Macromolecules of Life -1

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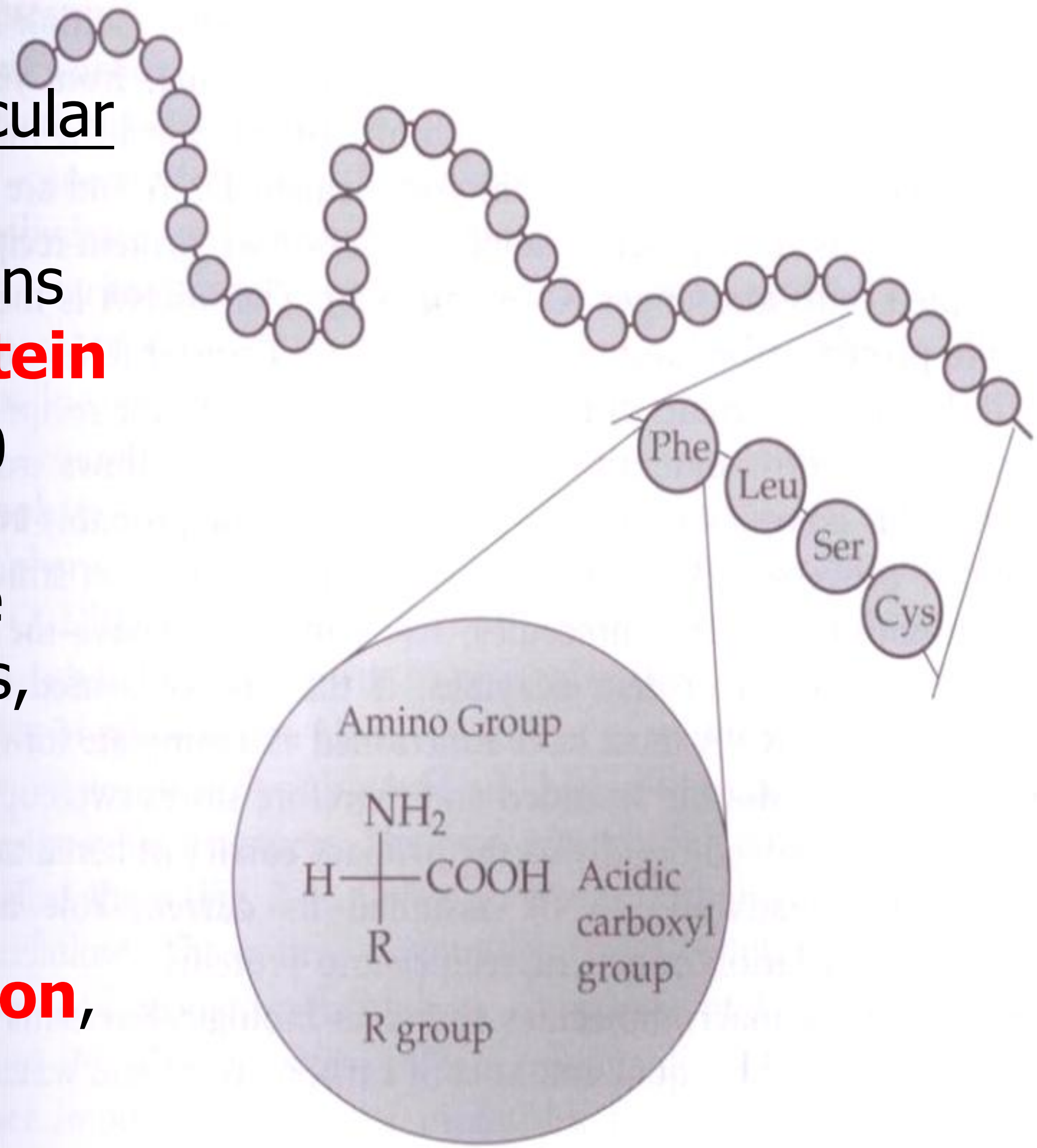
Introduction of Macromolecules

- Water constitutes about 70% of the weight of a living cell; the rest is composed of macromolecules containing thousands of atoms.
- Monomers (chains of smaller units) → biological macromolecules
  - **4** distinct monomers – **nucleotides** → the information macromolecule **deoxyribonucleic acid (DNA)**
  - **20** different monomers – **amino acids** → **proteins**
- The macromolecules of living organisms are classified into four groups: **proteins**, **nucleic acids**, **carbohydrates**, and **lipids**.

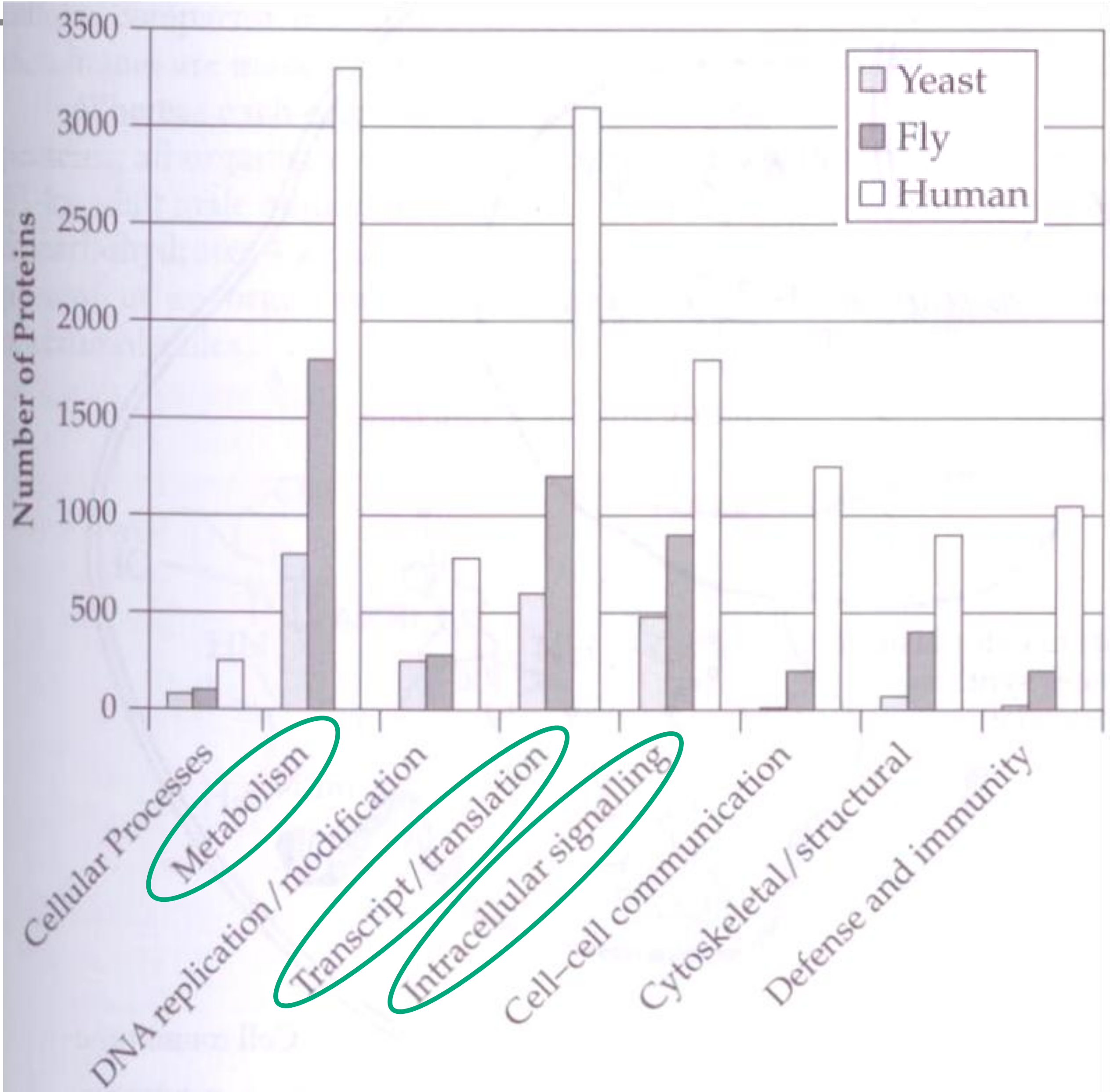
Proteins-1

- Make up <u>most of the molecular machinery of all organisms</u>
- Proteios (Greek word) means "**of the first rank**"→ **Protein**
- Linear chains of at most 20 different amino acids → constitute tissues, facilitate complex chemical reactions, and act as sensors, transducers, and energy transformers
- Contain the elements **carbon**, **hydrogen**, **oxygen**, **nitrogen**, and **sulfur**



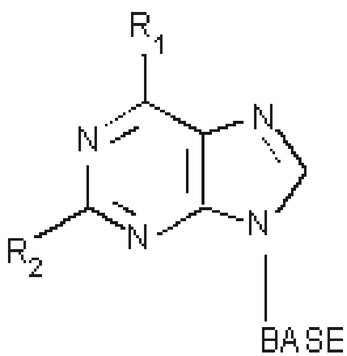
Proteins-2

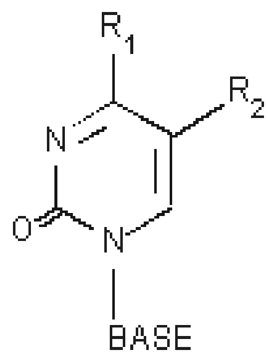
- Temporarily associated with a **phosphate group** → rapidly undergo shape changes and gain or lose enzymatic activity
- As enzyme, proteins bring substrates to appropriate configurations for chemical reactions to proceed.
- Proteins synthesized by various multicellular organisms group into major functional categories.



Nucleic Acids-1

Purine Nucleoside	Pyrimidine Nucleoside

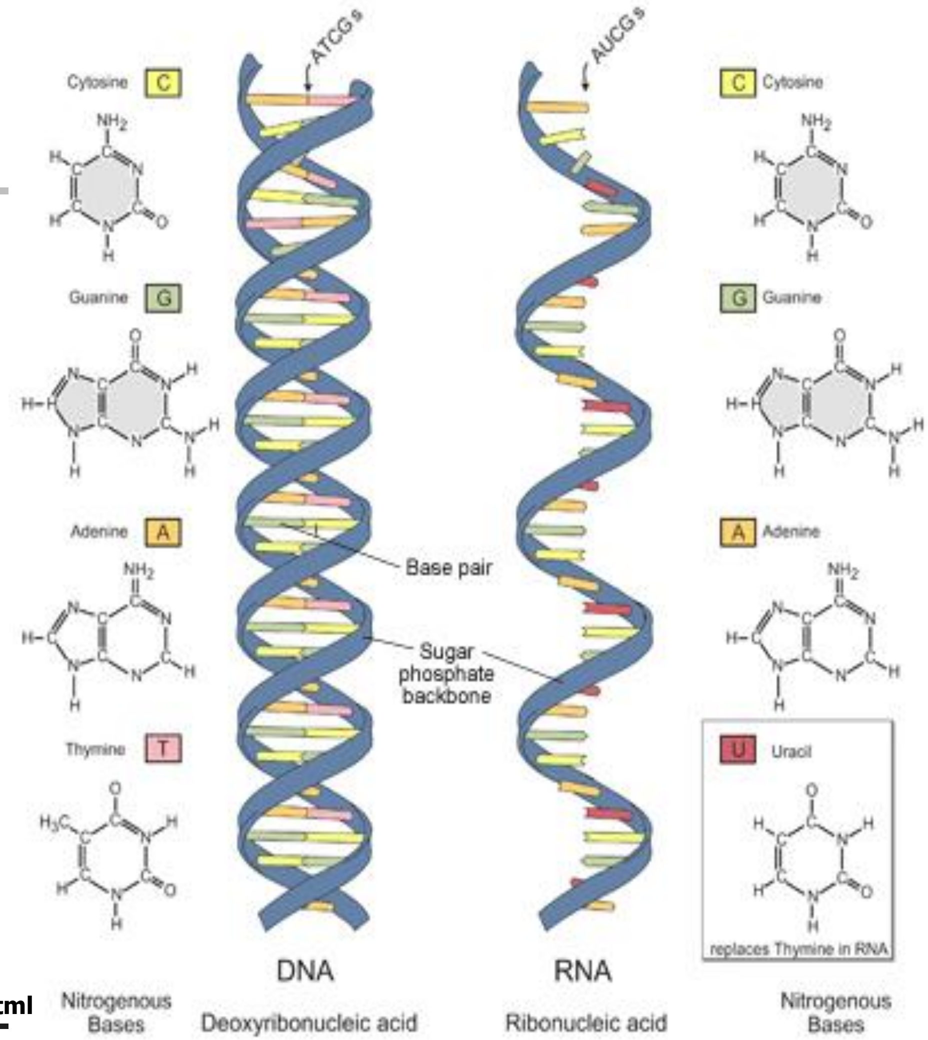




	R_1	R_2
Adenosine	NH_2	H
Guanosine	=O	NH_2

	R_1	R_2
Cytidine	NH_2	H
Thymidine	=O	CH_3
Uracil	=O	H

http://www.biotek.com/resources/articles/nucleic-acids-spectrophotometer.html

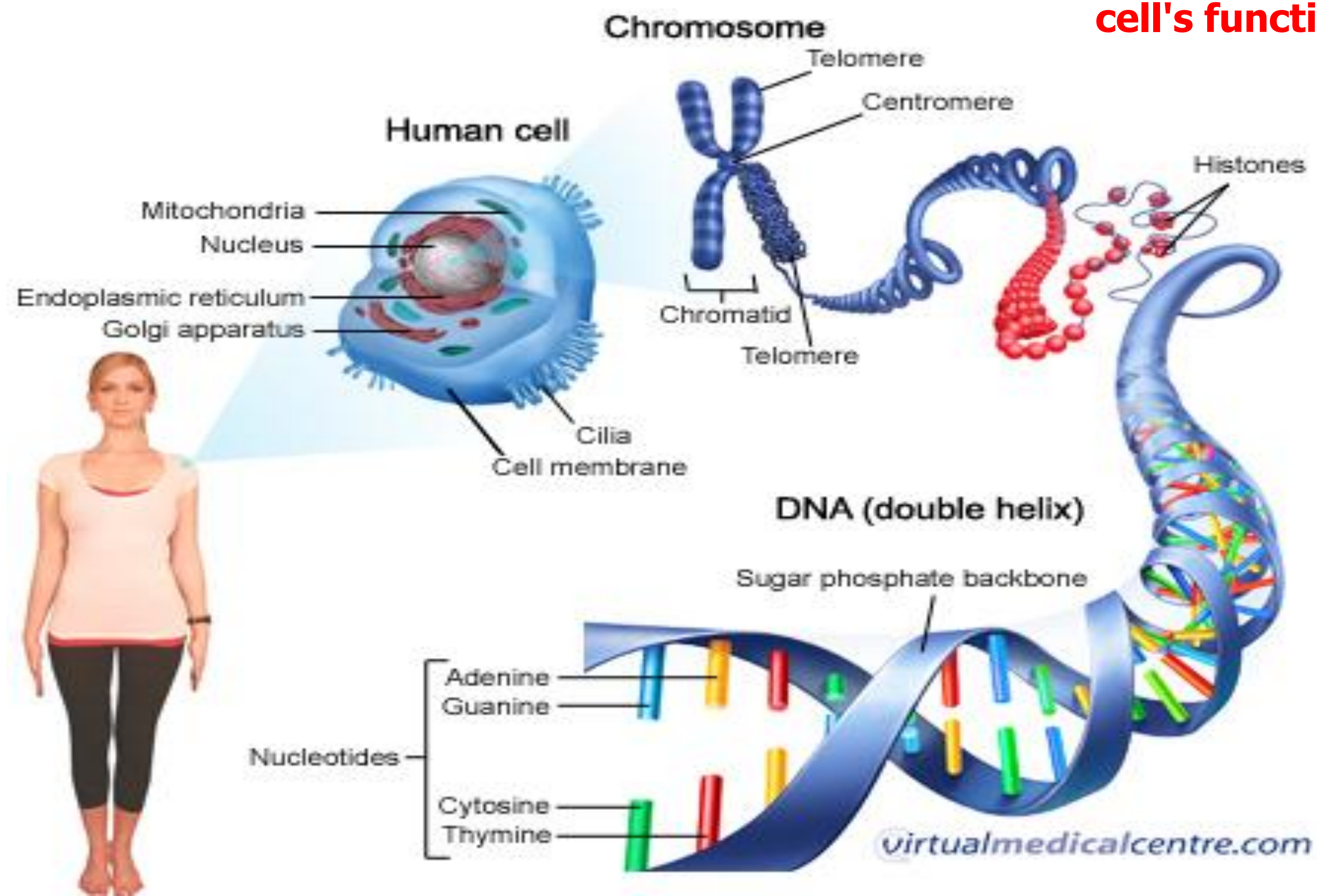


http://rst.gsfc.nasa.gov/Sect20/A12.html

- The information macromolecules of living systems
- Contain **carbon**, **hydrogen**, **oxygen**, and **nitrogen** (like proteins)
- Also contain **phosphorus**, **but do not contain sulfur**
- Group into 2 sets: **DNA (deoxyribonucleic acid)** and **RNA (ribonucleic acid)**

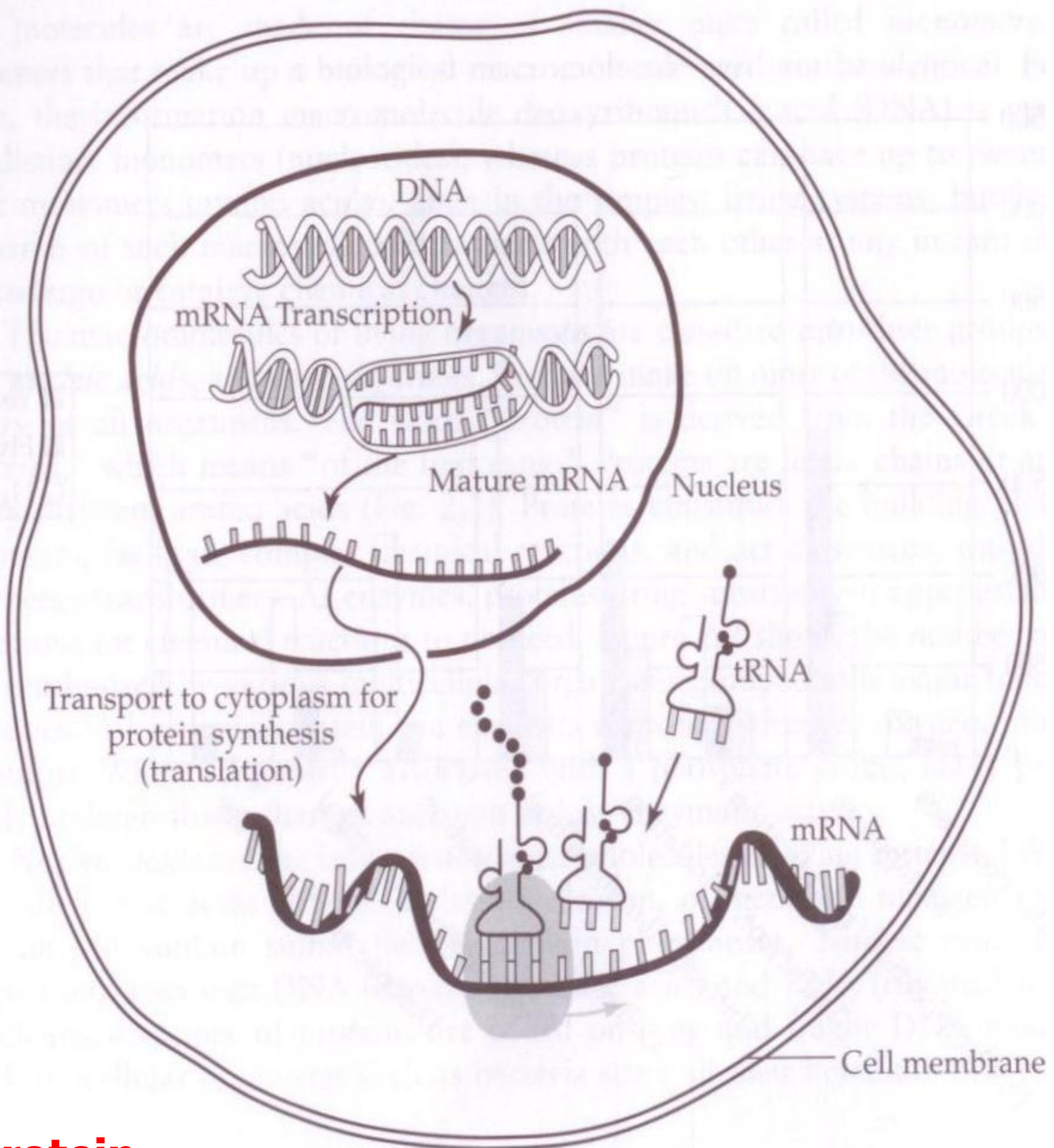
Nucleic Acids-2

- **Nucleic acids store genetic information and instructions for protein synthesis and all of the cell's functions**



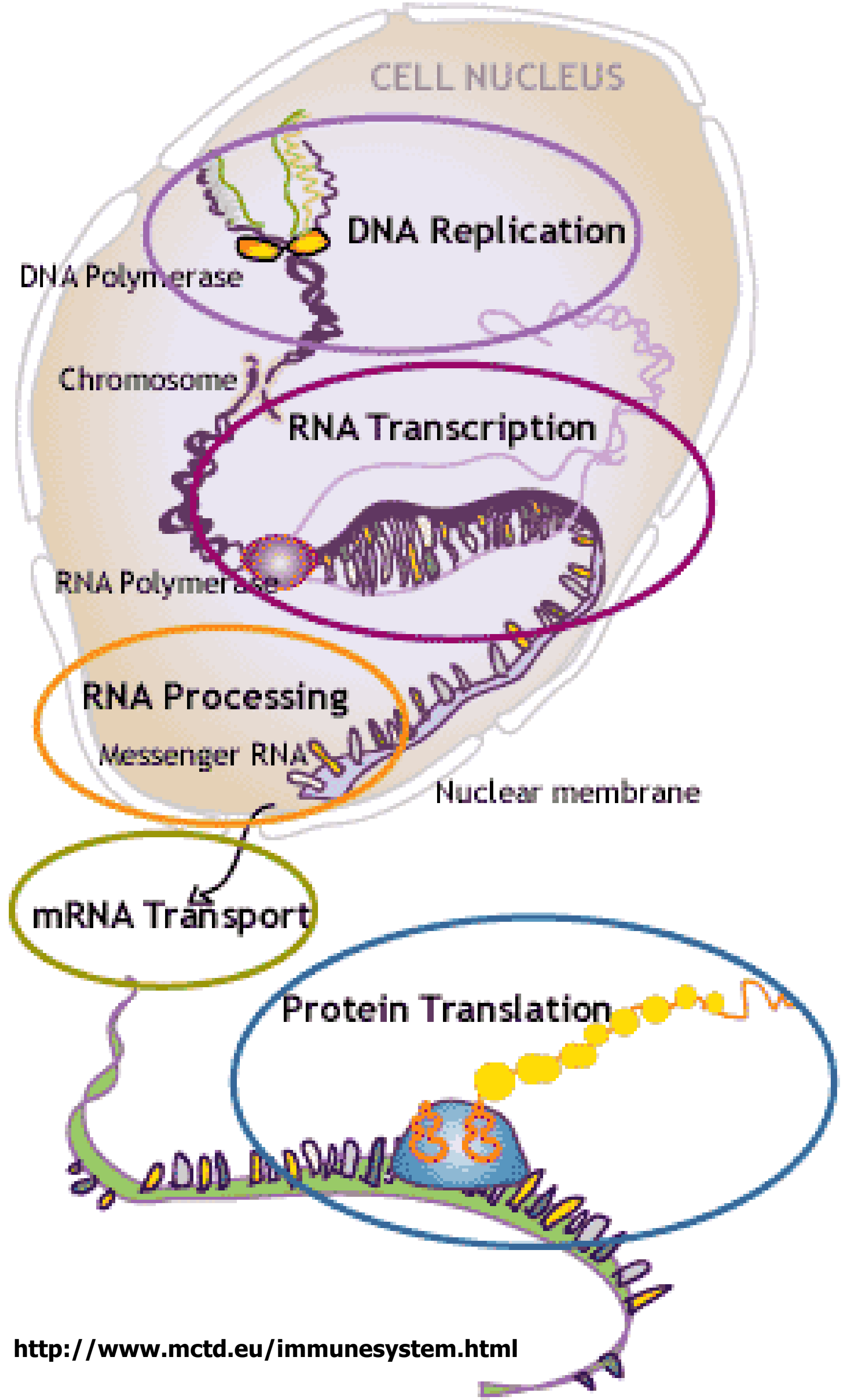
Nucleic Acids-3

- DNA and RNA, can always be found in all cells of everything from bacteria to humans. **DNA** is always found in the nucleus of the cell. **RNA** can also be found in the nucleus but also throughout the cell.
- **RNA** is broken down into three subcategories: messenger *RNA (mRNA)* - carries the genetic code from the DNA to the ribosome, transfer *RNA (tRNA)* - translates this code (called nucleotides) in the messenger RNA into amino acids structures, Ribosomal *RNA (rRNA)* - links the amino acid chains into proteins.
- **DNA** --- **Transcription** ---> **mRNA** └──> **Translation** **Protein**



Nucleic Acids-4

- DNA --Transcription--> mRNA --Translation--> Protein

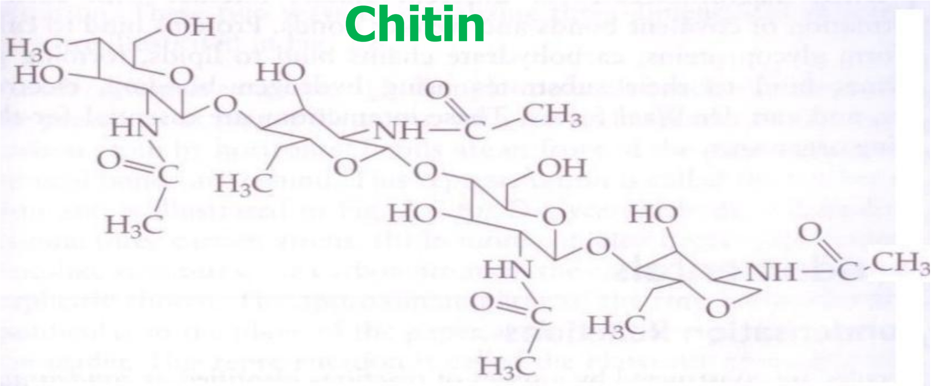


http://www.mctd.eu/immunesystem.html

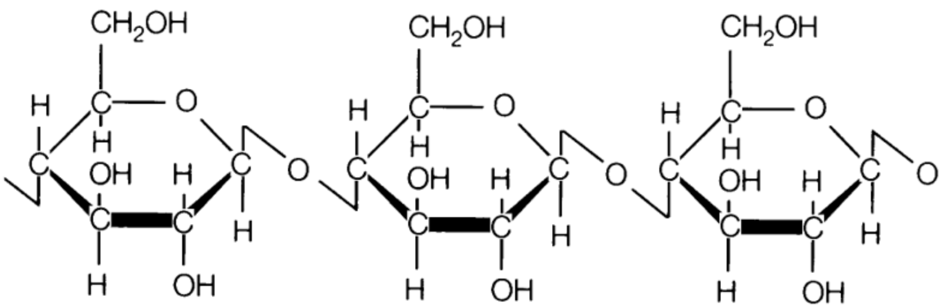
Carbohydrates

- Contain roughly equal amounts of **carbon atoms** and **water molecules**
- **Glucose** – important source of energy for driving cellular process
- Often present on proteins by forming covalent bonds with the free amino groups (asparagine) or hydroxyl groups (serine)
- Sialic acid – negative charge when present on proteins of cell membrane form a charge barrier known as glycocalyx
- **Carbohydrates** on the surface of proteins are often the source of immune or allergic reactions.
- Play important roles in **cell signaling and communication**

Chitin



Cellulose

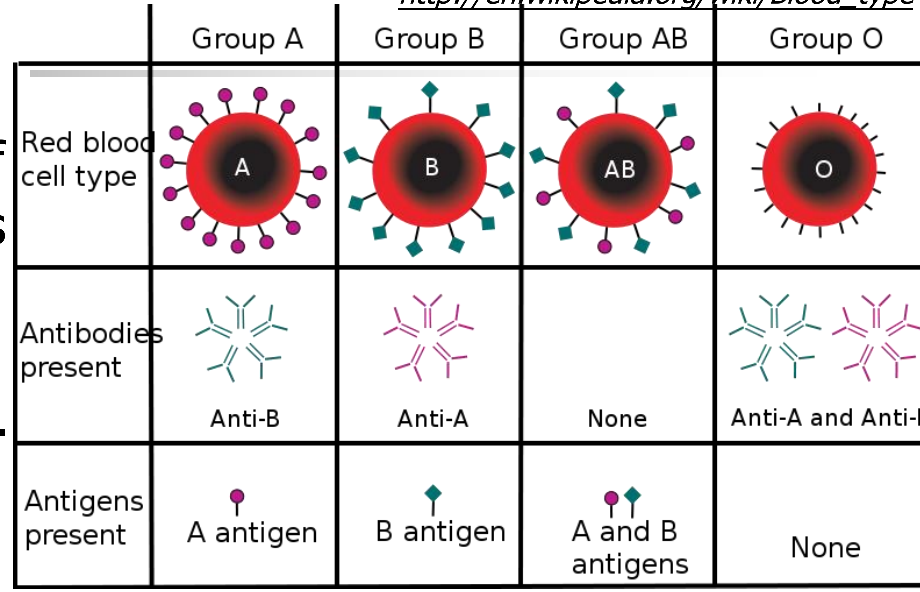


http://webspace.ship.edu/gspaul/animal%20behavior/cockroach/index.html

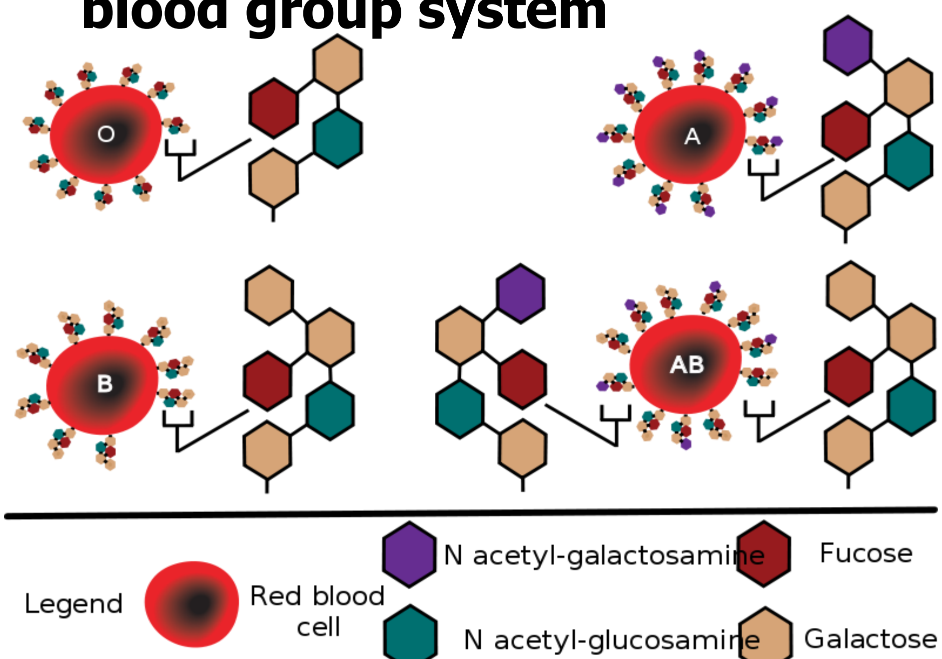
Blood Type (also called a **blood group**)

- A classification of blood based on the presence or absence of inherited antigenic substances on the surface of red blood cells (RBCs). These antigens may be proteins, carbohydrates, glycoproteins, or glycolipids, depending on the blood group system.
- **ABO blood group system & Rh blood group system**

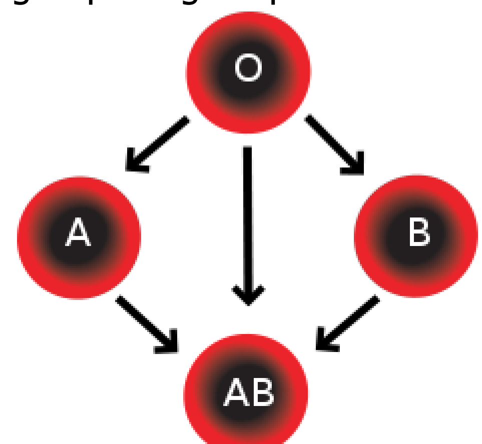
http://en.wikipedia.org/wiki/Blood_type



Blood type (or blood group) is determined, in part, by the ABO blood group antigens present on red blood cells.



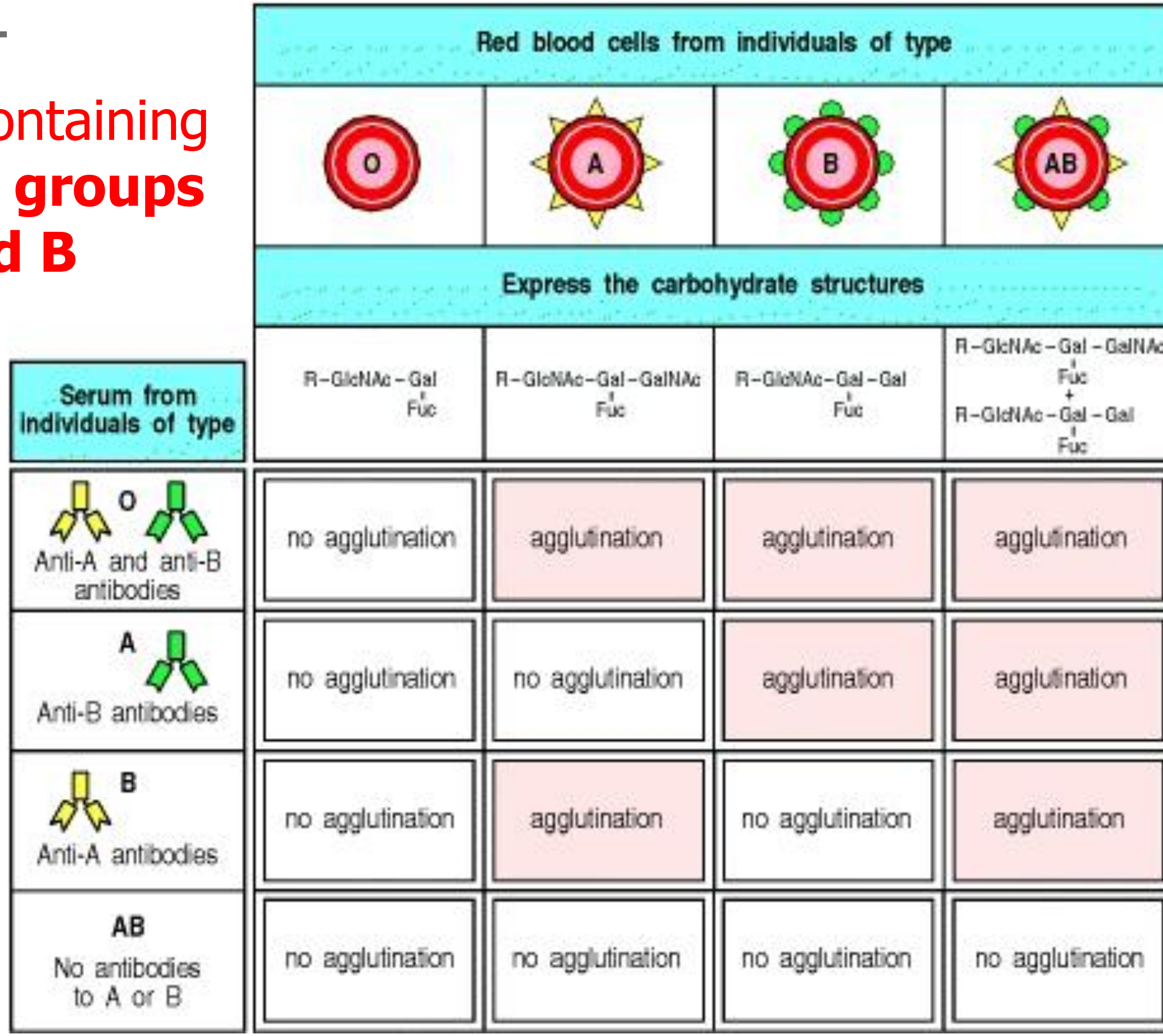
ABO blood group system: diagram showing the carbohydrate chains that determine the ABO blood group



RBC Compatibility chart
In addition to donating to the same blood group; type O blood donors can give to A, B and AB; blood donors of types A and B can give to AB.

Carbohydrates - Hemagglutination

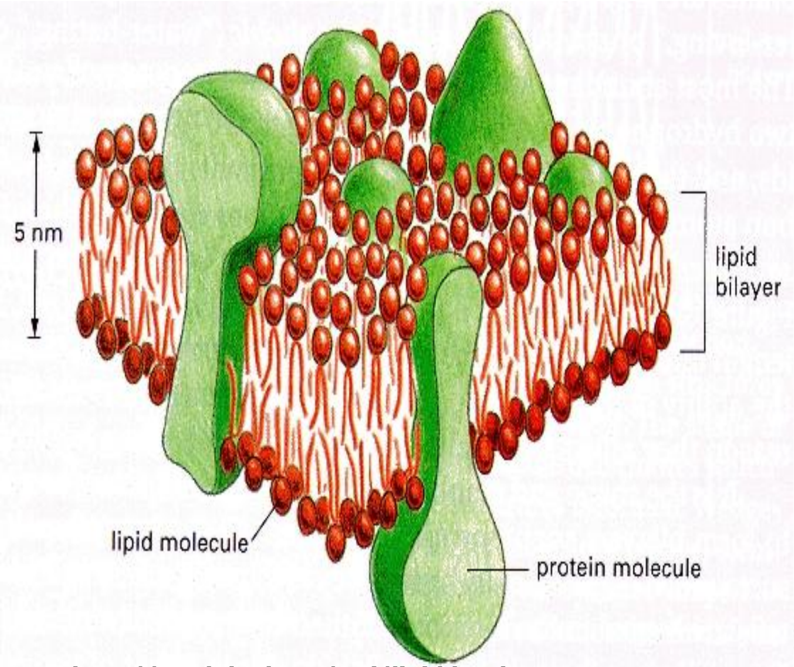
- Carbohydrate-containing proteins: **blood groups antigens A and B**
- Used to determine the ABO blood group of blood donors and transfusion recipients



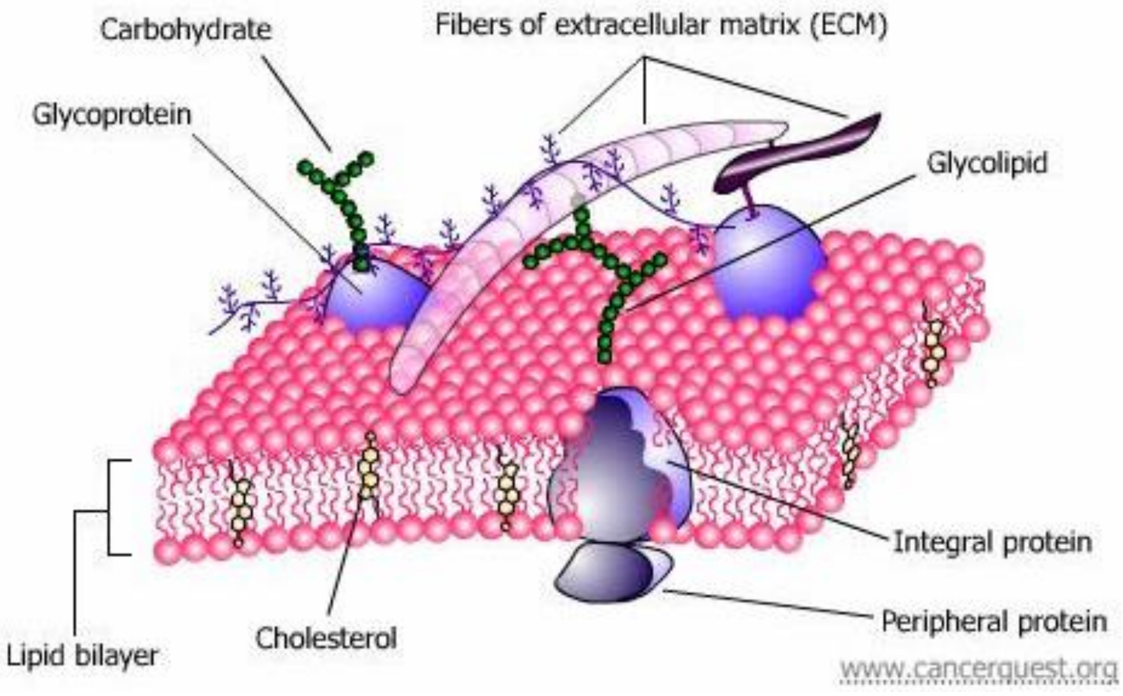
http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=imm&part=A2395&rendertype=figure&id=A2412

Lipid-1

- Are mostly made up of **carbon** and **hydrogen**
- Are not true macromolecules – because they **form large structures through associations** other than covalent bonding
- Form membranes for separating cells from each other, create cellular compartments, and perform other complex tasks

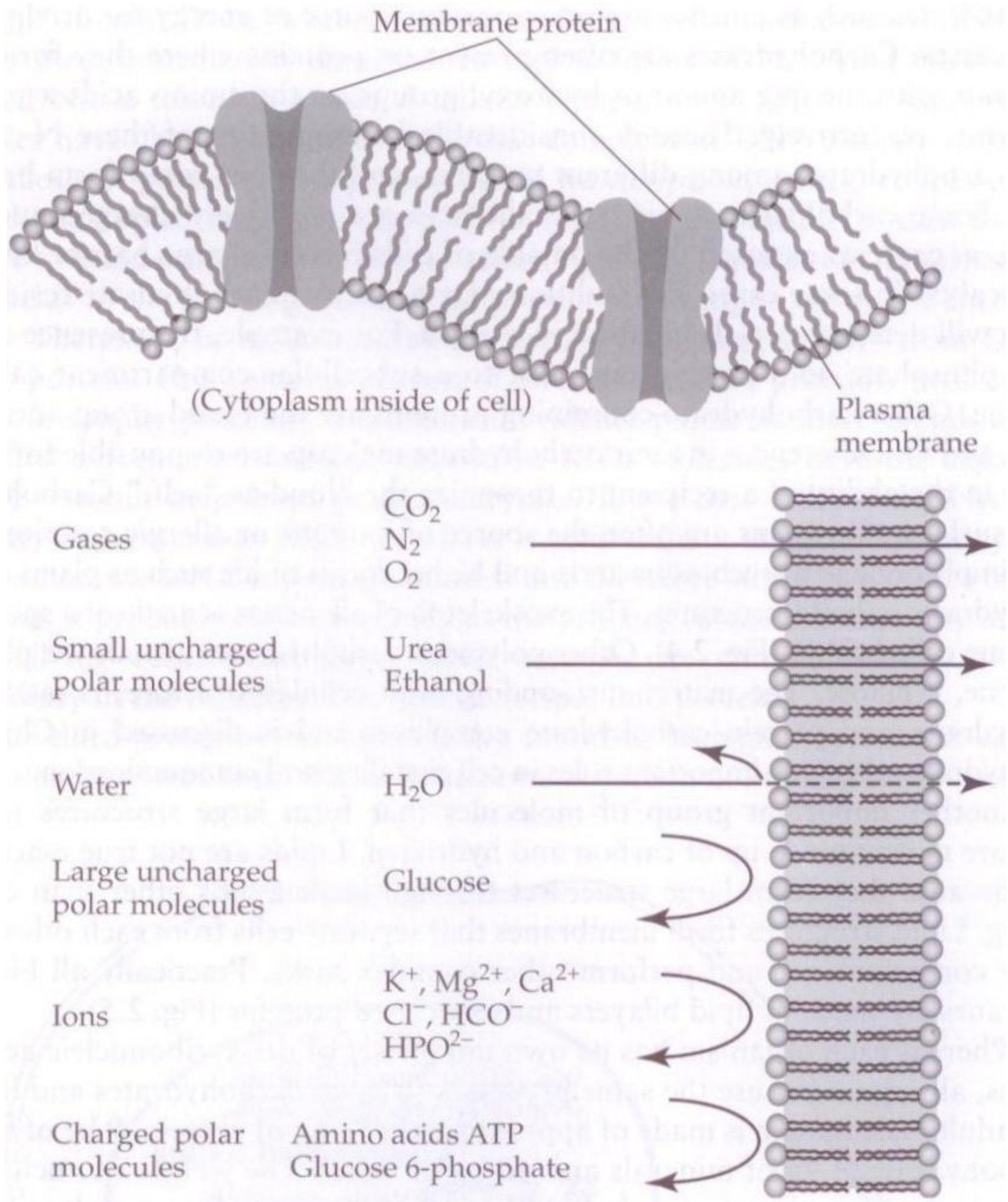


http://math.lanl.gov/~yi/lipid.html



Lipid-2

- All biological membranes are made of **lipid bilayers** and **associated proteins**
- Gases and small uncharged molecules can penetrate cell membrane



Summary

- 65-kg adult male human: 11kg of protein, 9 kg of fat, 1 kg of carbohydrate, 4 kg of minerals and 40 kg of water, **but the weight of nucleic acids** in an organism is much less than the corresponding weights of other macromolecules
- Macromolecules of different classes interact with each other by forming **covalent bonds** and **weaker bonds**
- Proteins bind to carbohydrates → **glycoproteins**, carbohydrate chains bind to lipid → **glycolipids**
- Enzymes bind to their substrates by **hydrogen bonding**, **electrostatic interactions**, and **ven der Waal forces**.

Condensation Reactions

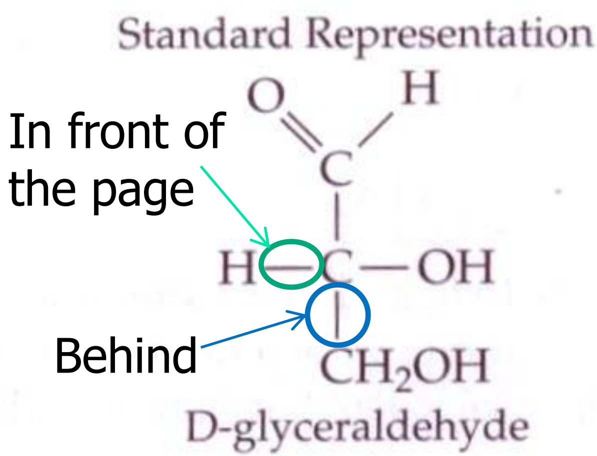
- Macromolecules are constructed by a series of reactions identified as **condensation reactions** or **dehydration reactions**

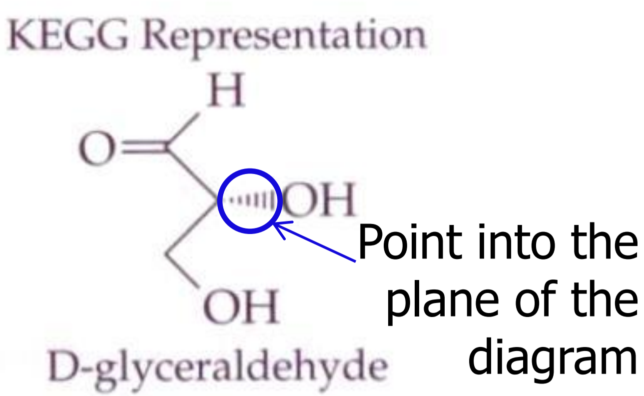
  BABBA—H + B—OH → BABBAB + H_2O

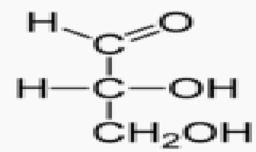
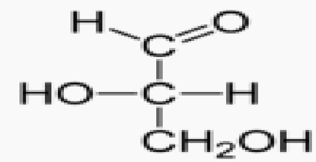
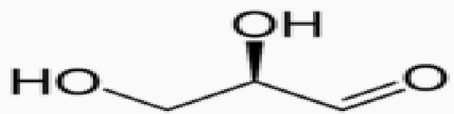
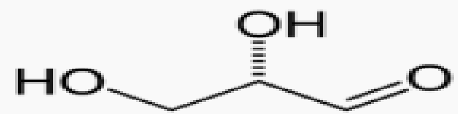
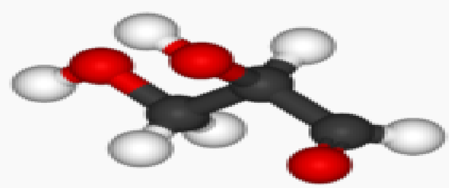
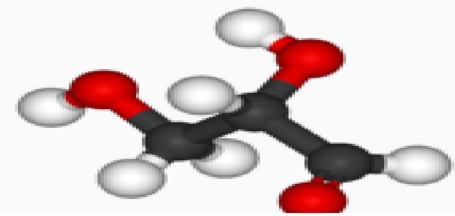
- Monomers are identified by the name of the building block followed by the word "residue", Ex: nucleotide residues.
- The synthesis of macromolecules occurs only if energy is added to the system. → the synthesis of macromolecules must be coupled to energy-releasing (**exergonic**) reactions
- Reverse reaction of condensation: **Hydrolysis** → releases energy to the environment (does not occur in the absence of mediating enzymes)
- Both condensation and hydrolysis reactions require the catalytic action of enzymes.

Structural Representation

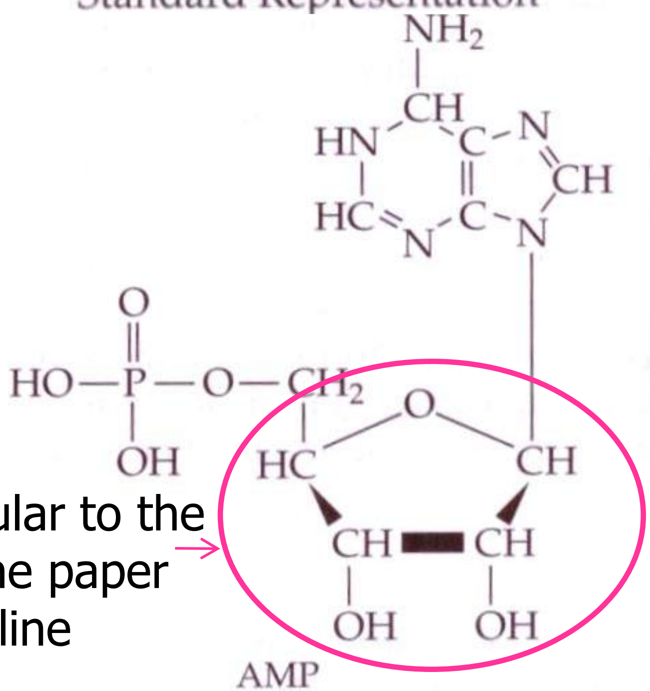
- The four types of macromolecules that are essential for living systems exhibit distinctly different 3-D structures.
- **Standard representation**: according to the Haworth projections
- **Second representation (KEGG)**: create digital databases for molecules**,** **do not indicate** the presence of **hydrocarbon bonds**





	D-glyceraldehyde (R)-glyceraldehyde (+)-glyceraldehyde	L-glyceraldehyde (S)-glyceraldehyde (−)-glyceraldehyde
Fischer projection		
Skeletal formula		
Ball-and-stick model		

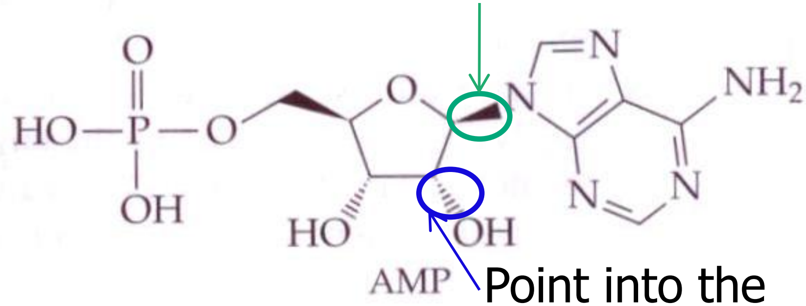
Standard Representation



Perpendicular to the plane of the paper with thick line

KEGG Representation

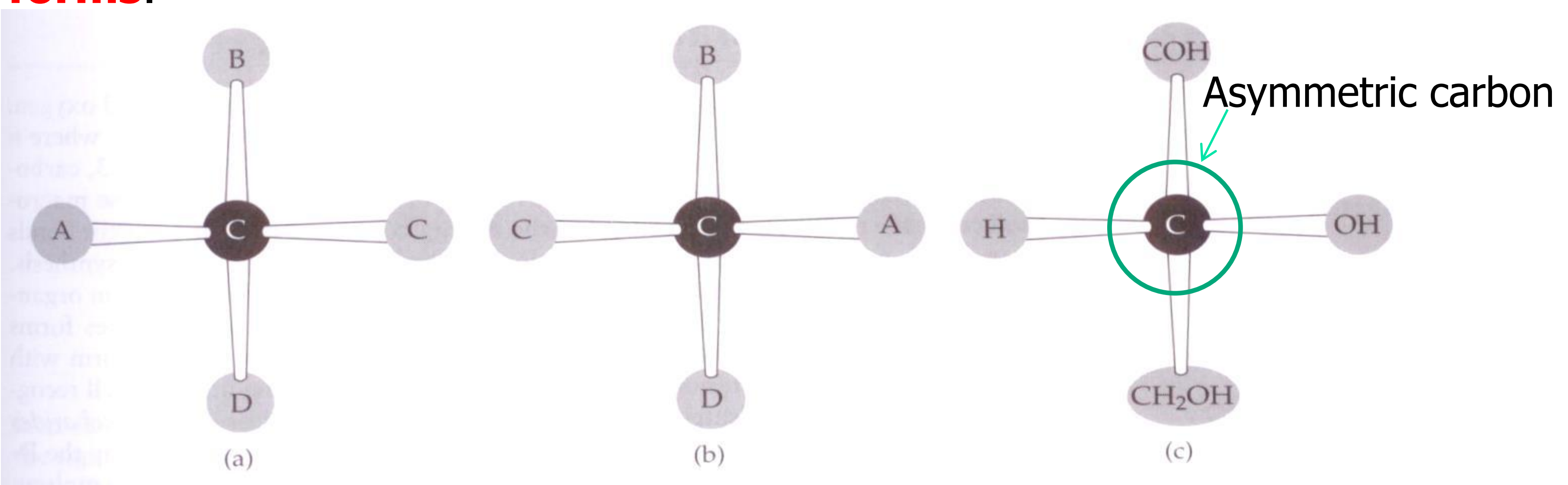
Toward the reader



Point into the plane of the diagram

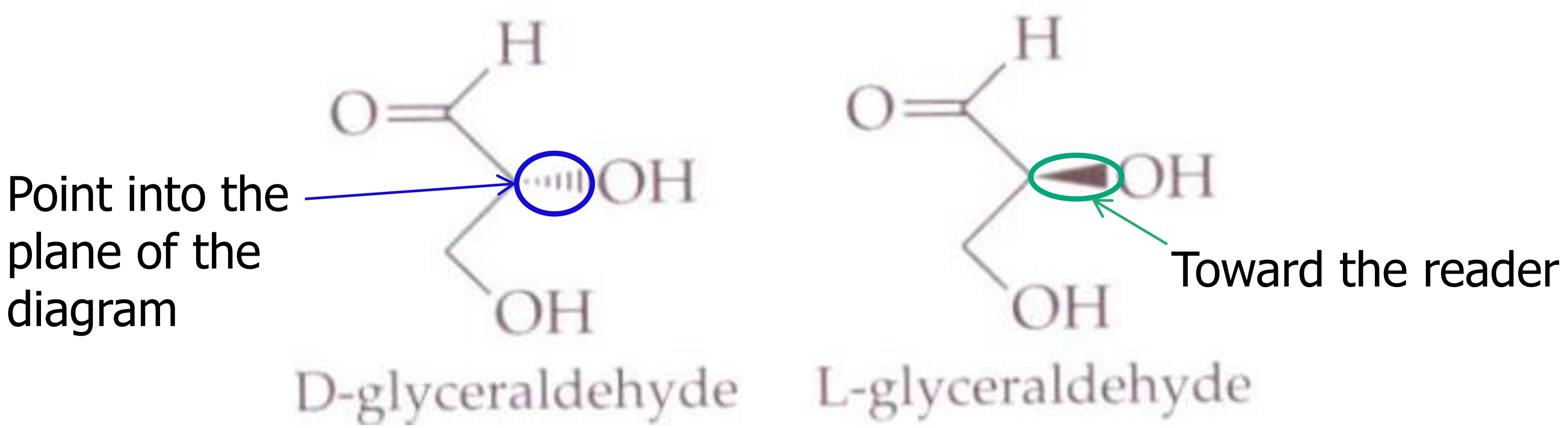
Stereoisomers and Biological Activity

- Molecules with identical chemical composition can have different spatial distributions of their atoms → significantly **different physical and chemical properties**
- **Isomers** – molecules with the same chemical composition, but with different 3D bond positioning
- **Stereoisomers** – isomers are mirror images of each other (like a left hand and right hand)
- Carbon atom gives rise to stereoisomers (binds to 4 different atoms or molecules) → **asymmetric or chiral carbon**
- A molecule with n asymmetric carbon atoms has **2^n stereoisomeric forms**.



Example of Stereoisomers

- Macromolecule family of **carbohydrates** contains many examples of stereoisomers.
- Example of stereoisomer: 3-carbon sugars D-glyceraldehyde and L-glyceraldehyde
- Central carbon atom is the asymmetric carbon:
  - hydroxyl group points inward → ***Dextro* (D) molecule**
  - hydroxyl group points outward → ***Levo* (L) molecule**



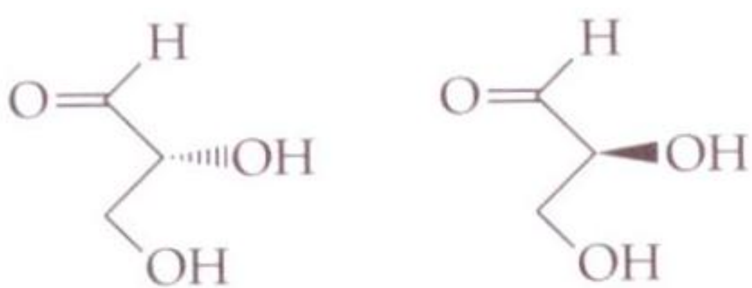
Carbohydrates

- Constructed of carbon, hydrogen, and oxygen
- **$C_n(H_2O)_m$**: n and m take the values of positive integers, called saccharides or sugars
- Carbohydrates are metabolized in cells and provide chemical energy for powering biological processes → the energy contained in their covalent bonds is used in locomotion, cell division, and protein synthesis
- Important functions as **structural building blocks in organism**, Ex: five-sugar carbohydrates
- Compounds that carbohydrates form with lipids and proteins play fundamental roles in protein trafficking and cell-cell recognition.
- Not all carbohydrates are sweet, D-sugars are more abundant than L-sugars in living organism

Monosaccharides

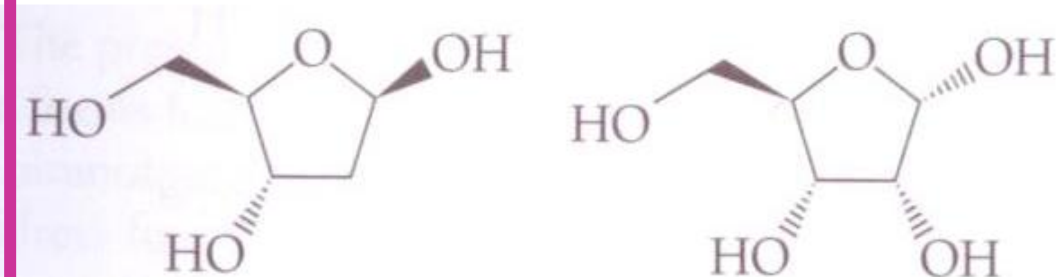
- Simplest carbohydrates
- The smallest monosaccharide molecules contain three and the largest contain seven carbon atoms.
- 3-carbon monosaccharide, Ex: D-glyceraldehyde → In living cells as intermediaries in the chemical reaction pathways that harvest energy from food
- **5-carbon sugars**, Ex: ribose and deoxyribose → Form parts of the backbones of the nucleic acids DNA and RNA

3-carbon sugars



D-glyceraldehyde L-glyceraldehyde

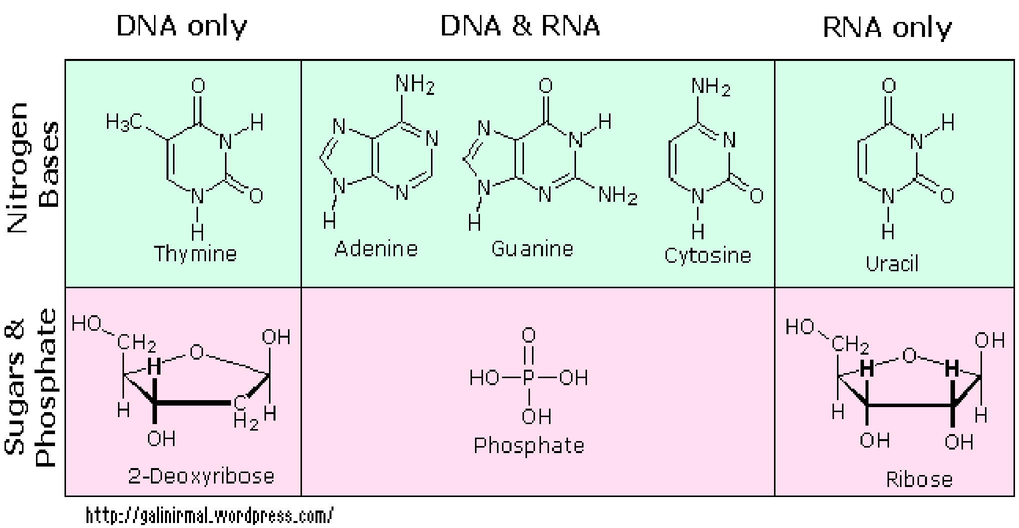
5-carbon sugars

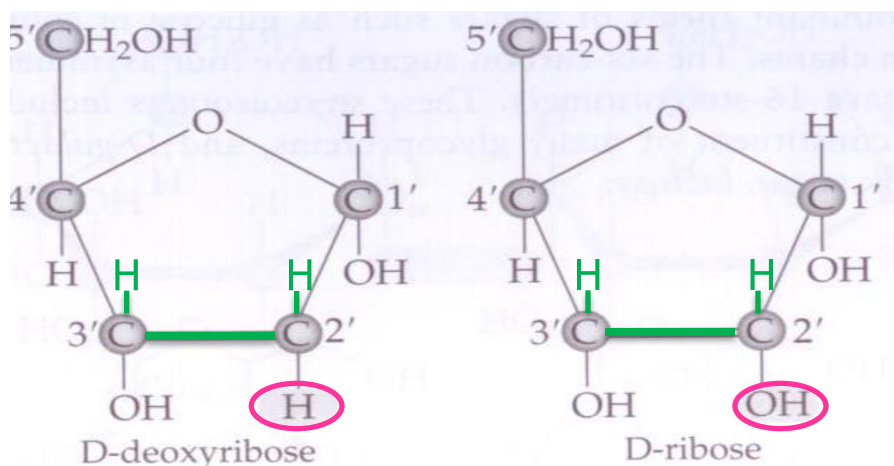


D-deoxyribose D-ribose

DNA and RNA

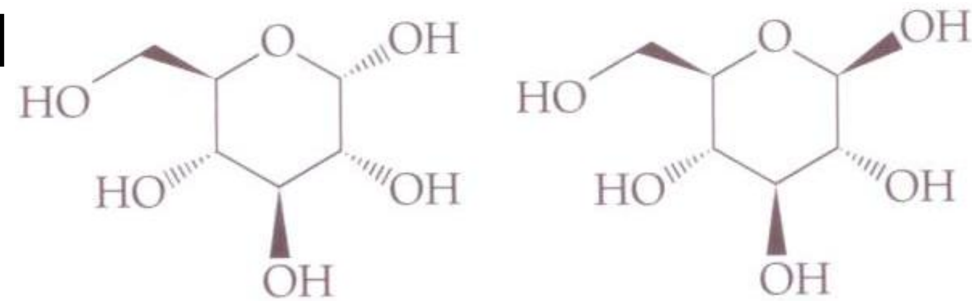
- Undergo condensation reactions by linking at different molecular sites
- Increase clockwise from central oxygen atom using primed integers 1′, 2′, 3′, 4′, and 5′
- Differ from each other by one atom → Oxygen atom is missing from carbon 2′ in DNA in relation to RNA (hydroxyl group is replaced by hydrogen atom)



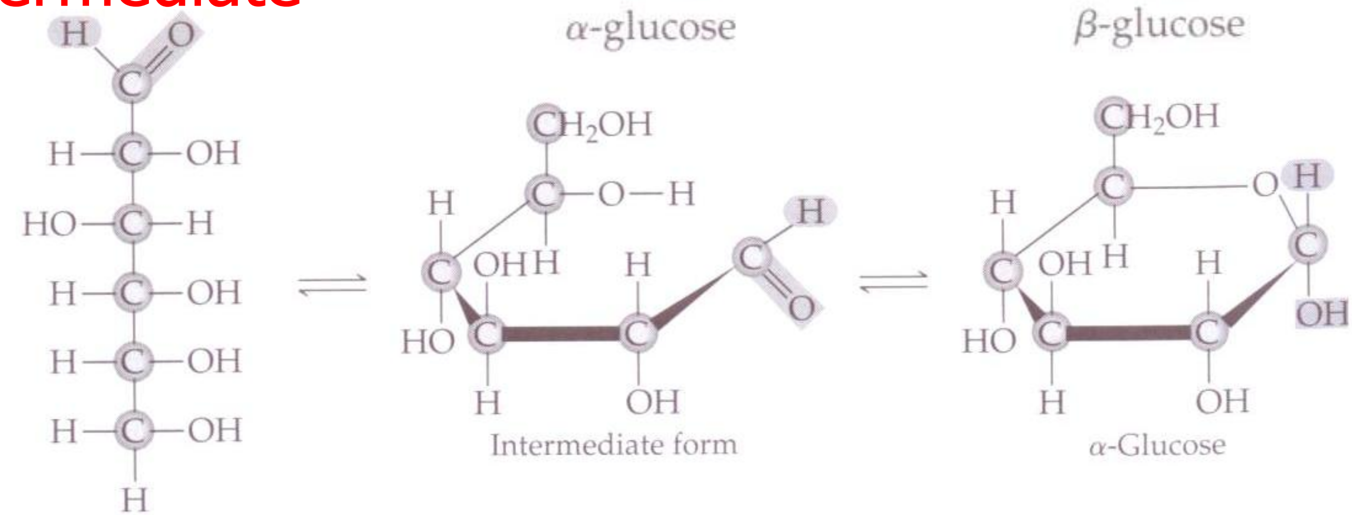


6-Carbon Sugars

- D-glucose ($C_6H_{12}O_6$) is also called grape sugar.
- The common stereoisomers of glucose are *α*- and *β*-glucose → Spatial placement of the –H and –OH attached to carbon 1’
- Ring structure forms *α*- and *β*-glucose can be obtained from the chain form through the intermediate form.
- Ring form is the dominant form in an aqueous environment.



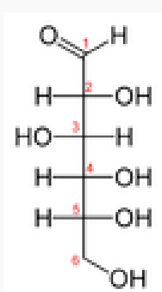
α-glucose β-glucose



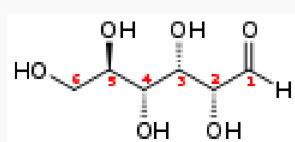
Straight-chain form Intermediate form α-Glucose

Stereoisomers of 6-Carbon Sugars

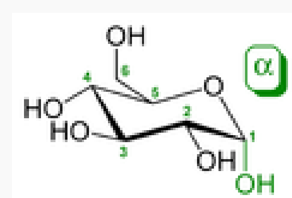
- 6-carbon sugars have four chiral centers in their acyclic forms (i.e. ignoring the anomeric carbon) → Four chiral centers give rise to 2^4 = 16 stereoisomers.
- These stereoisomers are classified into two classes with eight sugars in each, which are mirror images of each other. One class is labeled **L** and the other **D**.
- Only seven of these isomers are found in nature, of which D-glucose (Glu), D-galactose (Gal) and D-mannose (Man) are the most important. These eight isomers (including glucose itself) are diastereoisomers and belong to the **D series**.



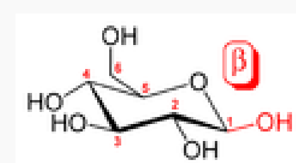
The Fischer projection of the chain form of D-glucose



The chain form of D-glucose



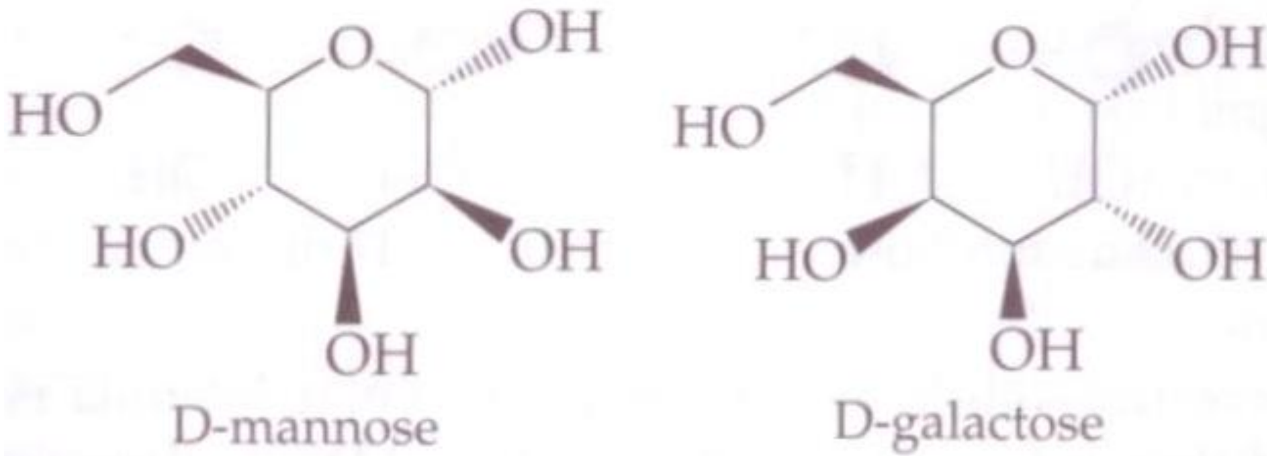
α-D-glucopyranose



β-D-glucopyranose

D-Mannose and D-Galatose

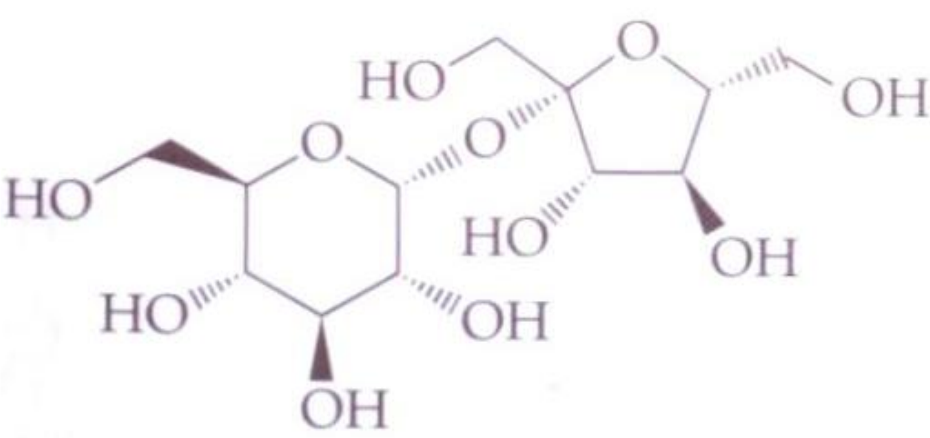
- **D-mannose** (fruit sugar) → A constituent of many glycoproteins
- **D-galactose** → The building block of the milk sugar (lactose)



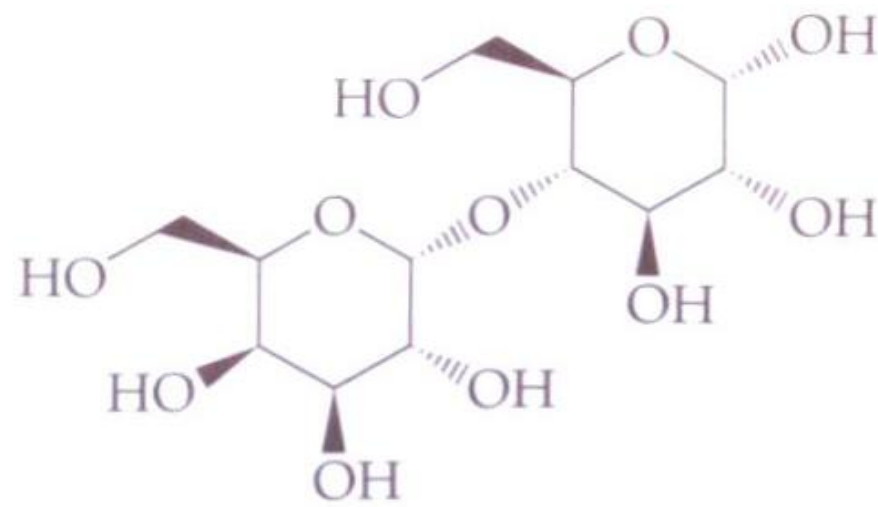
- D-glucose contained in all living cells → Green plants produce D-glucose by **photosynthesis**, others acquire it from plants.
- Cells uses glucose as primary energy source and harvest its chemical energy through energy-releasing reactions

Disaccharides

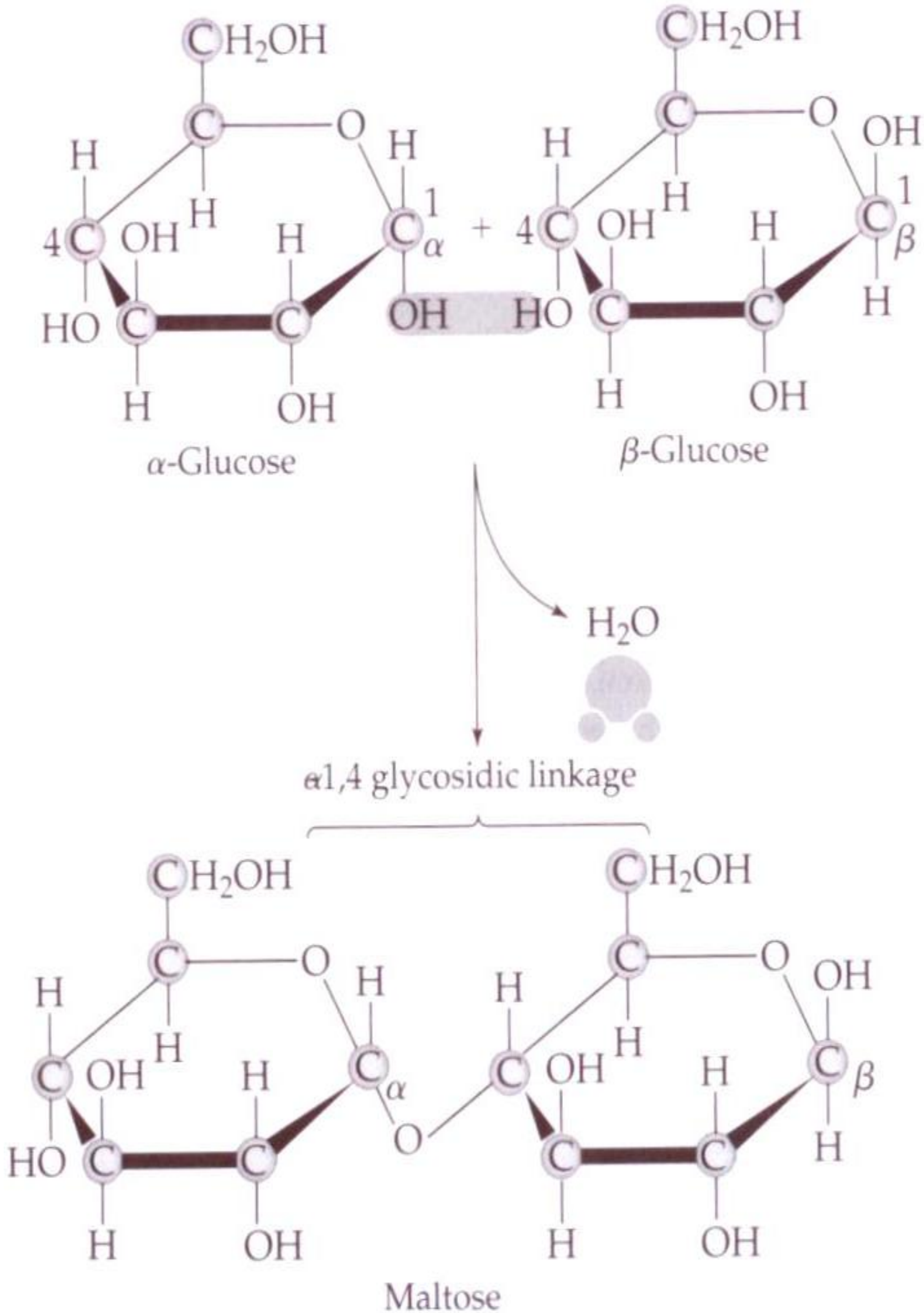
- Compose of two monosaccharide residues united **through a condensation reaction**
- Sucrose (table sugar) → The most abundant disaccharide throughout the plant kingdom
- Lactose is the milk sugar
- Chemical properties depend on the nature of the linked monosaccharides, the carbon atoms involved in bonding, and the form of the linkage.



Sucrose



Lactose



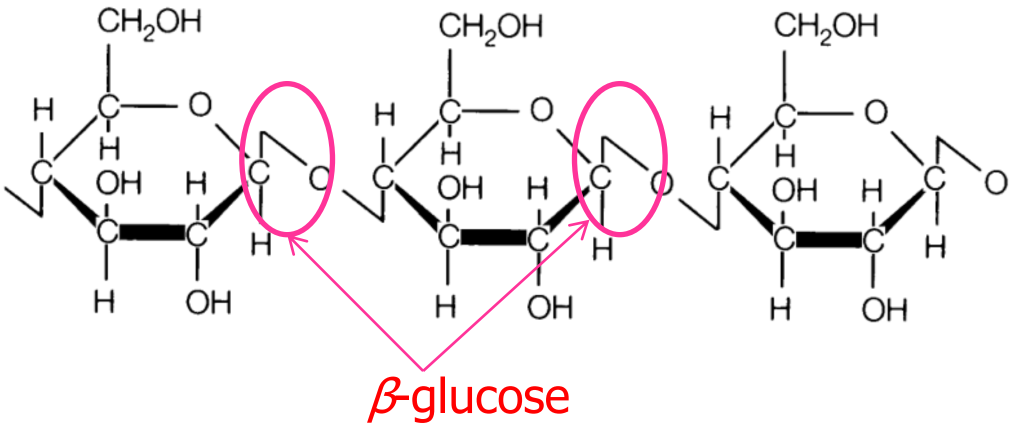
Disaccharides

- Maltose → from *α*- and *β*-glucose through a condensation reaction
- Disaccharides comprise an important food source for all organisms.
- Enzymes facilitate the degradation of these carbohydrates into smaller units to capture readily usable free energy.

Polysaccharides

- Giant chains of monosaccharide residues
- May be linear polymers or have many branches
- Starch and cellulose have the same chemical composition but different chemical structures and physical properties.
- Starch → Long chain of α-glucose, soluble in water, as a primary food for providing energy for humans
- Cellulose → Long chains of β-glucose, humans lack the enzymes to digest it, structural material for plants
- Chitin → Insect skeletons, an amino sugar (a sugar containing nitrogen), long straight chains that serve structural roles very similar to the bone of mammals

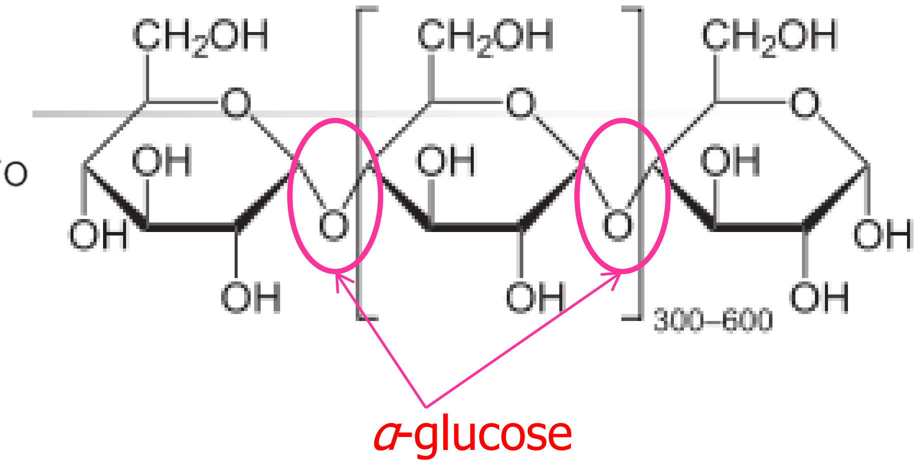
Cellulose



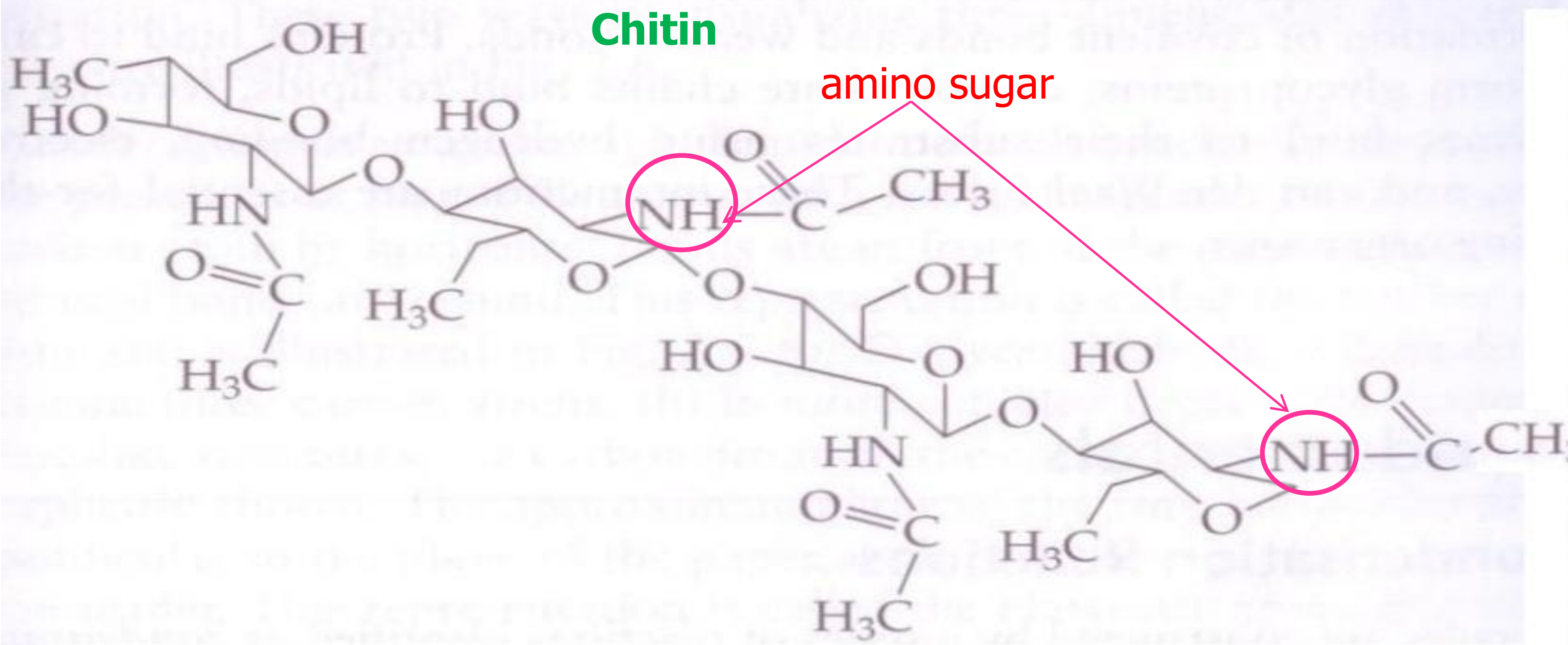
http://webspace.ship.edu/gspaul/animal%20behavior/cockroach/index.html

Starch

http://en.wikipedia.org/wiki/Starch

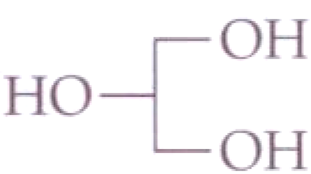


Chitin

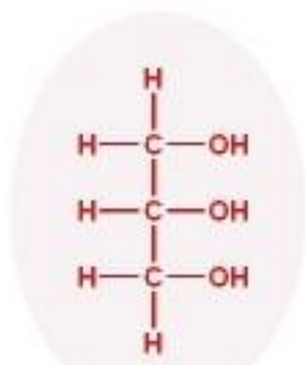


Lipids

- Insoluble in water, high hydrocarbon content
- Strictly speaking, are not macromolecules, but compounds of molecules by **hydrophobic interactions** and **van der Waals forces**
- Simple lipids, such as fats, oils, and waxes, are composed of two types of building blocks: **glycerol**, a small 3-carbon molecule with 3 hydroxyl groups, and 3 hydrocarbon chains called **fatty acids**.

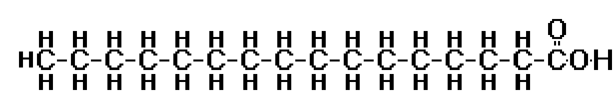


Glycerol

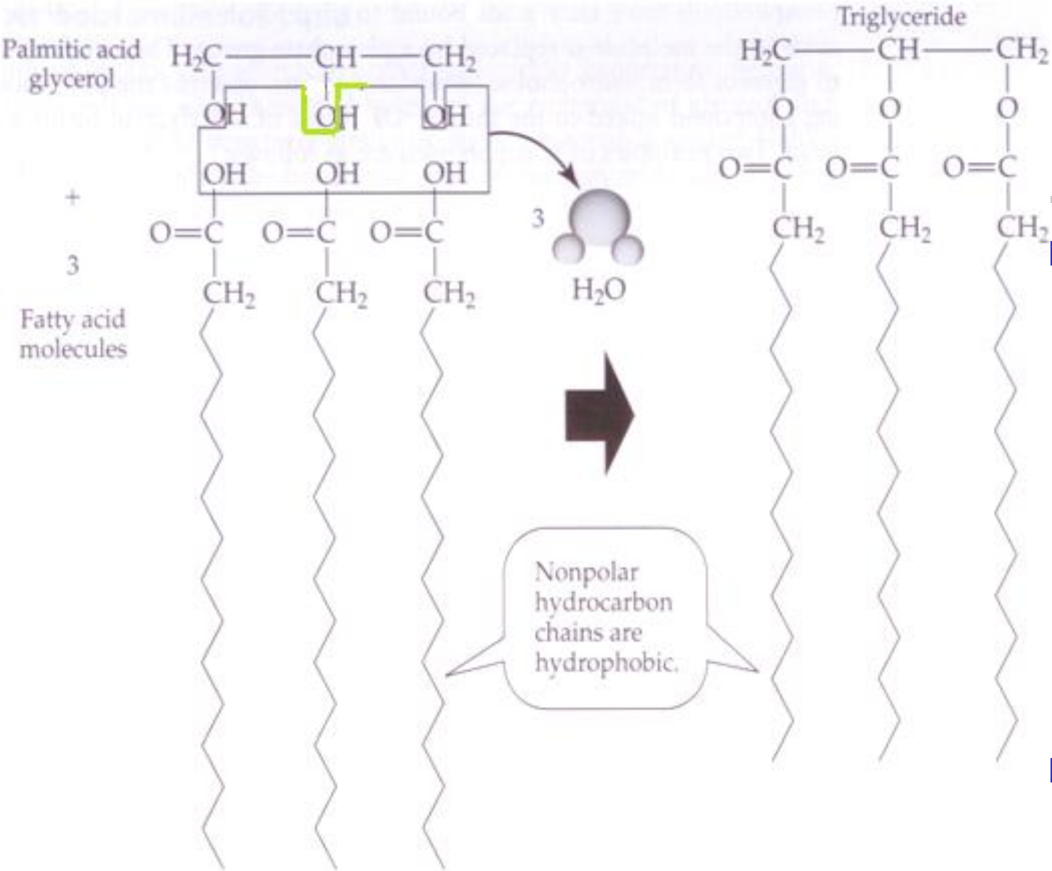


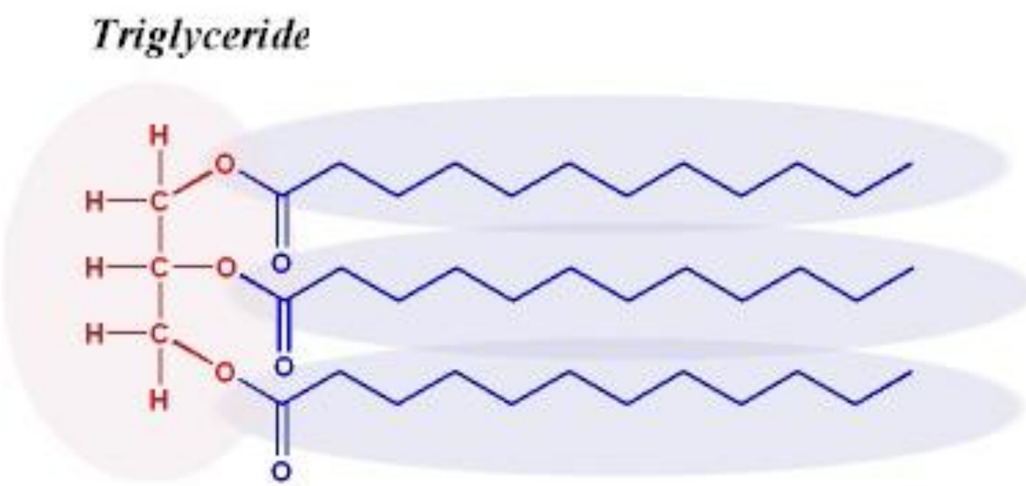
glycerol

http://thescienceoffat.blogspot.com/



http://www.cic-caracas.org/departments/science/Topic2.php

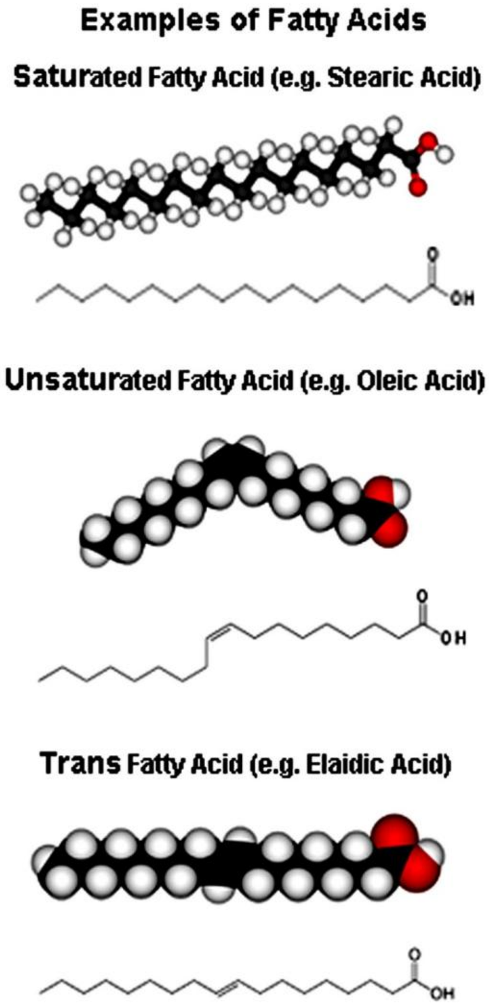




http://thescienceoffat.blogspot.com/

Lipid Molecule

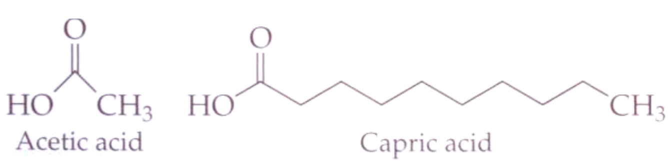
- Condensation reaction → Form 1 lipid molecule (triglyceride) and 3 molecules of water from a glycerol molecule and three fatty acids
- Physical properties: highly depend on the type of fatty acids used as building blocks
- Different lengths of the tail of a fatty acid and either saturated or unsaturated

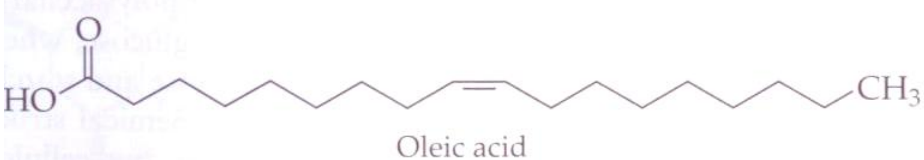


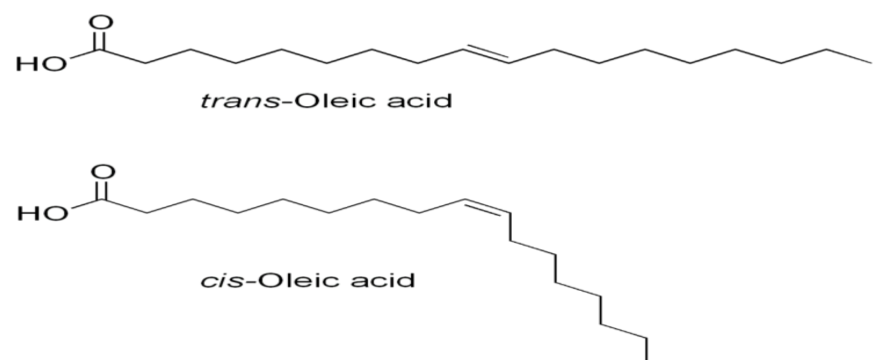
http://thescienceoffat.blogspot.com/

Saturated and Unsaturated Fatty Acids

- Depend on the presence of double carbon bonds
- Tail of a saturated fatty acids contains no double carbon bonds, Ex: capric acid
  - Hydrocarbon chains are relatively rigid and straight, pack together tightly when forming fat
  - Animal fats: solid at RT, tend to have long chain
- Unsaturated fatty acids contains one or more double bonds, causing a kink in the fatty acid and preventing from packing together tightly
  - Liquid plant oils have short or unsaturated fatty acids, Ex: oleic acid
- Kinks: associated with double bonds determine fluidity and melting point of lipid



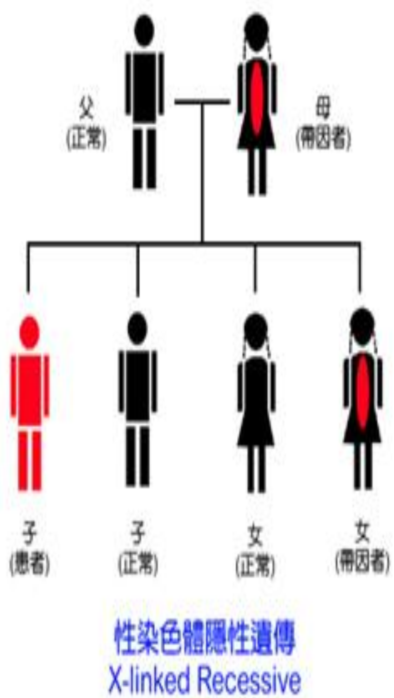




http://en.wikipedia.org/wiki/File:Isomers_of_oleic_acid.png

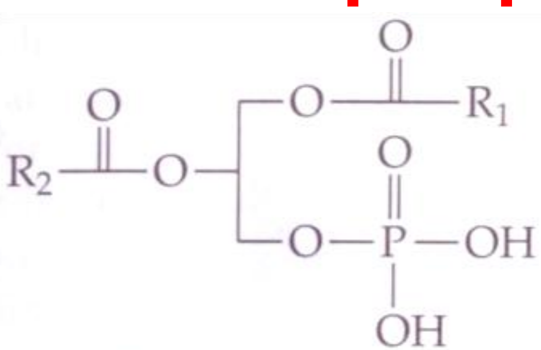
Adrenoleukodystrophy

- Adrenoleukodystrophy/ALD, ABCD1 Gene, ALD, ABCD1 gene -- inherited disorder that leads to progressive brain damage, failure of the adrenal glands and eventually death
- Damages the myelin sheath, a complex fatty that insulates many nerves of the central and peripheral nervous systems, eventually destroying it
- An essential protein, called a transporter protein (carry an enzyme which is used to break down very long-chain fatty acids found in the normal diet), is missing in ALD patients → Give rise to a build-up of very long-chain fatty acids (VLCFA) in the body and damage the brain and the adrenal gland
- Patients with X-linked ALD are all male, but about one in five women with the disease gene develop some symptoms
- No cure for the disease, some dietary treatments, for example, a 4:1 mixture of glyceryl trioleate and glyceryl trierucate (Lorenzo's oil) in combination with a diet low in VLCSFA (very long chain saturated fatty acids), have been used with limited success, especially before disease symptoms appear

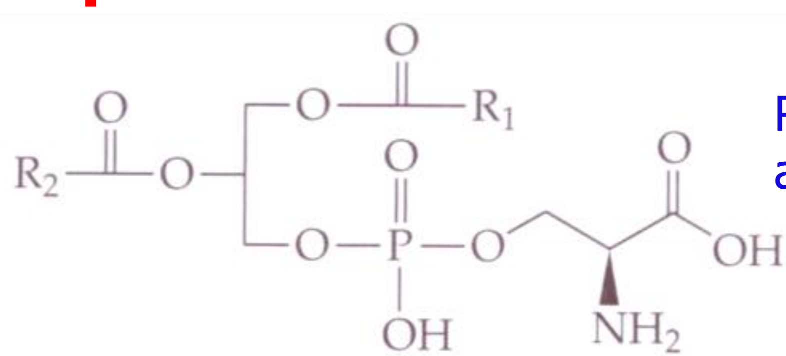


Phospholipids

- Core elements of biological membranes
- Form other structures such as micelles and liposomes in low levels of detergents
  - Liposomes are made in the presence of DNA and used as a vehicle for the delivery of genes in gene therapy.
  - Lipid membrane can fuse with plasma membrane of target cells and release the DNA into the cell.
- Fatty acids bound to glycerol, one of 3 fatty acids is replaced by a phosphate group (-OH, hydrophilic head), the other two fatty acids bound to glycerol form hydrophobic (nonopolar) chains→ **phospholipids**



Phosphatidic acid

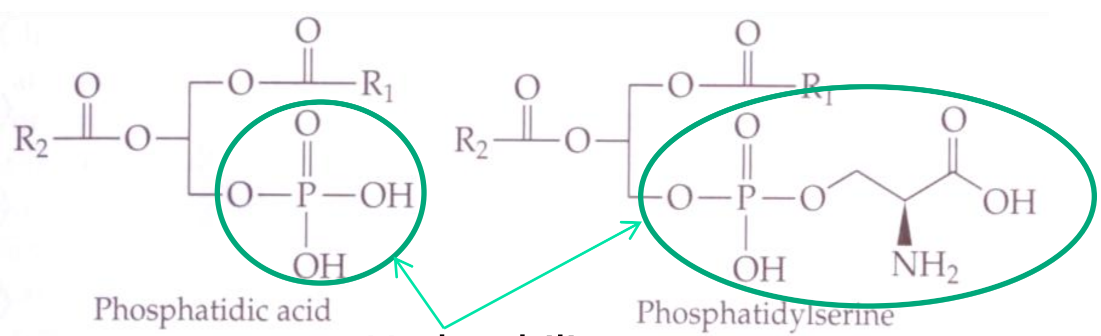


Phosphatidylserine

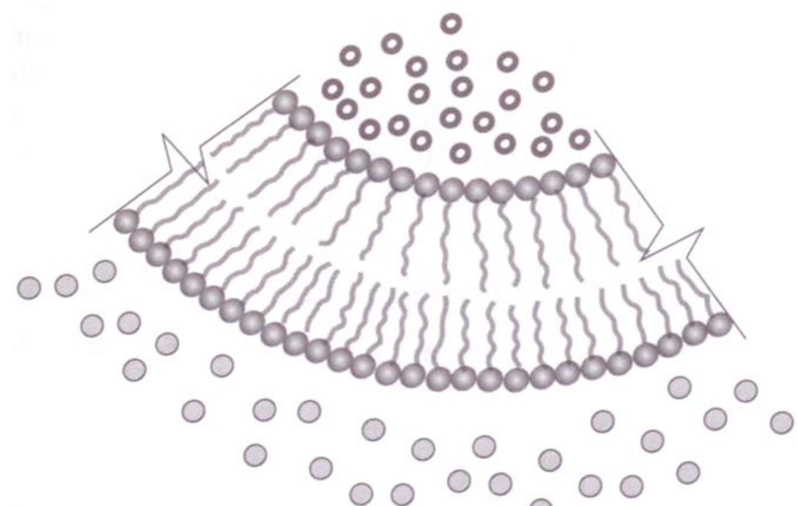
R1 & R2: represents fatty acids attached to glycerol

Biomembranes

- Phospholipids have one hydrophilic and one hydrophobic region.
- Phosphate group attached to glycerol has a negative charge → Hydrophilic → Globular subunits → Phospholipid heads
- Fatty acid tails are hydrocarbon chains → No charge → Hydrophobic → Long hydrophobic tail
- Phospholipids cluster together and form bilayer surfaces for shielding nonpolar fatty acid tails from water: hydrophilic heads face outward on both sides of bilayer (interacting with surrounding water), and hydrophobic tails remain in the interior of bilayer
- Enclosed in lipid bilayers, ex: nuclei and mitochondria

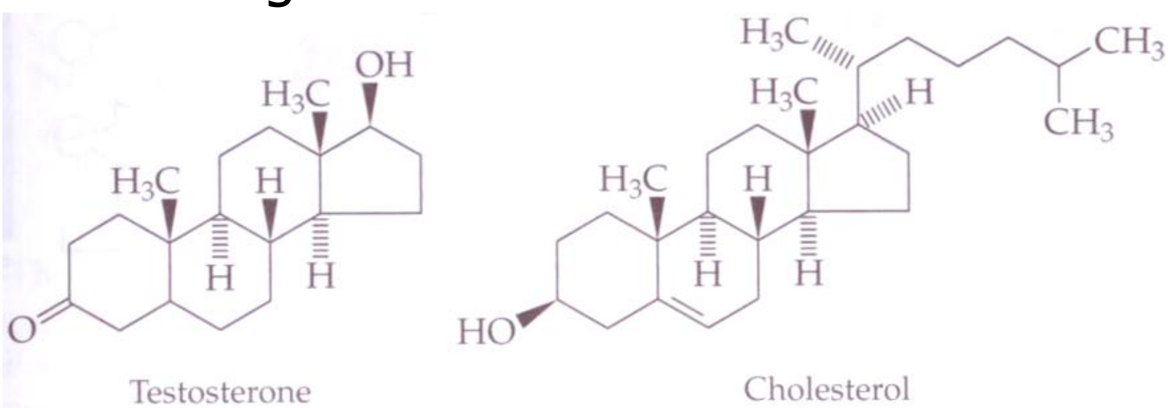


Hydrophilic
globular subunits



Other Subfamilies of Lipids

- Steroid hormones and steroids: not composed of glycerol and fatty acids, but have ringlike structures similar to sugars → **Consist mainly of hydrocarbons and are therefore hydrophobic**
- Testosterone: release into the blood stream from testis, development of male sexual characteristics, lipid soluble so as to regulate gene expression (across the plasma membranes of cells and enter nucleus)
- Cholesterol: deposit on the inner surface of vessels, clogging the arteries and altering mechanical properties
- **All steroids are synthesized from cholesterol and therefore have similar chemical structures**.
- Carotenoids, fat-soluble vitamins such as vitamins A and D, glycolipids such as glucocerebroside

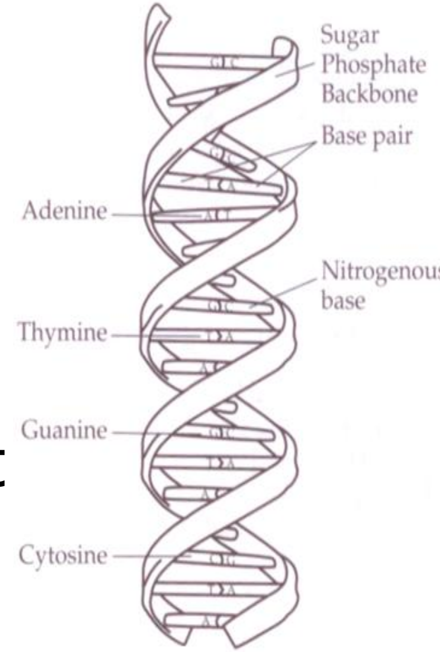


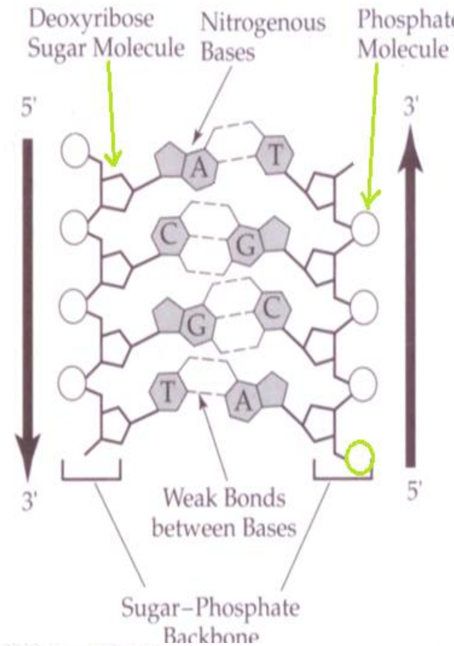
DNA

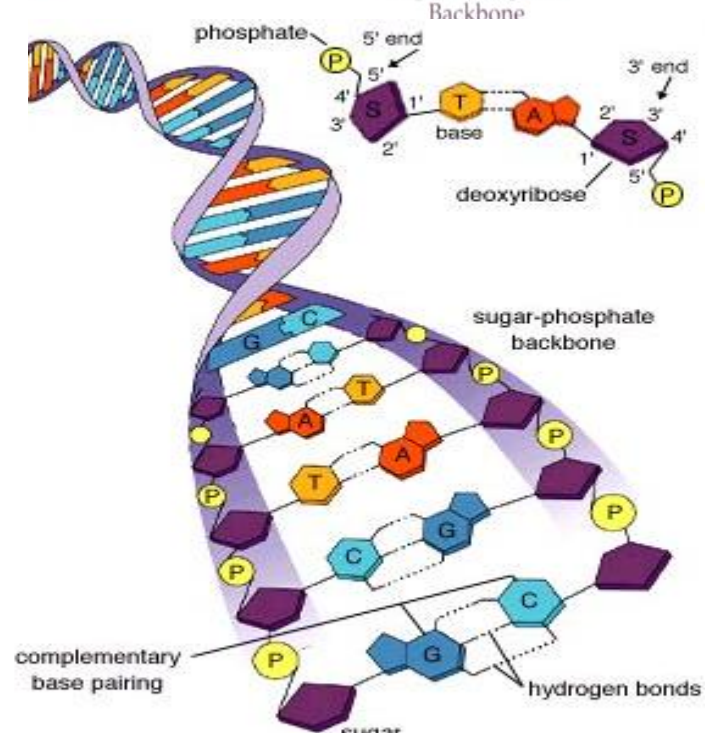
- Double-stranded helix with a uniform radius and angle of twist, run in opposite directions
- Each strand is made of different combinations of 4 molecular base beads A. G. C. and T
- Sugar-phosphate backbone, bases face toward each other and form hydrogen bonds

5-carbon sugar molecule (D-deoxyribose) + **phosphate molecule** + **nitrogenous bases**

- Beads in opposing strands complement each other by hydrogen bonds: **A=T** and **C≡G**



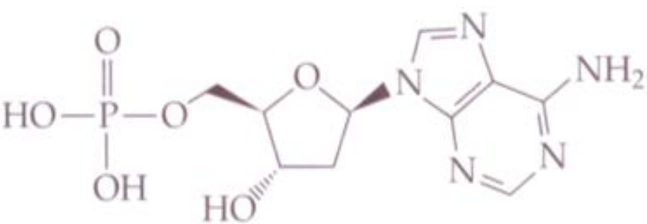




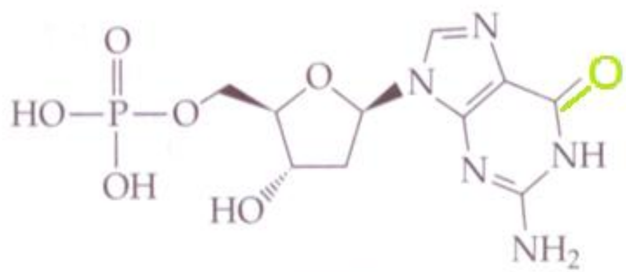
http://www.mhhe.com/biosci/esp/2001_gbio/folder_structure/ge/m4/s1/index.htm

Building Blocks

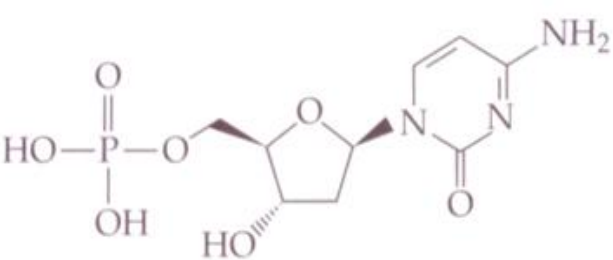
- **Nucleotides** (dAMP, dGMP, dTMP, and dCMP): 4 different types constitute the building blocks of DNA. → Composed of 3 subunits: **phosphate group**, **5-carbon sugar molecule (deoxyribose)**, **nitrogenous base**
- Identical groups in all 4 DNA nucleotides: **sugar** and **phosphate groups** (except the nitrogen bases)
- Nitrogenous bases in DNA:
  - Purines (composed of 2 rings): adenine (A) in dAMP and guanine (G) in dGMP
  - Pyrimidine (single ring): thymine (T) in dTMP and cytosine (C) in dCMP



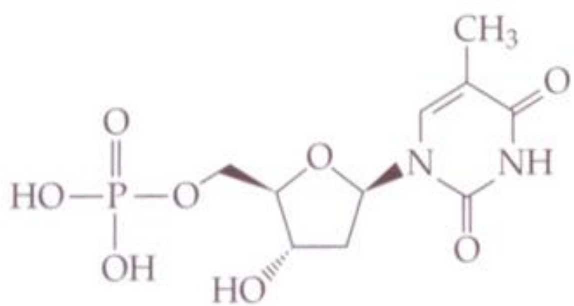
dAMP



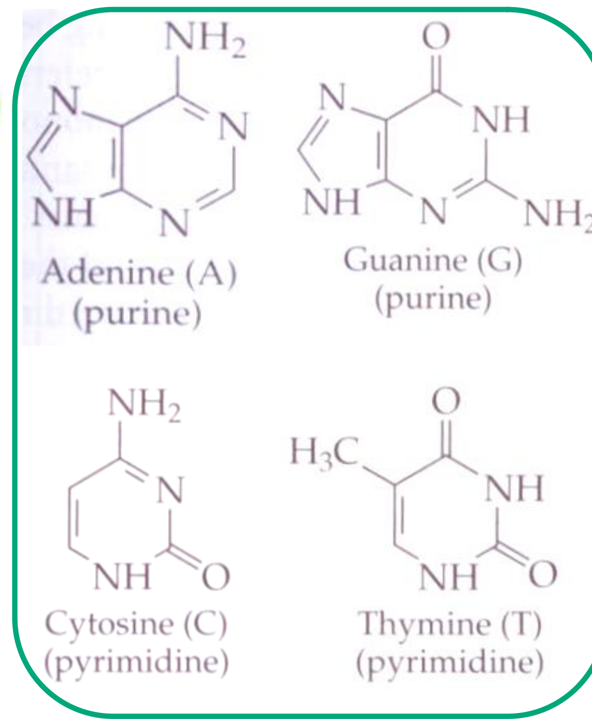
dGMP



dCMP

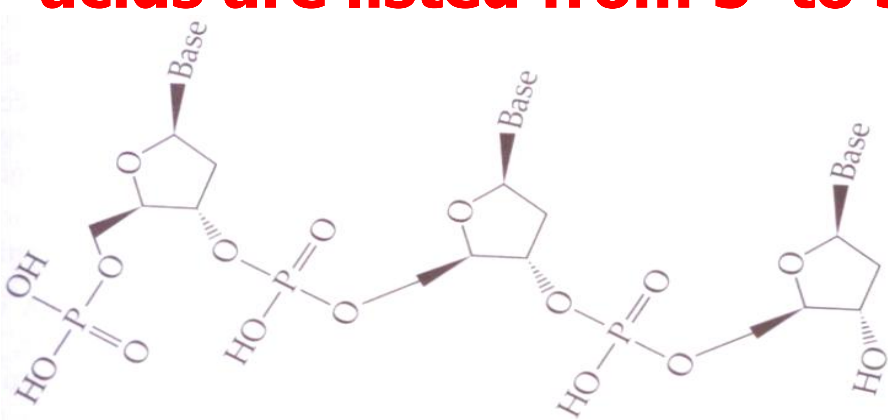


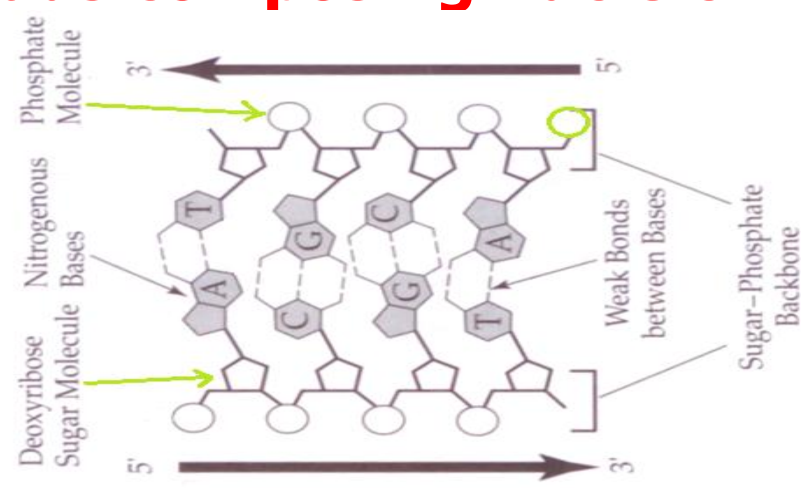
dTMP



Backbone

- Subunits of sugars and phosphates form the backbone of a DNA strand.
- Sugar subunit of one nucleotide binds to the phosphate group of the adjacent nucleotide.
- DNA strand has a sense of direction → Phosphate group attaches to 5′ carbon of sugar and one nucleotide attaches to sugar subunit of the adjacent nucleotide at 3′ carbon site
  - DNA strand has at one end a bound OH → **3′ end**
  - DNA strand has a bound phosphate → **5′ end**
- **The sequences of molecular beads composing nucleic acids are listed from 5′ to 3′.**





Complementary Base Pairs

- Double-stranded helix with constant radius: two strands of DNA twist like a screw, running in parallel but opposite directions → Two strands hold together by hydrogen bonding between monomers at the same positions in opposite strands.
- **Complementary base pairs**: **A=T** and **C≡G** → Assure the information stored in DNA is in duplicate, not identical but complementary, Ex: 5'AACTTG3' ←→ 3'TTGAAC5'
- **Constant diameter of the DNA helix is because** these **pairs have identical physical dimensions in the direction normal to the axis of DNA**
- In the human genome, G+C content is less than A+T content.