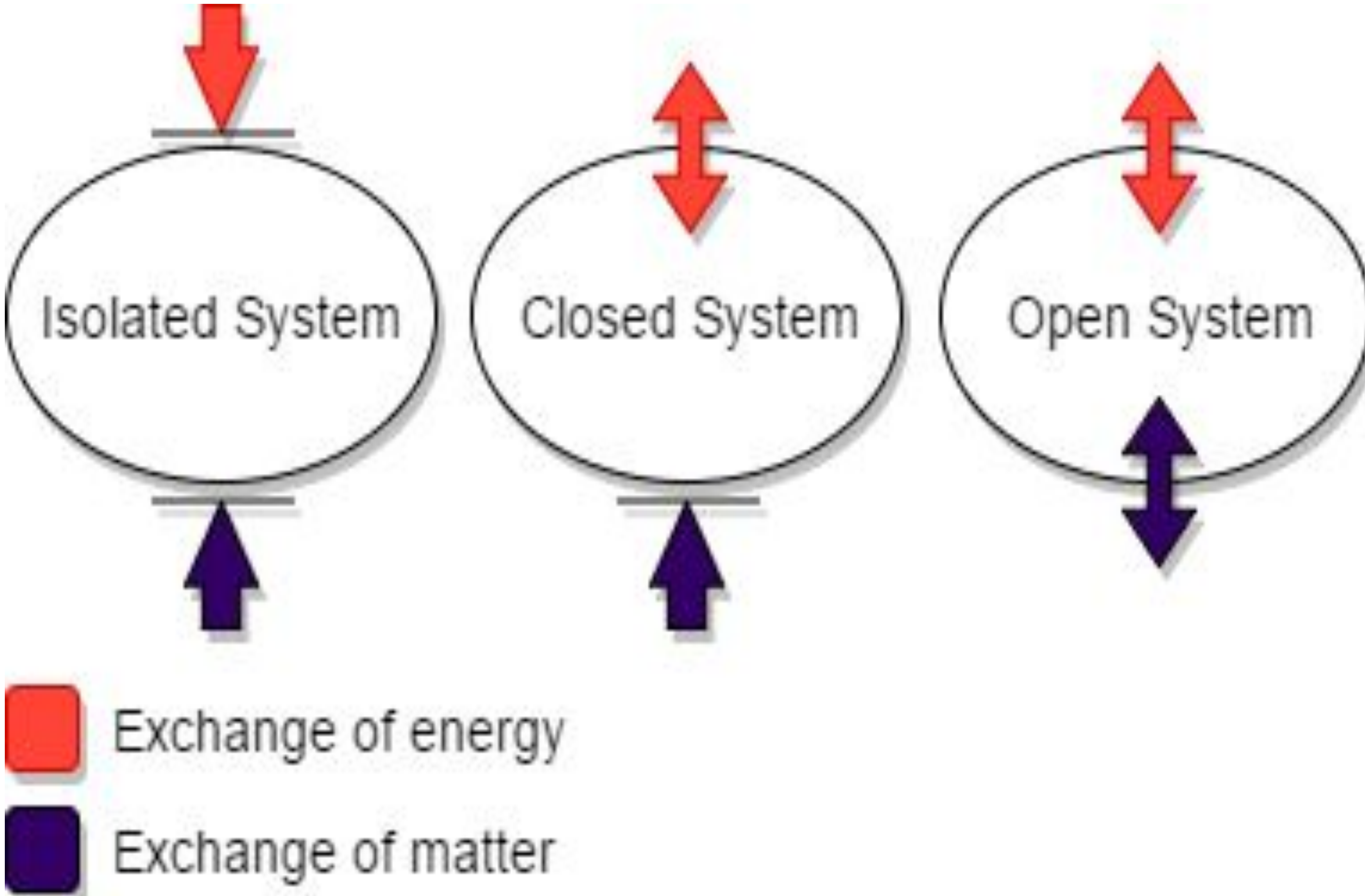
- A isolated system, such as that approximated by liquid in a thermos, is isolated from its surroundings

- In an open system, energy and matter can be transferred between the system and its surroundings

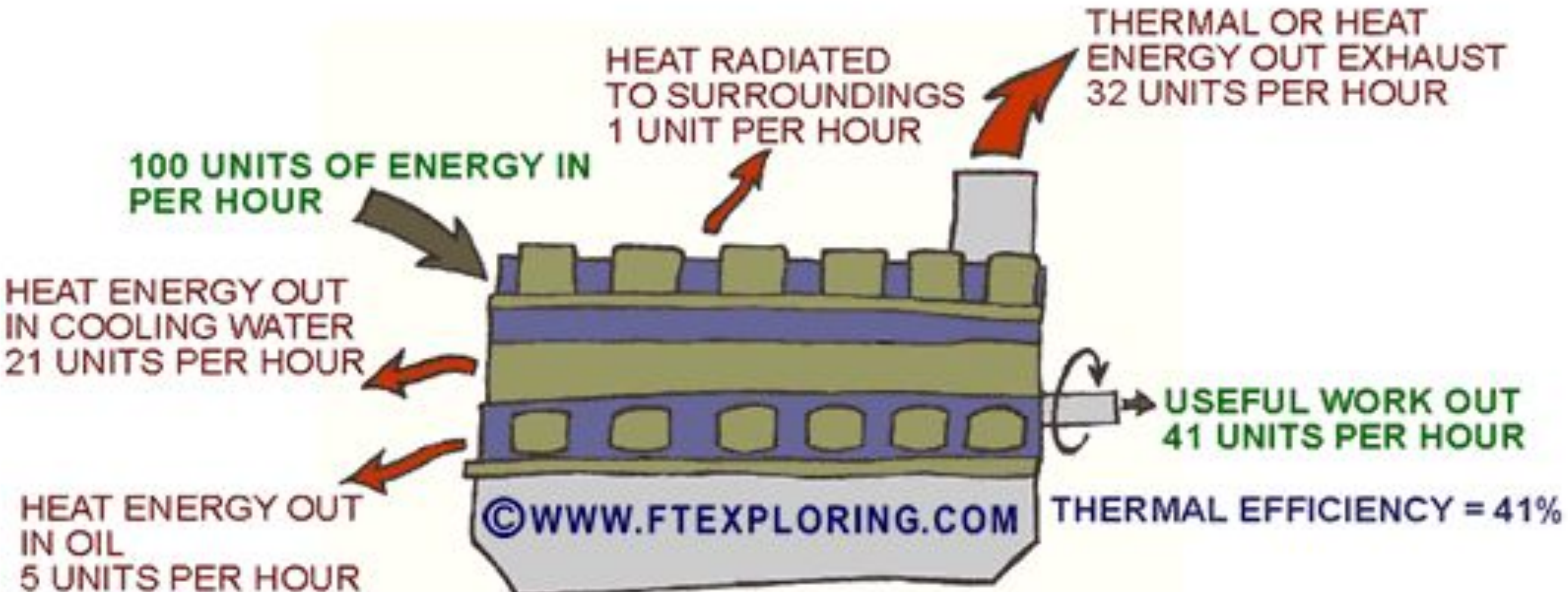
- Organisms are open systems



Types of Systems



ENERGY BALANCE IN A BIG EFFICIENT DIESEL ENGINE



100 UNITS OF FUEL POTENTIAL ENERGY INTO ENGINE

100 UNITS OF MECHANICAL & THERMAL ENERGY OUT OF ENGINE

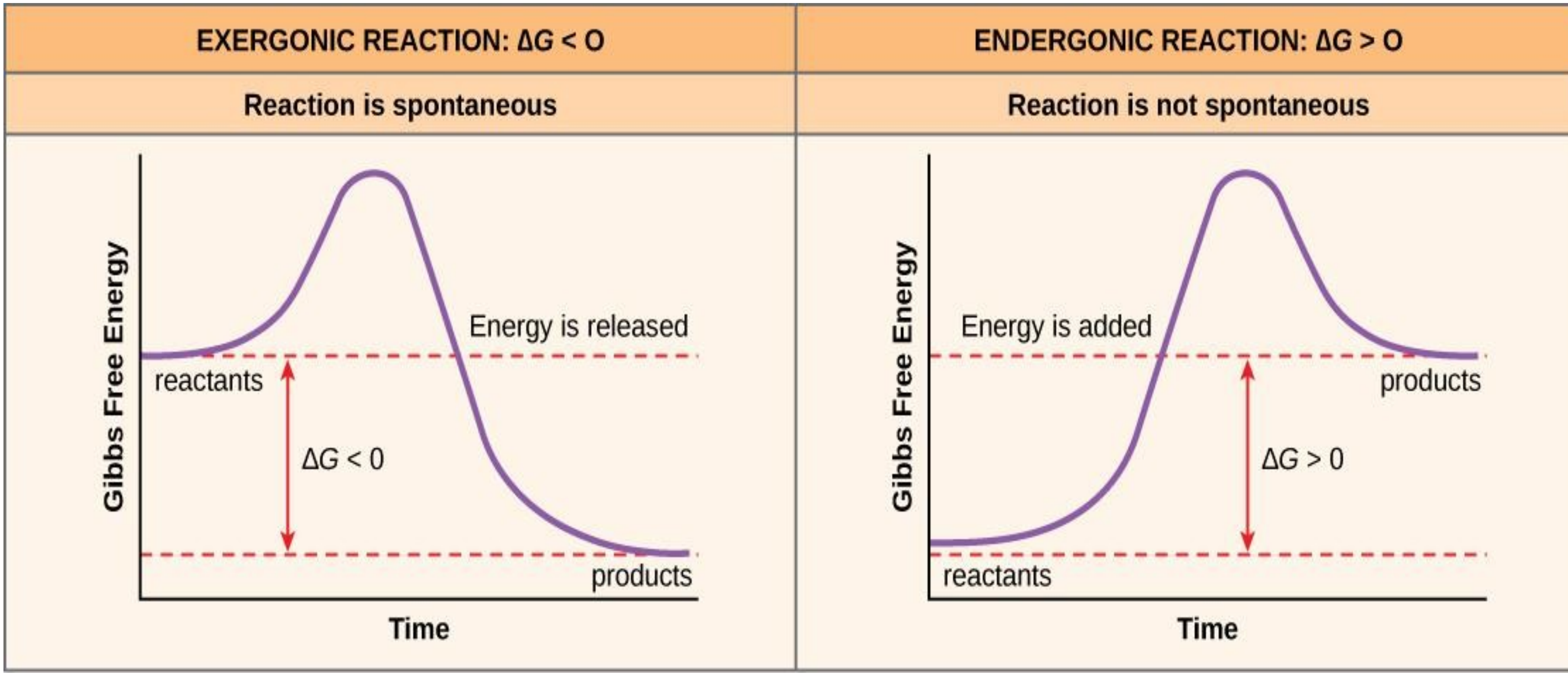
THE CHEMICAL ENERGY STORED IN THE FUEL IS CONVERTED TO MECHANICAL ENERGY AND THERMAL ENERGY. THE TOTAL MECHANICAL ENERGY AND THERMAL (HEAT) ENERGY OUT MUST EQUAL THE ENERGY AVAILABLE IN THE FUEL - FIRST LAW OF THERMODYNAMICS.

Gibbs free energy, G, expresses the amount of energy capable of doing work during a reaction at constant temperature and pressure. When a reaction proceeds with the release of free energy (that is, when the system changes so as to possess less free energy), the free-energy change, ΔG, has a negative value and the reaction is said to be exergonic. In endergonic reactions, the system gains free energy and ΔG is positive.

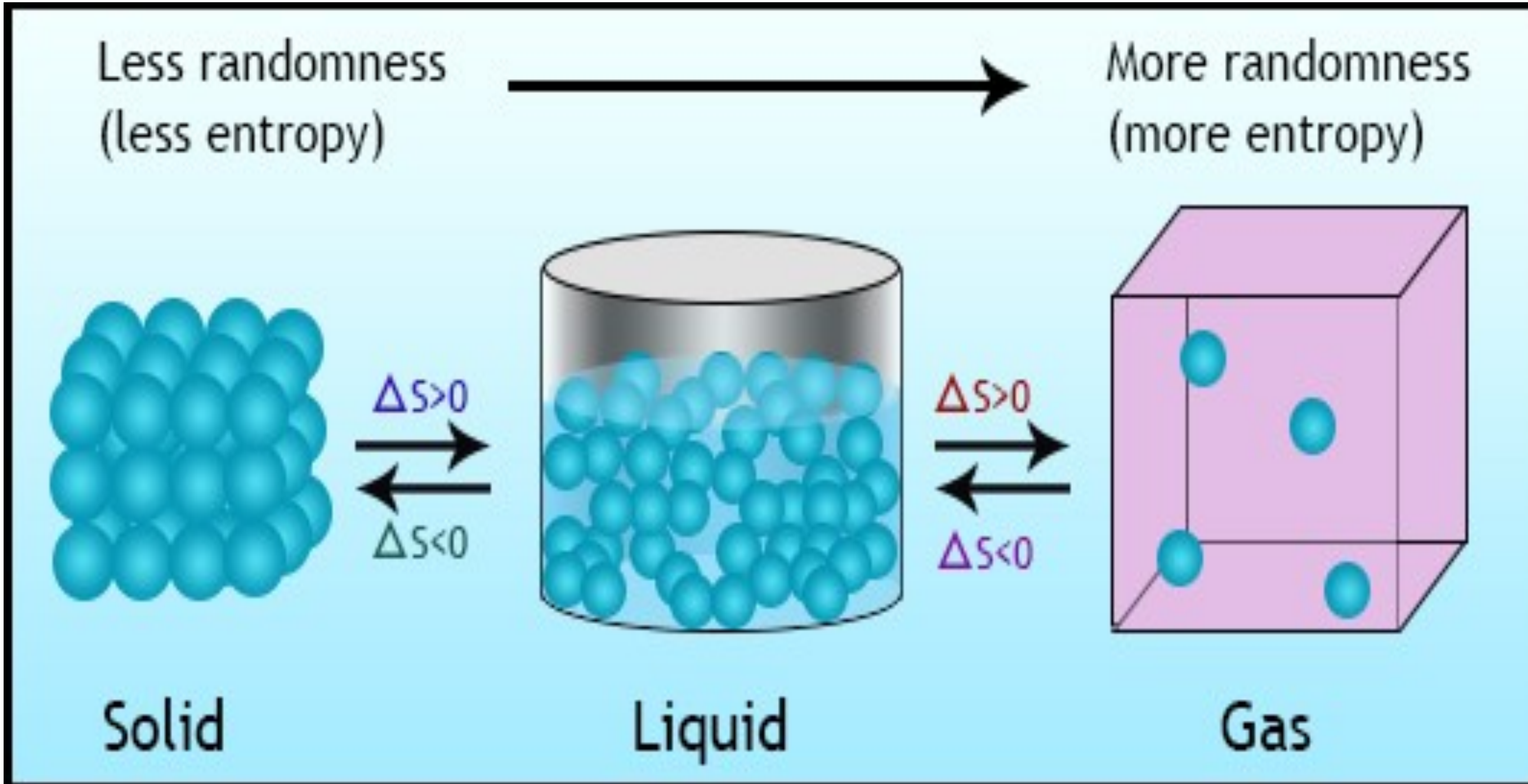
Enthalpy, H, is the heat content of the reacting system. It reflects the number and kinds of chemical bonds in the reactants and products. When a chemical reaction releases heat, it is said to be exothermic; the heat content of the products is less than that of the reactants and ΔH has, by convention, a negative value. Reacting systems that take up heat from their surroundings are endothermic and have positive values of ΔH.

Entropy, S, is a quantitative expression for the randomness or disorder in a system (see Box 1–3). When the products of a reaction are less complex and more disordered than the reactants, the reaction is said to proceed with a gain in entropy.

Enthalpy Change



Randomness - Entropy



The First Law of Thermodynamics

- According to the **first law of thermodynamics**, the energy of the universe is constant
- Energy can be transferred and transformed, but it cannot be created or destroyed
- The first law is also called the principle of conservation of energy

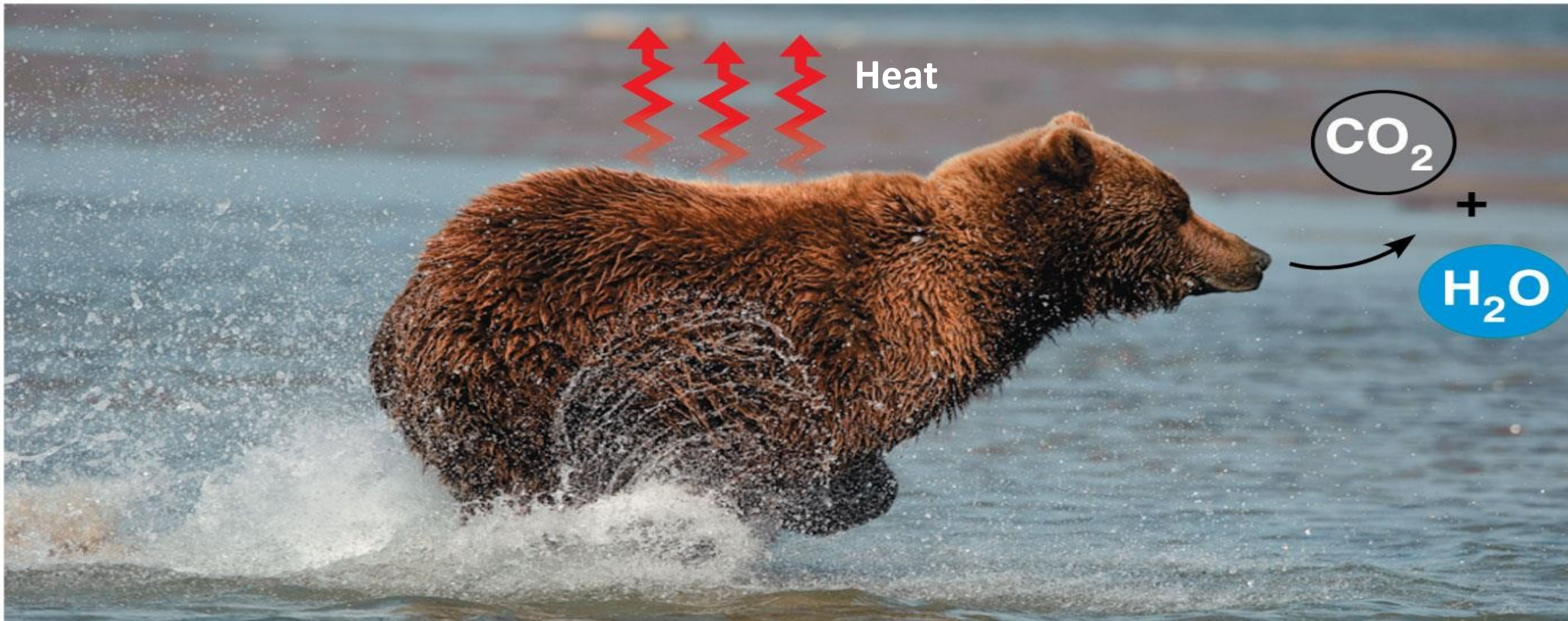
First law of thermodynamics

The Second Law of Thermodynamics

- During every energy transfer or transformation, some energy is unusable, and is often lost as heat

- Every energy transfer or transformation increases the **entropy** (disorder) of the universe

  - For a process to occur spontaneously, it must increase the entropy of the universe



Second law of thermodynamics

The Second Law of Thermodynamics

- Living cells unavoidably convert organized forms of energy to heat

- **Spontaneous processes** occur without energy input; they can happen quickly or slowly

- For a process to occur without energy input, it must increase the entropy of the universe

- The word **Spontaneous** does not imply that such a process would occur quickly; rather, the word signifies that the process is energetically favorable. (In fact, it may be helpful for you to think of the phrase "energetically favorable" when you read the formal term "spontaneous")

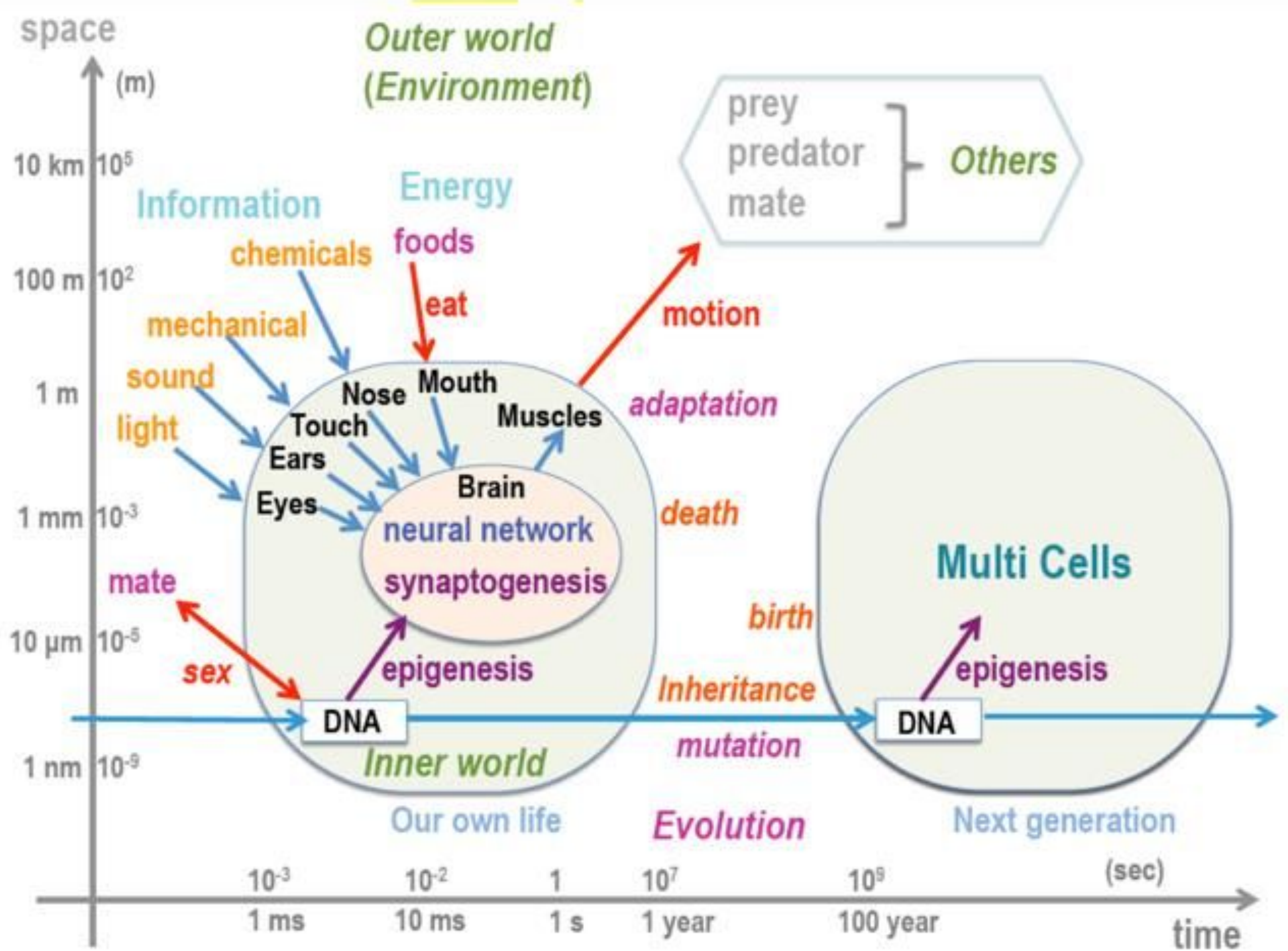
Biological Order and Disorder

- Cells create ordered structures from less ordered materials

- Organisms also replace ordered forms of matter and energy with less ordered forms

- Energy flows into an ecosystem in the form of light and exits in the form of heat

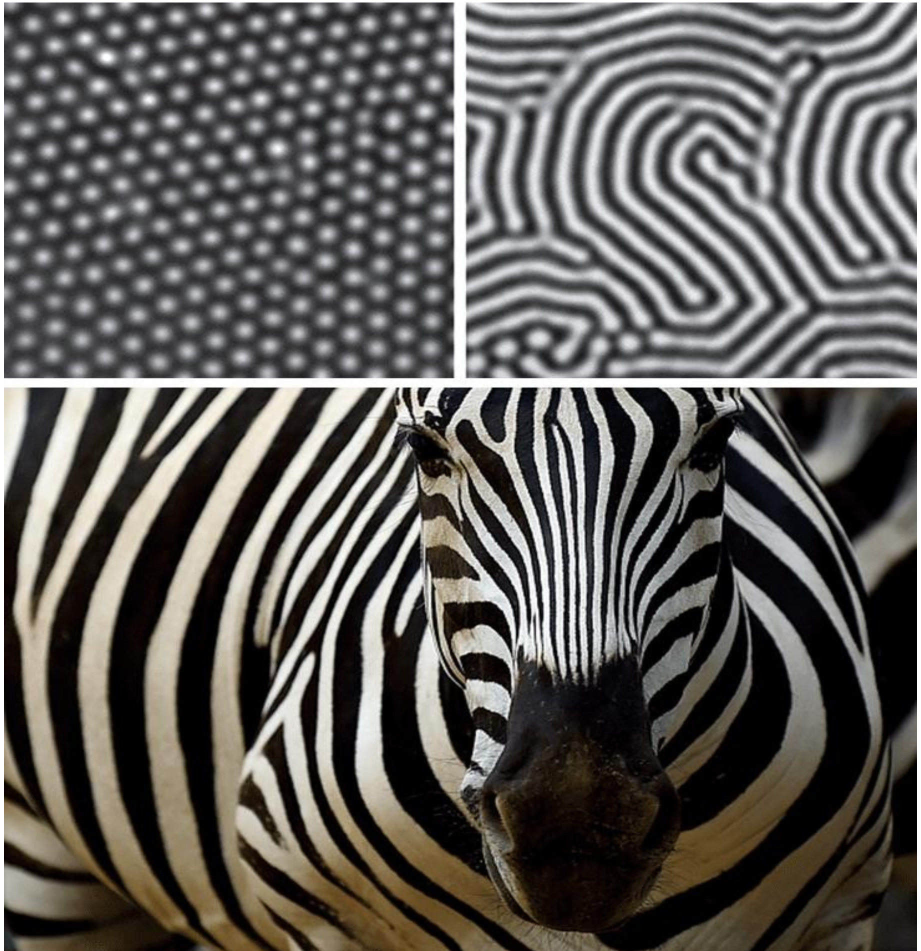
Biological Order and Disorder


space
(m)
Outer world
(Environment)
prey
predator
mate
Others
10 km
10^5
Information
Energy
chemicals
foods
100 m
10^2
eat
mechanical
motion
sound
Mouth
Nose
1 m
Muscles
adaptation
Touch
light
Ears
Brain
Eyes
1 mm
10^{-3}
neural network
death
synaptogenesis
Multi Cells
mate
birth
10 μm
10^{-5}
sex
epigenesis
epigenesis
Inheritance
DNA
DNA
mutation
1 nm
10^{-9}
Inner world
Our own life
Evolution
Next generation
10^{-3}
10^{-2}
1
10^7
10^9
(sec)
1 ms
10 ms
1 s
1 year
100 year
time

Biological Order and Disorder

- The evolution of more complex organisms does not violate the second law of thermodynamics???
- Entropy (disorder) may decrease in an organism, but the universe's total entropy increases

Biological Order and Disorder



Thermoregulation
Camouflage
Highly Efficient Design
Evolution of millions of years

Free-Energy Change, ΔG

- The change in free energy (ΔG) during a process is related to the change in enthalpy, or change in total energy (ΔH), change in entropy (ΔS), and temperature in Kelvin (T)

$$\Delta G = \Delta H - T\Delta S$$

- Only processes with a negative ΔG are spontaneous
- Spontaneous processes can be harnessed to perform work

Free Energy, Stability, and Equilibrium

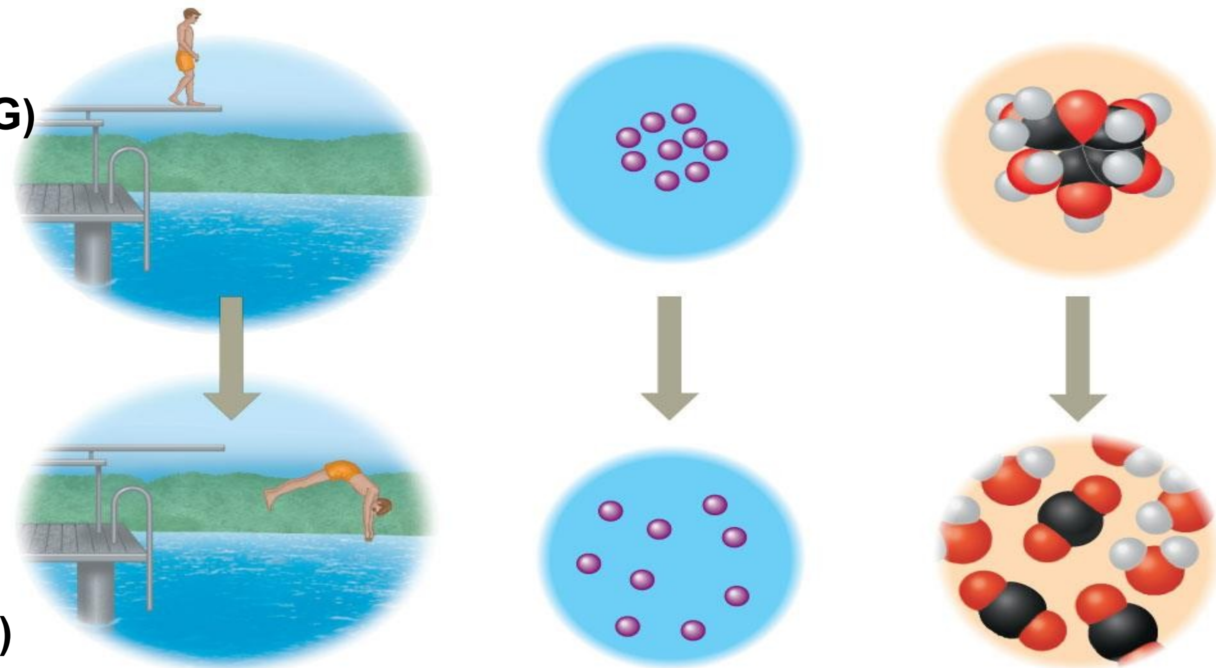
- Free energy is a measure of a system’s instability, its tendency to change to a more stable state
- During a spontaneous change, free energy decreases and the stability of a system increases
- Equilibrium is a state of maximum stability
- A process is spontaneous and can perform work only when it is moving toward equilibrium

Free Energy, Stability, and Equilibrium

- **More free energy (higher G)**
- **Less stable**
- **Greater work capacity**

In a spontaneous change
- The free energy of the system decreases ($\Delta G < 0$)
- The system becomes more stable
- The released free energy can be harnessed to do work

- **Less free energy (lower G)**
- **More stable**
- **Less work capacity**



(b) Diffusion

(c) Chemical reaction

(a) Gravitational motion

- Living cells constantly perform work. They require energy for maintaining their highly organized structures, synthesizing cellular components, generating electric currents, and many other processes.
- Bioenergetics is the quantitative study of energy relationships and energy conversions in biological systems. Biological energy transformations obey the laws of thermodynamics.
- All chemical reactions are influenced by two forces: the tendency to achieve the most stable bonding state (for which enthalpy, H, is a useful expression) and the tendency to achieve the highest degree of randomness, expressed as entropy, S. The net driving force in a reaction is ΔG, the free-energy change, which represents the net effect of these two factors: $\Delta G = \Delta H - T\Delta S$.

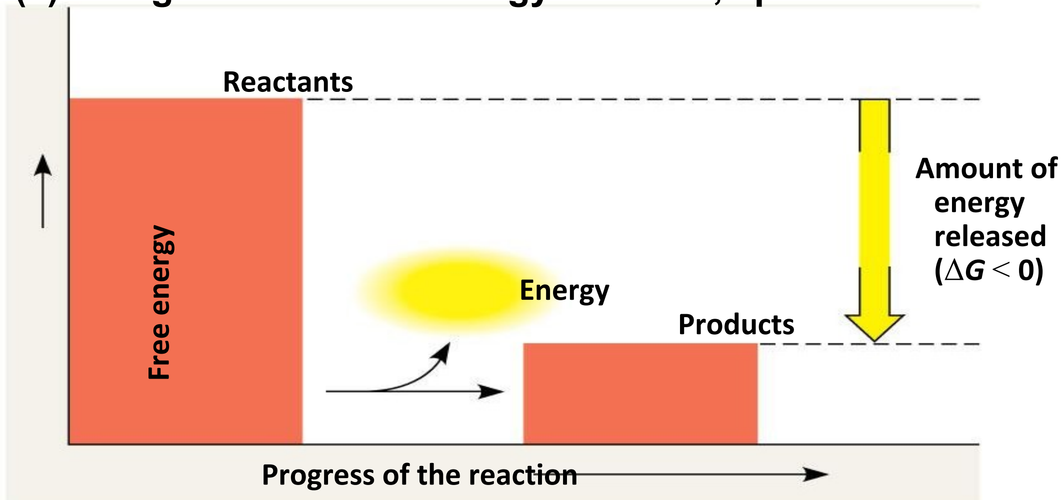
- The standard transformed free-energy change, $\Delta G'^{\circ}$, is a physical constant that is characteristic for a given reaction and can be calculated from the equilibrium constant for the reaction: $\Delta G'^{\circ} = -RT \ln K'_{eq}$.
- The actual free-energy change, ΔG, is a variable that depends on $\Delta G'^{\circ}$ and on the concentrations of reactants and products: $\Delta G = \Delta G'^{\circ} + RT \ln$ ([products]/[reactants]).
- When ΔG is large and negative, the reaction tends to go in the forward direction; when ΔG is large and positive, the reaction tends to go in the reverse direction; and when $\Delta G = 0$, the system is at equilibrium.
- The free-energy change for a reaction is independent of the pathway by which the reaction occurs. Free-energy changes are additive; the net chemical reaction that results from successive reactions sharing a common intermediate has an overall free-energy change that is the sum of the ΔG values for the individual reactions.

Exergonic and Endergonic Reactions in Metabolism

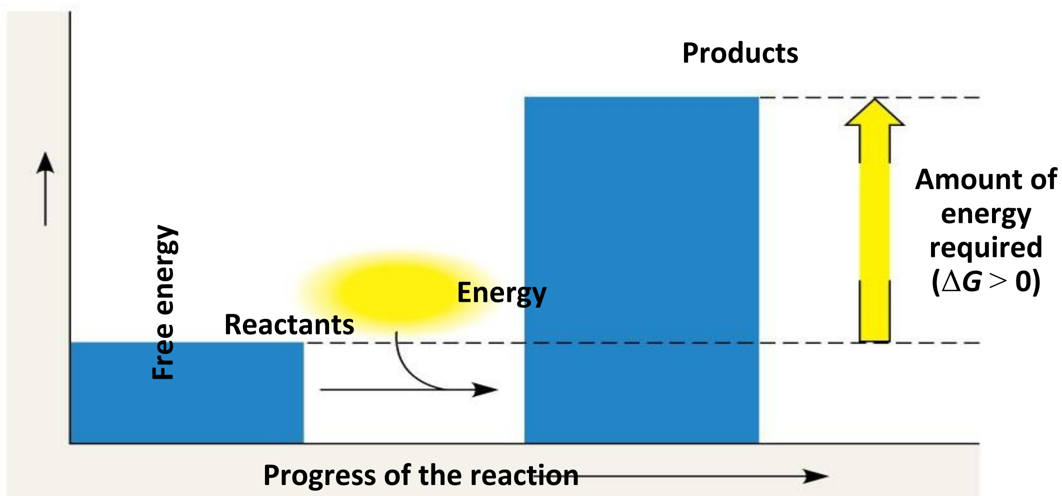
- An Exergonic **reaction** proceeds with a net release of free energy and is spontaneous

- An **Endergonic reaction** absorbs free energy from its surroundings and is non-spontaneous

(a) Exergonic reaction: energy released, spontaneous

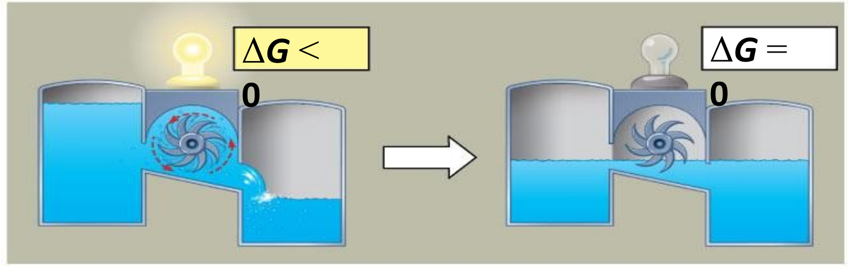


(b) Endergonic reaction: energy required, nons-pontaneous



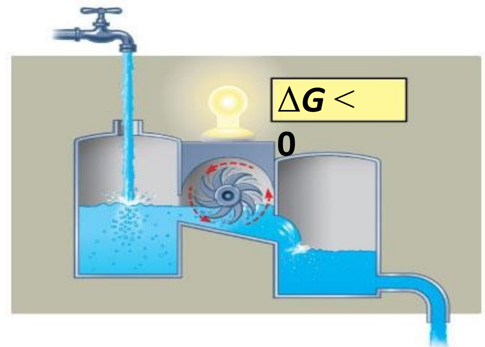
Equilibrium and Metabolism

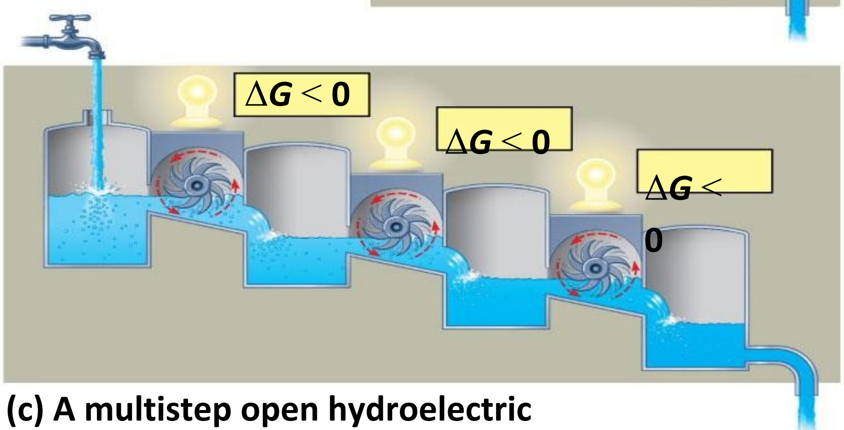
- Reactions in a closed system eventually reach equilibrium and then do no work
- Cells are not in equilibrium; they are open systems experiencing a constant flow of materials
- A defining feature of life is that metabolism is never at equilibrium
- A catabolic pathway in a cell releases free energy in a series of reactions
- Closed and open hydroelectric systems can serve as analogies



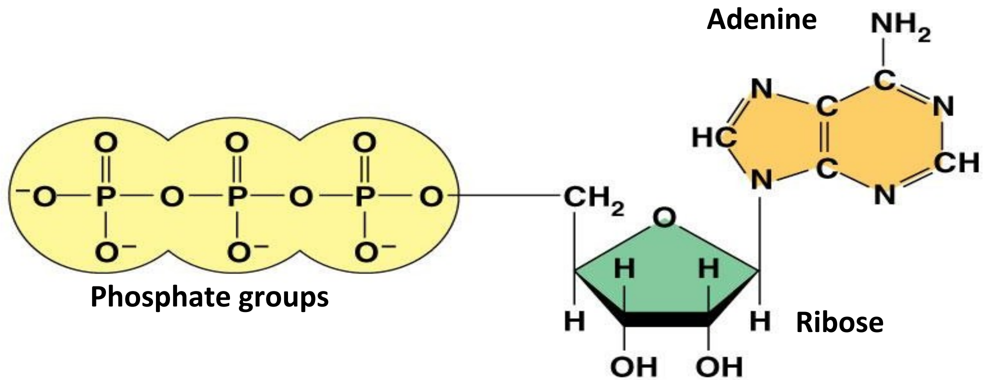
(a) An isolated hydroelectric system

(b) An open hydro-electric system

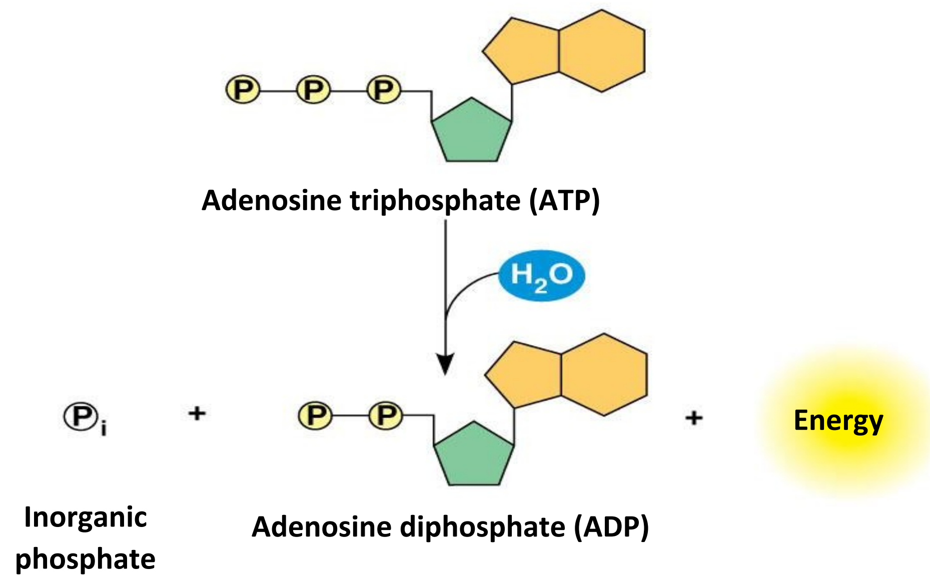




(c) A multistep open hydroelectric system



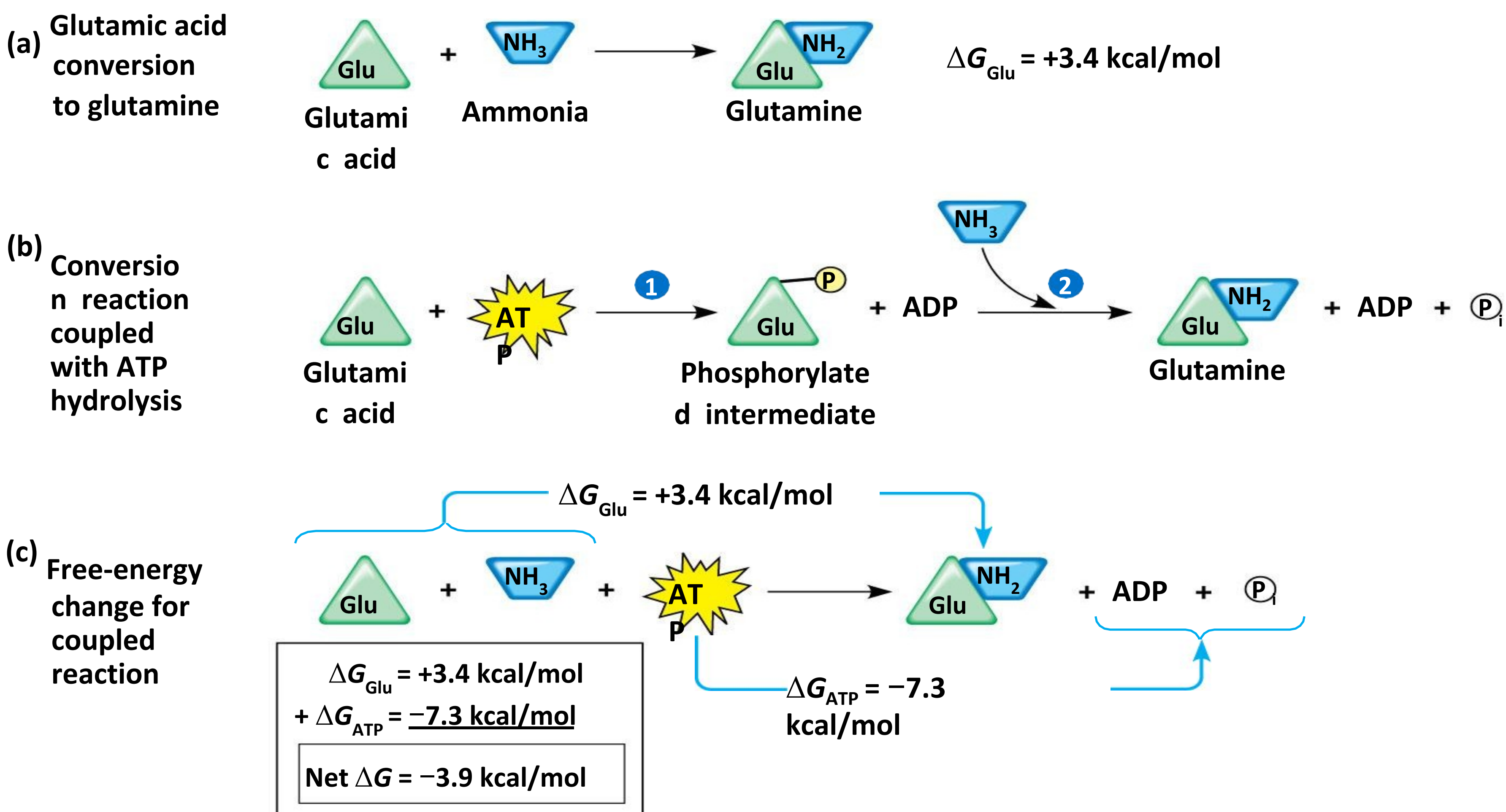
(a) The structure of ATP

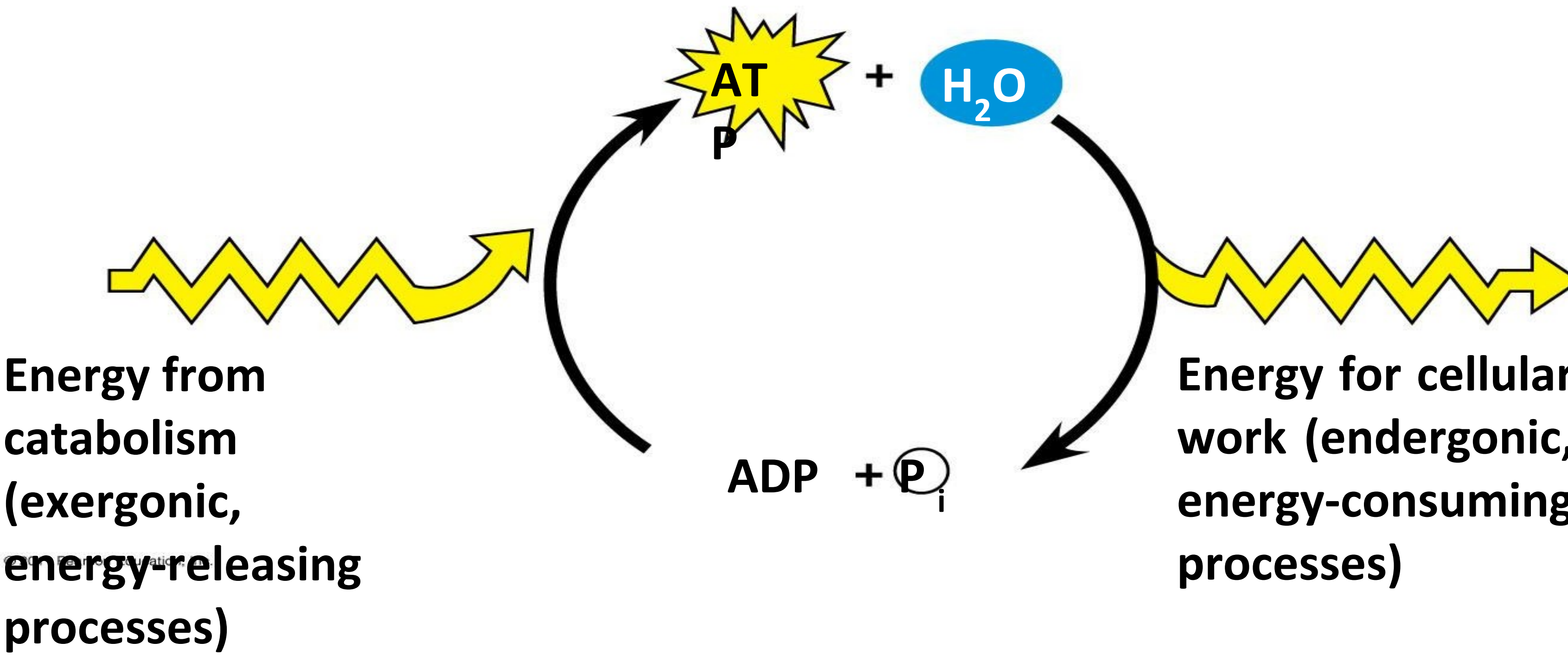


(b) The hydrolysis of ATP

How the Hydrolysis of ATP Performs Work

- The three types of cellular work (mechanical, transport, and chemical) are powered by the hydrolysis of ATP
- In the cell, the energy from the exergonic reaction of ATP hydrolysis can be used to drive an endergonic reaction
- Overall, the coupled reactions are exergonic


(a) Glutamic acid conversion to glutamine
Glu
+
NH3
Glu
NH2
Glutami c acid
Ammonia
Glutamine
ΔG Glu = +3.4 kcal/mol
(b) Conversio n reaction coupled with ATP hydrolysis
Glu
+
AT P
1
Glu
P
+ ADP
NH3
2
Glu
NH2
+ ADP + P i
Glutami c acid
Phosphorylate d intermediate
Glutamine
(c) Free-energy change for coupled reaction
ΔG Glu = +3.4 kcal/mol
Glu
+
NH3
+
AT P
Glu
NH2
+ ADP + P i
ΔG Glu = +3.4 kcal/mol
+ ΔG ATP = −7.3 kcal/mol
Net ΔG = −3.9 kcal/mol
ΔG ATP = −7.3 kcal/mol



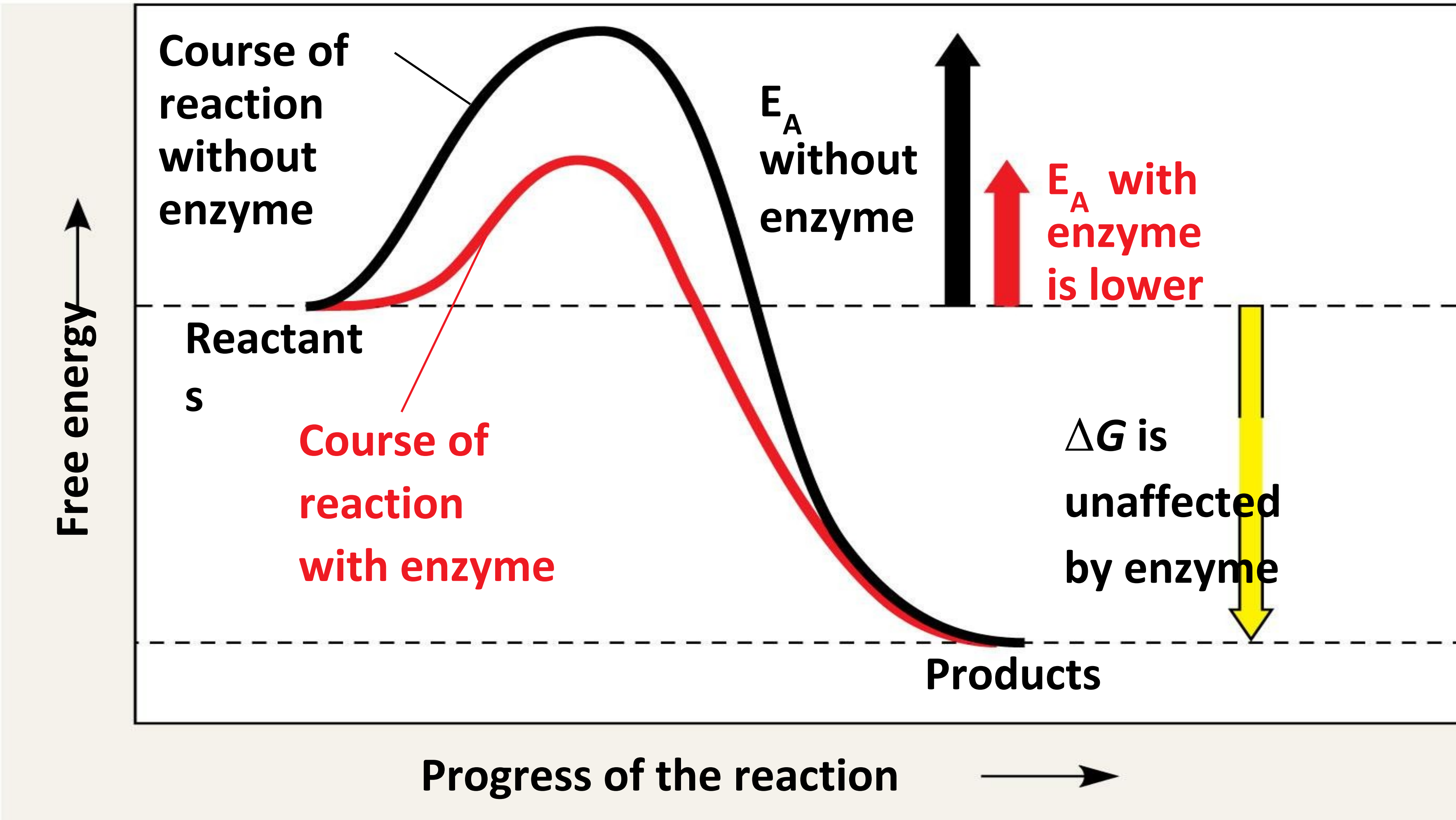
ATP
+
H_2O
Energy from catabolism (exergonic, energy-releasing processes)
Energy for cellular work (endergonic, energy-consuming processes)
ADP + P_i

Enzymes speed up metabolic reactions by lowering energy barriers

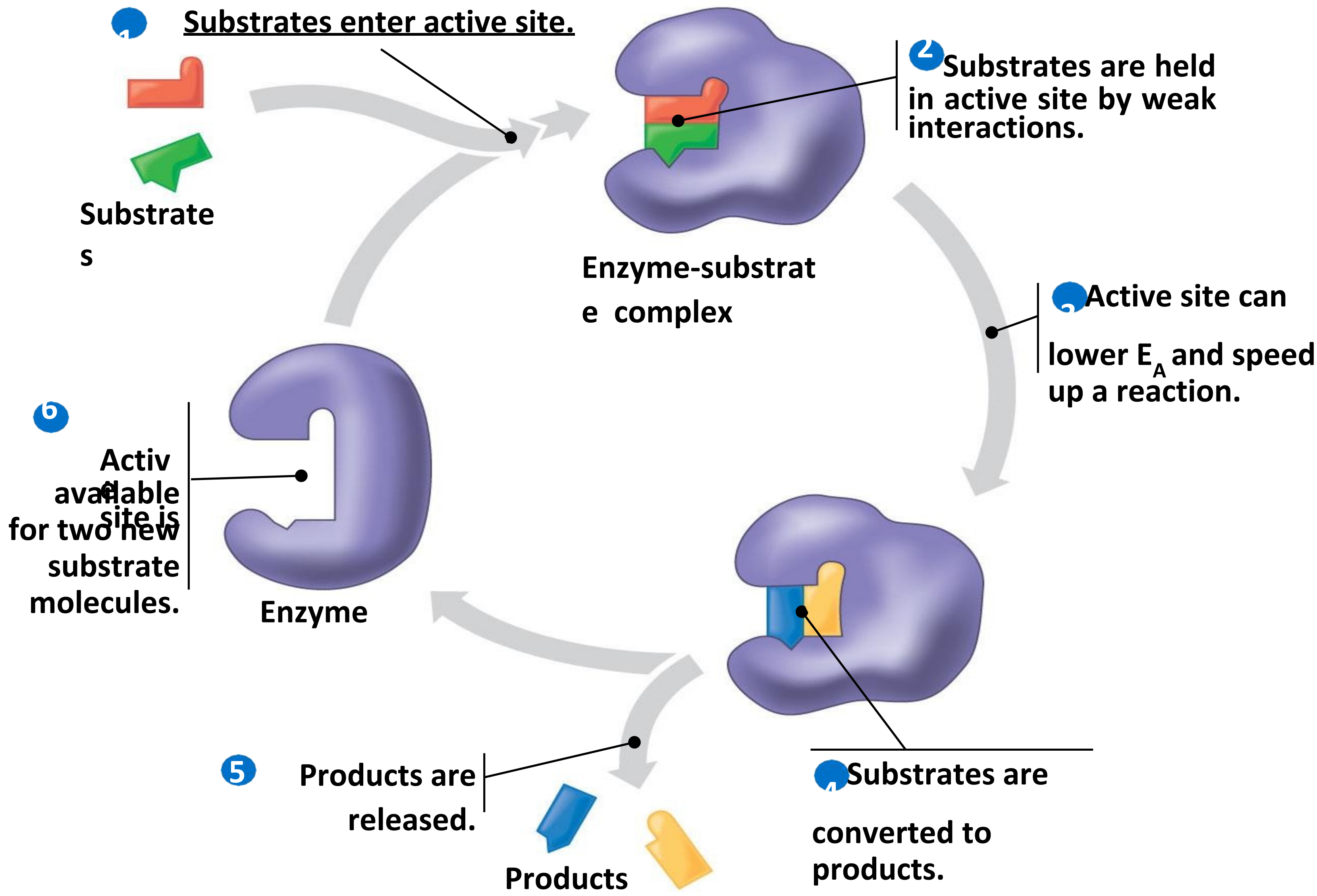
- A **catalyst** is a chemical agent that speeds up a reaction without being consumed by the reaction
- An **enzyme** is a catalytic protein
- Hydrolysis of sucrose by the enzyme sucrase is an example of an enzyme-catalyzed reaction

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



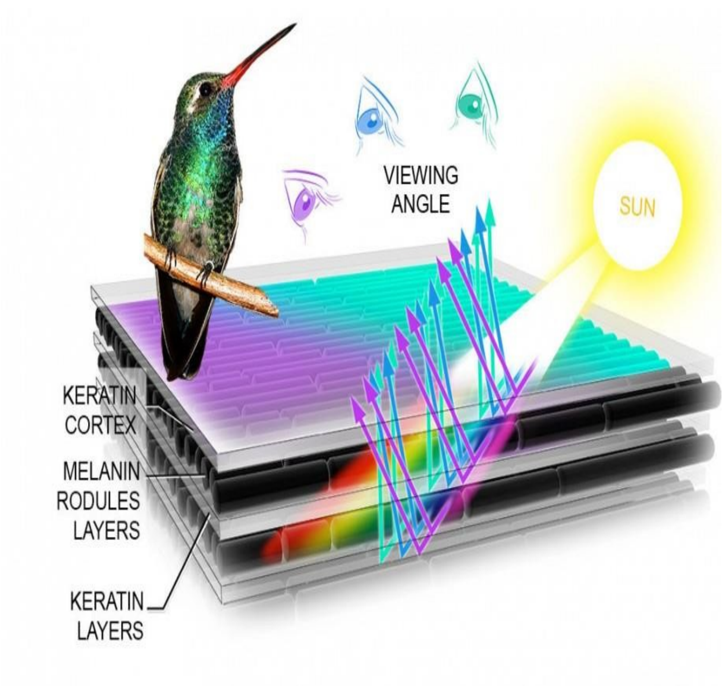
Course of reaction without enzyme
E_A without enzyme
E_A with enzyme is lower
Reactant
s
Course of reaction with enzyme
ΔG is unaffected by enzyme
Products
Free energy
Progress of the reaction



1 Substrates enter active site.
Substrate
s
2 Substrates are held in active site by weak interactions.
Enzyme-substrat
e complex
3 Active site can
lower E_A and speed up a reaction.
4 Substrates are
converted to products.
5 Products are
released.
Products
6 Activ
e
site is
available for two new substrate molecules.
Enzyme

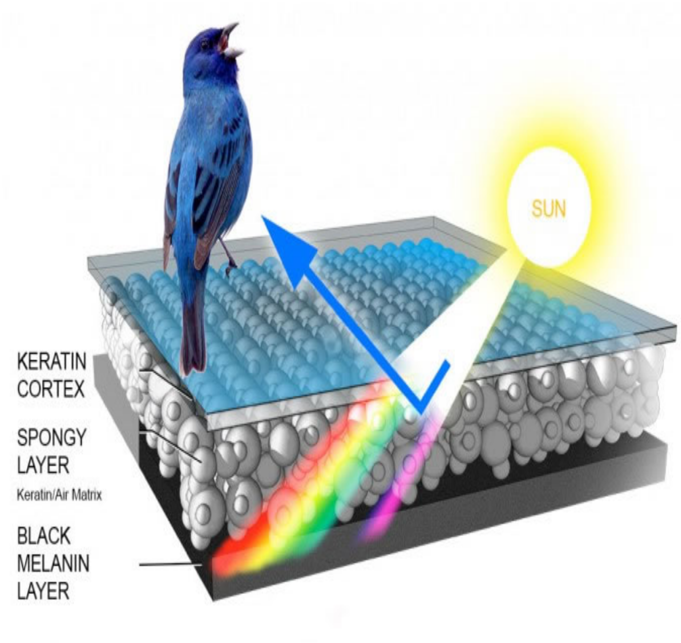
Structural colours are like Diffraction Gratin

- **IRIDESCENT FEATHERS**



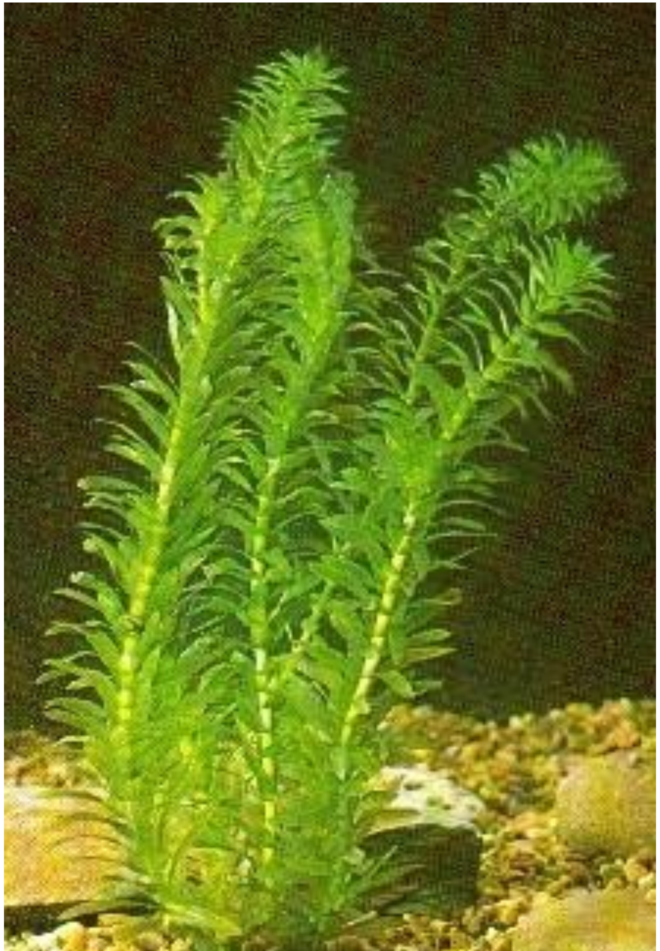
- The best known example is the gorget (throat feathers) of many hummingbird species.
- The iridescent colors of the gorget are the result of the refraction of incident light caused by the microscopic structure of the feather barbules.
- The refraction works like a prism, splitting the light into rich, component colors.
- As the viewing angle changes, the refracted light becomes visible in a glowing, shimmering iridescent display.
- Including: the Purple Gallinule and Tricolored Heron.

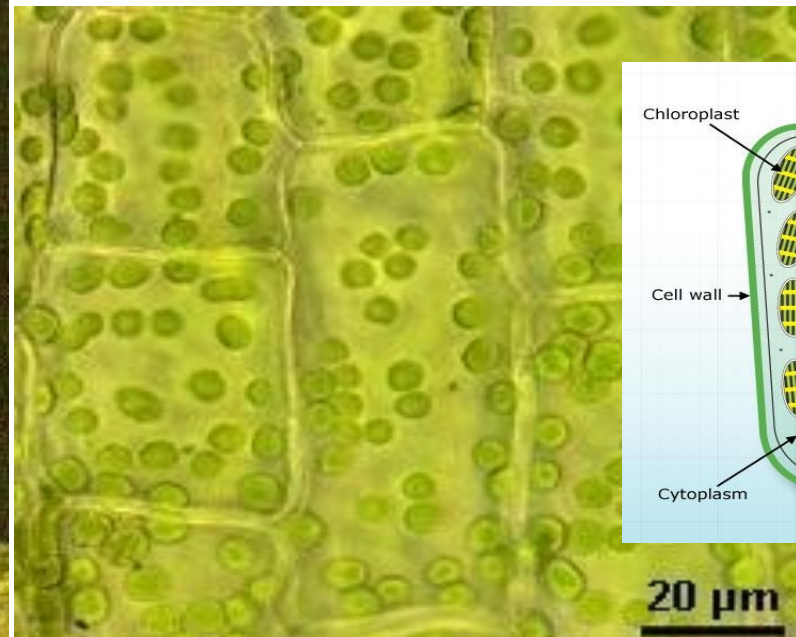
Structural colours

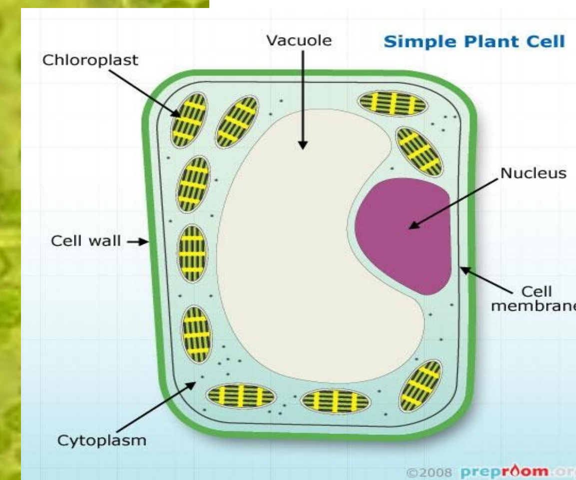


- Not all structural colors are iridescent.
- Tiny air pockets in the barbs of feathers can scatter incoming light, resulting in a specific, non-iridescent color.
- Blue colors in feathers are almost always produced in this manner.
- Examples include the blue feathers of bluebirds, Indigo Buntings, Blue Jays and Steller's Jays.

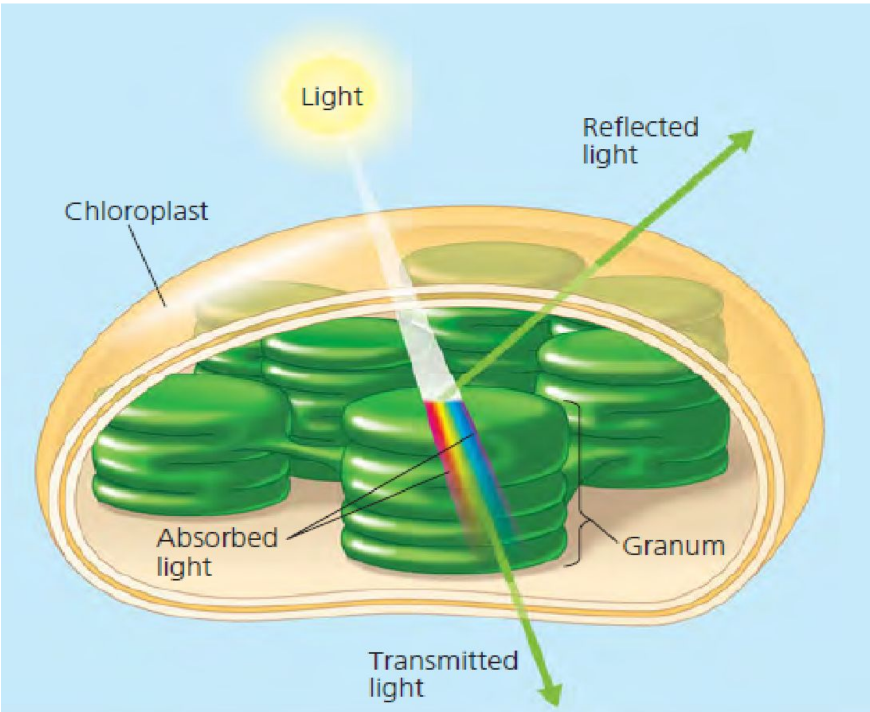
Why are Plants Green?







Chloroplasts

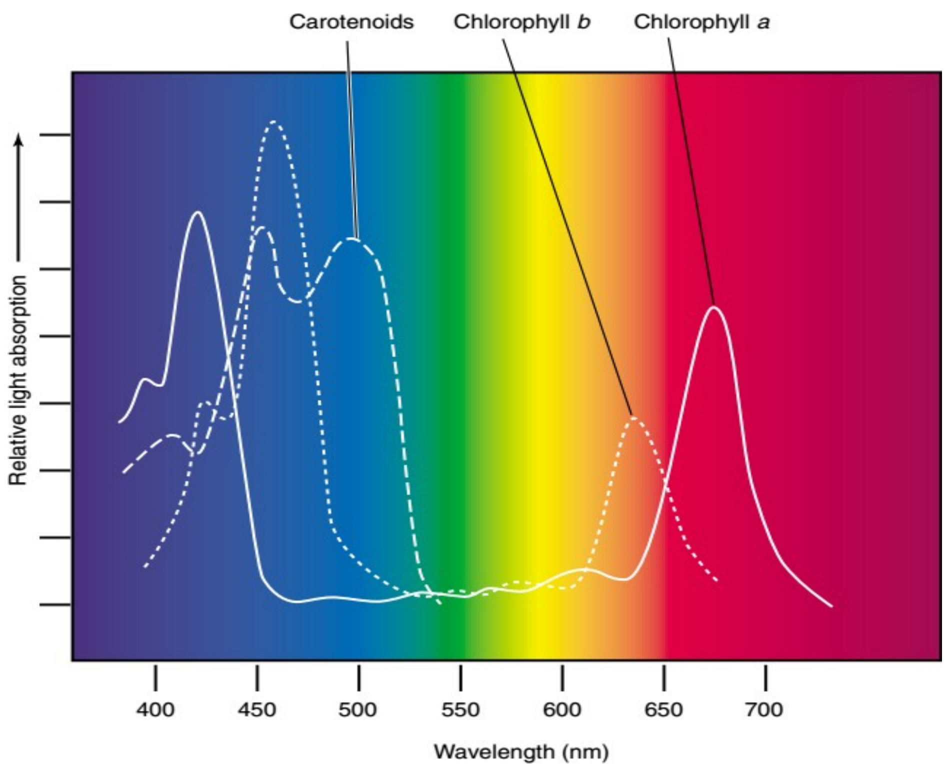


Why leaves are green: interaction of light with chloroplasts.
The chlorophyll molecules of chloroplasts absorb violet-blue and red light (the colors most effective in driving hotosynthesis) and reflect or transmit green light. This is why leaves appear green.

Photosynthetic pigments: Light receptors

- When light meets matter, it may be reflected, transmitted, or absorbed.
- Different pigments absorb light of different wavelengths, and the wavelengths that are absorbed disappear.
- If a pigment is illuminated with white light, the color we see is the color most reflected or transmitted by the pigment.
- We see green when we look at a leaf because chlorophyll absorbs violet-blue and red light while transmitting and reflecting green light
- The ability of a pigment to absorb various wavelengths of light can be measured with an instrument called a **spectrophotometer**.
- A graph plotting a pigment's light absorption versus wavelength is called an **absorption spectrum**

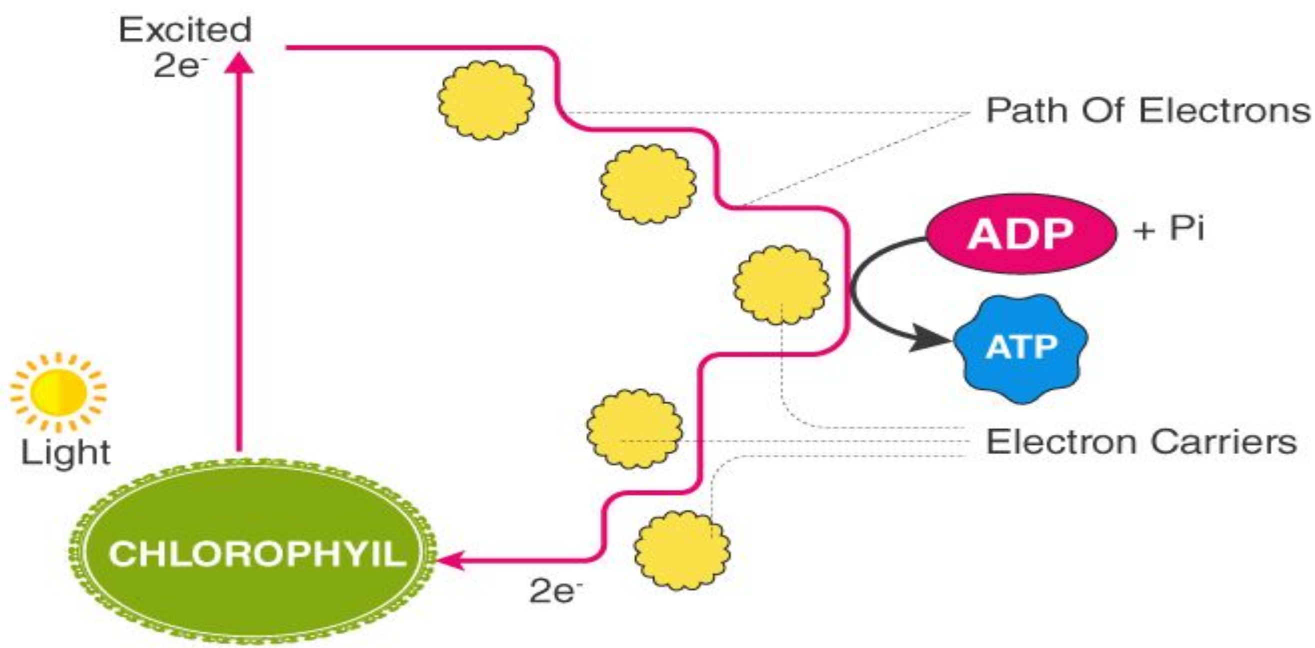
Absorption Spectra of chlorophyll pigments



- **The Figure** shows the absorption spectra of three types of pigments in chloroplasts:
- ***chlorophyll a***, which participates directly in the light reactions; the accessory pigment *chlorophyll b*; and a group of accessory pigments called carotenoids.
- The spectrum of chlorophyll *a* suggests that violet-blue and red light work best for photosynthesis, since they are absorbed, while green is the least effective

Cyclic Photophosphorylation

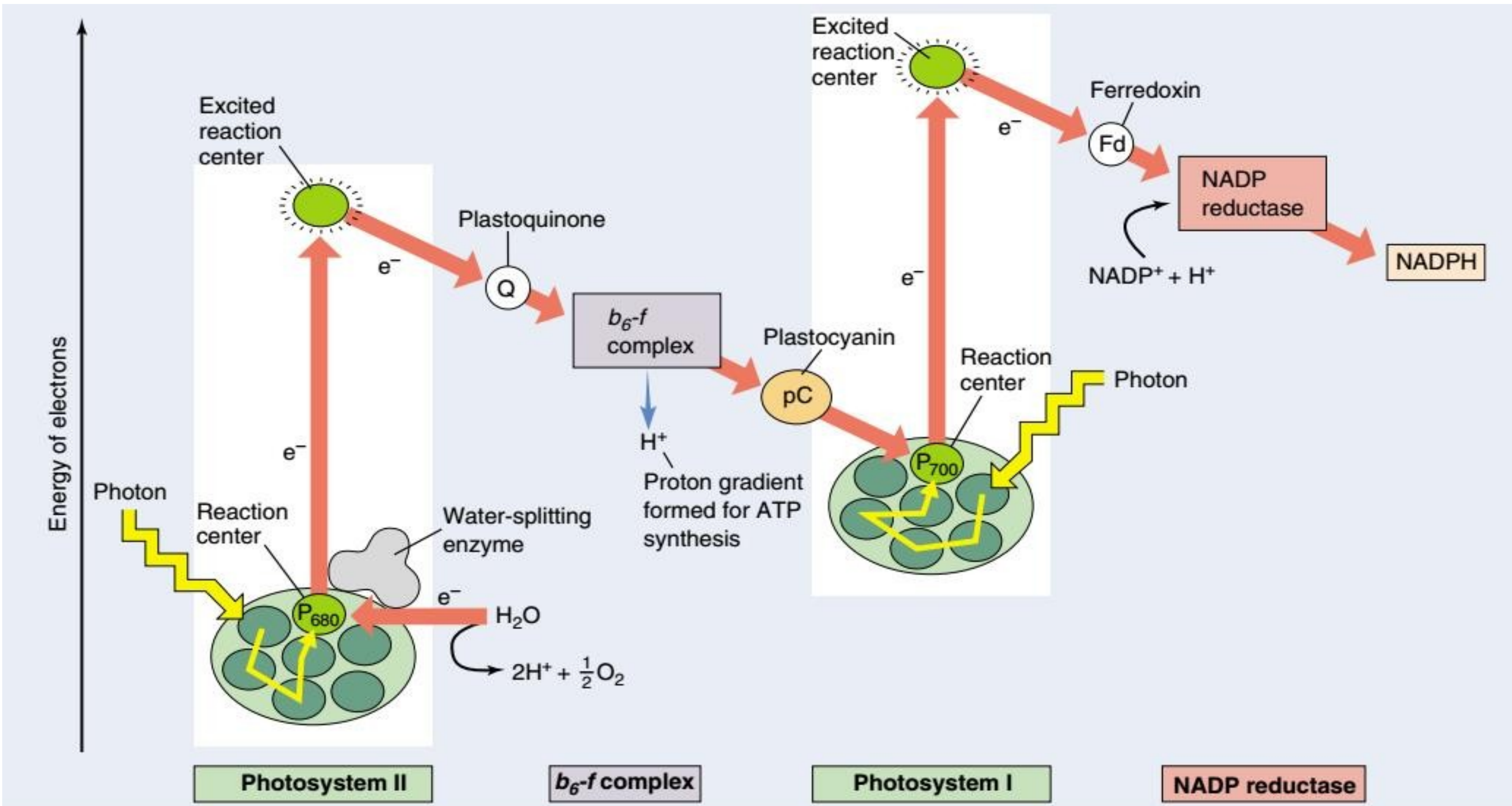
- Process for ATP generation associated with some Photosynthetic Bacteria
- Reaction Center => 700 nm



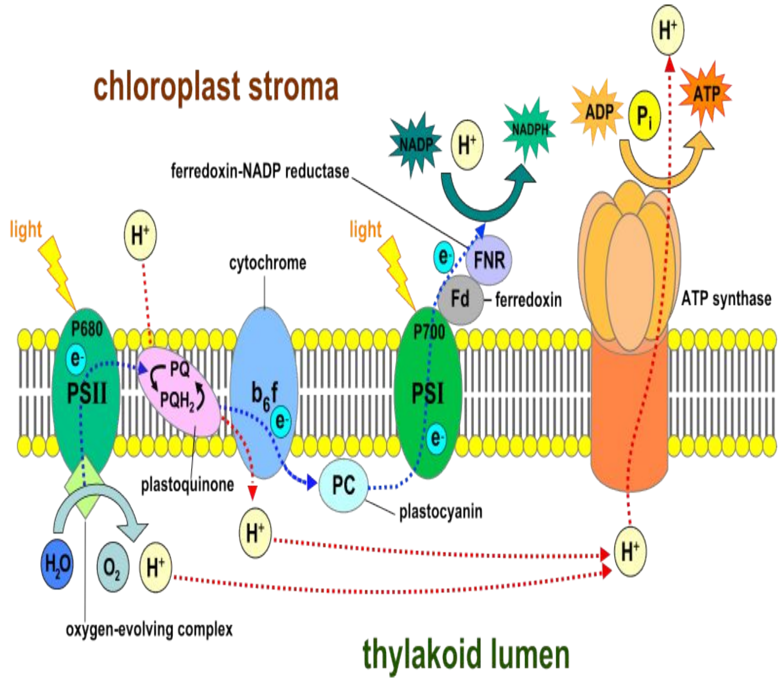
Photosynthesis

- Inside a chloroplast, there are thylakoid disks, that have their own phospholipid bilayer membrane,
- One of the components in the thylakoid membrane is a photosystem, which is packed with chlorophyl.
- The chlorophyl absorbs the light energy and uses it to excite the electron.
- The electron is then passed to an electron acceptor protein, which passes it along an electron transport chain.
- As the electron is passed along the transport chain, the electron looses energy, which is used to make ATP from ADP and Pi.
- The electron is then recycled and enters the photosystem again.
- The mechanism of ATP production is that when the electron is being passed along the chain, the electron is passed over a proton pump, which uses the negative charge of the electron to pump the proton across the membrane into the thylakoid space.
- There is a high proton gradient built up inside the thylakoid space. They then move down the gradient, out of an ATPase out of the thylakoid space.

Non-cyclic Photophosphorylation



Non-cyclic Photophosphorylation



- This process is referred to as non- cyclic photophosphorylation because the lost electrons by P680 of Photosystem II are occupied by P700 of Photosystem I and are not reverted to P680.

- Here the complete movement of the electrons is in a unidirectional or in a non-cyclic manner.
- During non-cyclic photophosphorylation, the electrons released by P700 are carried by primary acceptor and are finally passed on to NADP.

- Here, the electrons combine with the protons – H+ which is produced by splitting up of the water molecule and reduces NADP to NADPH2.

Engineering Connection

1. Engineers are faced with the challenge of designing energy efficient systems for heating buildings, for example, or creating fuel-efficient vehicles.

2. The photosynthetic process serves as an excellent model for highly efficient engineering design.

3. Plants convert readily available resources (water, sunlight and carbon dioxide) into plant fuel (glucose).

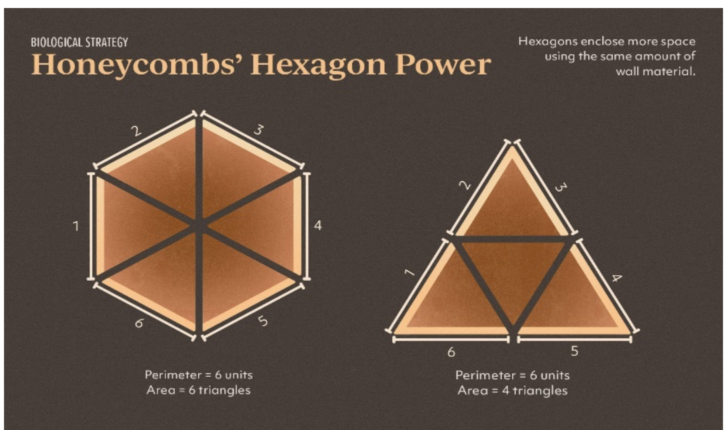
4. The only byproduct of the process is oxygen, which is an environmentally friendly product that is consumable by other organisms.

Fibonachi series

Module 2

Mathematics in Biology (Part 1)

Mendelian Genetics



LECTURE 7 : GENETICS

- Introduction to Genetics and heredity
- Gregor Mendel – a brief bio
- Genetic terminology (glossary)
- Monohybrid crosses
- Patterns of inheritance
- Dihybrid crosses
- Test cross
- Beyond Mendelian Genetics – incomplete dominance

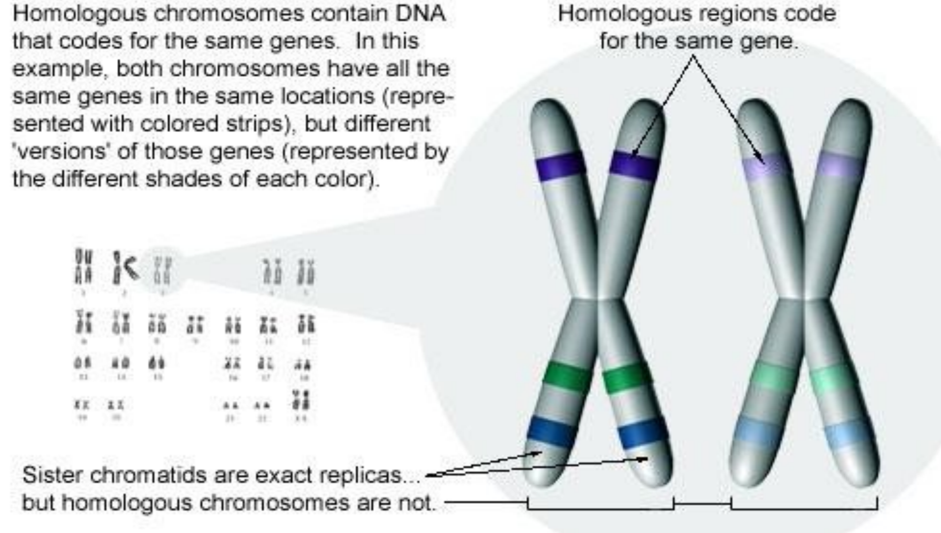
Introduction to Genetics

- **GENETICS** – branch of biology that deals with heredity and variation of organisms.

- **Chromosomes** carry the hereditary information (genes)
  - Arrangement of nucleotides in DNA
  - DNA RNA Proteins

- Chromosomes (and genes) occur in pairs **Homologous Chromosomes**
- New combinations of genes occur in sexual reproduction
  - Fertilization from two parents

Figure B-11: Homologous Chromosomes



Gregor Johann Mendel

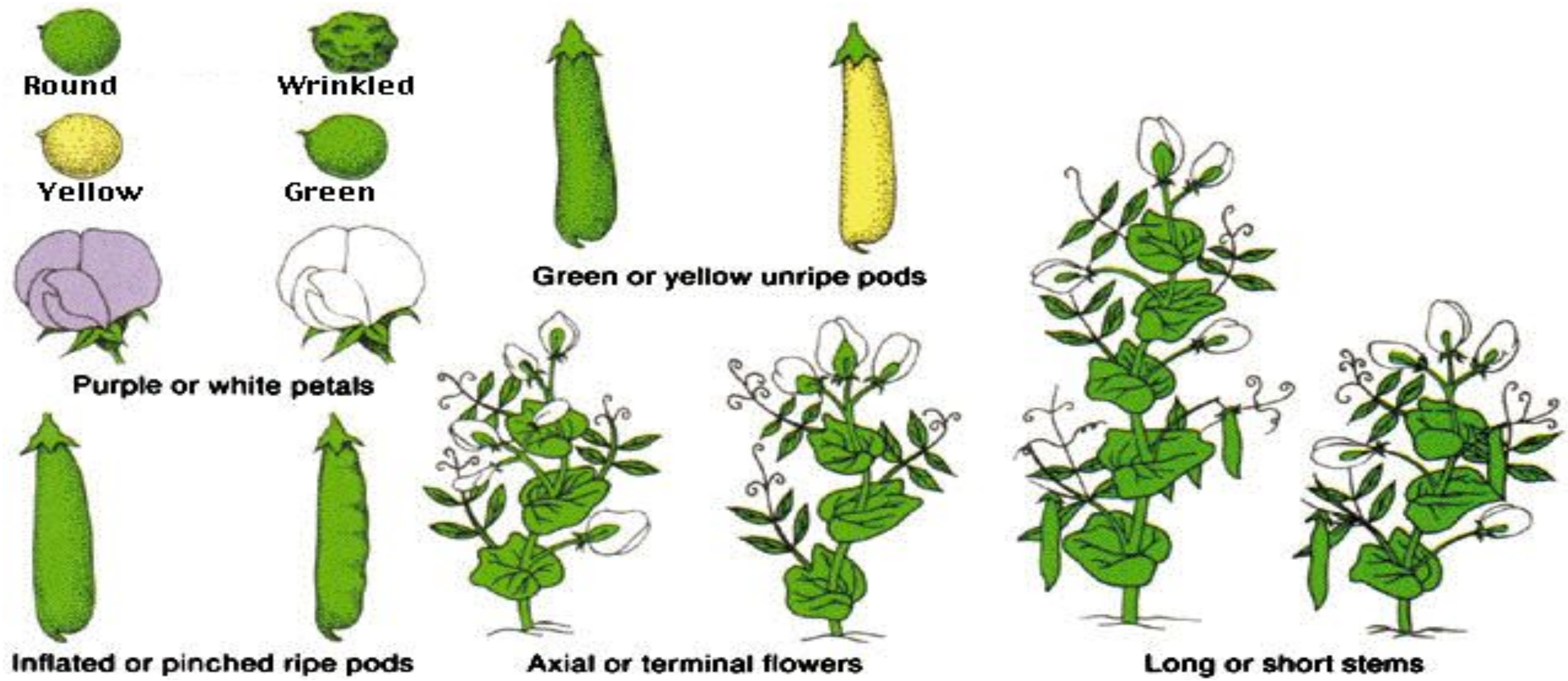
- Austrian Monk, born in what is now Czech Republic in 1822

Gregor Mendel

- Son of peasant farmer, studied Theology and was ordained priest Order St. Augustine.
- Went to the university of Vienna, where he studied botany and learned the Scientific Method
- Worked with pure lines of peas for eight years
- Prior to Mendel, heredity was regarded as a "blending"

Mendel's peas

- Mendel looked at seven traits or characteristics of pea plants:



- In 1866 he published *Experiments in Plant Hybridization*, (*Versuche über Pflanzen-Hybriden*) in which he established his three Principles of Inheritance

- He tried to repeat his work in another plant, but didn't work because the plant reproduced asexually! If…
- Work was largely ignored for 34 years, until 1900, when

- Mendel was the first biologist to use Mathematics – to explain his results quantitatively.
- Mendel predicted

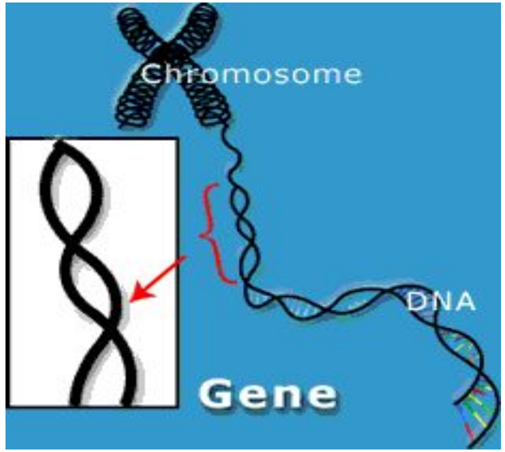
The concept of genes

That genes occur in pairs

That one gene of each pair is present in the gametes

Genetics terms you need to know:

- **Gene** – a unit of heredity; a section of DNA sequence encoding a single protein
- **Genome** – the entire set of genes in an organism



- **Alleles** – two genes that occupy the same position on homologous chromosomes and that cover the same trait (like 'flavors' of a trait).
- **Locus** – a fixed location on a strand of DNA where a gene or one of its alleles is located.

- **Homozygous** – having identical genes (one from each parent) for a particular characteristic.
- **Heterozygous** – having two different genes for a particular characteristic.

- **Dominant** – the allele of a gene that masks or suppresses the expression of an alternate allele; the trait appears in the heterozygous condition.
- **Recessive** – an allele that is masked by a

- **Genotype** – the genetic makeup of an organisms
- **Phenotype** – the physical appearance of an organism (Genotype + environment)

- **Monohybrid cross**: a genetic cross involving a single pair of genes (one trait); parents differ by a single trait.
- **P** = Parental generation
- **F_1** = First filial generation; offspring from a genetic cross.
- **F_2** = Second filial generation of a genetic cross

7 Characteristics in Peas

Trait	Stem length	Pod shape	Seed shape	Seed color	Flower position	Flower color	Pod color
Characteristics	Tall	Inflated	Smooth	Yellow	Lateral	Purple	Green
	Dwarf	Constricted	Wrinkled	Green	Terminal	White	Yellow

Monohybrid cross

- Parents differ by a single trait.
- Crossing two pea plants that differ in stem size, one tall one short

T = allele for Tall

t = allele for dwarf

TT = homozygous tall plant

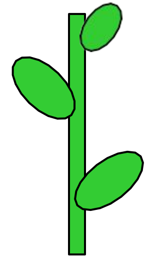
t t = homozygous dwarf plant

Long or short stems

$$TT \times tt$$

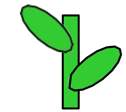
Monohybrid cross for stem length:

P = parentals
true breeding,
homozygous plants:



T T × *t t*

(tall) (dwarf)

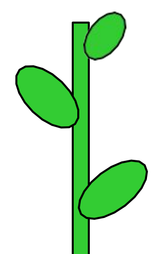


↓

F_1 generation
is heterozygous:

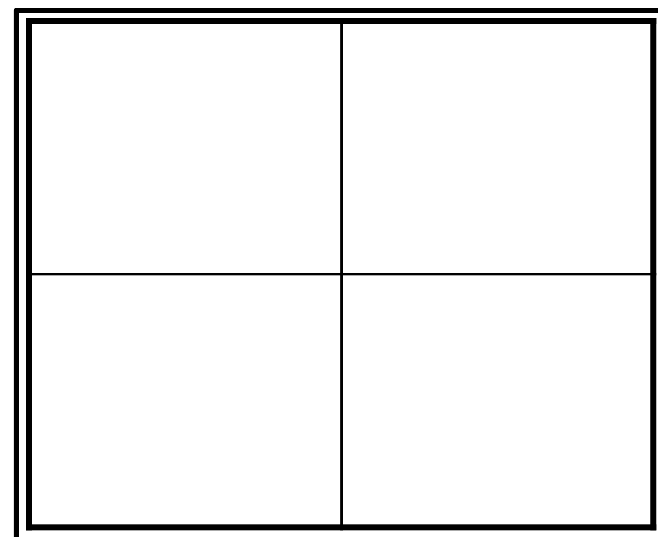
T *t*

(all tall plants)



Punnett square

- A useful tool to do genetic crosses
- For a monohybrid cross, you need a square divided by four….
- Looks like a window pane… We use the Punnett square to predict the genotypes and phenotypes of



Using a Punnett Square

STEPS:

1. determine the genotypes of the parent organisms
2. write down your "cross" (mating)
3. draw a p-square

Parent genotypes:

TT and *t t*

Cross

T T × ***t t***

Punnett square

4. **"split" the letters of the genotype for each parent & put them "outside" the p-square**
5. determine the possible genotypes of the offspring by filling in the p-square
6. summarize results (genotypes & phenotypes of offspring)

T T × ***t***
t

	T	**T**
t	T *t*	T *t*
t	T *t*	T *t*

Genotypes:
100% T
t

Phenotypes:
100% Tall plants

Monohybrid cross: F_2 generation

- If you let the F1 generation self-fertilize, the next monohybrid cross would be:

T *t* × **T *t***
(tall) (tall)

	T	***t***
T	T T	T *t*
t	T *t*	*t t*

<u>Genotypes:</u>
1 TT=
Tall 2 T*t*
= Tall
1 *tt* = dwarf
Genotypic ratio= 1:2:1

<u>Phenotype:</u>
3 Tall
1 dwarf
Phenotypic ratio= 3:1

Secret of the Punnett Square

- Key to the Punnett Square:
- Determine the <u>gametes</u> of each parent…
- How? By “splitting” the genotypes of each parent:

If this is your cross **T T** × ***t t***

The gametes are: **T** **T** ***t*** ***t***

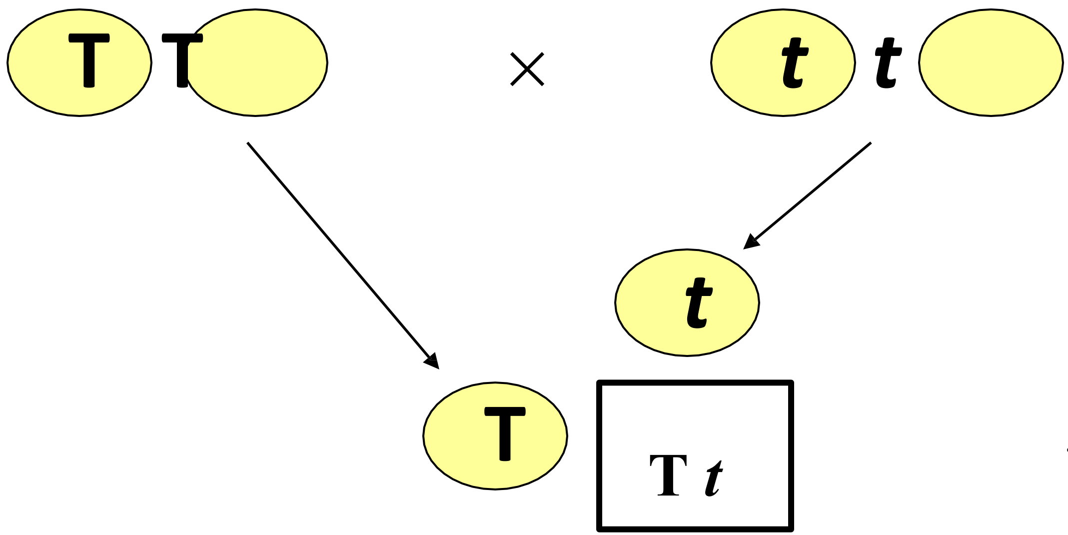
Once you have the gametes…

T T × *t t*

	t	*t*
T	T*t*	T*t*
T	T*t*	T*t*

Shortcut for Punnett Square...

- If either parent is HOMOZYGOUS



Genotypes:
100% T
t

Phenotypes:
100% Tall
plants

- **You only need <u>one</u> box!**

Understanding the shortcut…

	t	*t*
T	T *t*	T *t*
T	T *t*	T *t*

=

	t
T	T *t*

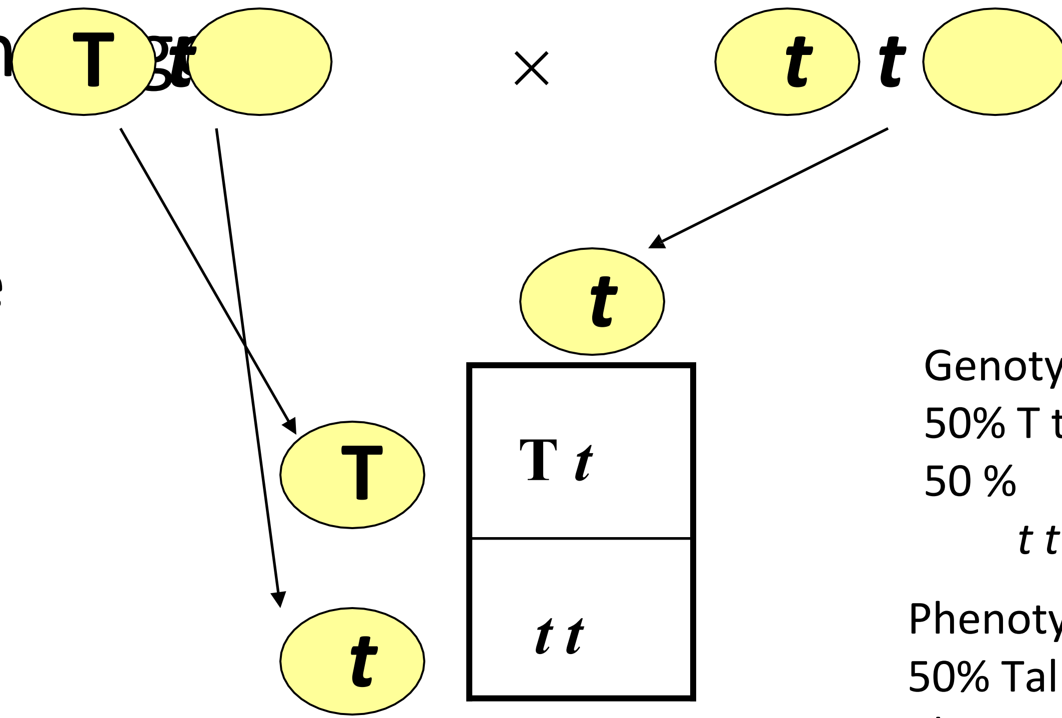
Genotypes:
100% T t

Phenotypes:
100% Tall

If you have another cross…

- A heterozygous with a homozygous

You can still use the shortcut!



Genotypes:
50% T t
50 %
t t

Phenotypes:
50% Tall plants
50% Dwarf plants

Another example: Flower color

For example, flower color:

P = purple (dominant)

p = white (recessive)

If you cross a homozygous Purple (PP) with a homozygous white (*pp*):

$$\mathrm{P\,P} \times p\,p \downarrow \mathrm{P}\,p$$

ALL PURPLE (P*p*)

Cross the F1 generation:

$Pp \times Pp$

	P	*p*
P	P P	P *p*
p	P *p*	*p p*

Genotypes:
1 PP
2 Pp
1 pp

Phenotypes:
3 Purple
1 White

Mendel's Principles

- **1. Principle of Dominance**:

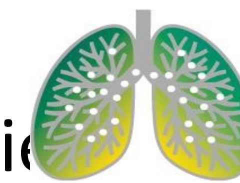
  One allele masked another, one allele was dominant over the other in the F_1 generation.

- **2. Principle of Segregation**:

  When gametes are formed, the pairs of hereditary factors (genes) become separated, so that each sex cell (egg/sperm) receives only one kind of gene.

Human case: CF

- Mendel's Principles of Heredity apply universally to all organisms.
- Cystic Fibrosis: a lethal genetic disease affecting Caucasians.
- Caused by mutant recessive gene carried by 1 in 20 people of European descent (12M)
- One in 400 Caucasian couples will be both carrie



of CF – 1 in 4 children will have it.
- CF disease affects transport in tissues – mucus is accumulated in lungs, causing

Inheritance pattern of CF

IF two parents <u>carry</u> the recessive gene of Cystic Fibrosis (*c*), that is, they are heterozygous (C *c*), one in four of their children is expected to be homozygous for *cc* and have the disease:

	C	*c*
C	C C	C *c*
c	C *c*	*c c*

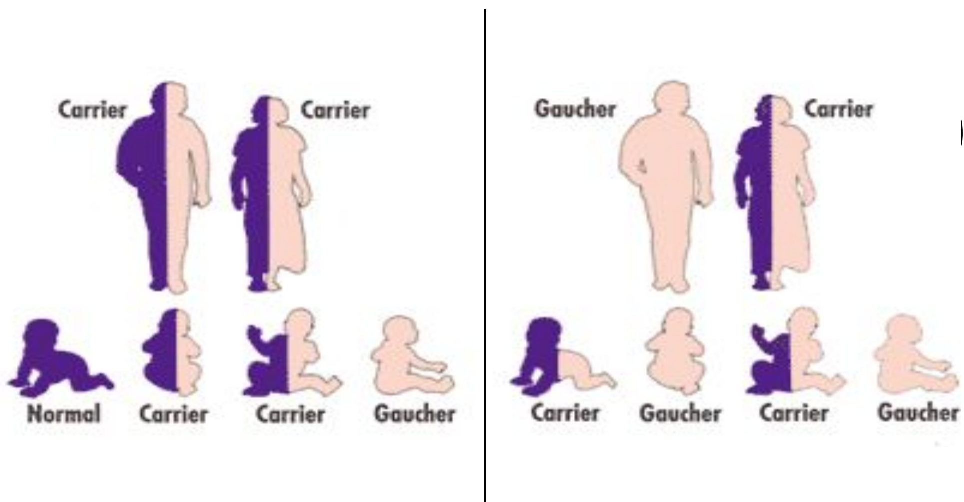
C C = normal
C *c* = carrier, no symptoms
c c = has cystic fibrosis

Probabilities…

- Of course, the 1 in 4 probability of getting the disease is just an **expectation**, and in reality, any two carriers may have normal children.
- However, the greatest probability is for 1 in 4 children to be affected.
- Important factor when prospective parents are concerned about their chances of having affected children.
- Now, 1 in 29 Americans is a symptom-less carrier (Cf *cf*) of the gene.

Gaucher Disease

- **Gaucher Disease** is a rare, genetic disease. It causes lipid-storage disorder (lipids accumulate in spleen, liver, bone marrow)
- It is the most common genetic **disease** affecting Jewish people of Eastern European ancestry
  (1 in 50 ,000)



Dihybrid crosses

- Matings that involve parents that differ in **two** genes (two independent traits)

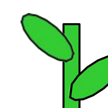
For example, flower color:

P = purple (dominant)

p = white (recessive)

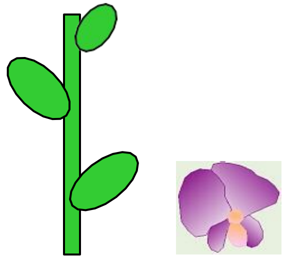
and stem length:

T = tall



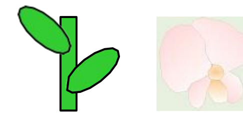
t = short

Dihybrid cross: flower color and stem length



TT PP× *tt pp*

(tall, purple) (short, white)



Possible Gametes for parents

T P and *t p*

	tp	*tp*	*tp*	*tp*
TP	T*t*P*p*	T*t*P*p*	T*t*P*p*	T*t*P*p*
TP	T*t*P*p*	T*t*P*p*	T*t*P*p*	T*t*P*p*
TP	T*t*P*p*	T*t*P*p*	T*t*P*p*	T*t*P*p*
TP	T*t*P*p*	T*t*P*p*	T*t*P*p*	T*t*P*p*

F1 Generation: All tall, purple flowers (T*t* P*p*)

Dihybrid cross: flower color and stem length (shortcut)

TT PP × *tt pp*

(tall, purple) (short, white)

Possible Gametes for parents

T P *t p*

	T P
t *p*	T *t* P *p*

F1 Generation: All tall, purple flowers (T*t* P*p*)

Dihybrid cross F_2

If F_1 generation is allowed to self pollinate, Mendel observed 4 phenotypes:

T*t* P*p* × T*t* P*p*

(tall, purple) $_T$(t$_P$all, pu$_{Tp}$rple)

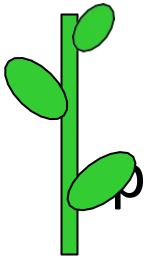
Possible gametes: TP T*p* *t*P *tp*

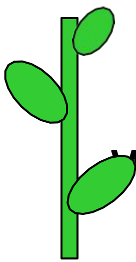
	TP	T*p*	*t*P	*tp*
TP	TTPP	TTP*p*	T*t*PP	T*t*P*p*
T*p*	TTP*p*	TT*pp*	T*t*P*p*	T*tpp*
*t*P	T*t*PP	T*t*P*p*	*tt*PP	*tt*P*p*
tp	T*t*P*p*	T*tpp*	*tt*P*p*	*ttpp*

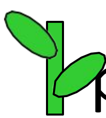
Four phenotypes observed

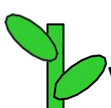
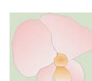
Tall, purple (9); Tall, white (3); Short, purple (3); Short white (1)

Dihybrid cross

9 Tall  purple 

3 Tall  white 

3 Short  purple 

1 Short  white 

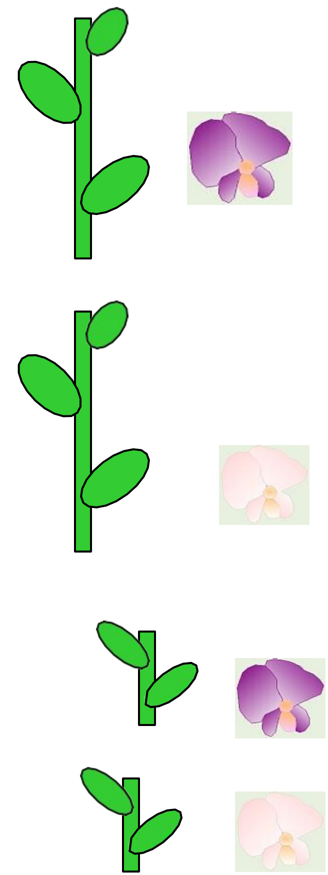
	TP	T*p*	*t*P	*tp*
TP	TTPP	TTP*p*	T*t*PP	T*t*P*p*
T*p*	TTP*p*	TT*pp*	T*t*P*p*	T*tpp*
*t*P	T*t*PP	T*t*P*p*	*tt*PP	*tt*P*p*
tp	T*t*P*p*	T*tpp*	*tt*P*p*	*ttpp*

Phenotype Ratio = 9:3:3:1

Dihybrid cross: 9 genotypes

Genotype ratios (9): Four Phenotypes:

1	TTPP	Tall, purple (9)
2	TTP*p*	
2	T*t*PP	
4	T*t*P*p*	
1	TT*pp*	Tall, white (3)
2	T*tpp*	
1	*tt*PP	Short, purple (3)
2	*tt*P*p*	
1	*ttpp*	Short, white (1)



Principle of Independent Assortment

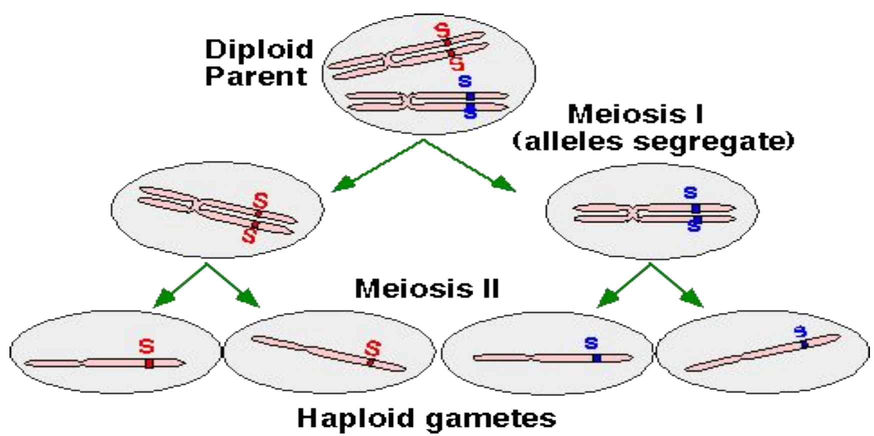
- Based on these results, Mendel postulated the **3. Principle of Independent Assortment**:

  "Members of one gene pair segregate independently from other gene pairs during gamete formation"

Genes get shuffled – these many combinations are one of the advantages of sexual reproduction

Relation of gene segregation to meiosis…

- There’s a correlation between the movement of chromosomes in meiosis and the segregation of alleles that occurs in meiosis

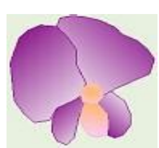


Test cross

When you have an individual with an unknown genotype, you do a **test cross.**

Test cross: Cross with a homozygous recessive individual.

For example, a plant with **purple** flowers can either be **PP** or **P*p***…therefore, you cross the plant with a *pp* (white flowers, homozygous recessive)



P ? × *pp*

Test cross

- If you get all 100% purple flowers, then the unknown parent was PP…

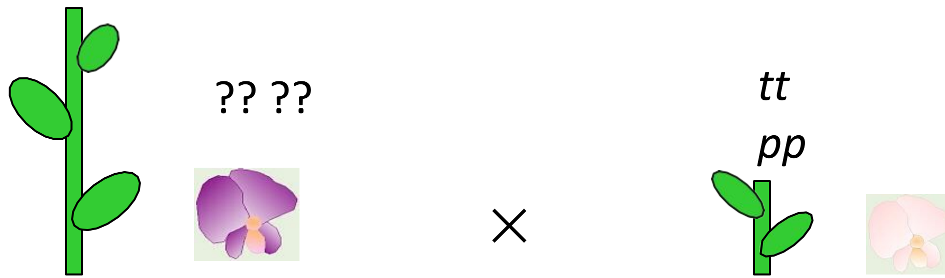
	P	**P**
p	P*p*	P*p*
p	P*p*	P*p*

- If you get 50% white, 50% purple flowers, then the unknown parent was P*p*…

	P	***p***
p	P*p*	*p p*
p	P*p*	*p p*

Dihybrid test cross??

If you had a tall, purple plant, how would you know what genotype it is?



1. TTPP
2. TTP*p*
3. T*t*PP
4. T*t*P*p*

Beyond Mendelian Genetics: Incomplete Dominance

Mendel was lucky! Traits he chose in the pea plant showed up very clearly…

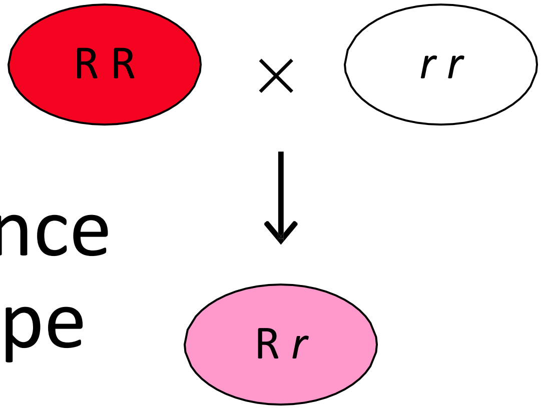
One allele was dominant over another, so phenotypes were easy to recognize.

Incomplete Dominance

Snapdragon flowers come in many colors.

If you cross a red snapdragon (RR) with a white snapdragon (rr)

You get PINK flowers (Rr)!



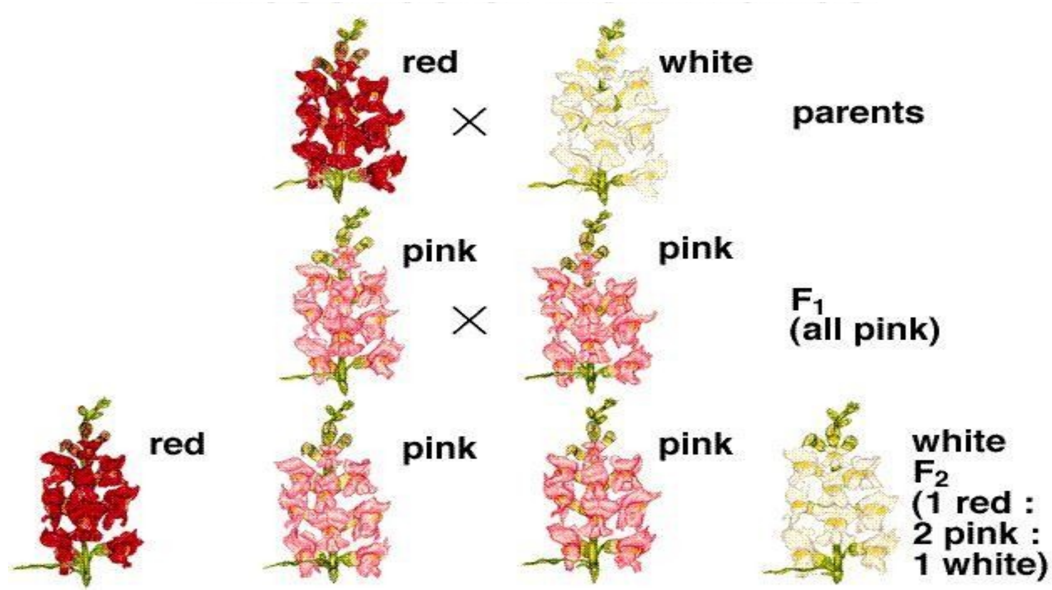
Genes show incomplete dominance when the heterozygous phenotype is intermediate.

Incomplete dominance

When F1 generation (all pink flowers) is self pollinated, the F2 generation is 1:2:1 red, pink, white

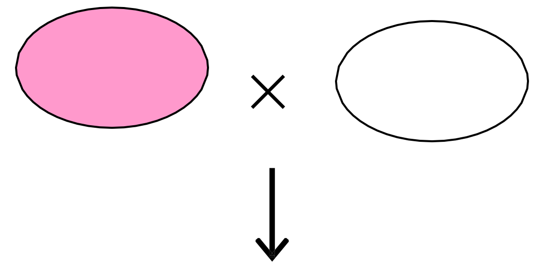
	R	***r***
R	**R R**	**R *r***
r	**R *r***	***r r***

Incomplete Dominance

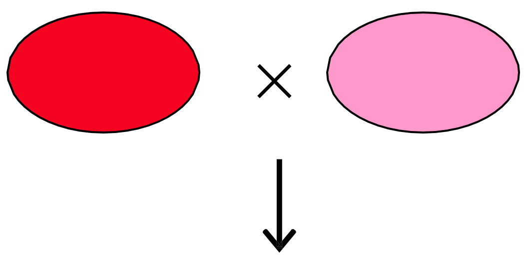


Incomplete dominance

What happens if you cross a pink with a white?



A pink with a red?



Summary of Genetics

- Chromosomes carry hereditary info (genes)
- Chromosomes (and genes) occur in pairs
- New combinations of genes occur in sexual reproduction
- Monohybrid vs. Dihybrid crosses
- Mendel’s Principles:
  - Dominance: one allele masks another
  - Segregation: genes become separated in gamete formation
  - Independent Assortment: Members of one gene pair segregate independently from other gene pairs during gamete formation

What is Mathematical Biology?

- **Talking to biologists and getting familiar with their experiments and data with respect to a biological process.**
- **Developing a mathematical model that describes the biological process (e.g., by differential equations).**
- **Simulating and comparing the numerical results with experimental results – and keep revising until the fit is satisfactory.**
- **Using the model to make a new hypothesis and suggest new experiments.**

What is Mathematical Modeling?

- A mathematical model is the formulation in mathematical terms of the **assumptions** believed to underlie a particular real-world problem
- Mathematical modeling is the **process** of deriving such a formulation

Value of Models

- Mathematical modelling is fundamental to engineering research. A mathematical model may be simple or complex:

- Qualitative model formulation, is the conversion of an objective statement and a set of hypotheses and assumptions into an informal, conceptual model

- Qualitative model is then converting this to a quantitative model.

- Model may consist of no more than one mathematical equation or may involve hundreds of equations.

- Its subject may be a comprehensive overview of a total system or it may be the tiniest piece of a microminiature subsystem

Types of models

- The theoretical model is based on well-established basic principles, such
- as Ohm's Law ($I = E/R$) or Newton's Second Law ($F = ma$).

- Empirical models are mathematical descriptions of observations, and they often involve a good deal of fitting curves to data.

- A large number of mathematical models of biological systems are empirical because the subject matter is often very complex and far removed from the simple application of basic principles.

- To construct an empirical model, one would begin with a set of numerical
- observations and attempt to fit the data with a mathematical expression that preserved the essence of the variation of the data without reproducing the unessential (or *noise*) aspects of data variation.

Steps in model formulation

steps recommended for modeling. These are

1. Conceptualize.

2. Separate model elements.

3. Capture the essence of each element.

4. Maintain interface ability.

5. Mathematically describe each element.

6. Solve numerically for parameter values (calibration).

7. Compare model results against experimental results (validation).

8. Revise model.

Why is it Worthwhile to Model Biological Systems

- To help reveal possible underlying mechanisms involved in a biological process
- To help interpret and reveal contradictions/incompleteness of data
- To help confirm/reject hypotheses
- To predict system performance under untested conditions
- To supply information about the values of experimentally inaccessible parameters
- To suggest new hypotheses and stimulate new experiments

What do you do with the model?

- Solutions—Analytical/Numerical
- Interpretation—What does the solution mean in terms of the original problem?
- Predictions—What does the model suggest will happen as parameters change?
- Validation—Are results consistend with experimental observations?