Chapter 5 (Campbell)

The Structure and Function of Large Biological Molecules

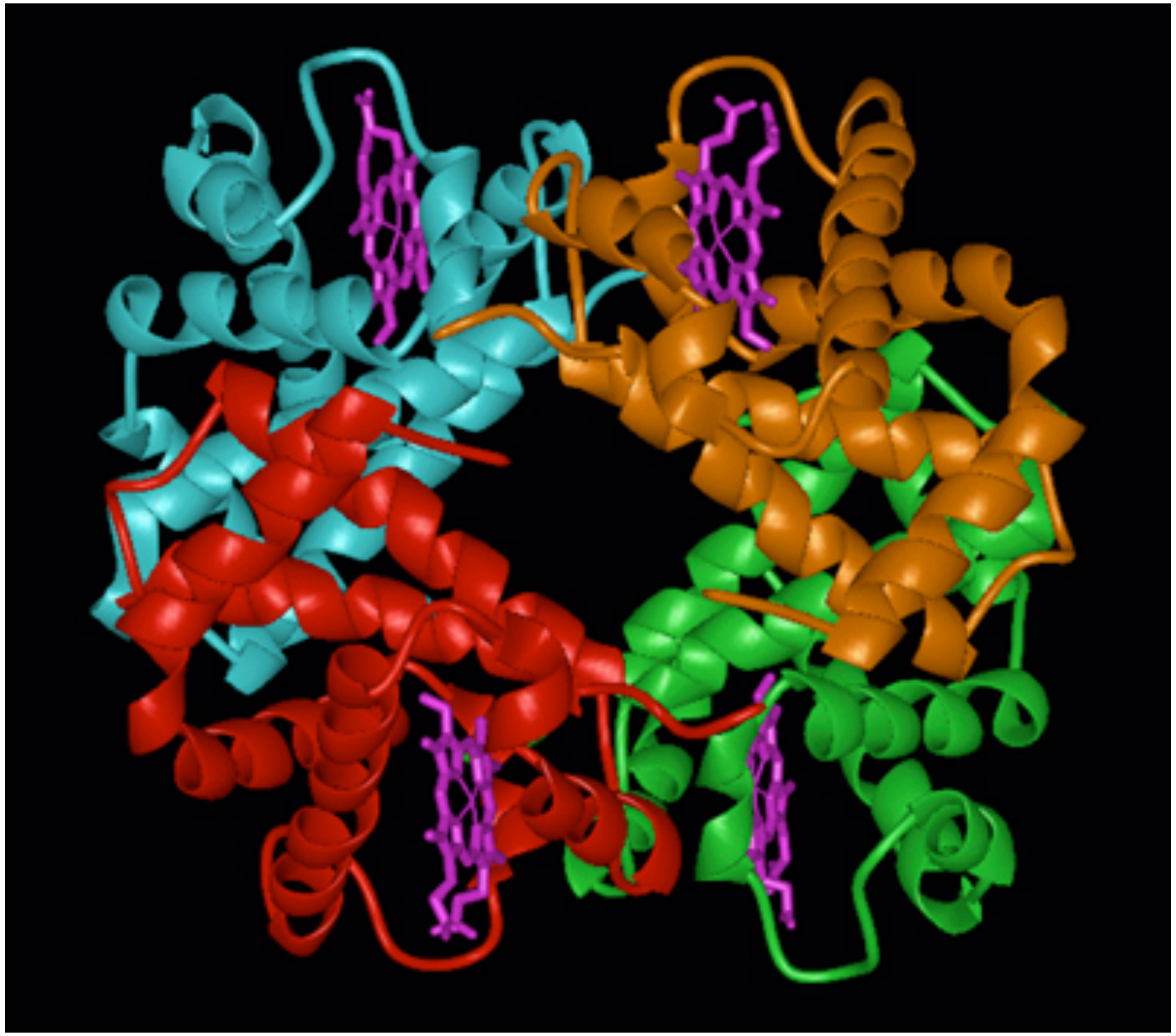
PREFACE

- Remarkably the most important molecules of life fall into just 4 categories: carbs, lipids, proteins and nucleic acids
- Three of these classes contain huge molecules (macromolecules)
- The architecture of these molecules helps explain how the molecules work
- Also, like water, these molecules exhibit emergent properties

(5) Biochemistry

I.

Main Idea: These macromolecules are often long chains that consist of small units bond together.

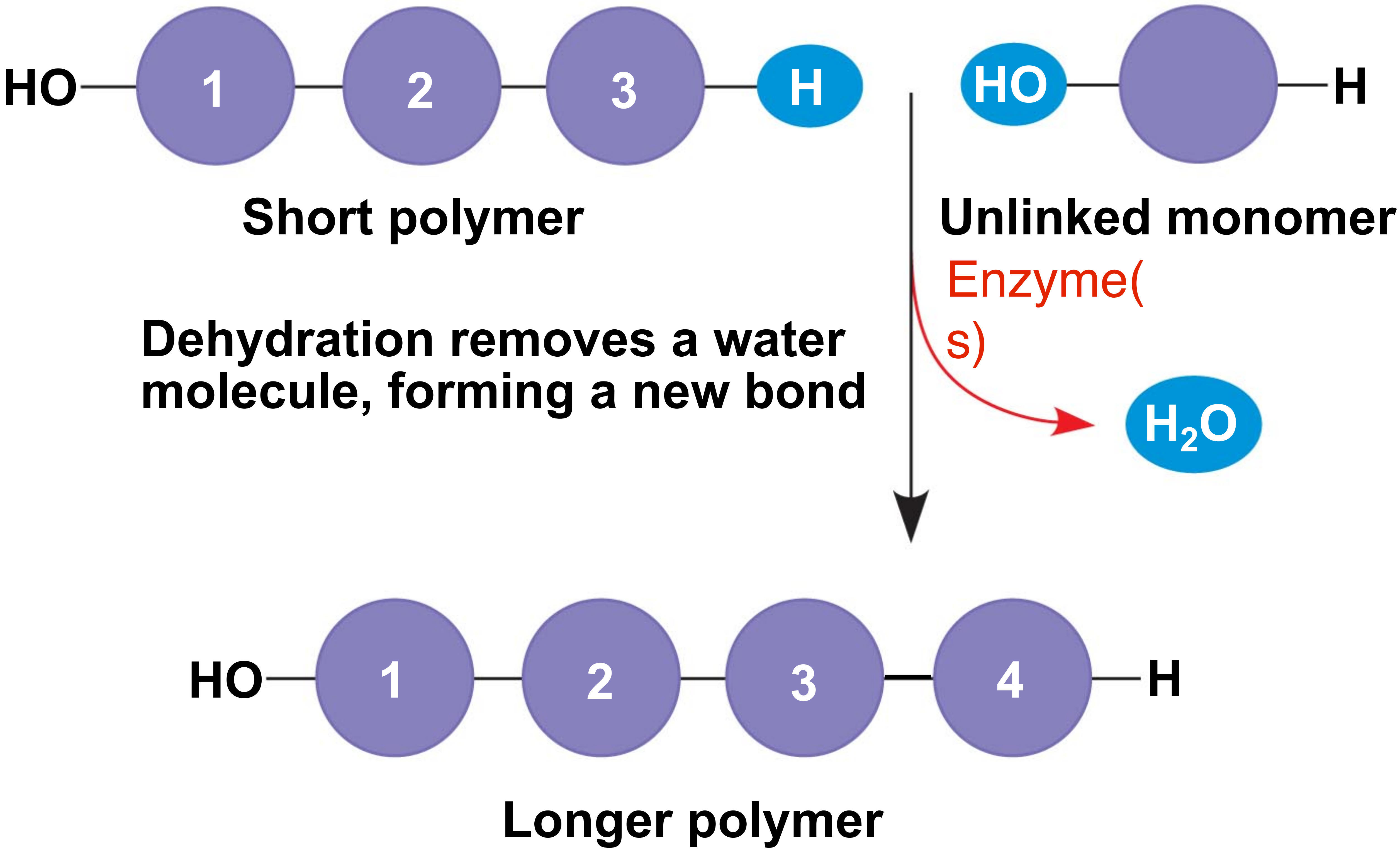


MACROMOLECULES ARE POLYMERS, BUILT FROM MONOMERS

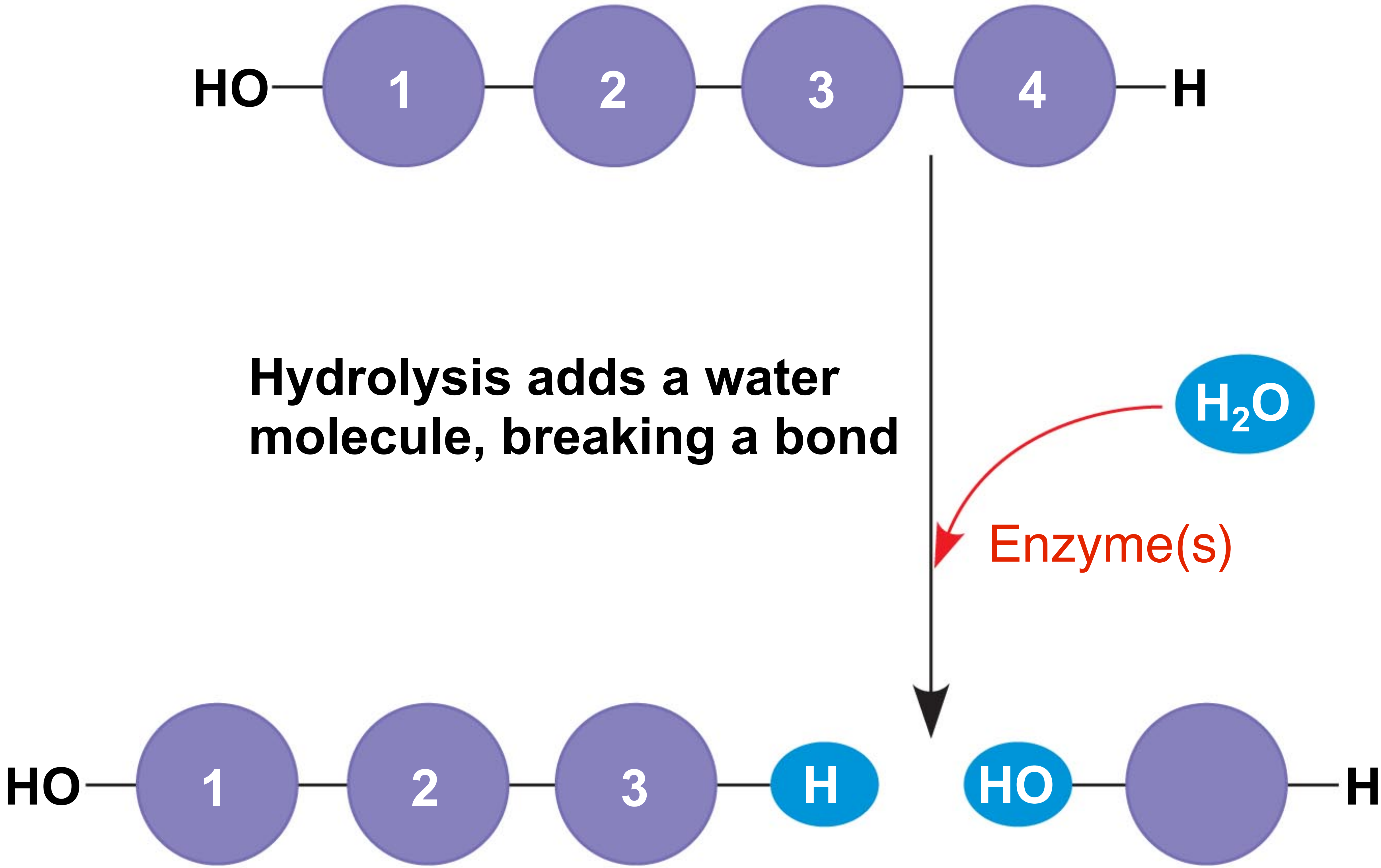
- *Polymers* are long chain-like molecules made up of smaller subunits
- *Monomers* are serve as the building blocks or subunits for polymers

A. The Synthesis and Breakdown of Polymers

- Although *polymers* and *monomers* vary, the mechanism by which they are built and broken down is the roughly the same
- These building and breaking reactions occur in aqueous solutions and they are facilitated by *enzymes*.
  - *Enzymes* are proteins that speed up the rate of chemical reactions.
- Monomers are covalently bonded to each other through the loss of water, in a reaction called **dehydration synthesis**
- Monomers are separated by a reaction that is essentially the reverse of dehydration synthesis, this reaction is called **hydrolysis.**
  - Here we see enzymes catalyzing a reaction that uses water to split the bonds between monomers.



(a) Dehydration reaction in the synthesis of a polymer



(b) Hydrolysis of a polymer

B. The Diversity of Polymers

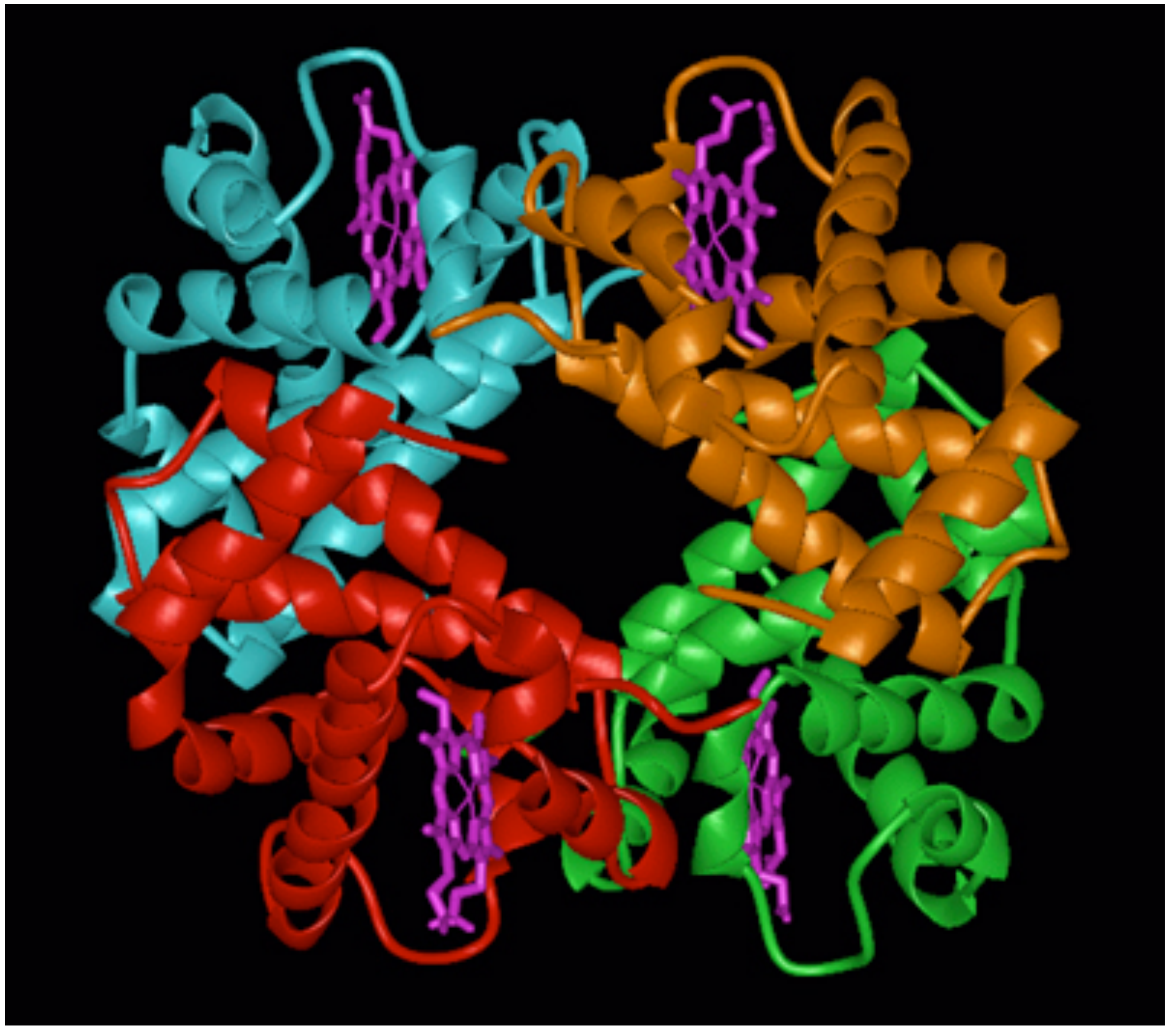
- Each cell has thousands of different macromolecules
  - One cell can differ greatly from another cell even when these cells are part of the same organism
  - The differences in cells between species is even greater yet
- The molecular logic of life is both simple and elegant!
  - Small molecules (monomers) common in all organisms are ordered and arranged into unique macromolecules specific to cell types and species.
- Despite such great molecular diversity these macromolecules can be grouped into 4 common classes.

(5) Biochemistry

II.

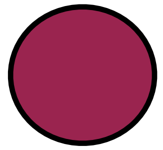
Main Idea: Carbohydrates' structure consists of atoms of carbon, hydrogen and oxygen, in a 1:2:1 ratio ($C_1H_2O_1$).

Main Idea: Carbohydrates function as a fuel source and building material.

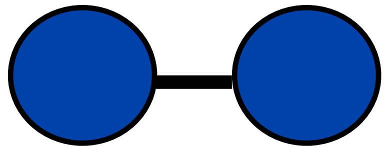


CARBOHYDRATES SERVE AS FUEL AND BUILDING MATERIAL

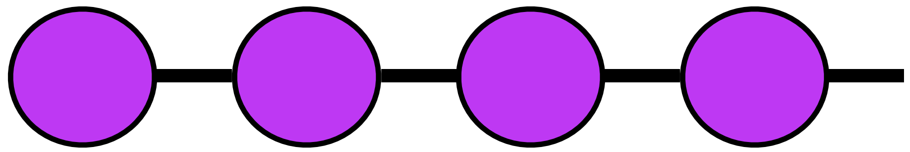
- *Carbohydrates* include both simple sugars and polymers of sugars.
  - *Monosaccharides;* simple monomers of sugars



  - *Disaccharides;* two monomers of sugar bonded together



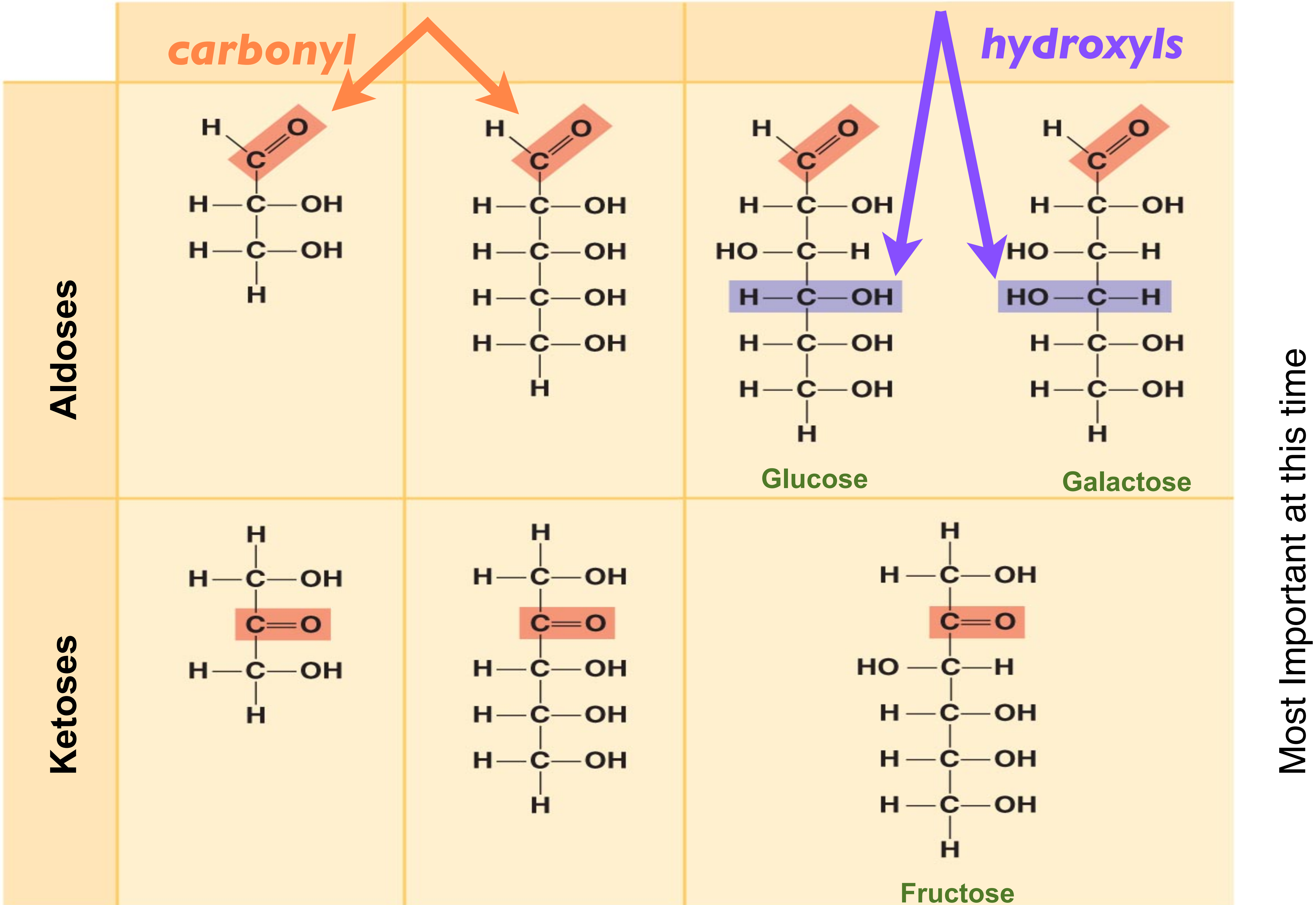
  - *Polysaccharides;* monomers of sugars bonded together



A. Sugars

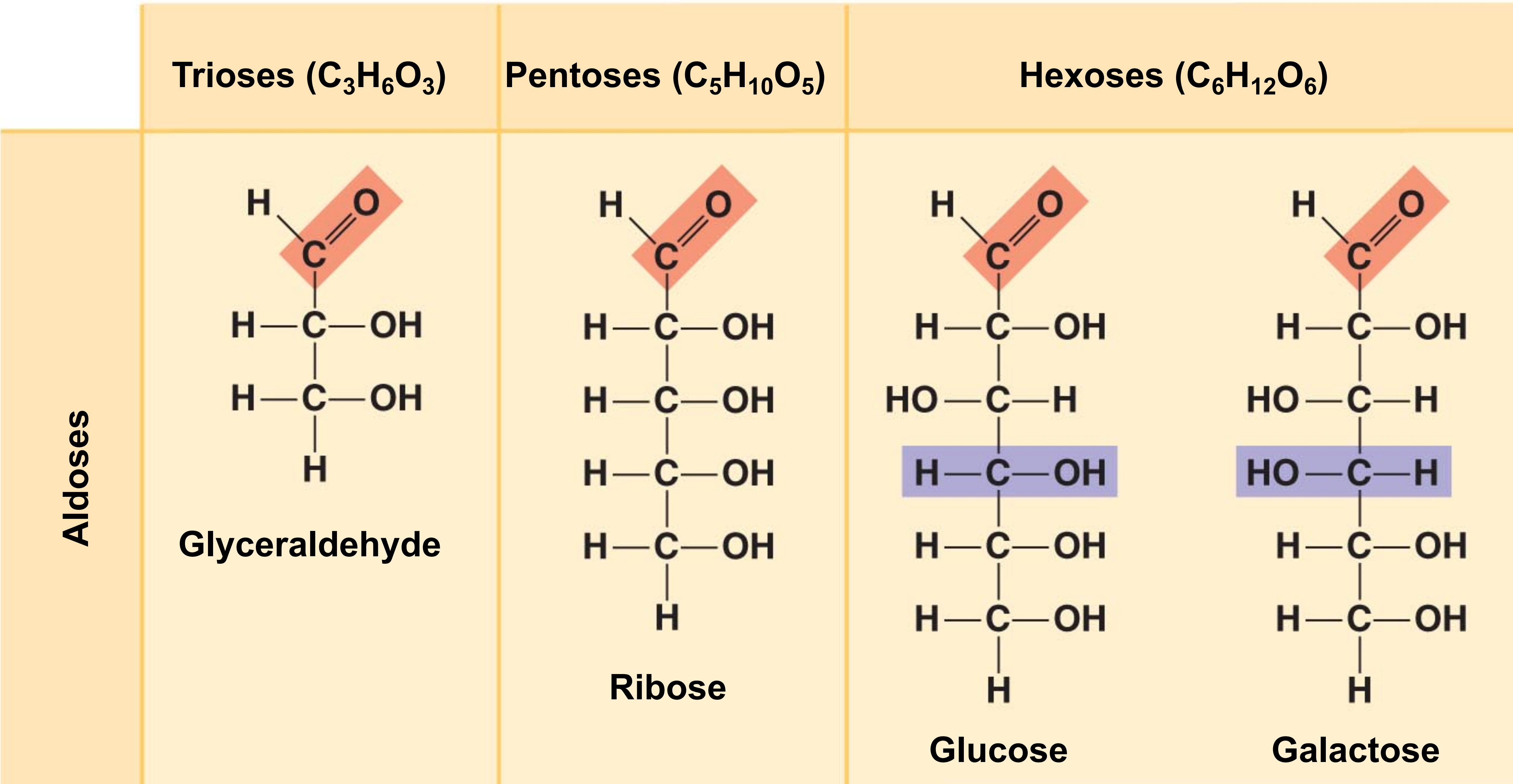
- *Monosaccharides;* simple monomers of sugars

Structural "Trademarks"



Difference
s

1) #of carbons (range = 3-7)
2) spatial arrangement of parts around asymmetrical carbons

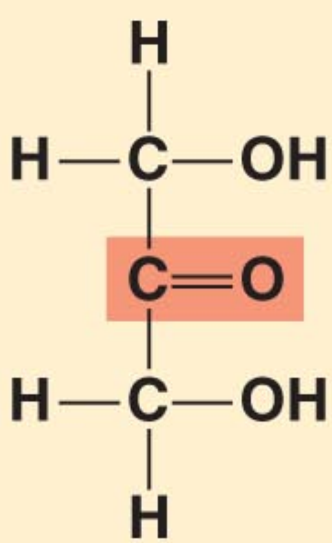
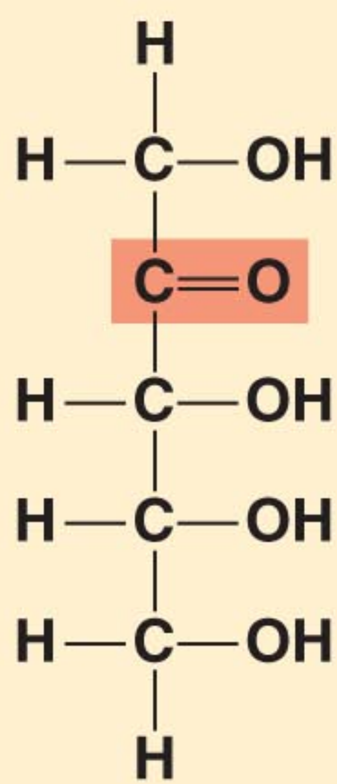
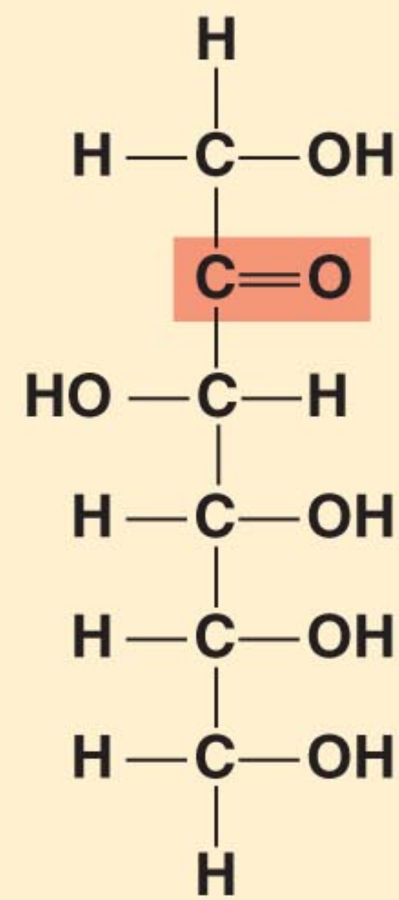


What these molecules called?

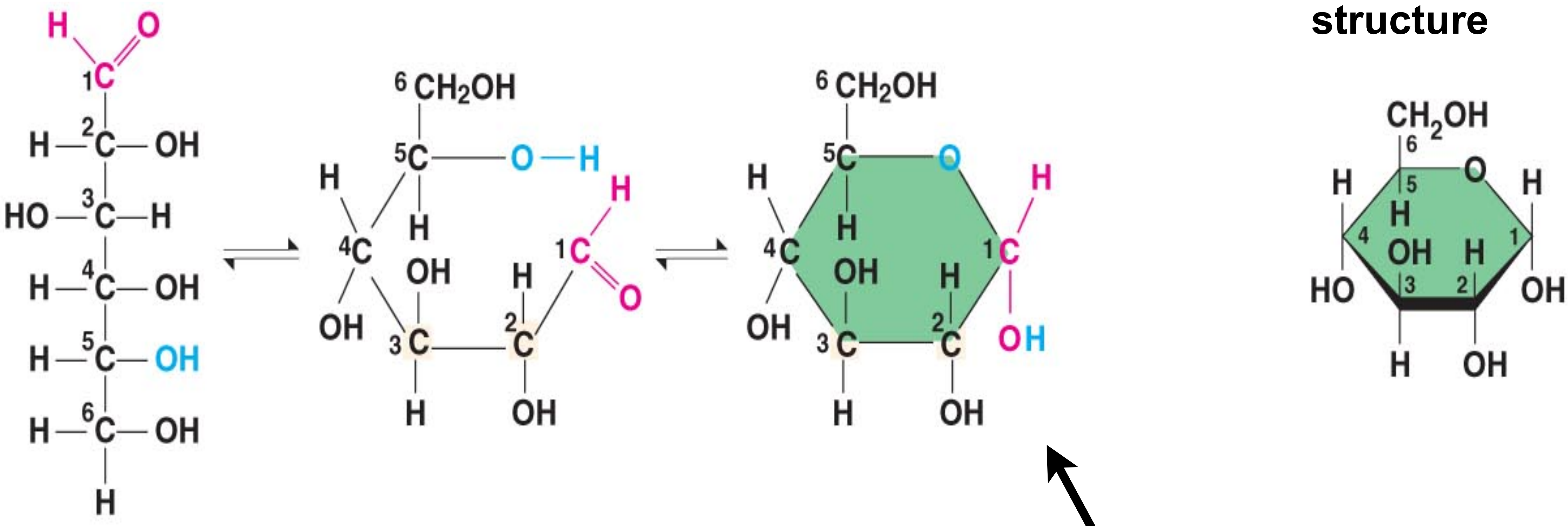
Structural Isomers

Differences

1) #of carbons (range = 3-7)
2) spatial arrangement of parts around asymmetrical carbons

	Trioses ($C_3H_6O_3$)	Pentoses ($C_5H_{10}O_5$)	Hexoses ($C_6H_{12}O_6$)
Ketoses	 Dihydroxyacetone	 Ribulose	 Fructose

(c) Abbreviated ring structure



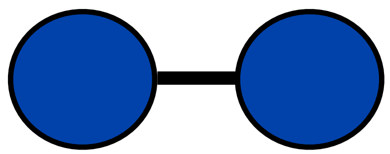
(b) ring forms

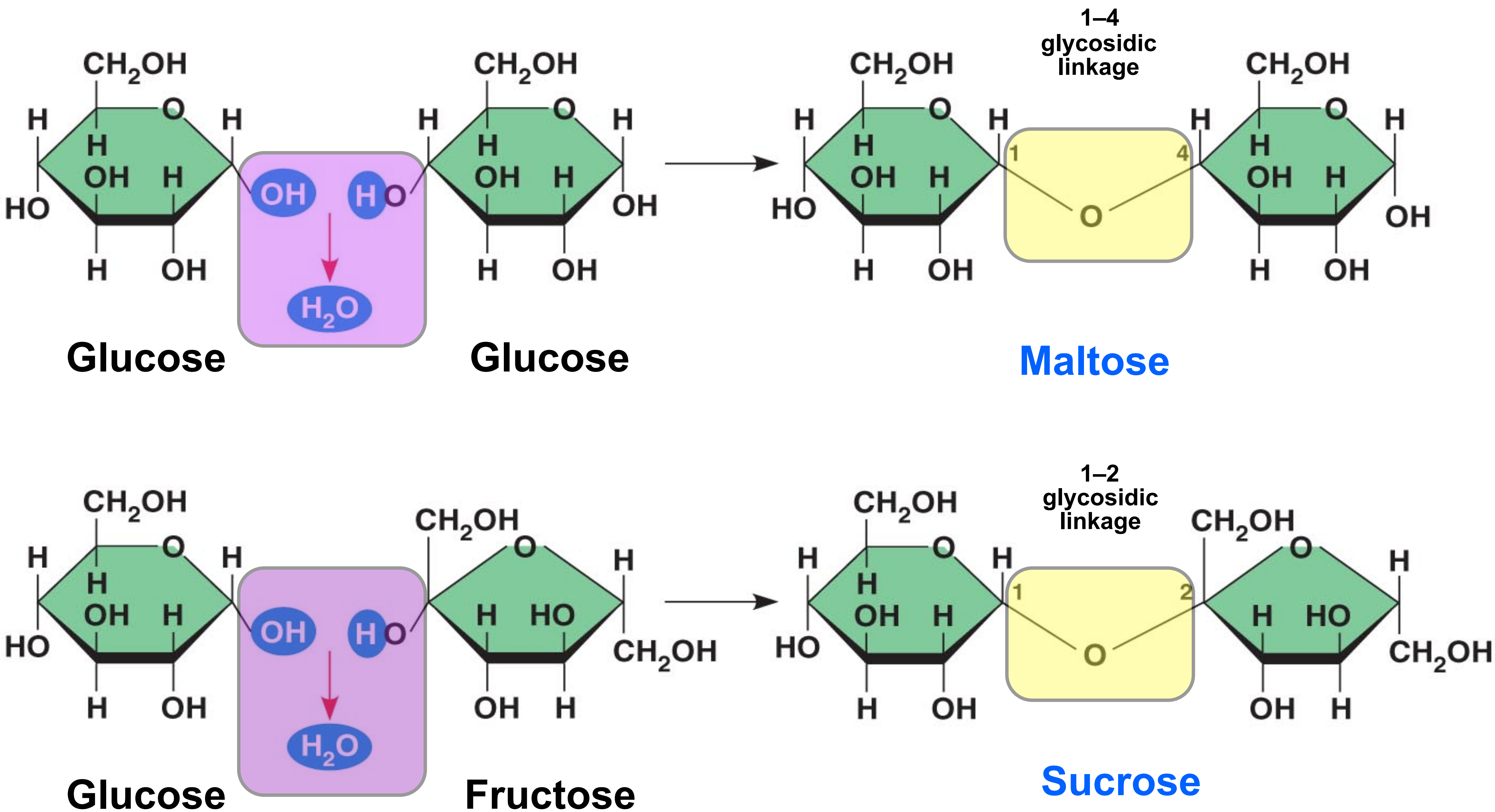
Wet (in cells)

(a) Linear

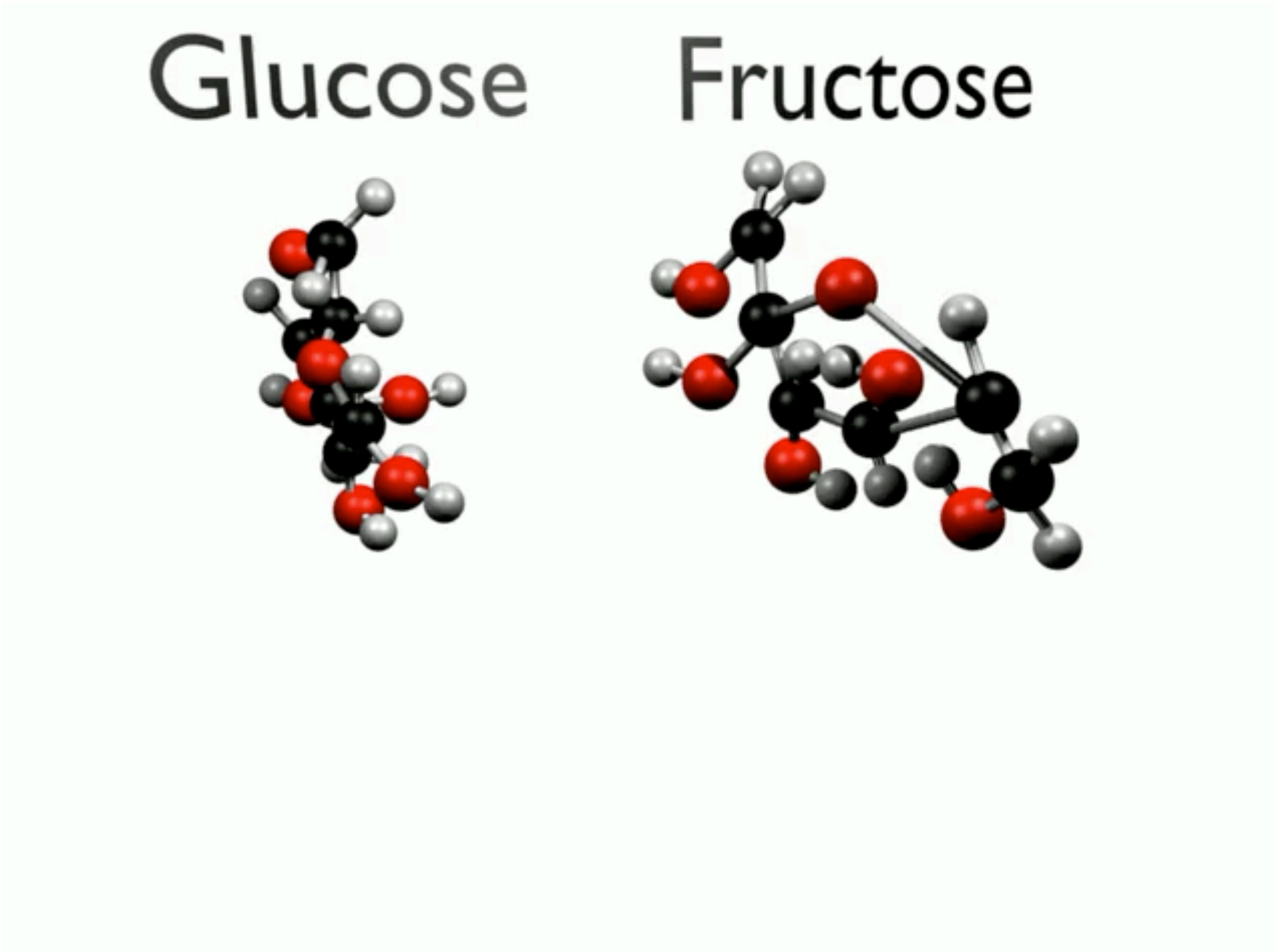
Dry (on lab bench)

- *Disaccharides;* two monomers of sugar bonded together



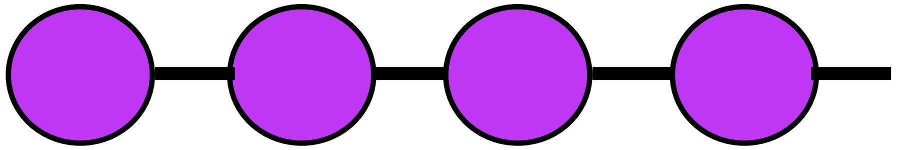


Glucose + Galactose = ? **Lactose**



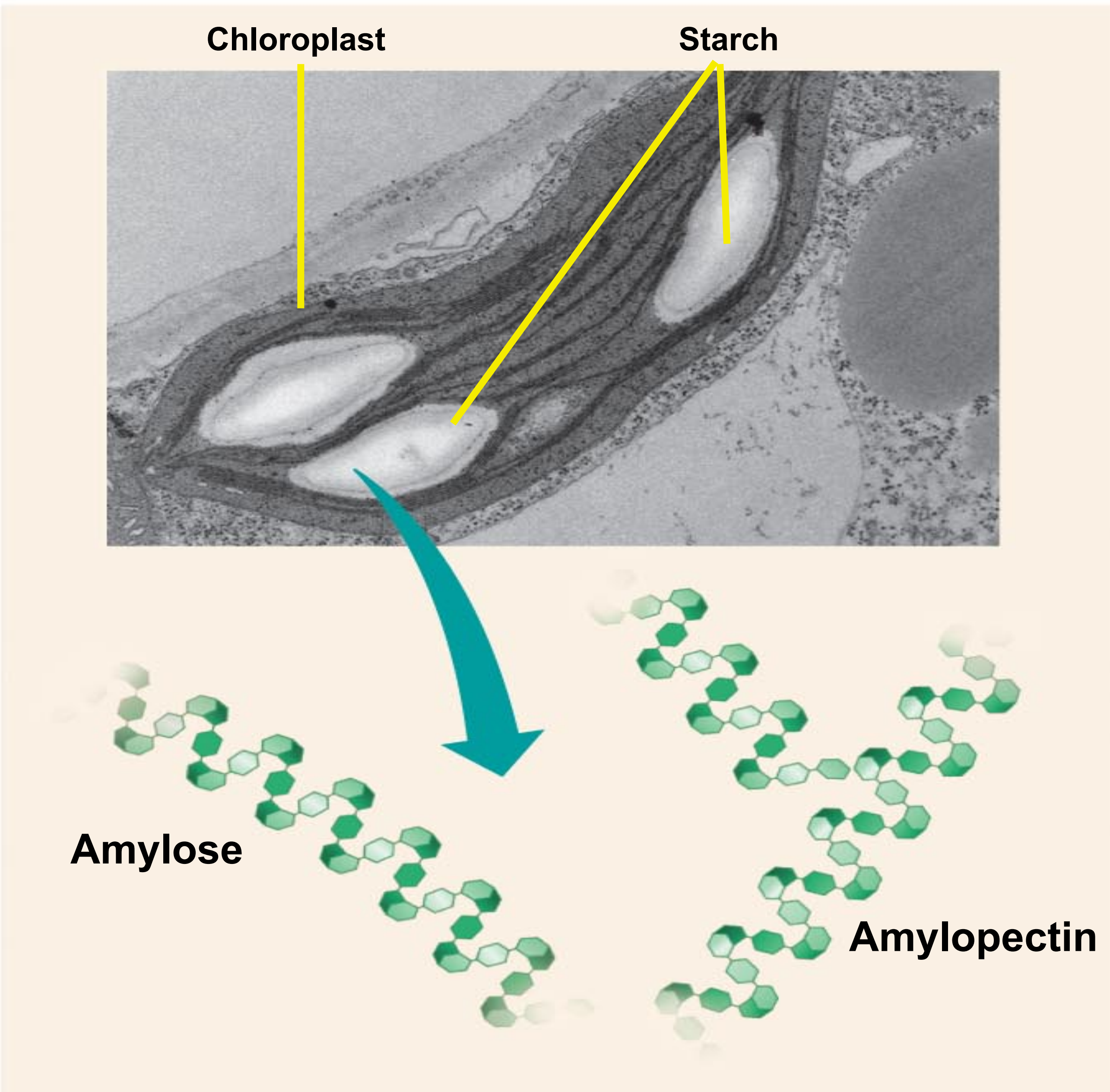
Dehydration Synthesis of Sucrose

- *Polysaccharides;* monomers of sugars bonded together

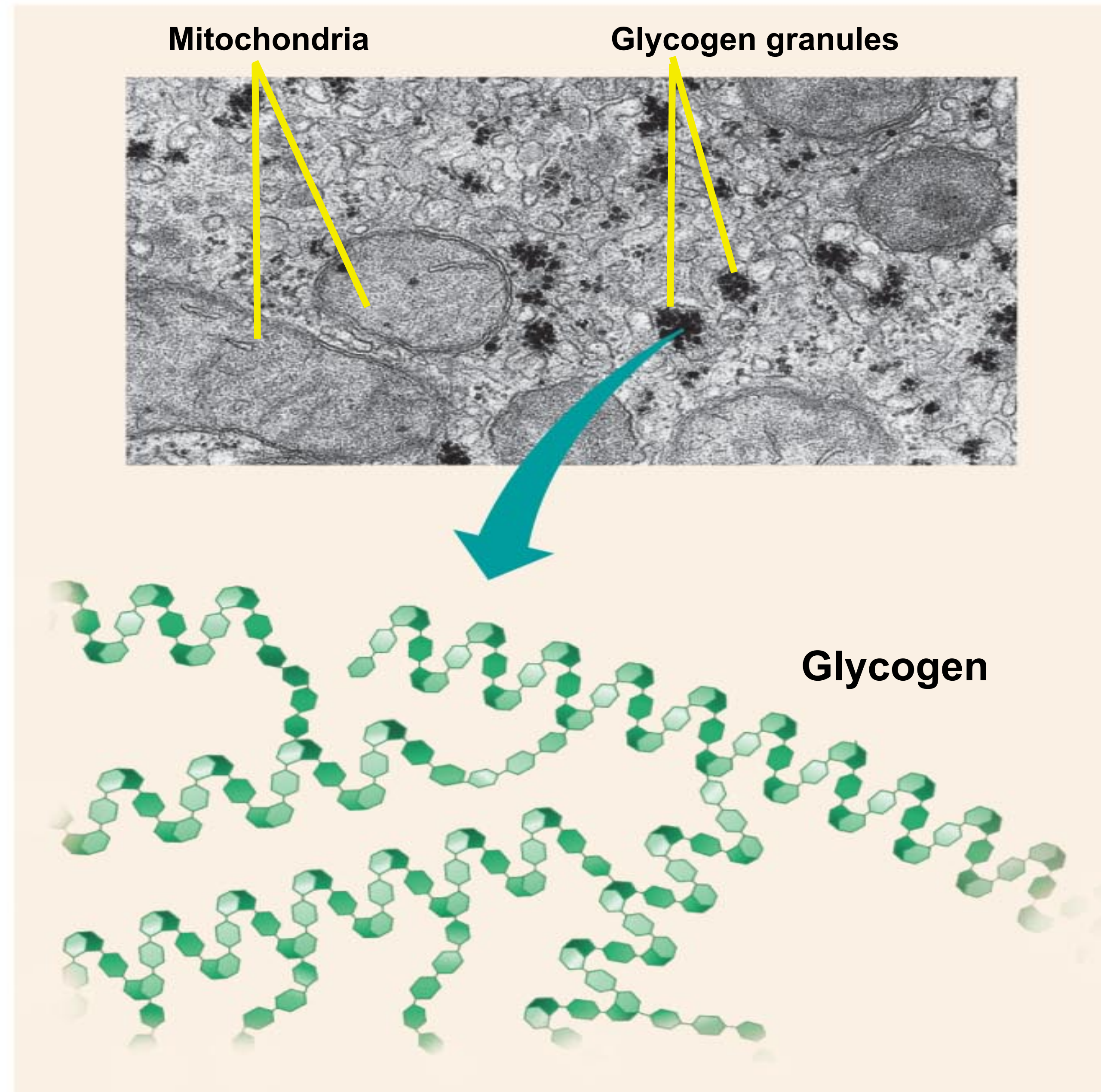


a few hundred to a few thousand

1. Storage Polysaccharides

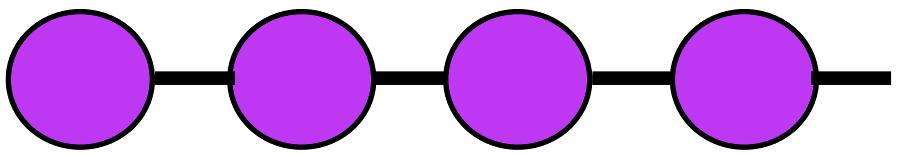


(a) Starch: a plant polysaccharide



(b) Glycogen: animal polysaccharide

- *Polysaccharides;* monomers of sugars bonded together

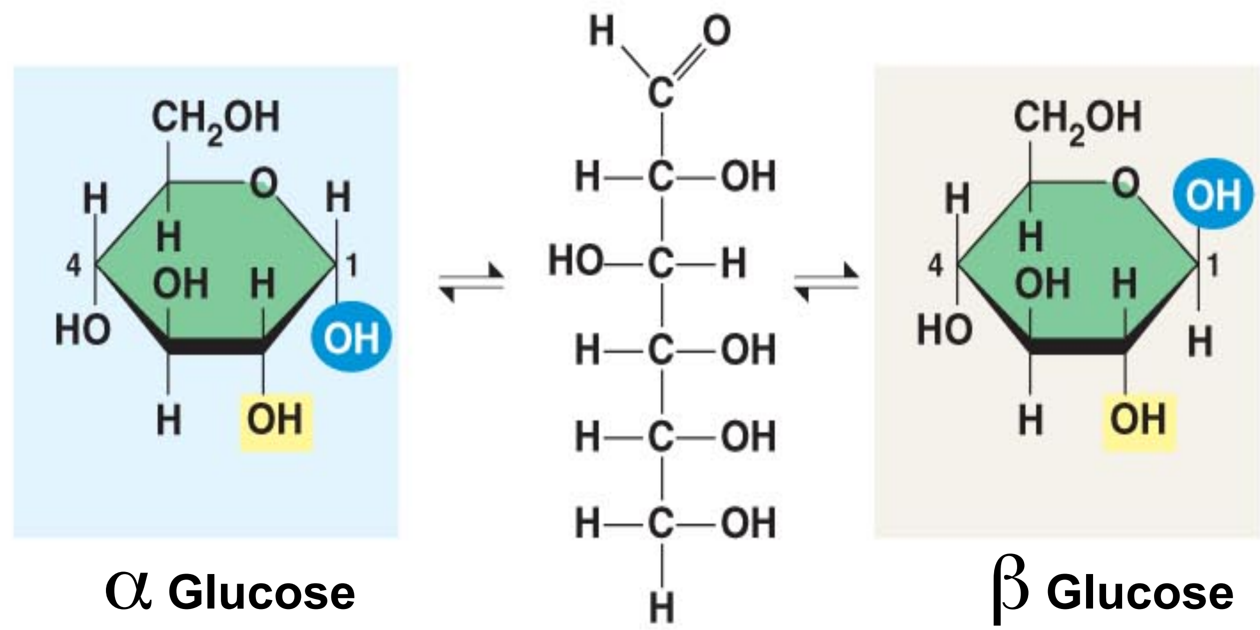


a few hundred to a few thousand

2. Structural Polysaccharides

α and β glucose ring structures

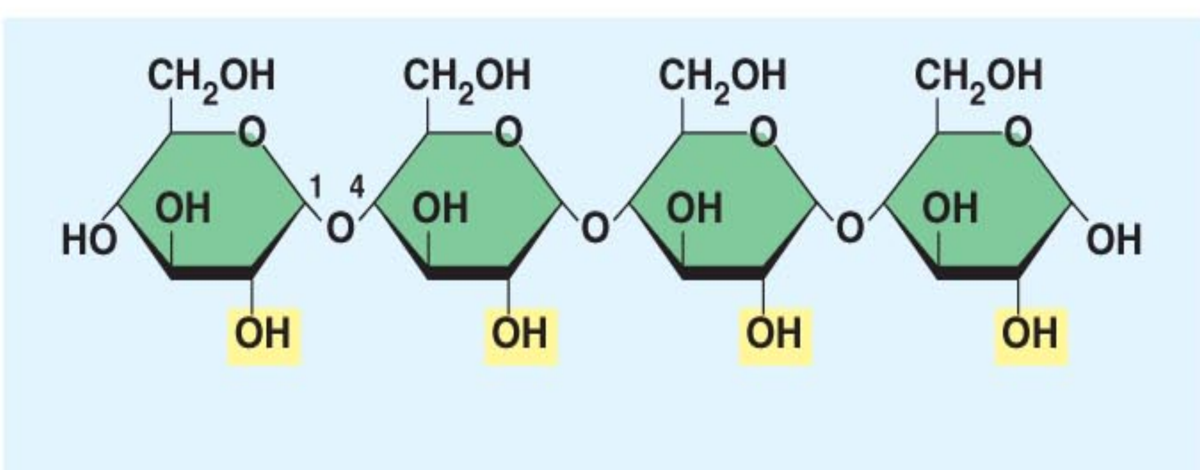
Helical



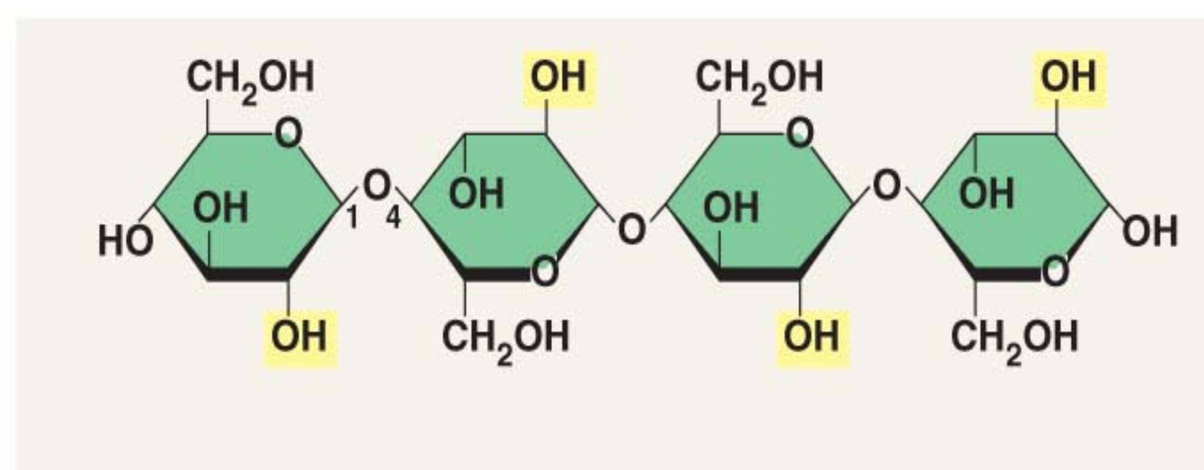
α Glucose

β Glucose

Straight

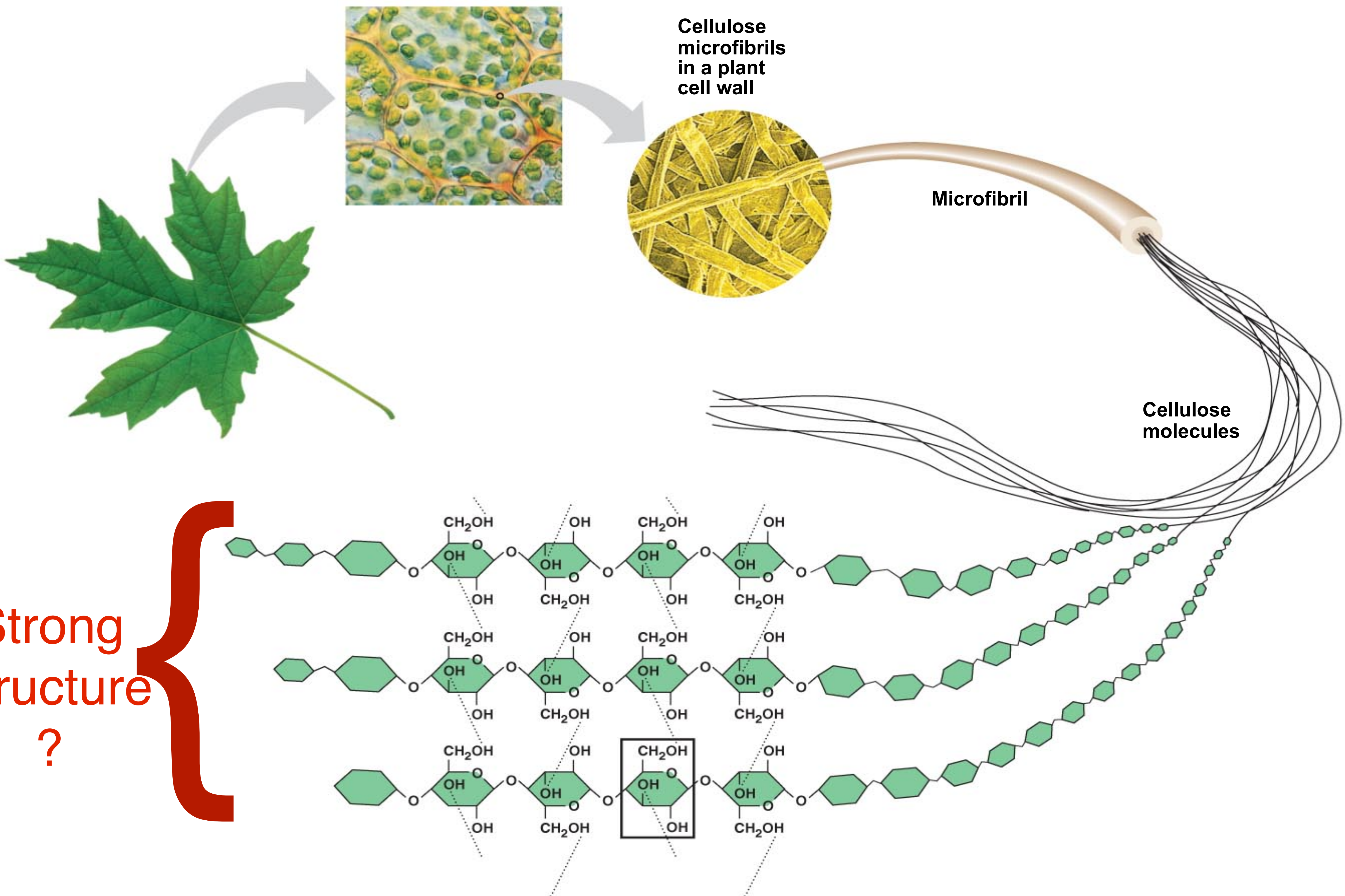


Starch: 1–4 linkage of α glucose monomers



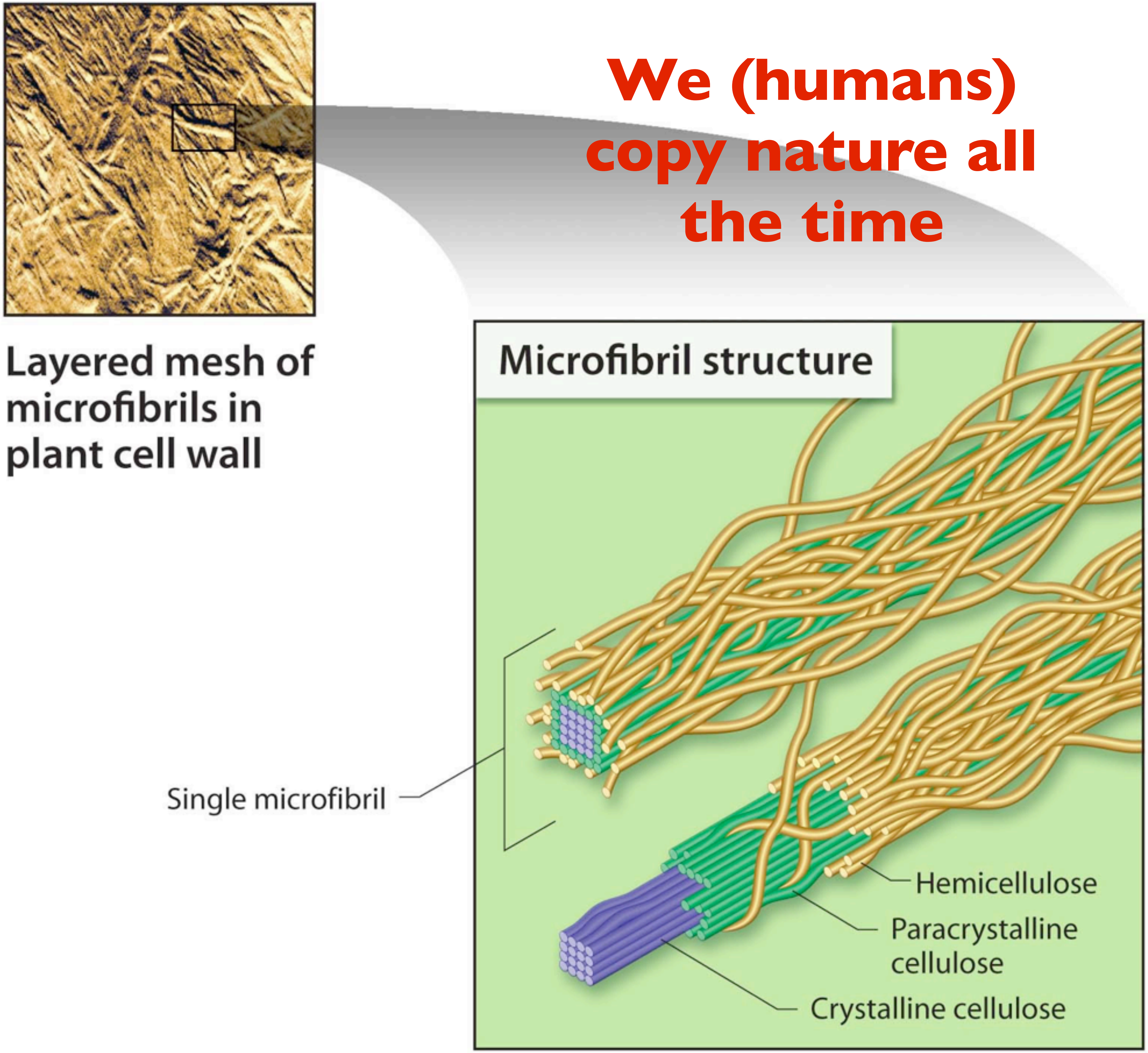
Cellulose: 1–4 linkage of β glucose monomers

2. Structural Polysaccharides



Strong Structure ?

We (humans) copy nature all the time



Are still questioning the strength of cellulose?

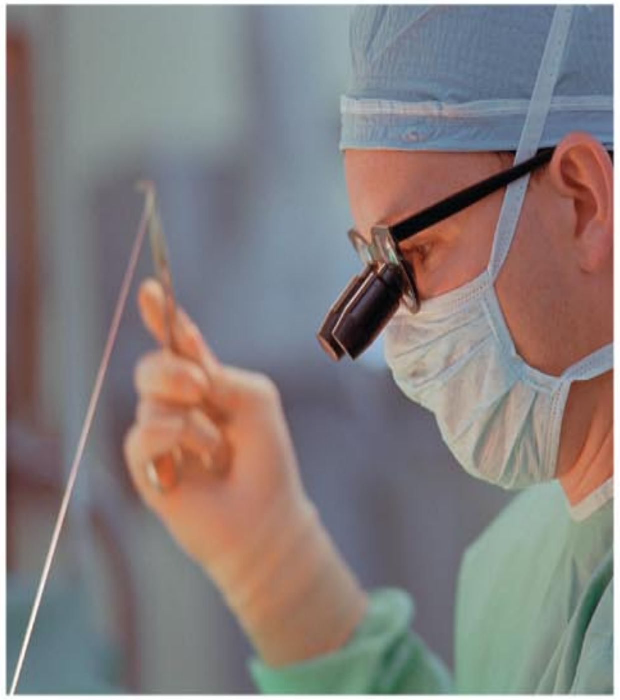
Cellulose

- **Major component in plant cell walls**
  - **It is the most abundant organic compound on earth!**
- **Few organisms possess the enzyme(s) necessary to digest the β bonds found in cellulose**
  - **Some prokaryotes & protists**
  - **Many herbivores, from cows to termites, have symbiotic relationships with these microbes.**
- **Humans can not digest cellulose and get no energy from these sugars however cellulose is still important in a healthy diet.**

Chitin

- Found in arthropods (insects, spiders and crustaceans)
    - Major component in exoskeletons
- Pure Chitin is leathery and flexible
    - Becomes very hard when encrusted with calcium carbonate.
- Fungi build their cell walls from chitin.





Functions of Carbohydrates

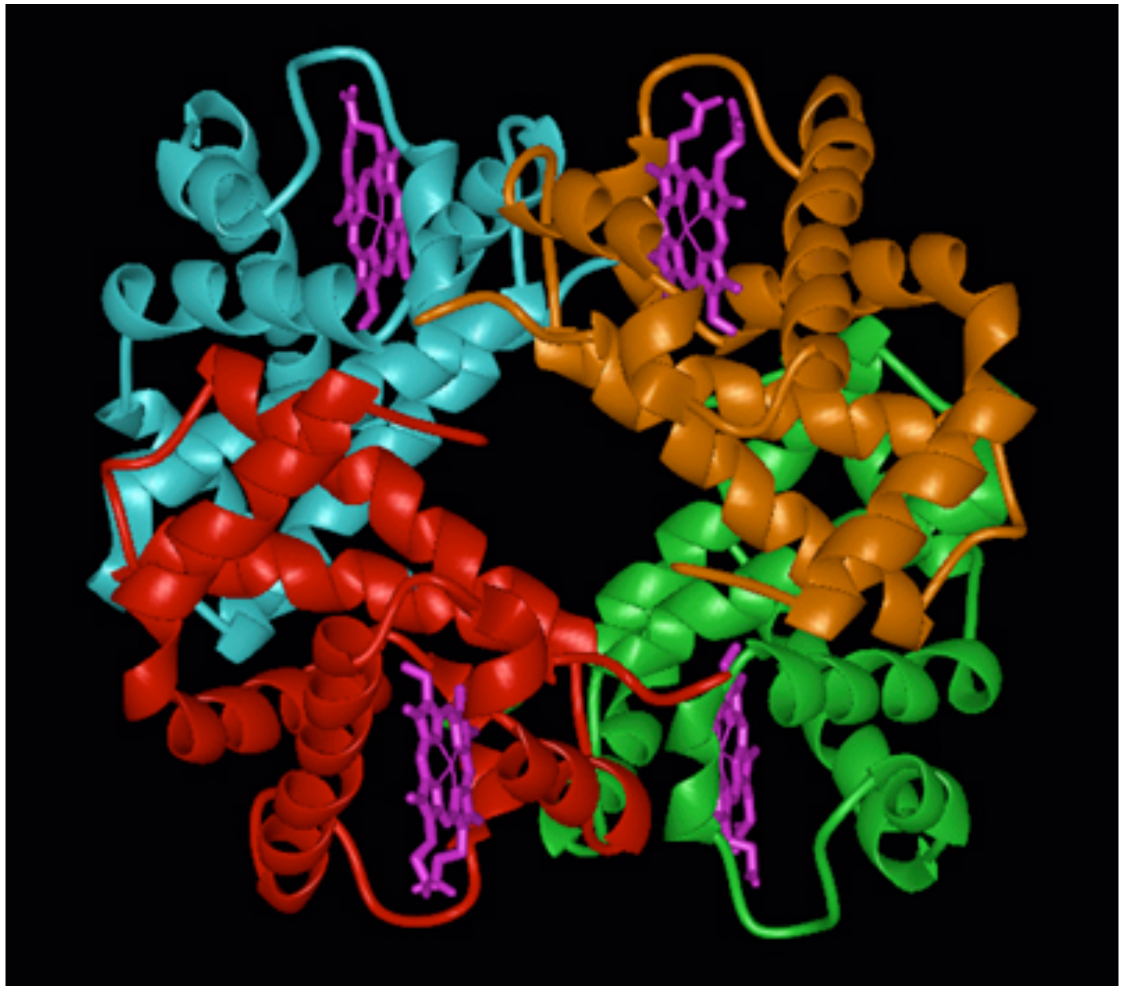
- They are major fuel source for cellular work
  - Sugars are used indirectly to power cellular processes, ATP is the direct cellular fuel
- They act as building blocks for other types of organic molecules
  - Sugars are used structurally by organisms
  - Sugars also serve as cellular ID tags

(5) Biochemistry

III.

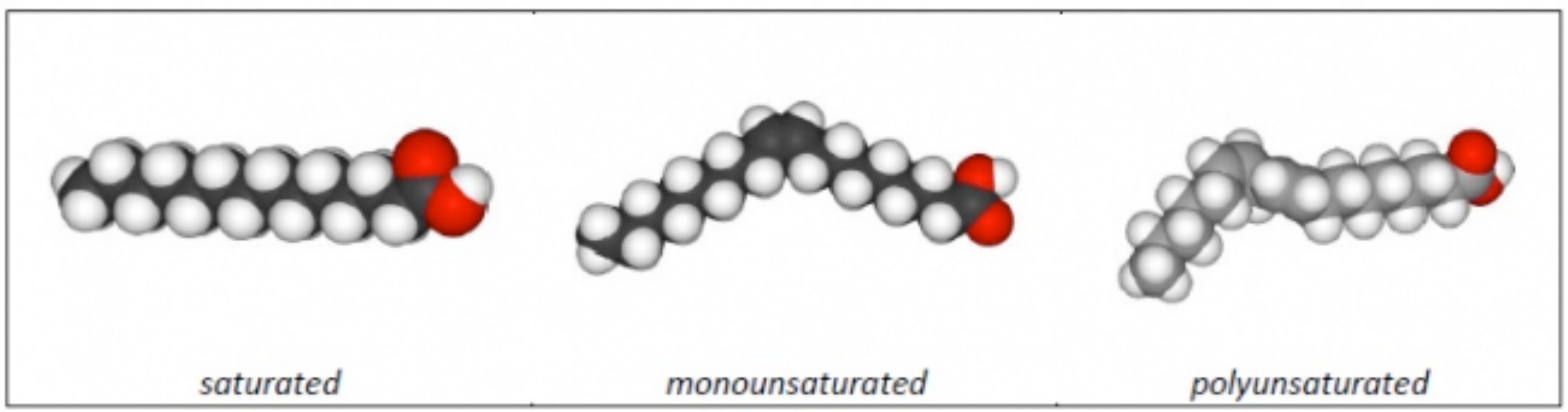
Main Idea: Lipids are a structurally diverse group of hydrophobic molecules and they smaller than the other macromolecules.

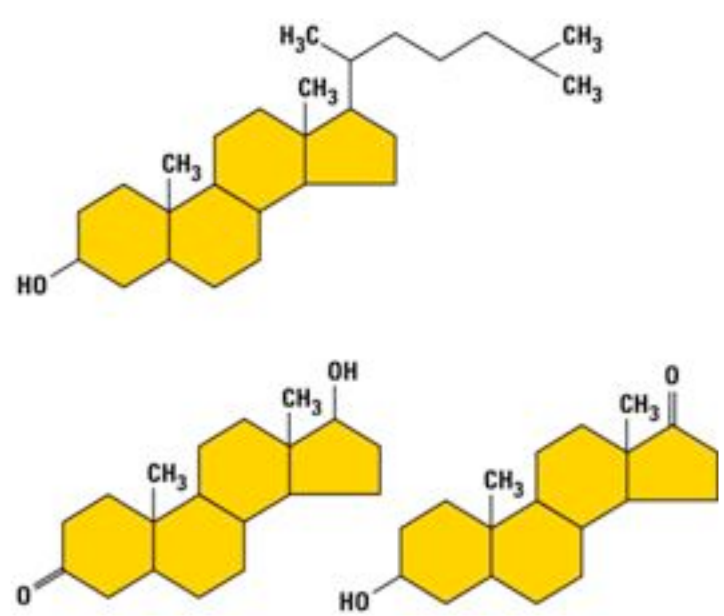
Main Idea: Lipids are functionally as diverse, they are used as energy molecules, structural molecules and chemical messengers.

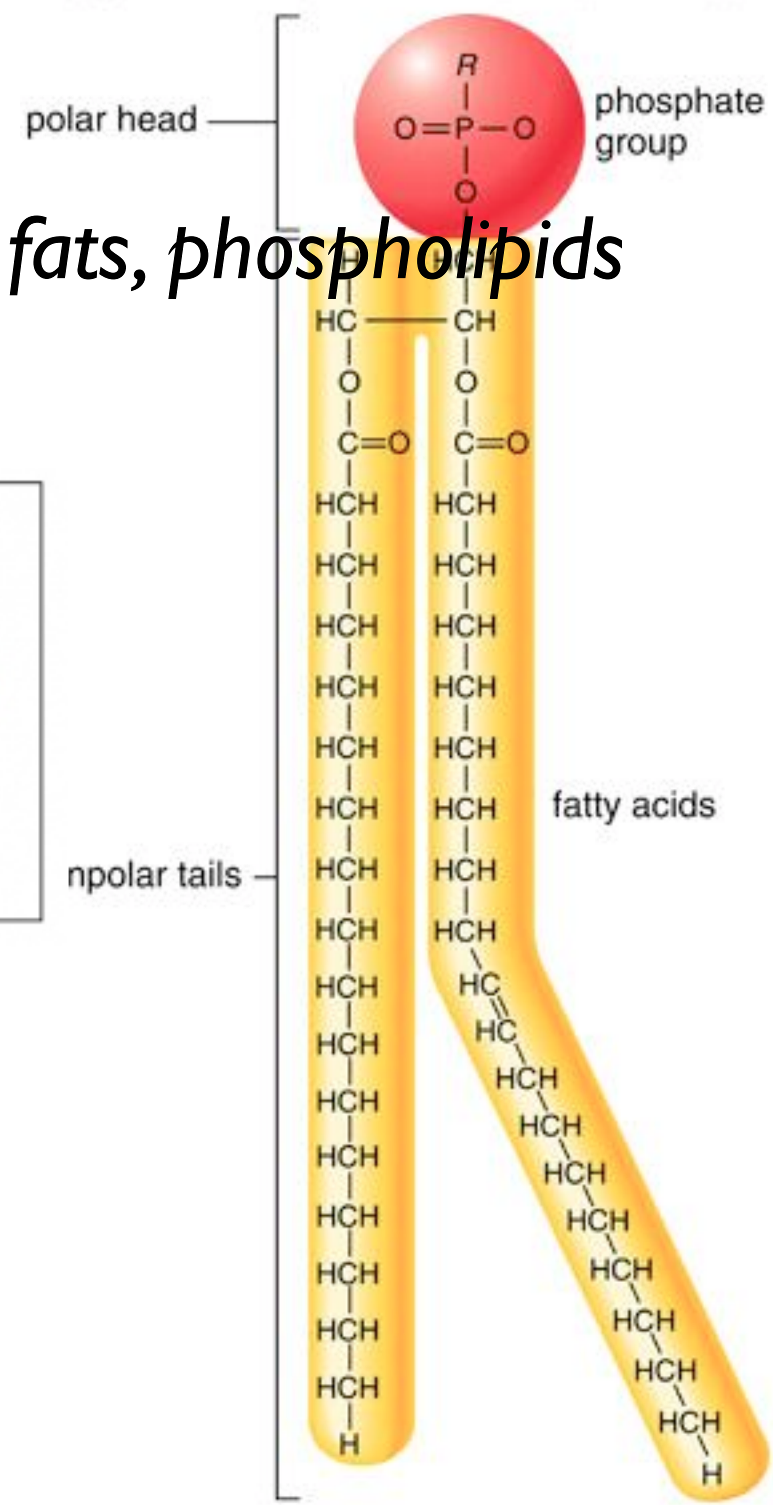


LIPIDS ARE A DIVERSE GROUP OF HYDROPHOBIC MOLECULES

- They are not true polymers.
- The most biologically important lipids include: *fats*, *phospholipids* and *steroids*.





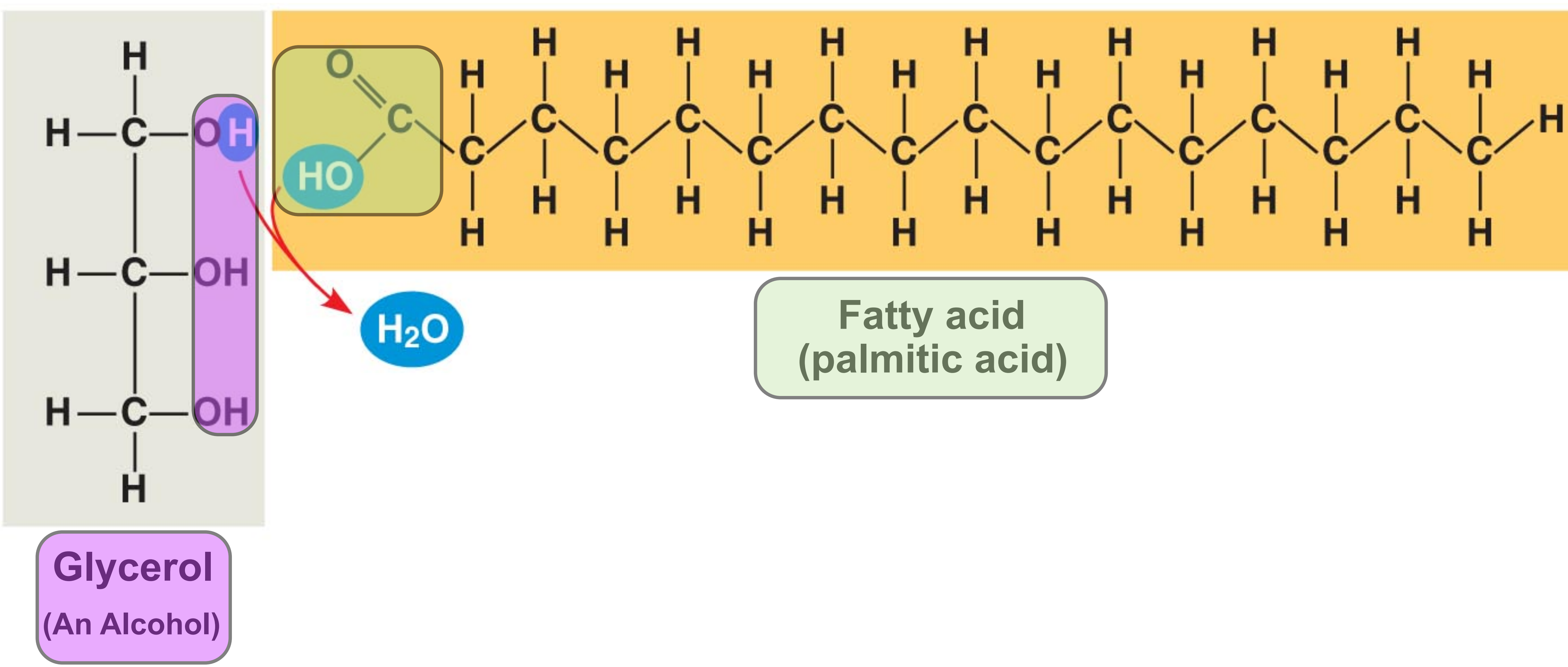


Phospholipid structure

A. Fats

- A fat has two parts: *a Glycerol backbone and a fatty acid(s)*
- They are hydrophobic.

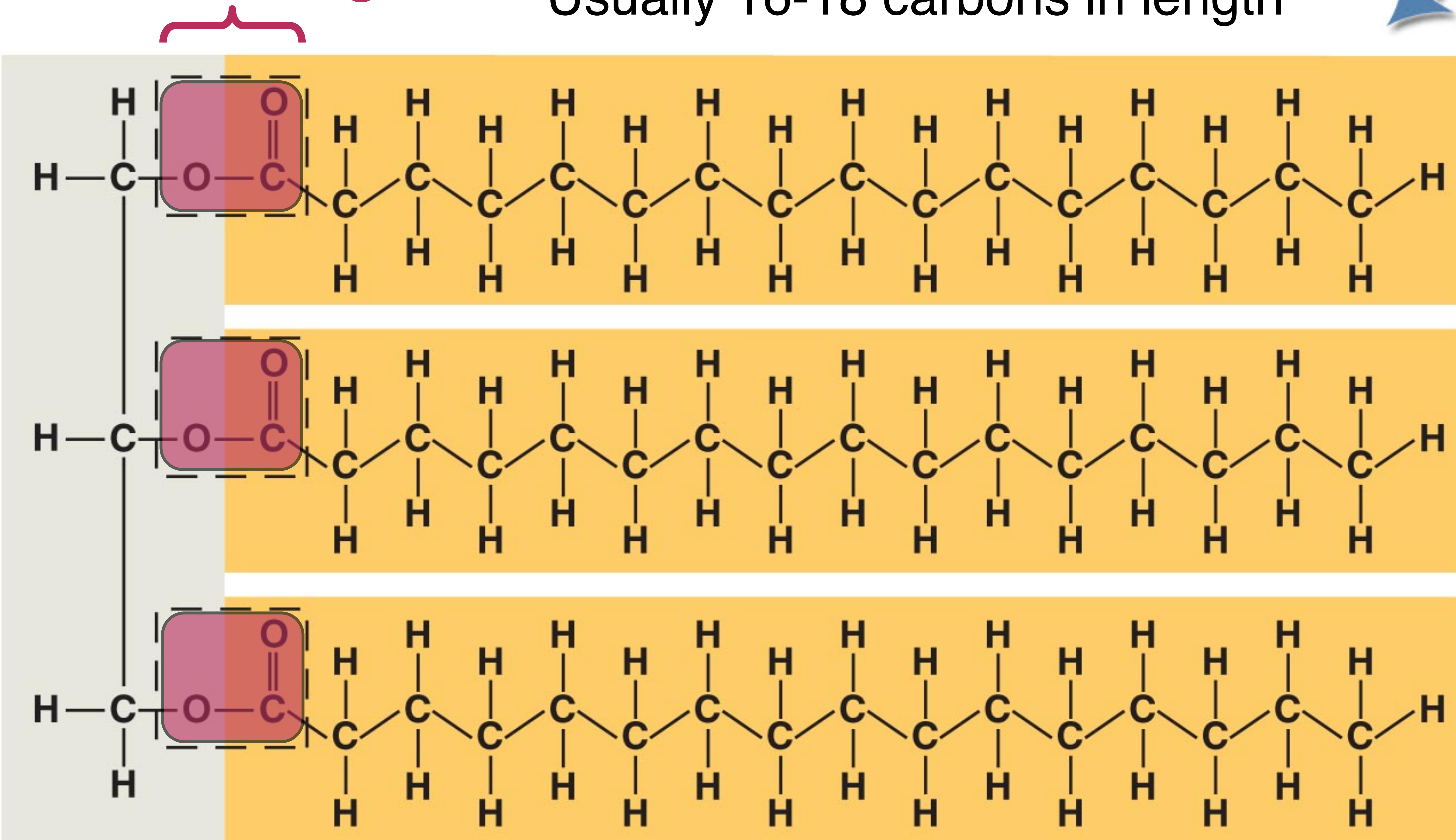
Dehydration reaction in the synthesis of a fat



Fatty acids can same or each can be different

Ester linkage

Usually 16-18 carbons in length

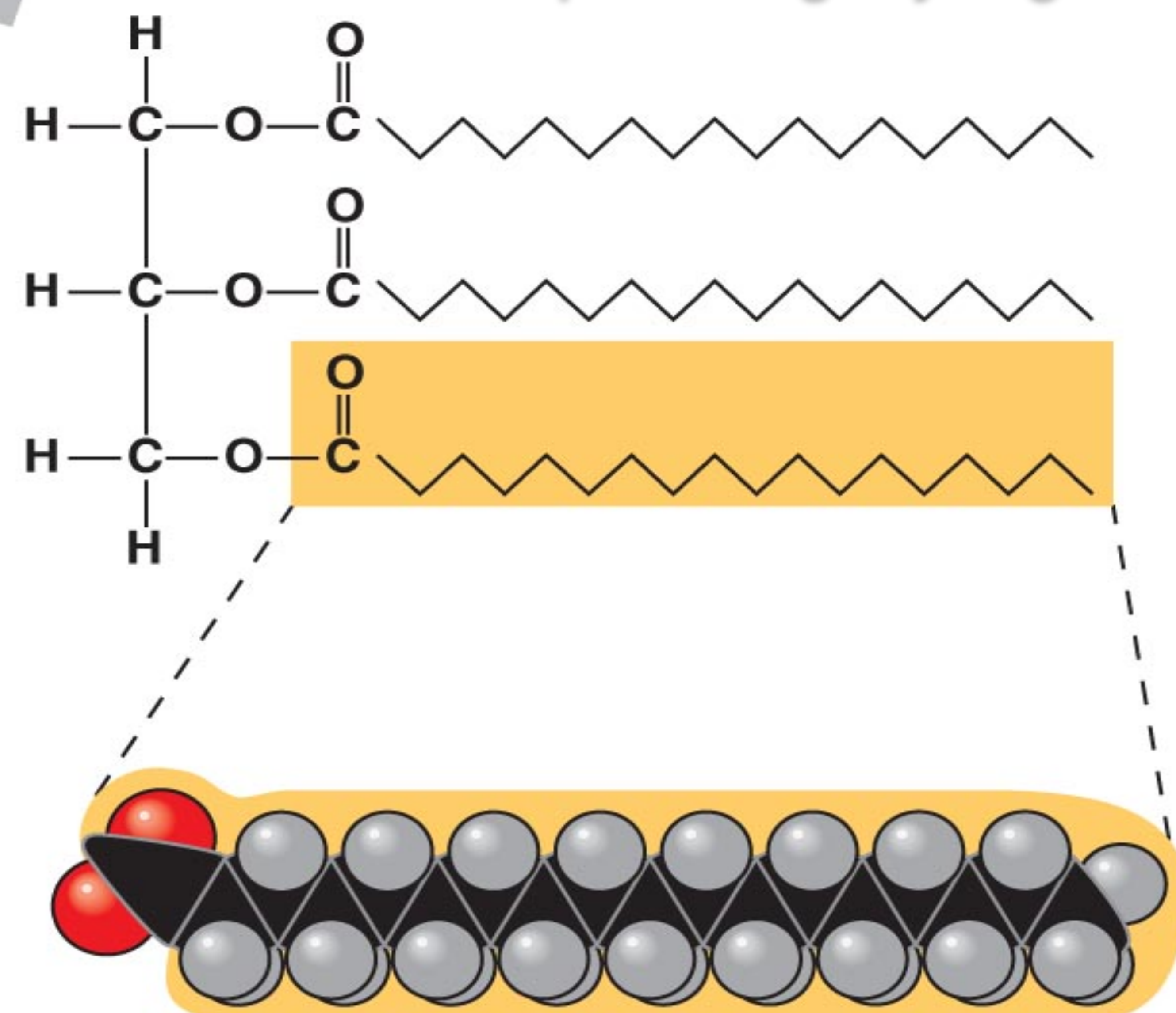


Fat molecule (triacylglycerol)

saturated fats

-no double bonds
-packs tightly together

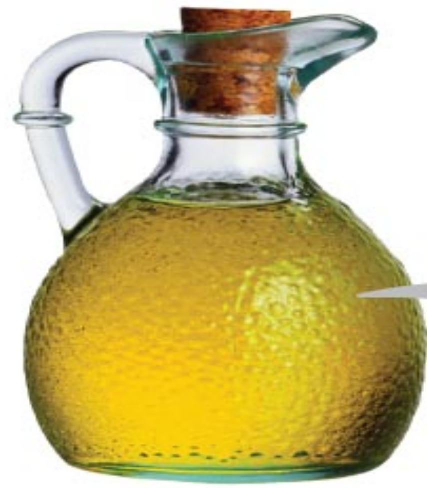
Solid at room temp



Contributes to cardiovascular disease

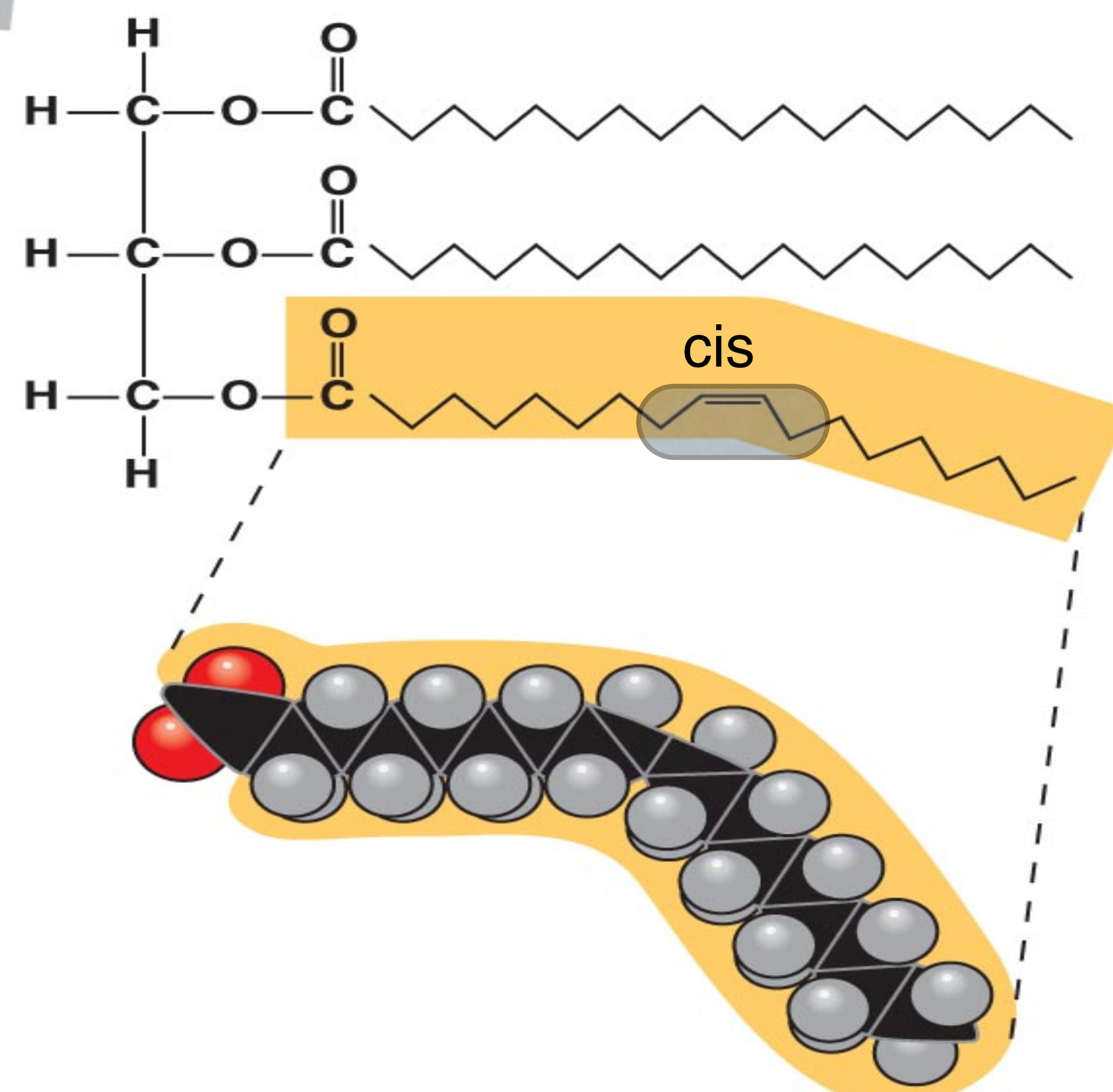
Animal fats

unsaturated fats



-one or more double bonds

-packs less tightly together



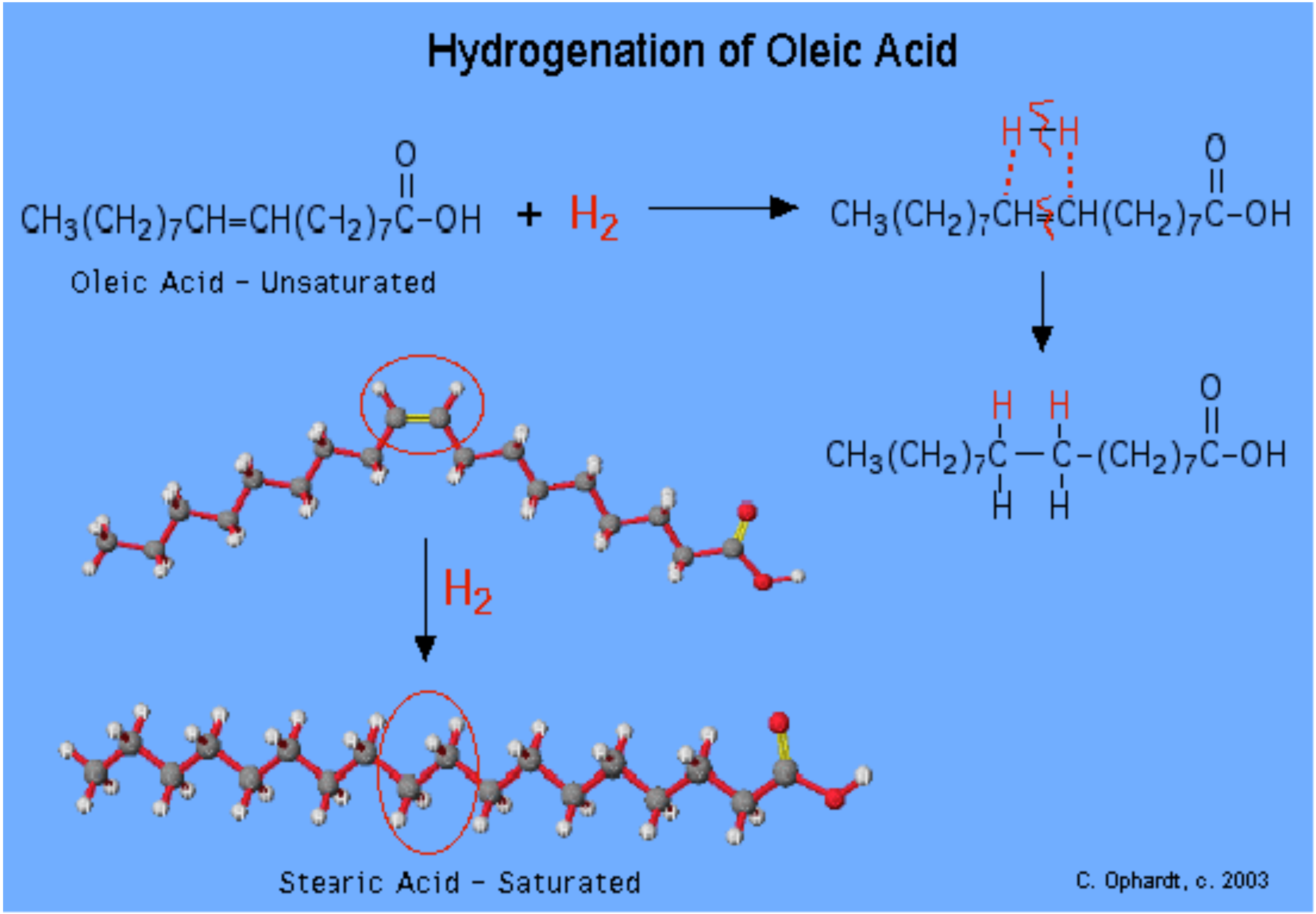
Liquid at room temp

Helps eliminate “bad” fats

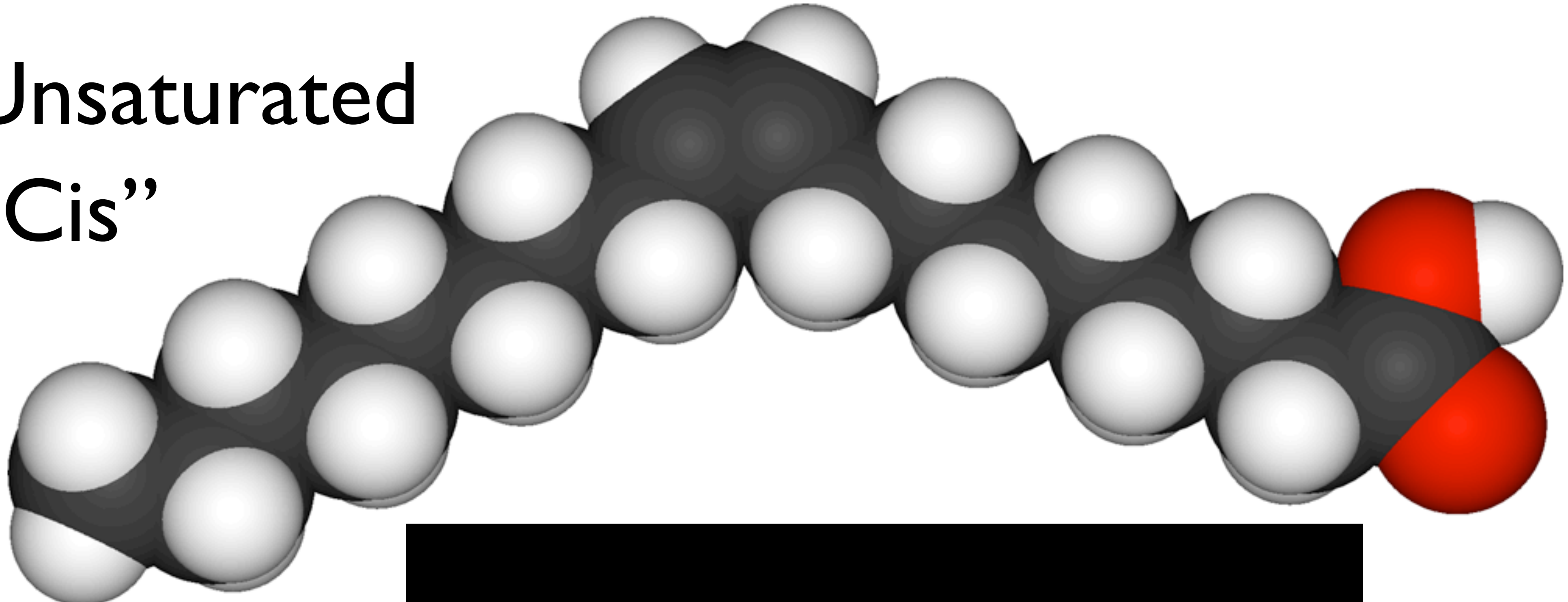
Fish & Plant fats

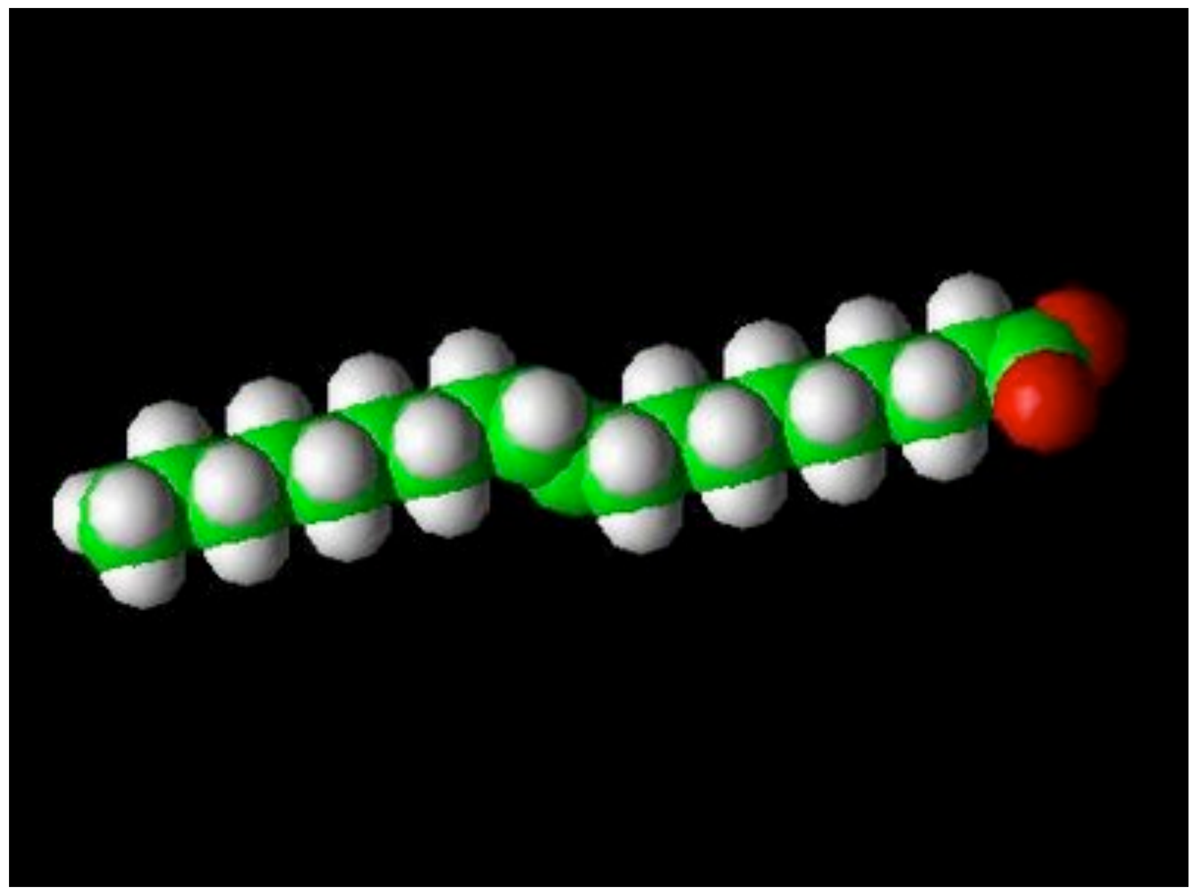
hydrogenated oils

aka...trans-fats

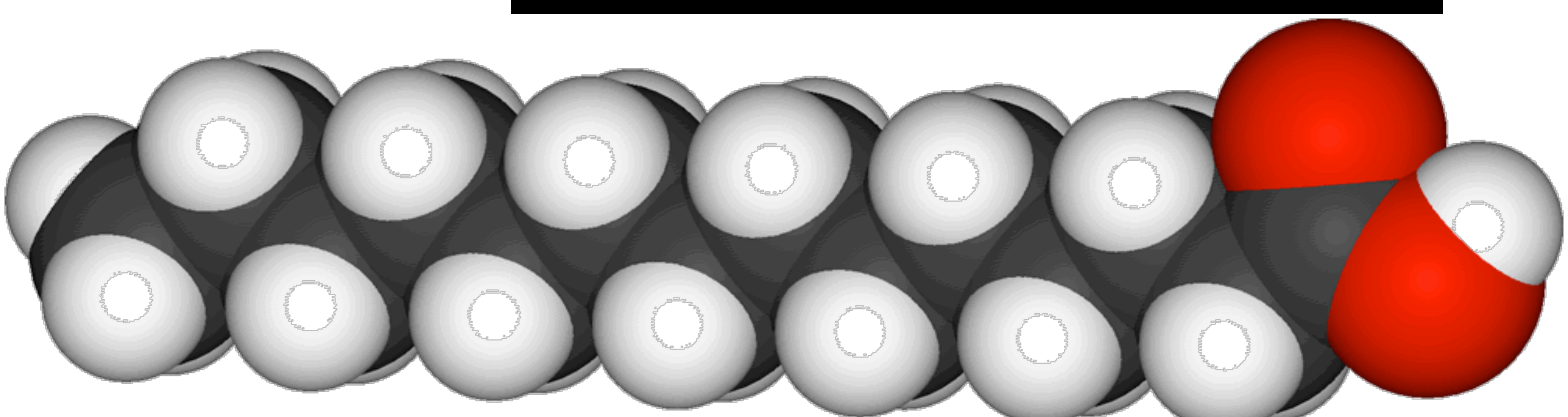


Unsaturated
“Cis”





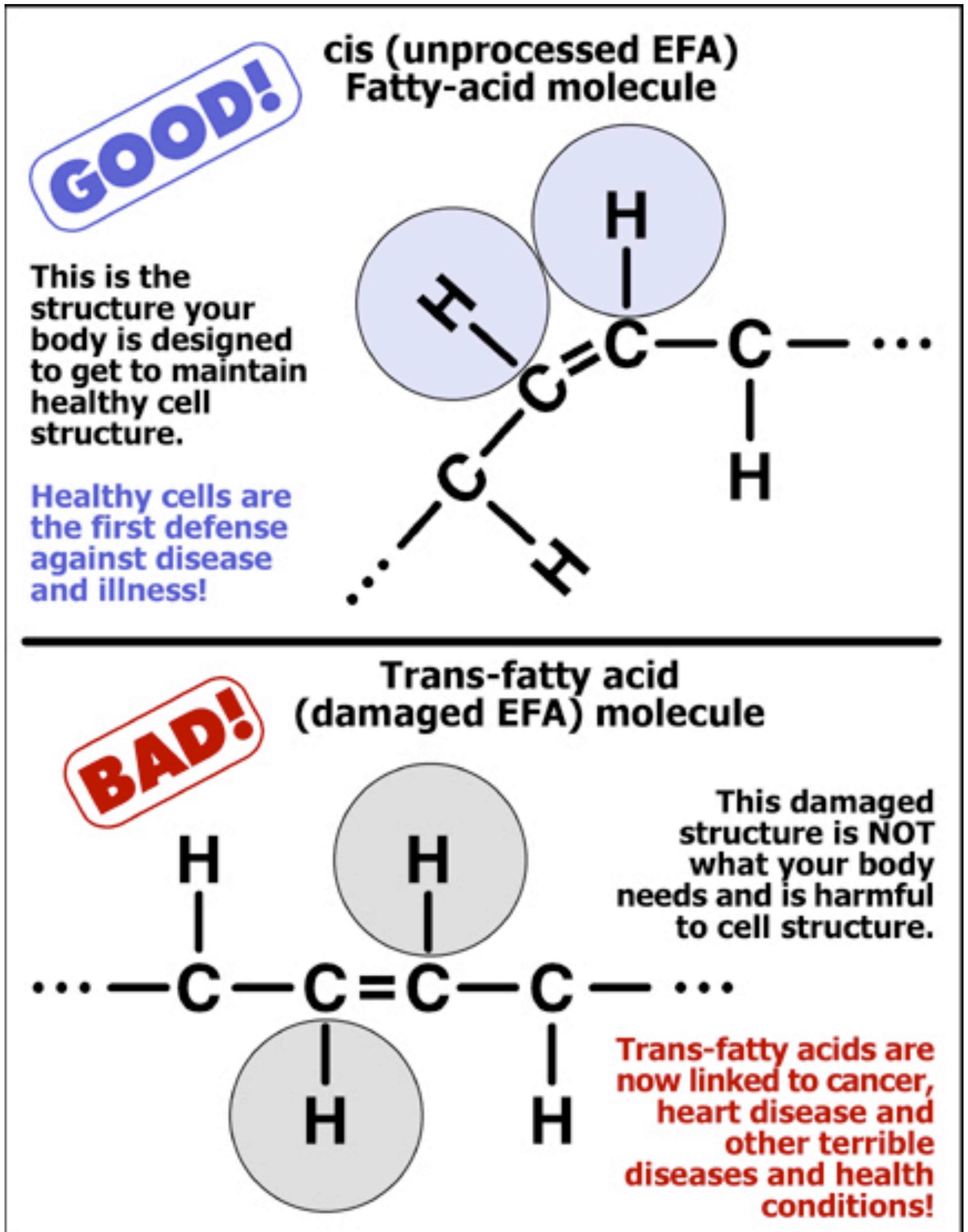
Unsaturated
“Trans”

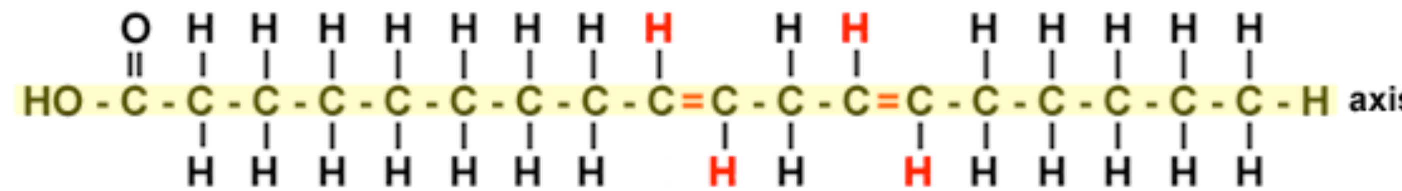


Saturated

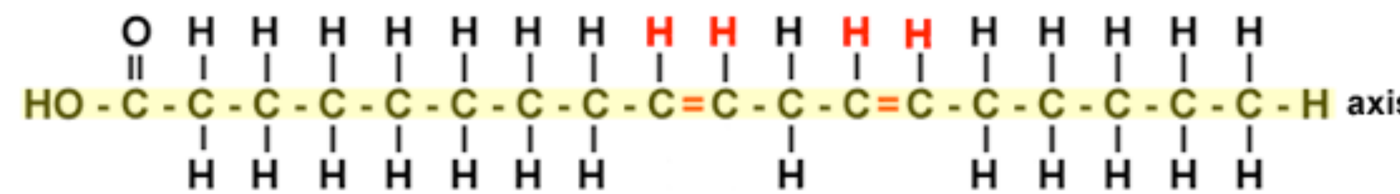
hydrogenated oils

aka...trans-fats

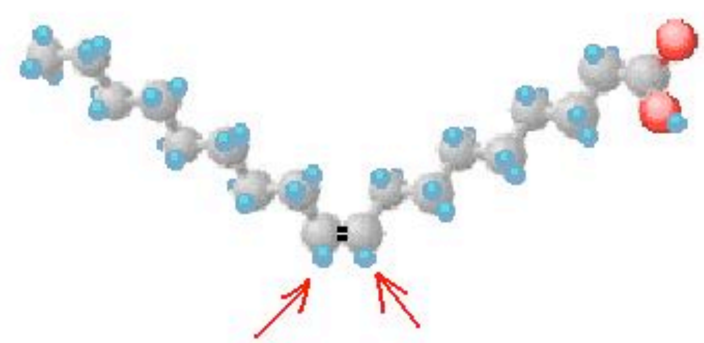




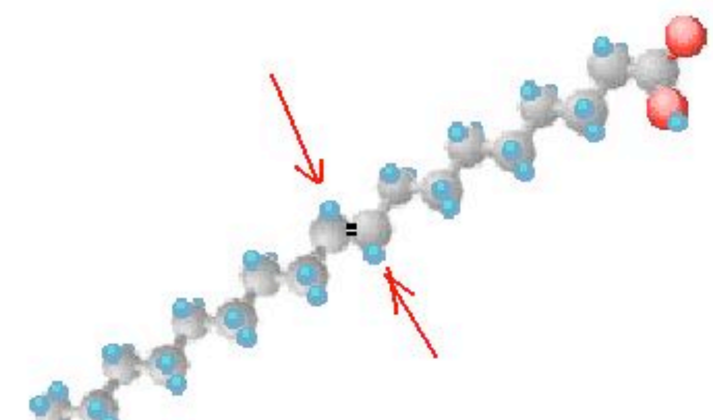
linoleic acid: *trans* configuration (*trans* isomer)



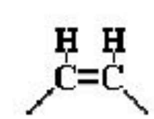
linoleic acid: *cis* configuration (*cis* isomer)



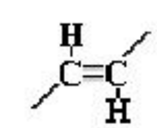
Cis-9-octadecenoic acid
(Oleic acid)



Trans-9-octadecenoic acid
(Elaidic acid)



Cis Configuration



Trans Configuration


FUEL the FUN!
SKIPPY
CREAMY
PEANUT BUTTER
importladen.de


Nilla wafers
Reduced Fat
KRAFT
Stove Top
CHICKEN
Sociables
MY-T-FINE
Fudge Brownie
Sugar Free
SnackWell's
Nutter Butter
Newtons
Andes
OLD EL PASO
Taco

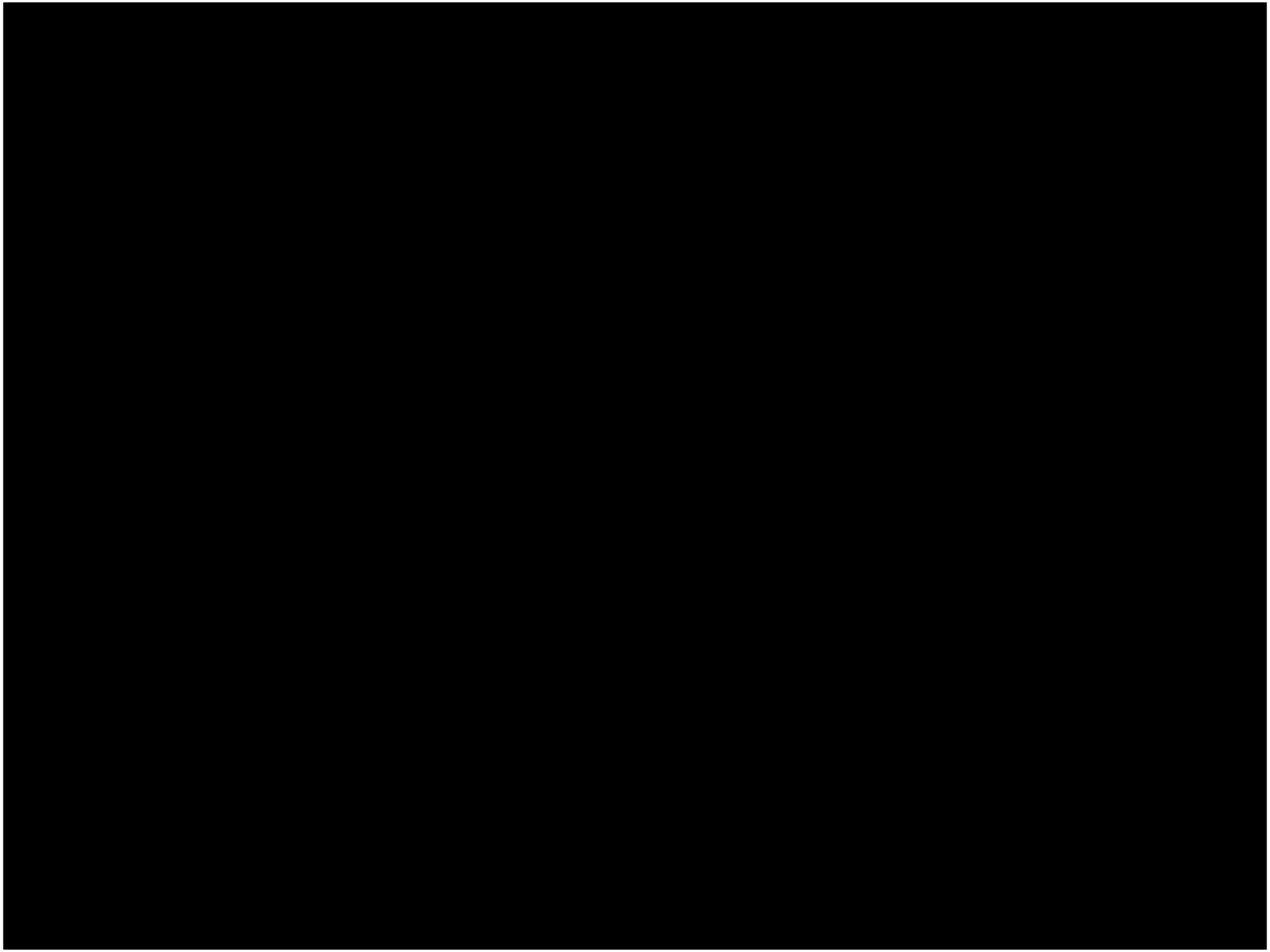

Pringles
CHEEZ-IT
REDUCED FAT
Chips Ahoy!

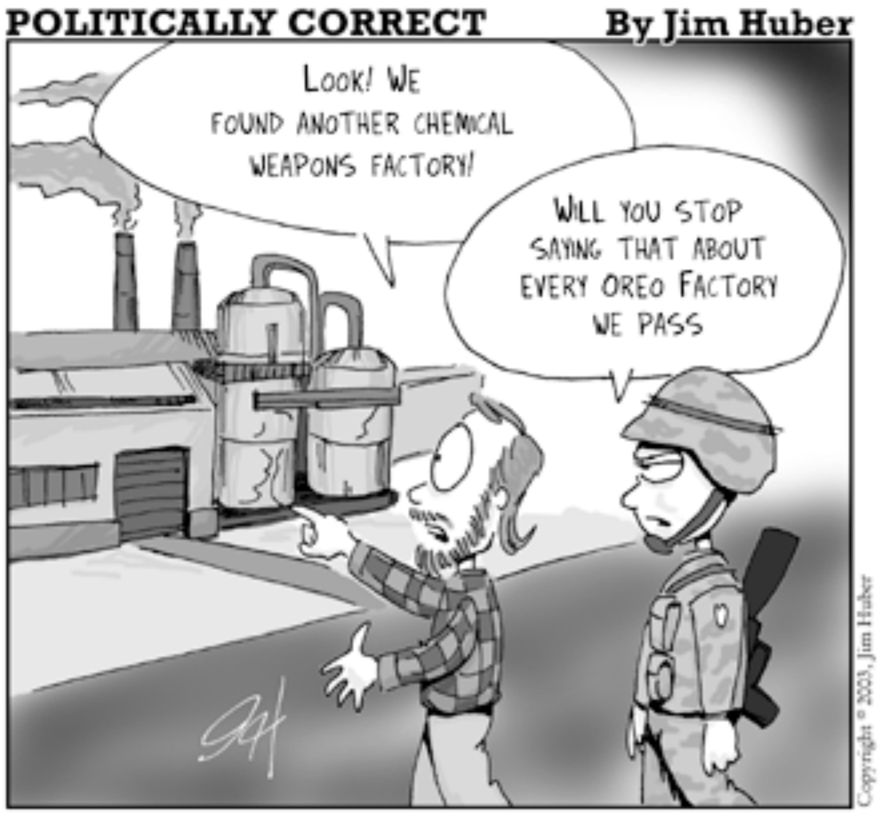

TRANS
FATS

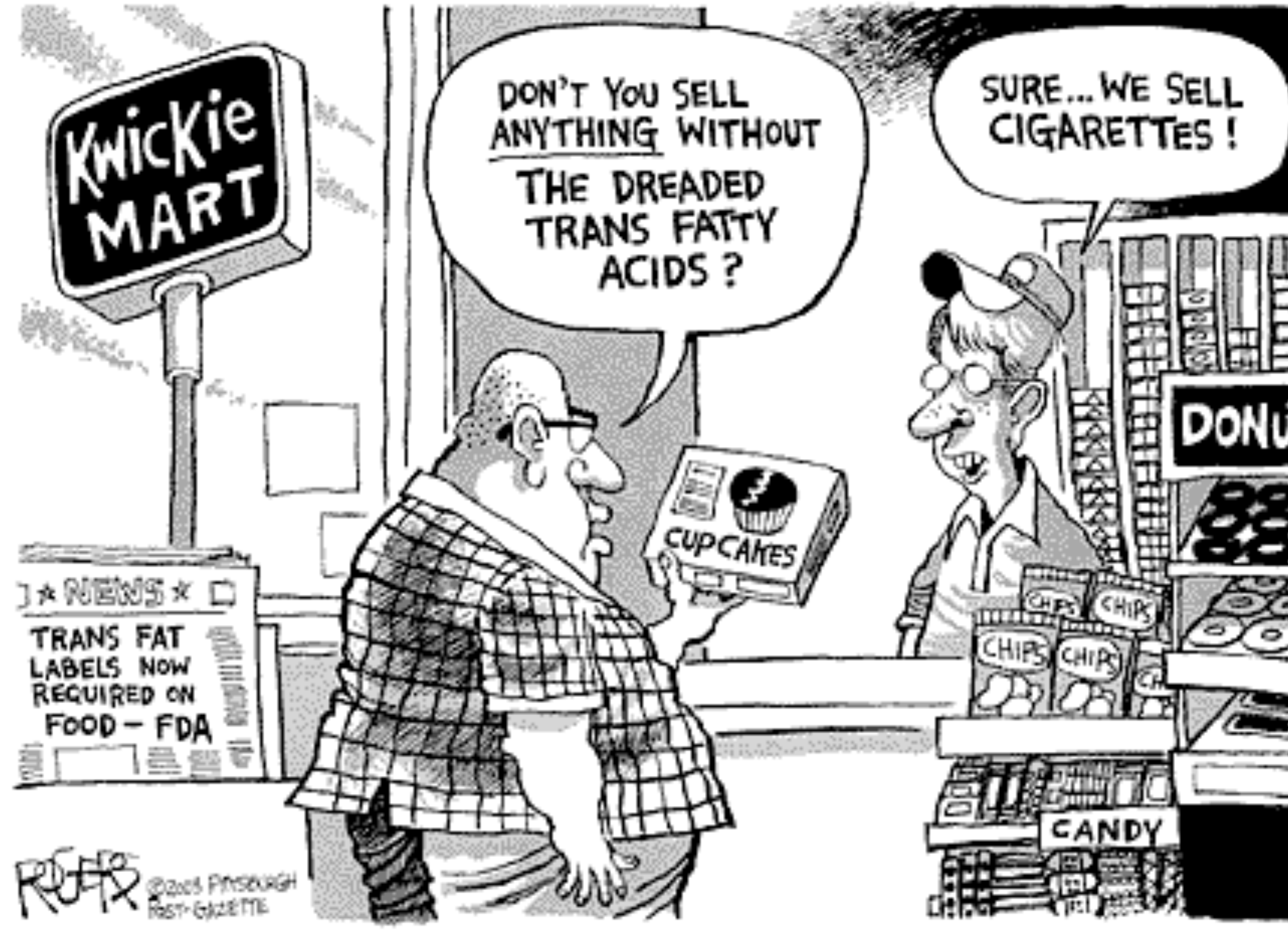

© AP

Peanut Butter

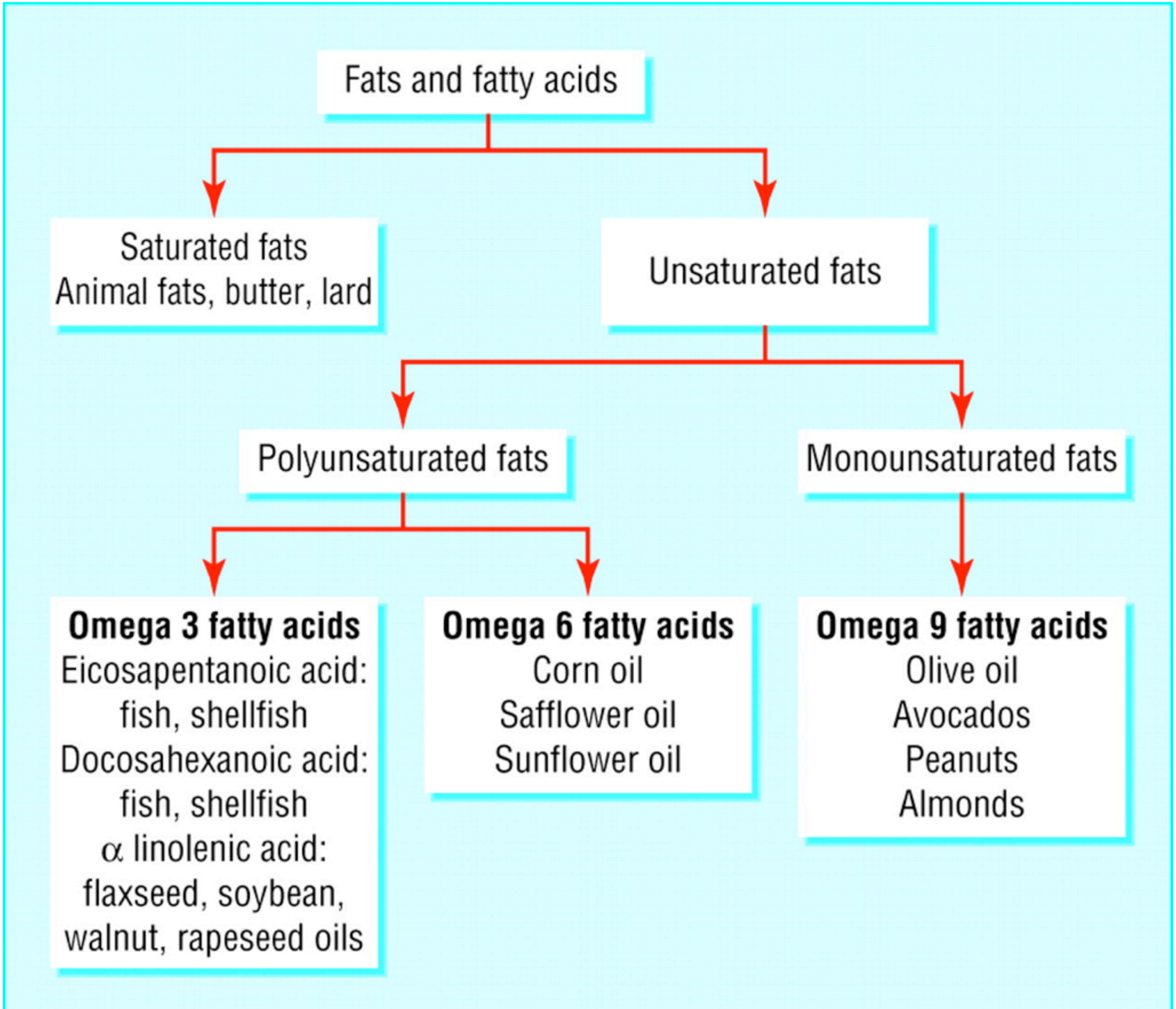
Processed Foods Loaded with Hydrogenated

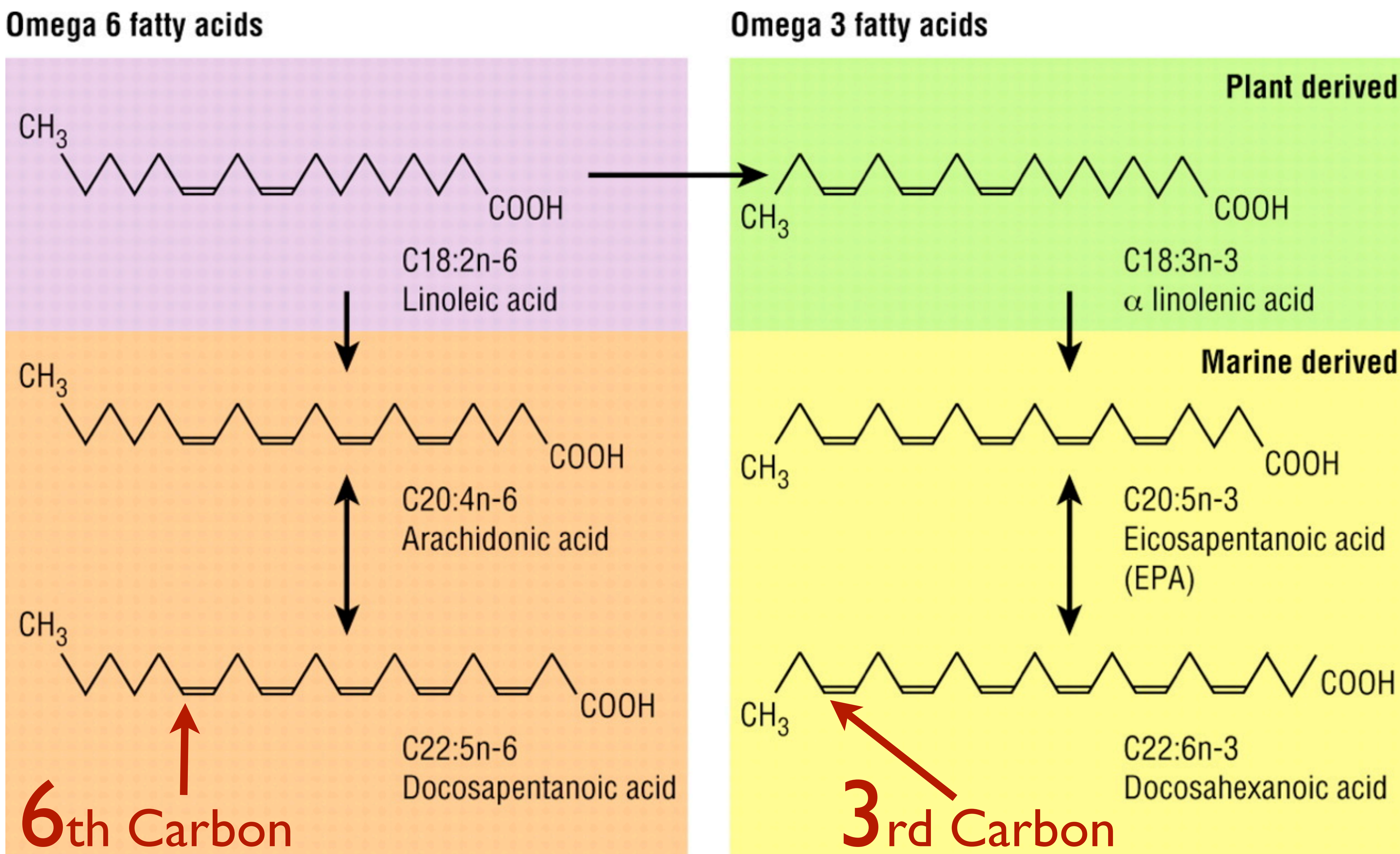




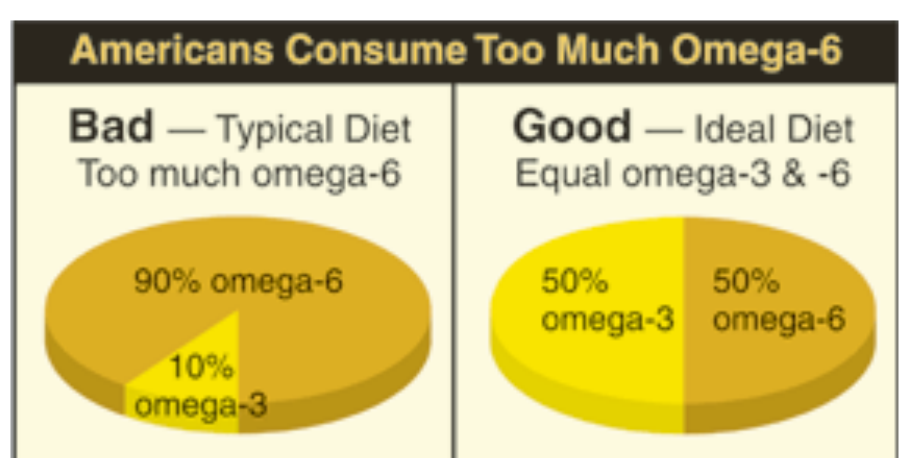



"How do you guys want your trans fatty acids prepared?"


Fats and fatty acids
Saturated fats
Animal fats, butter, lard
Unsaturated fats
Polyunsaturated fats
Monounsaturated fats
Omega 3 fatty acids
Eicosapentanoic acid: fish, shellfish
Docosahexanoic acid: fish, shellfish
α linolenic acid: flaxseed, soybean, walnut, rapeseed oils
Omega 6 fatty acids
Corn oil
Safflower oil
Sunflower oil
Omega 9 fatty acids
Olive oil
Avocados
Peanuts
Almonds



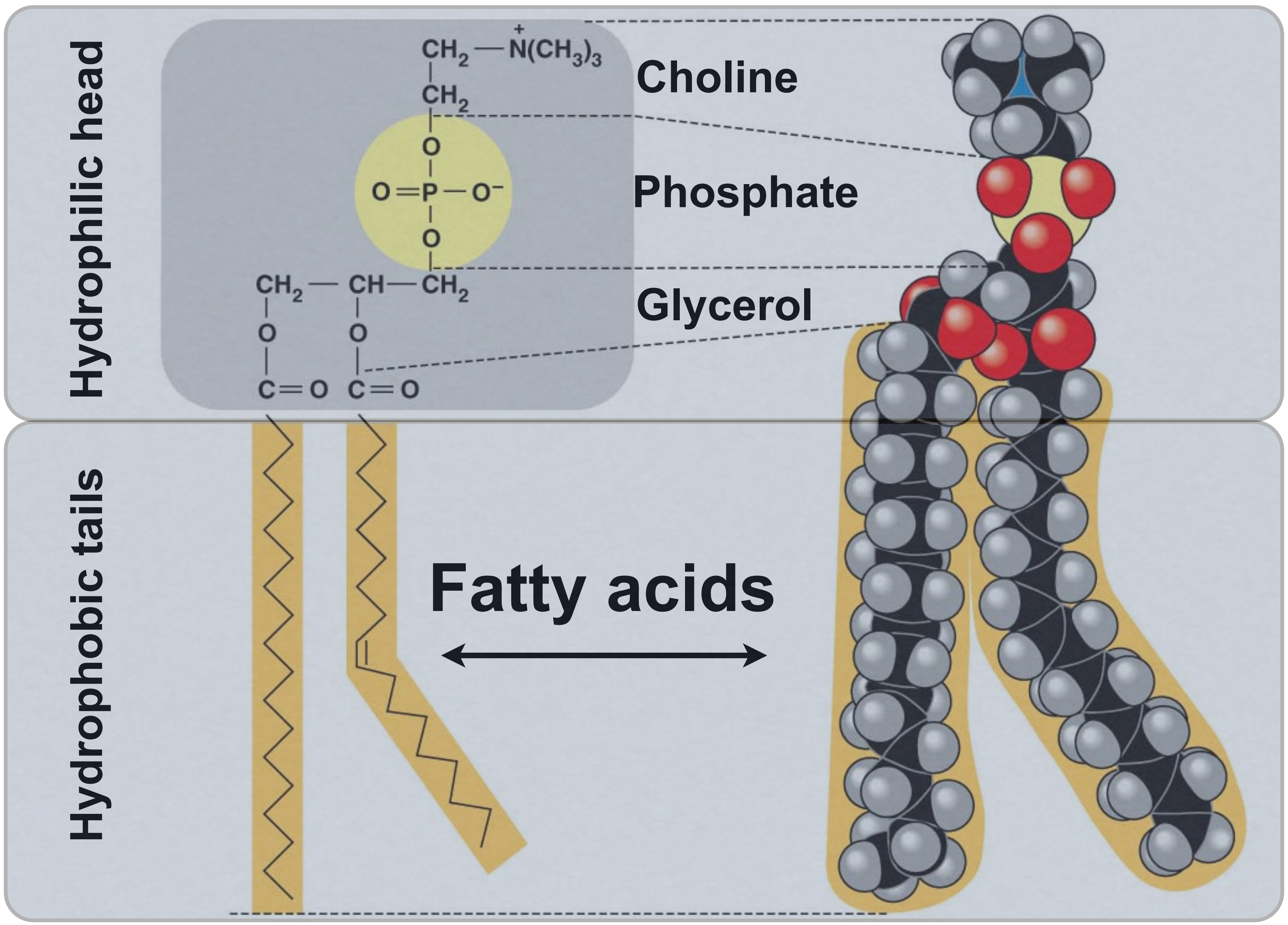
Omega 6 fatty acids
Omega 3 fatty acids
Plant derived
CH3
COOH
C18:2n-6
Linoleic acid
C18:3n-3
α linolenic acid
Marine derived
C20:4n-6
Arachidonic acid
C20:5n-3
Eicosapentanoic acid (EPA)
C22:5n-6
Docosapentanoic acid
C22:6n-3
Docosahexanoic acid
6th Carbon
3rd Carbon



Americans Consume Too Much Omega-6
Bad — Typical Diet
Too much omega-6
90% omega-6
10% omega-3
Good — Ideal Diet
Equal omega-3 & -6
50% omega-3
50% omega-6

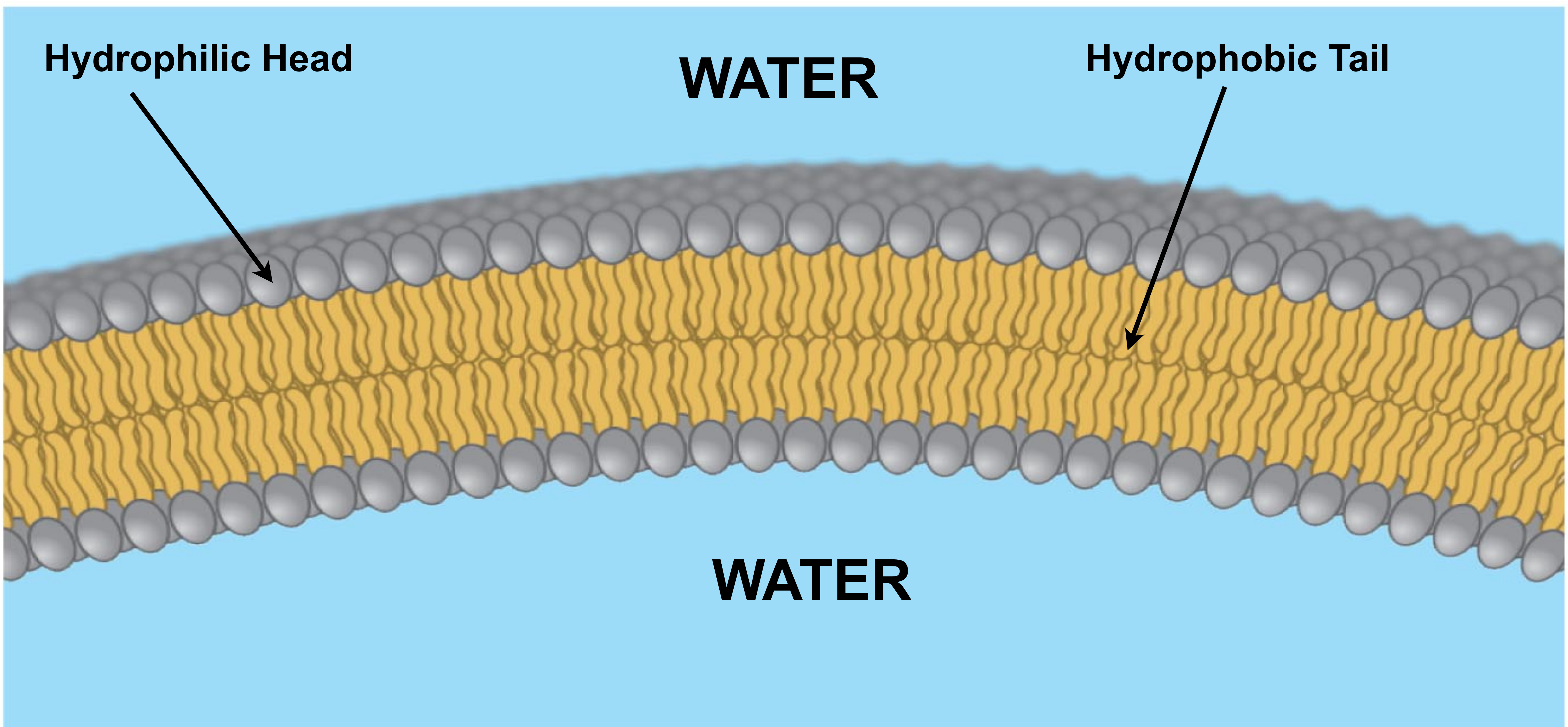
B. Phospholipids

- *Phospholipids* are essential, they make up membranes
- A fat has two parts: *Hydrophilic head* and *Hydrophobic tail*



B. Phospholipids

- *Phospholipids* are essential, they make up membranes
- A fat has two parts: *Hydrophilic head* and *Hydrophobic tail*
- ***Membranes separate internal from external environments, cells could not exist without them***



C. Steroids

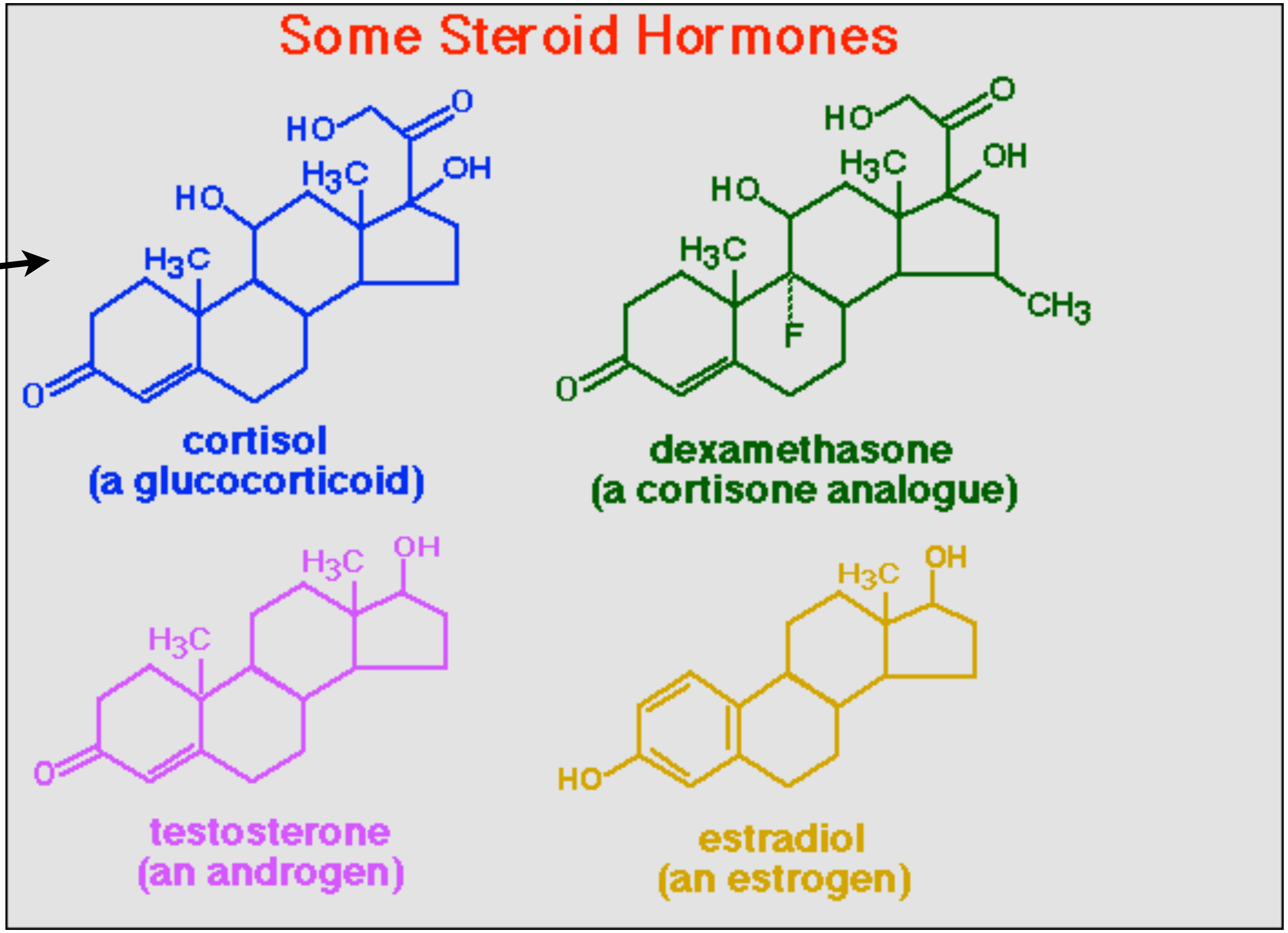
- *Steroids* are lipids, they are made of 4 fused rings
- Steroids include: Cholesterol and Sex Hormones
- They play an important role in membrane structure and function
- They are also important precursors to other organic molecules

Cortisol

-increasing blood sugar through <u>gluconeogenesis</u>

-suppressing the immune system

-aiding in fat, protein, and carbohydrate metabolism



Functions of Lipids

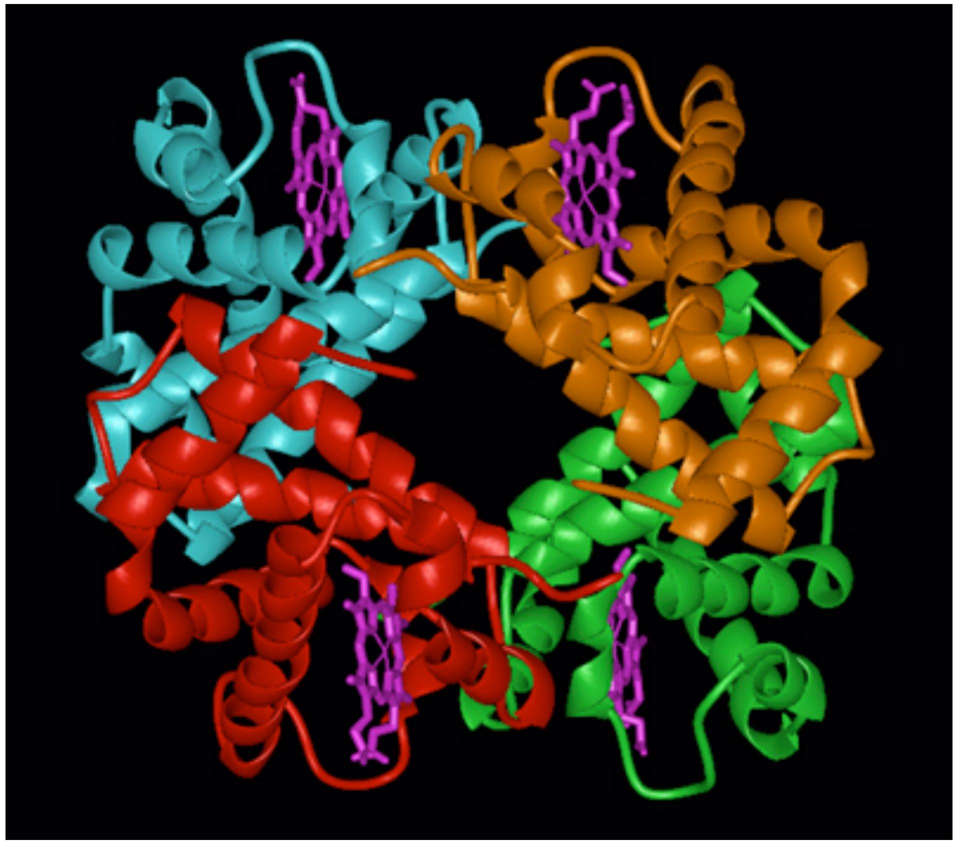
- They are major fuel source for cellular work
  - Lipids are used indirectly to power cellular processes, ATP is the direct cellular fuel
- They act as building blocks for membranes
- They cushion and insulate
- They are chemical messengers (hormones)

(5) Biochemistry

IV.

Main Idea: Proteins have the most sophisticated structures and make up over 50% of every cells biomass.

Main Idea: Proteins play a role in virtually every vital process important to life, they have the widest diversity of functions.



PROTEINS INCLUDE A DIVERSITY OF STRUCTURES, RESULTING IN A WIDE RANGE OF FUNCTIONS

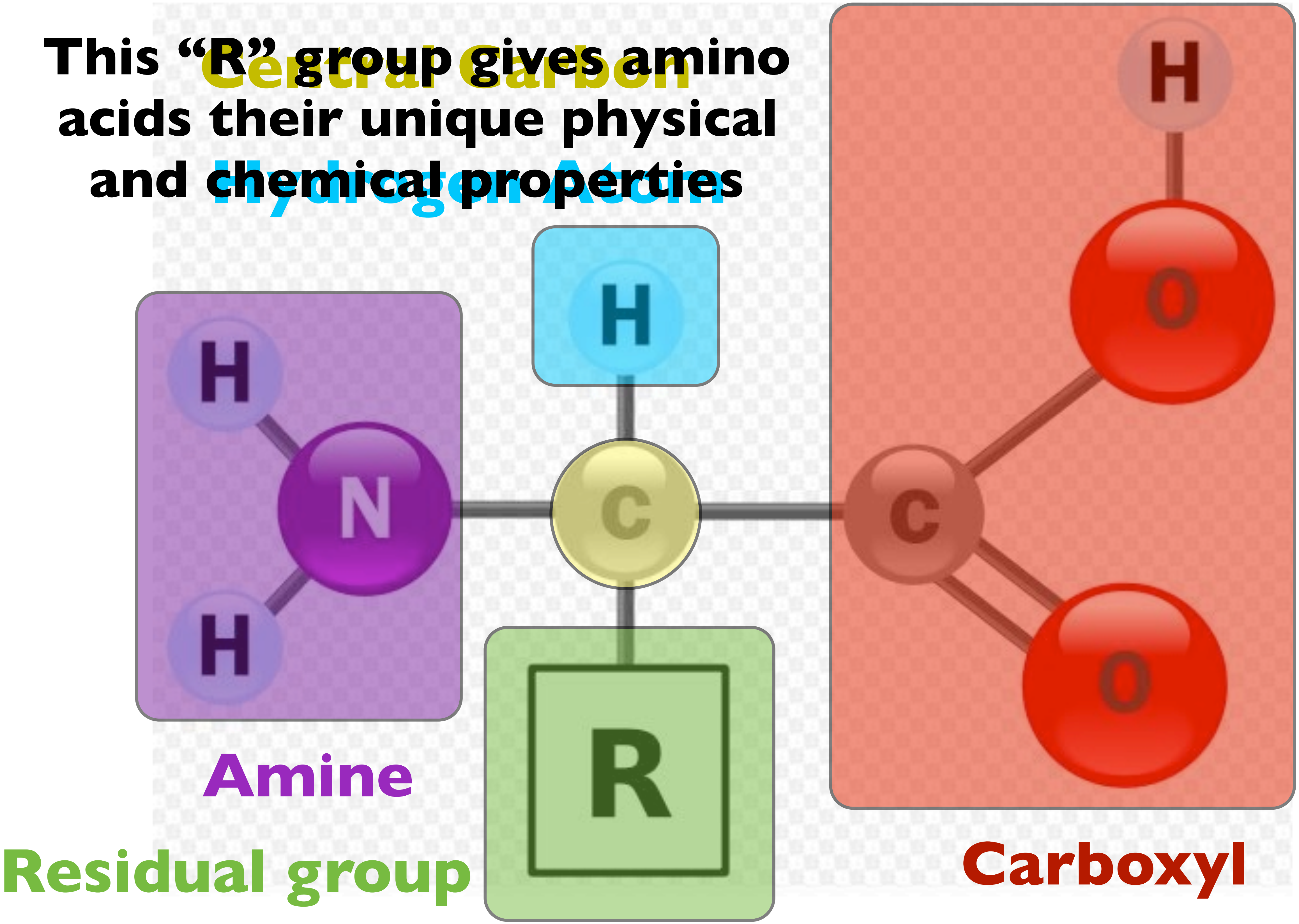
- Humans have tens of thousands of differently shaped proteins, each with its unique role or function.
- Proteins are the main building blocks of life and proteins control life's necessary functions.

A. Polypeptides (aka proteins)

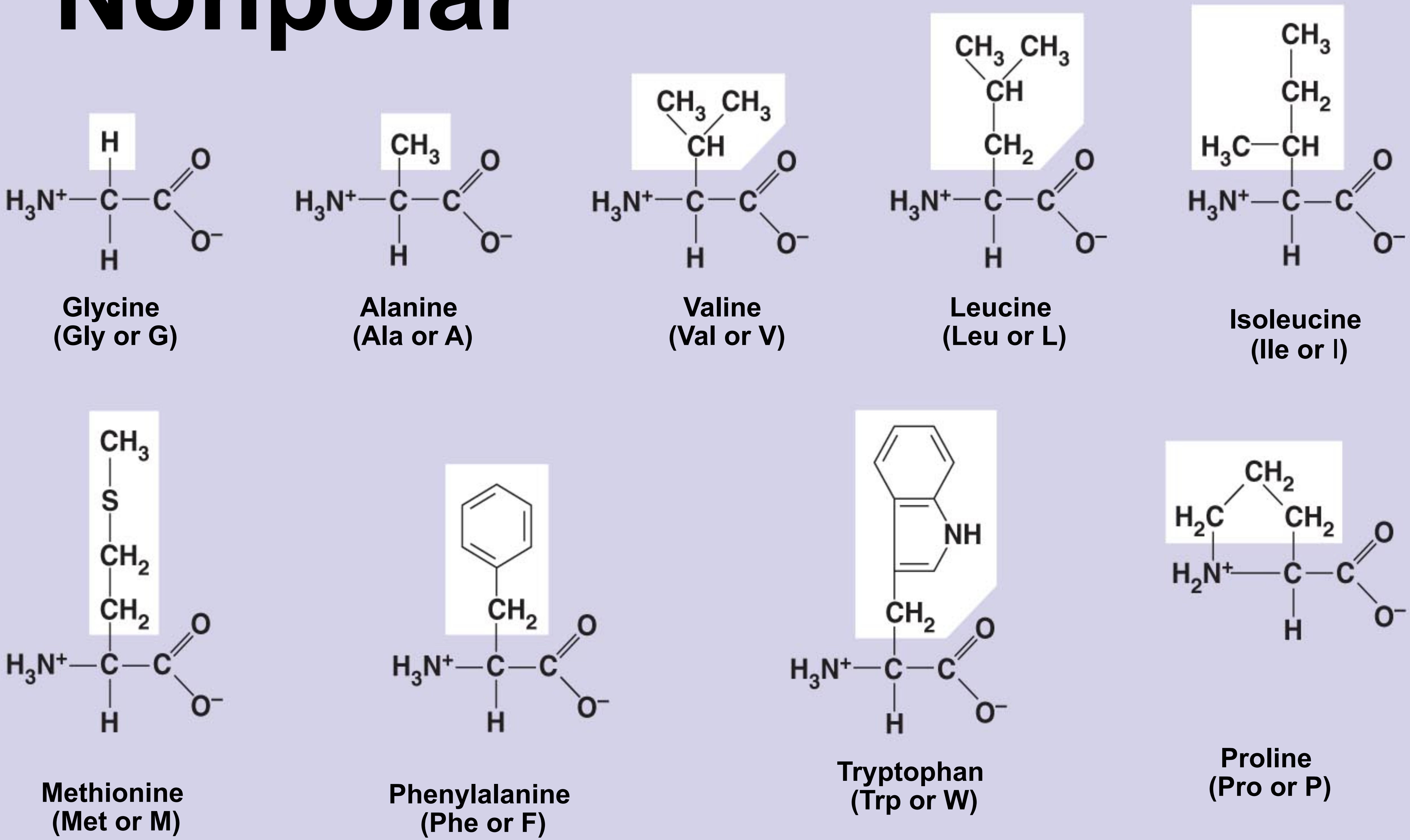
- Proteins are true polymers constructed from 20 different monomers called *amino acids*.

1. Amino Acid monomers

- The amino acid below is non-ionized (dry) .



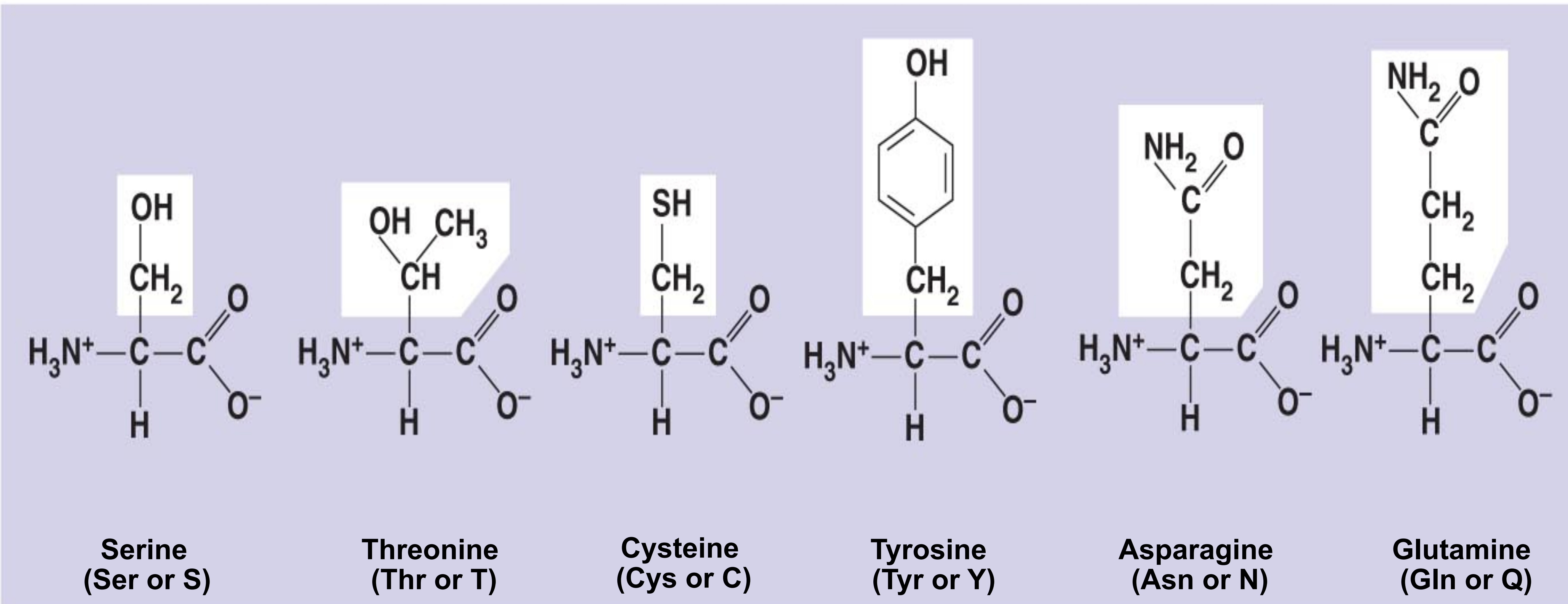
Nonpolar



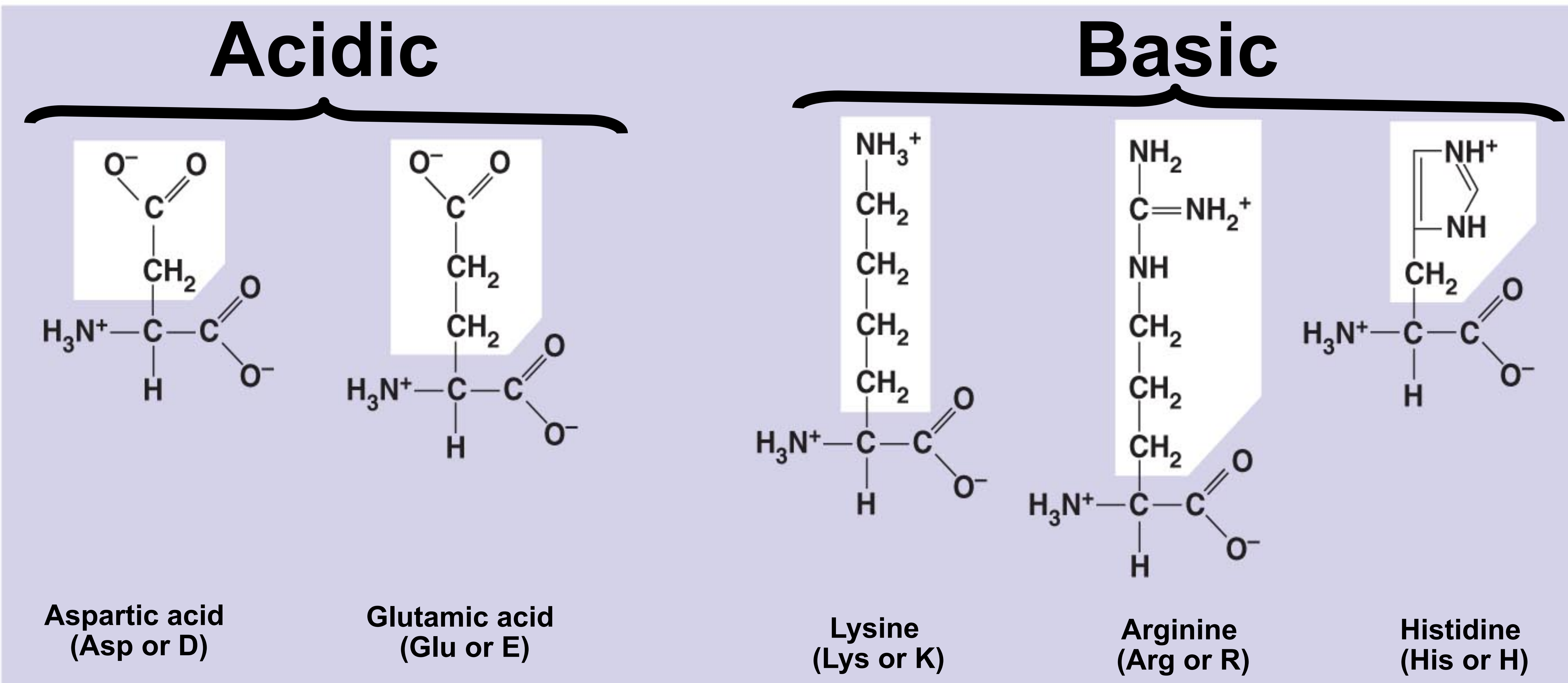
What is different about these side groups?

Ionized

Polar

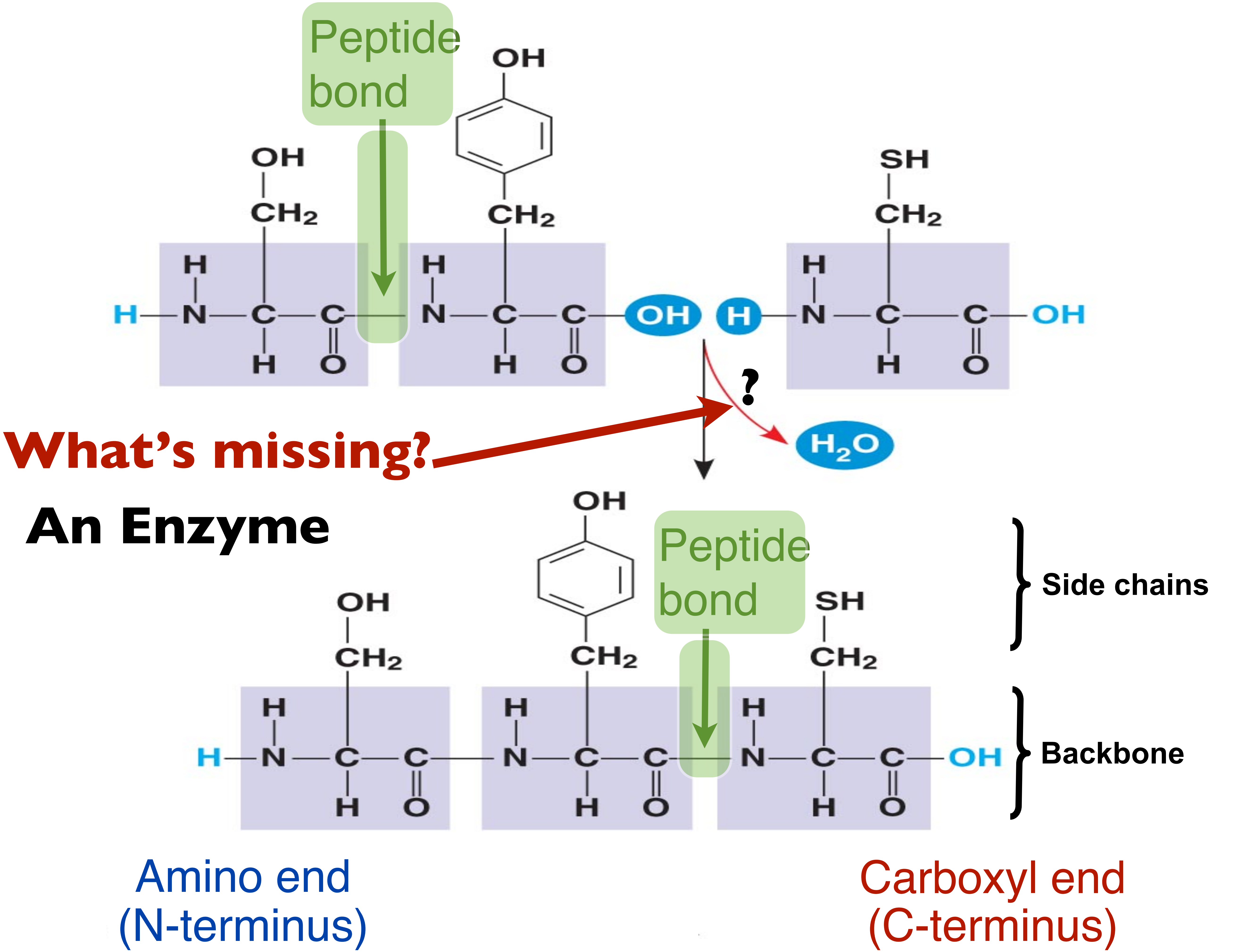

OH
CH2
H3N+ — C — C
O
O−
H
OH CH3
CH
SH
NH2 O
C
Serine
(Ser or S)
Threonine
(Thr or T)
Cysteine
(Cys or C)
Tyrosine
(Tyr or Y)
Asparagine
(Asn or N)
Glutamine
(Gln or Q)

Electrically charged

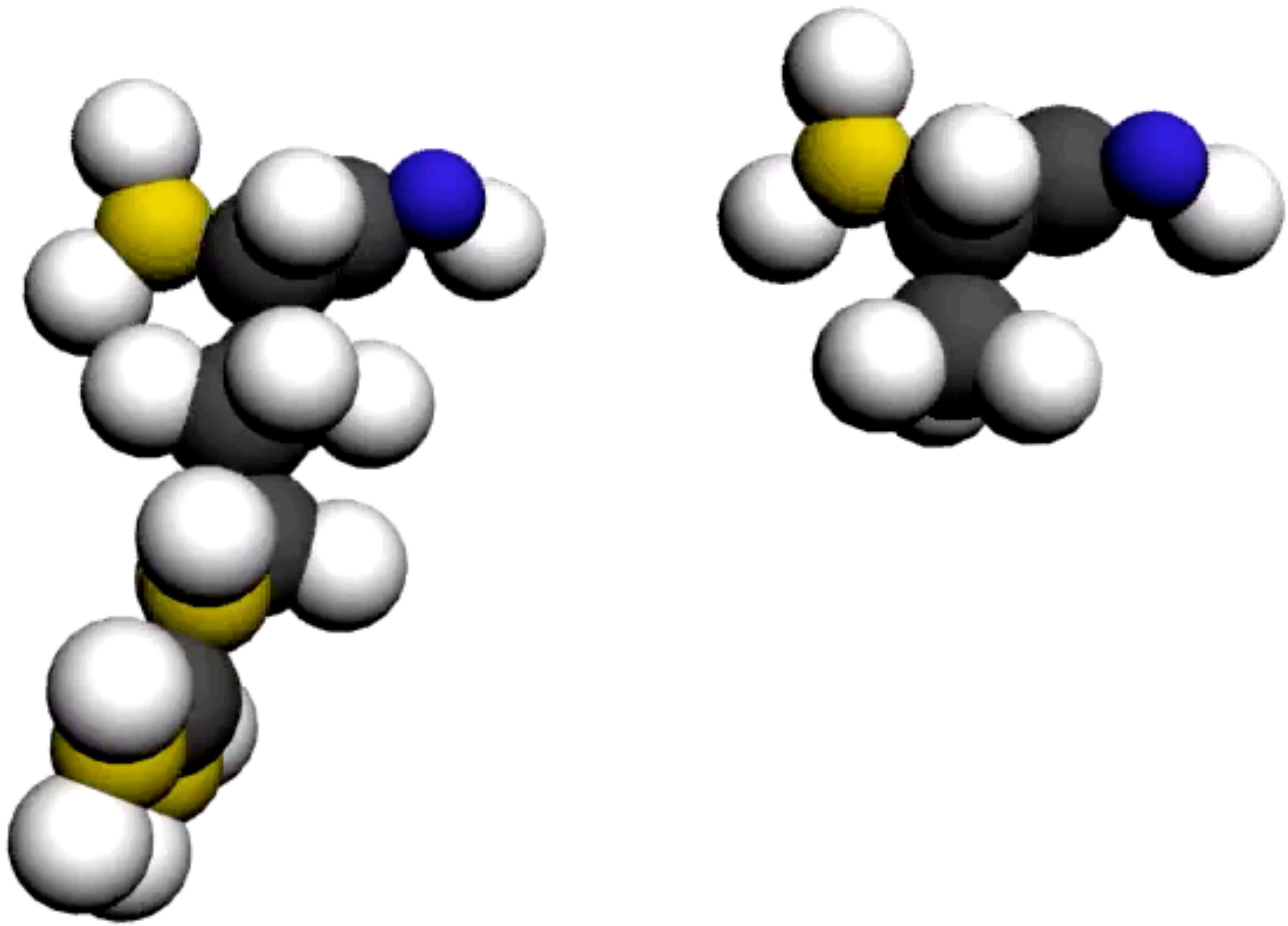


2. Amino Acid polymers

- **The amino acids are joined by dehydration synthesis reactions.**
  - **The resulting bond is a *peptide bond*.**
- **This process repeated over and over yields a polypeptide.**
  - **Polypeptide chains range in length from 3 amino acids to 1000's of amino acids**
- **Each protein is unique due to the types of amino acids, the number of amino acids and their order.**

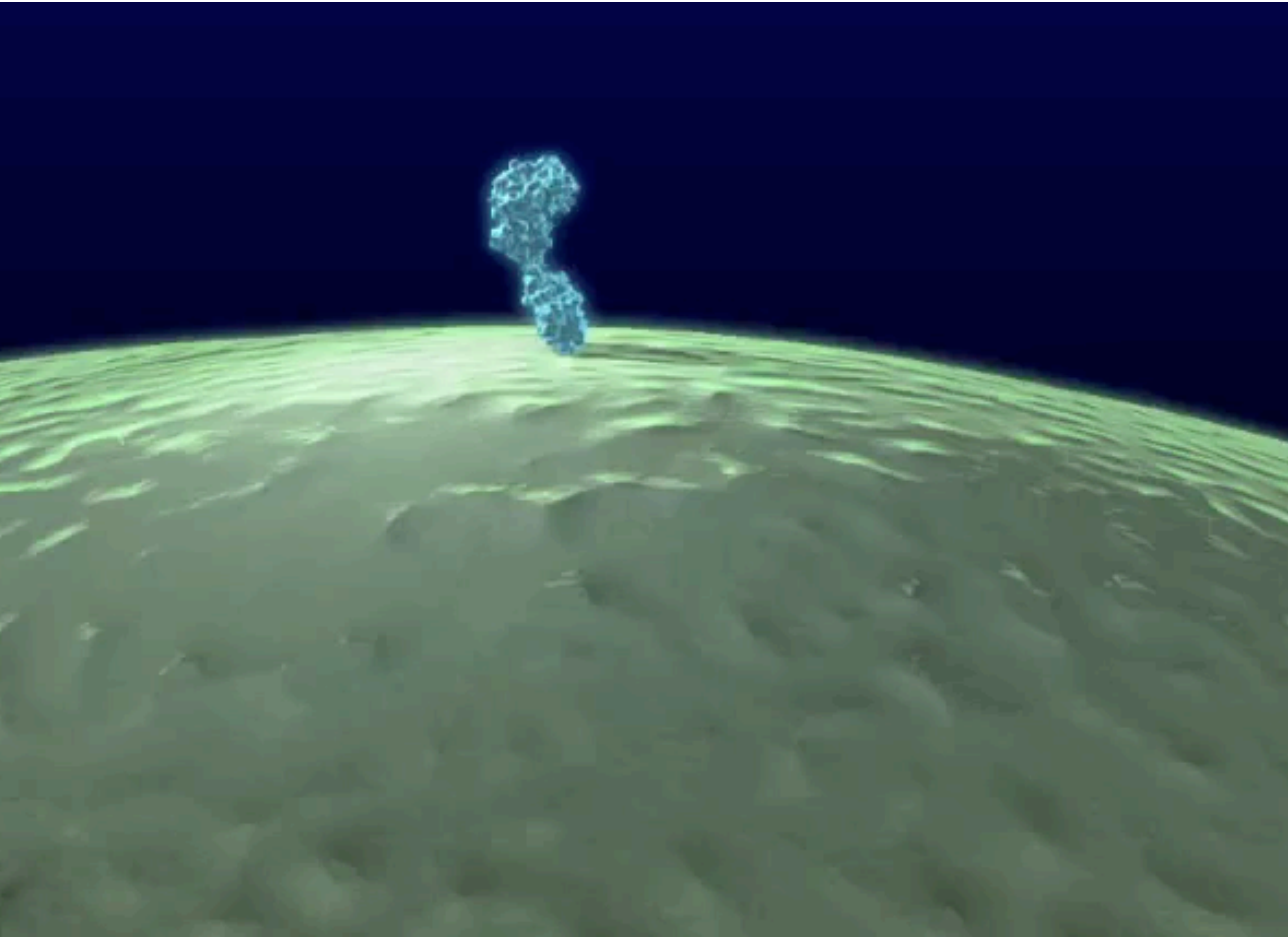

Peptide bond
OH
OH
CH2
CH2
SH
CH2
H
H
H
H
N
C
C
N
C
C
OH
H
N
C
C
OH
H
O
H
O
H
O
?
What's missing?
H2O
An Enzyme
OH
Peptide bond
OH
SH
CH2
CH2
CH2
Side chains
Backbone
Amino end (N-terminus)
Carboxyl end (C-terminus)

Formation of a Peptide Bond



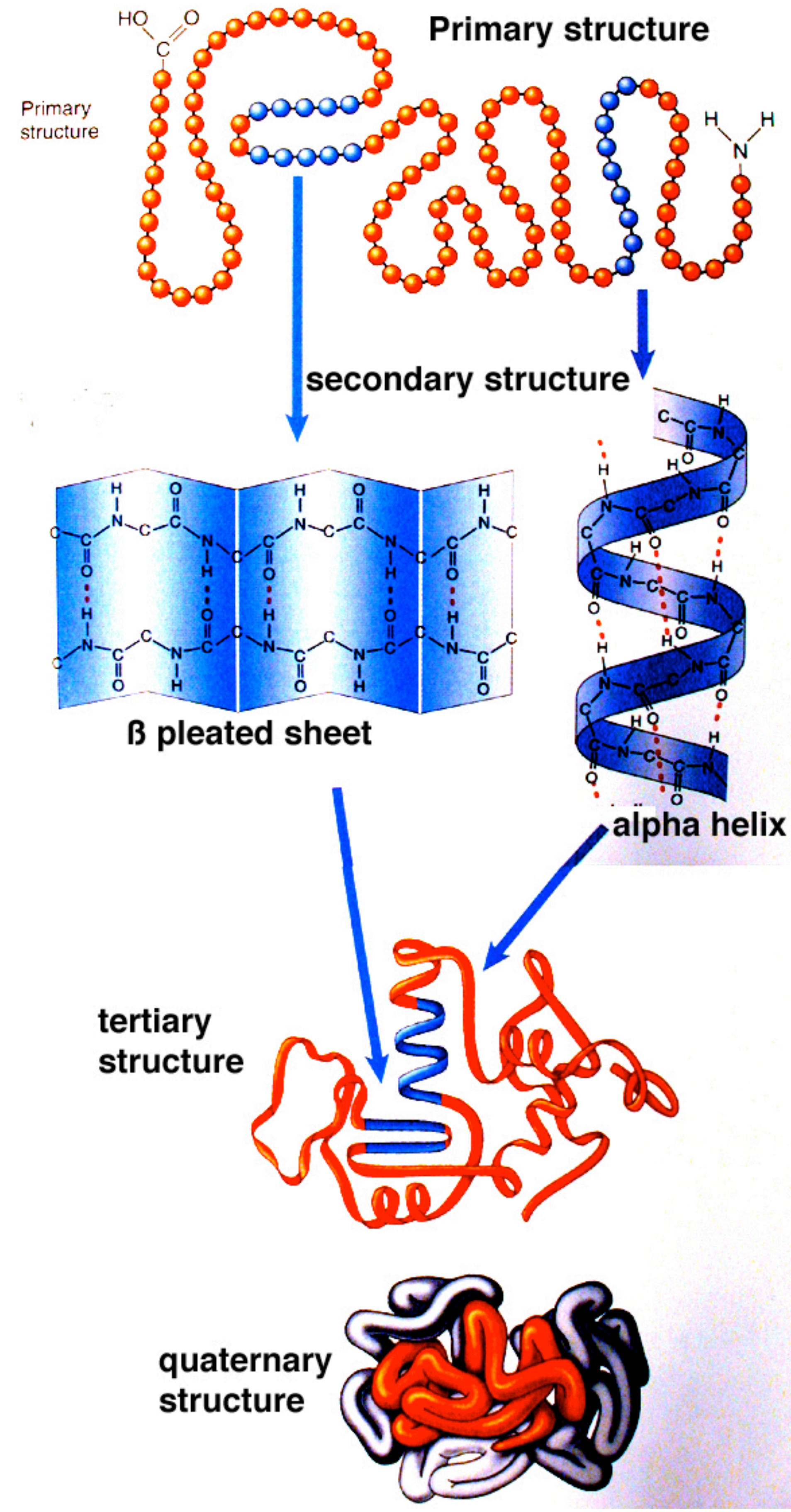
B. Protein Structure and Function

- **Functions of proteins depend on their architecture.**
  - **This architecture is dependent upon the amino acid sequence.**
- **Proteins are more than just a polypeptide chain, proteins must be <u>twisted</u>, <u>folded</u> and <u>coiled</u> into a specific shape.**
- **The twisting, folding and coiling is <u>held in place</u> by a variety of <u>bonds</u> between the groups on the amino acids.**
- **Proteins generally take one of two shapes:**
  - **Round... *globular proteins***
  - **Linear... *fibrous proteins***
- **In almost every case the function of a protein depends on its ability to recognize and bind with some other molecule.**



1. Four Levels of Protein Structure

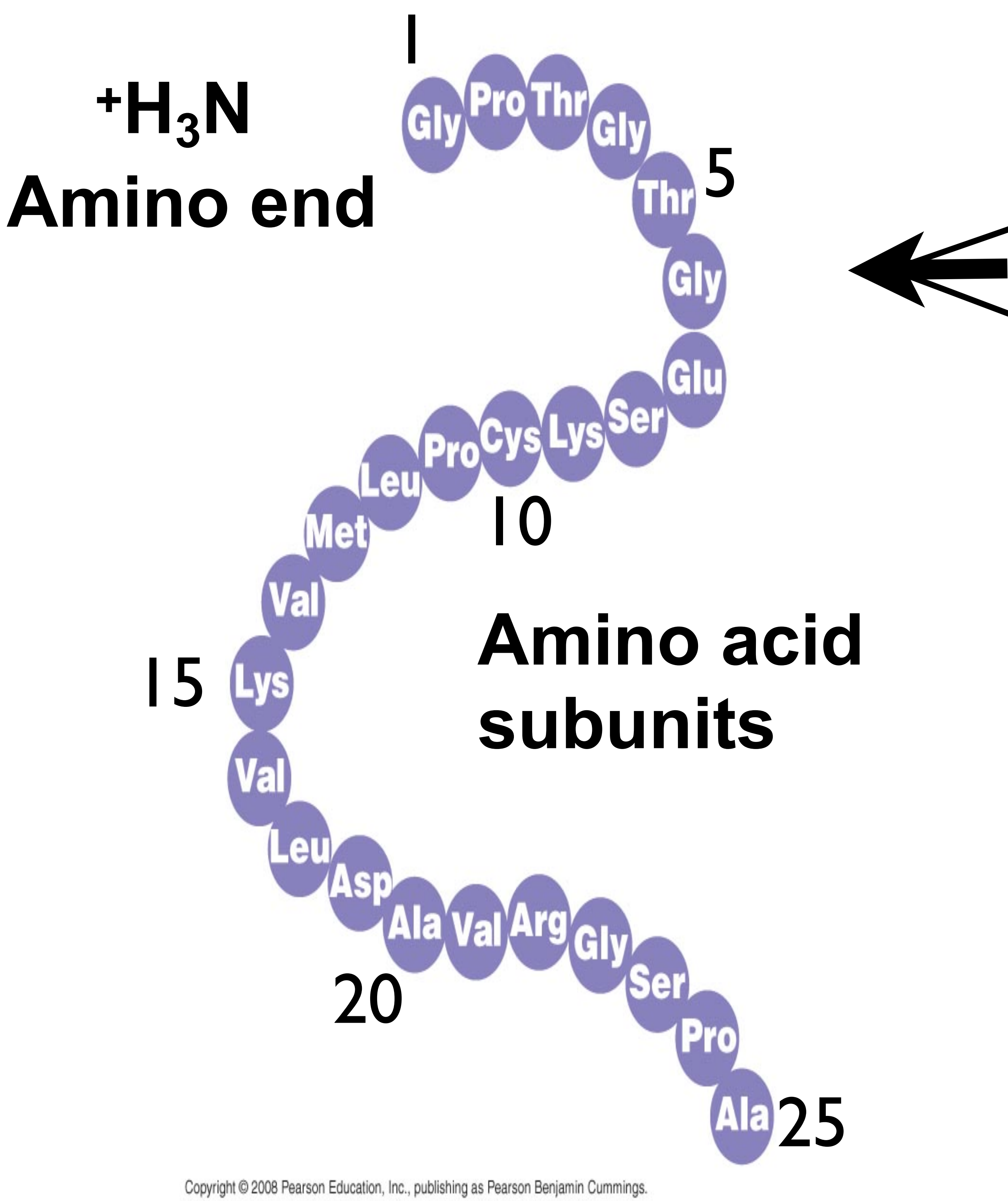
- With a goal to understand a proteins function its productive to begin by dissecting its structure.
- All proteins have levels of structure: *primary, secondary* and *tertiary*. Some have proteins have a fourth level, *quaternary*.

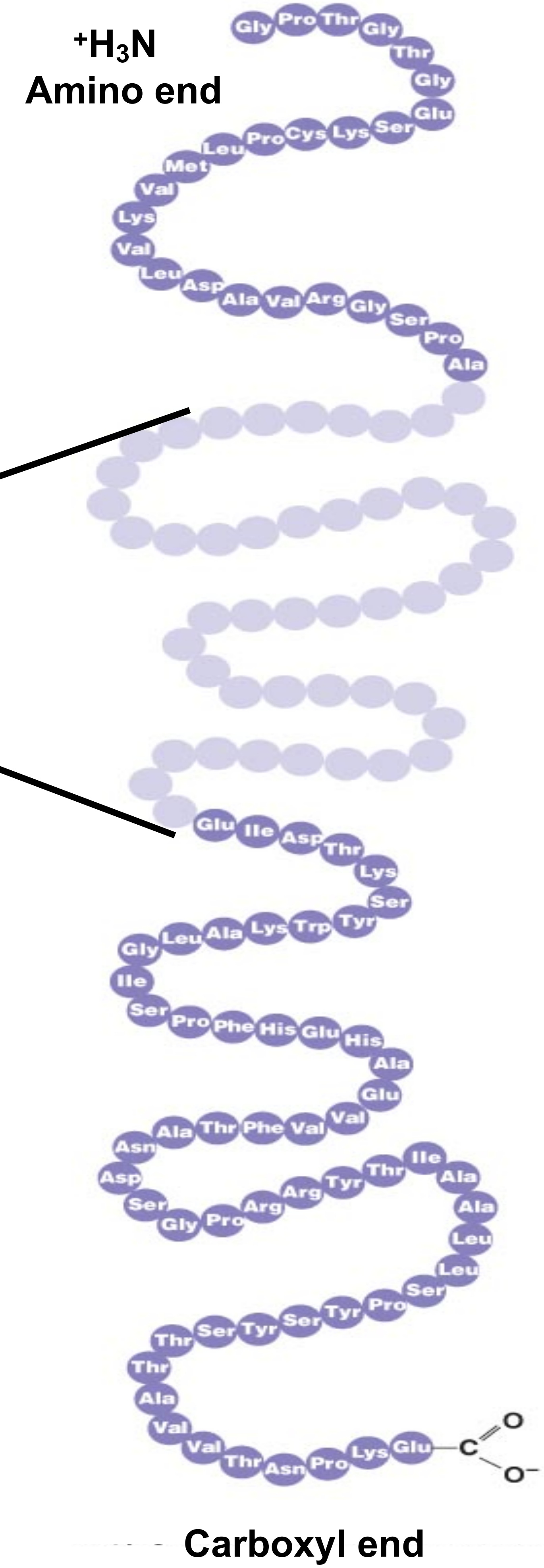


[redacted]

Primary Structure

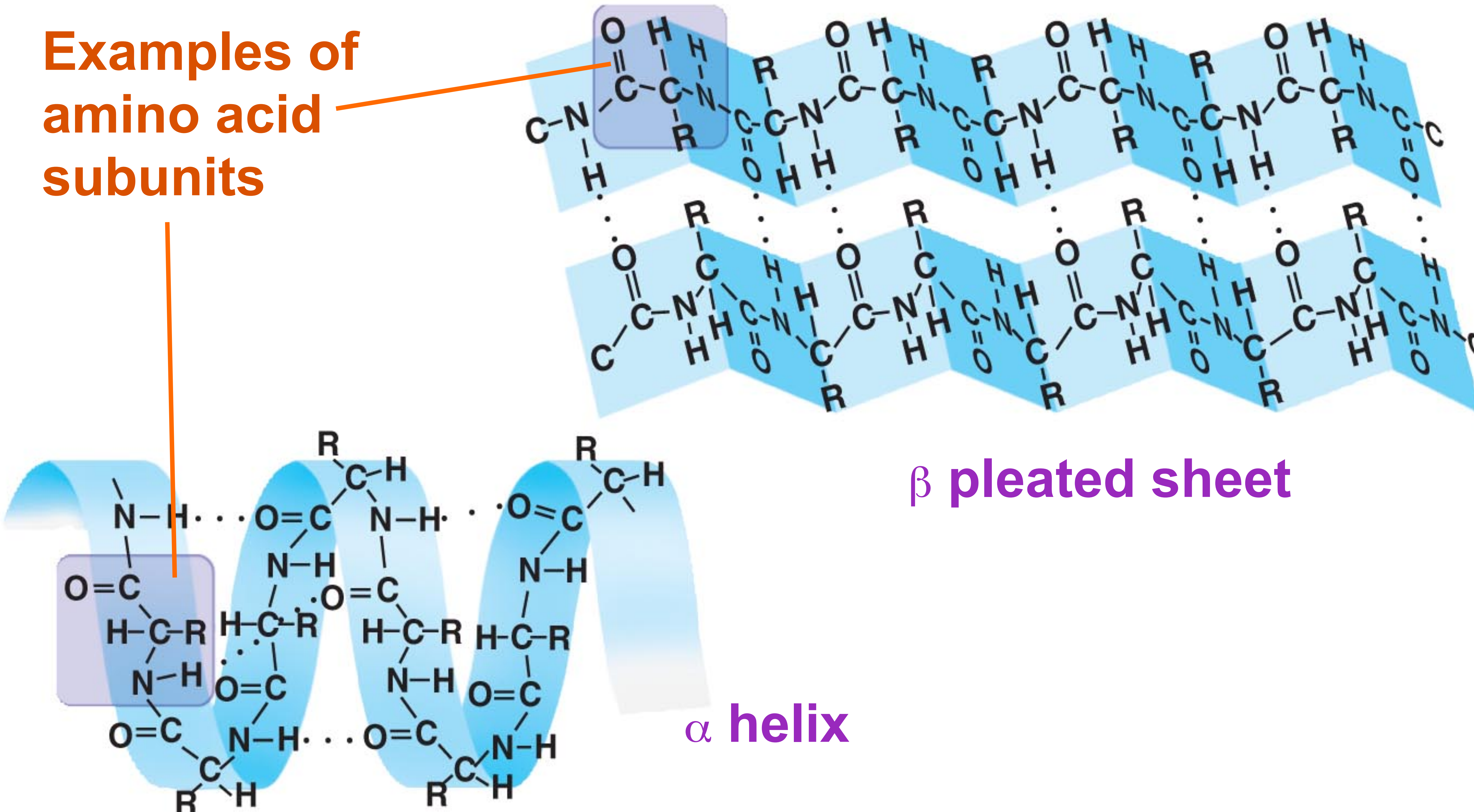
Linear Chain of Amino Acids





Secondary Structure

Regions stabilized by hydrogen bonds between polypeptide chains



DISCUSSION

Physical properties

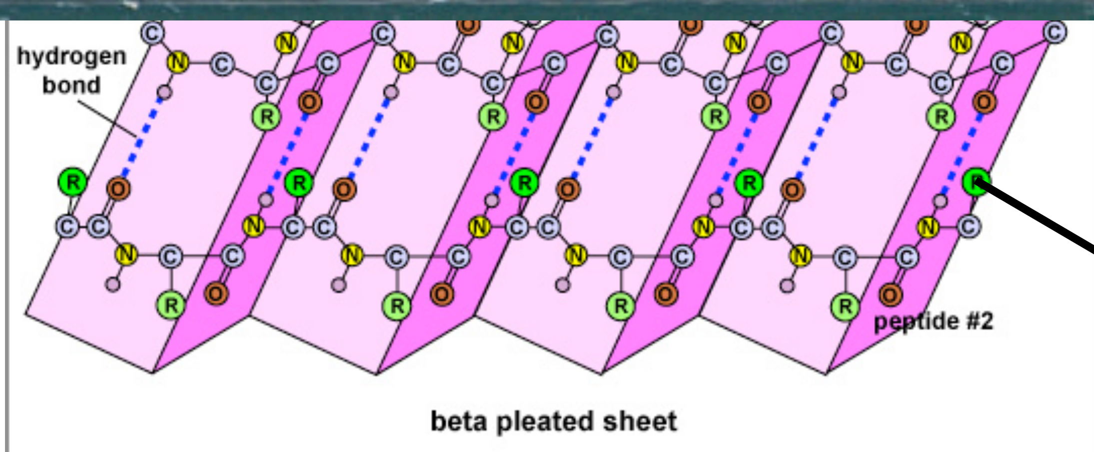
On the basis of information existing in the literature an hypothesis may be formulated concerning the molecular structure responsible for the physical properties of spider's silk. The molecular characteristics of frame silk appear to be typical of silks in general. The frame silk of *Araneus diadetnatus,* a close relative of *A. sericatus,* consists largely of small side-chain amino acids (Andersen, 1970; Lucas, 1964; Peakall, 1964, 1968) and is highly bi-refringent (Zemlin, 1968). X-ray diffraction analyses show this silk to be a partially crystalline substance (Lucas, 1964; Warwicker, i960). It appears likely, then, that the molecular configuration of frame silk is similar to that of *Bombyx mori* silk, the amino acids of the fibroin sequenced such that long segments of the poly- peptide chains consist solely of residues with small side groups packed into a /?-pleated sheet-crystalline formation, with the bulky side-chain amino acids confined to non- crystalline regions (Lucas, 1964).

The amino acid composition of the base strands of *A. diadematus* viscid silk does not differ substantially from that of frame silk (Andersen, 1970). No report is to be found of an X-ray diffraction analysis of viscid silk. It is noted, however, that viscid silk is only weakly, if at all, bi-refringent (personal observation), making it unlikely that this silk contains crystals of the size found in frame silk. The difference can be accounted for if a different amino acid sequence exists in viscid silk; if the bulky side-chain amino acids, rather than being grouped together, are scattered throughout the poly- peptide chains, the small side-group amino acids may be prevented from forming stable crystals.

Such a difference in crystallinity between frame and viscid silks may account for the primary difference in their physical properties, the greater extensibility of viscid silk. The vast majority of amino acid links in the polypeptide chains of viscid silk, rather than being bound up in highly oriented and inextensible crystals, would be free to participate in the extension of the material, a situation more typical of a rubber than a silk. The physical properties of frame silk will be dominated by the interaction of the crystalline and amorphous regions to yield a stiffer, less extensible material. However, since the strength of both silks will be limited by the strength of the non- crystalline portion of the polypeptide chains, their breaking stresses should be the same, and are.

Abdominal glands of the spider secrete silk fibers made of a structural protein containing b pleated sheets.

The radiating (base) strands, made of dry silk fibers, maintain the shape of the web.



Rigid

Flexible

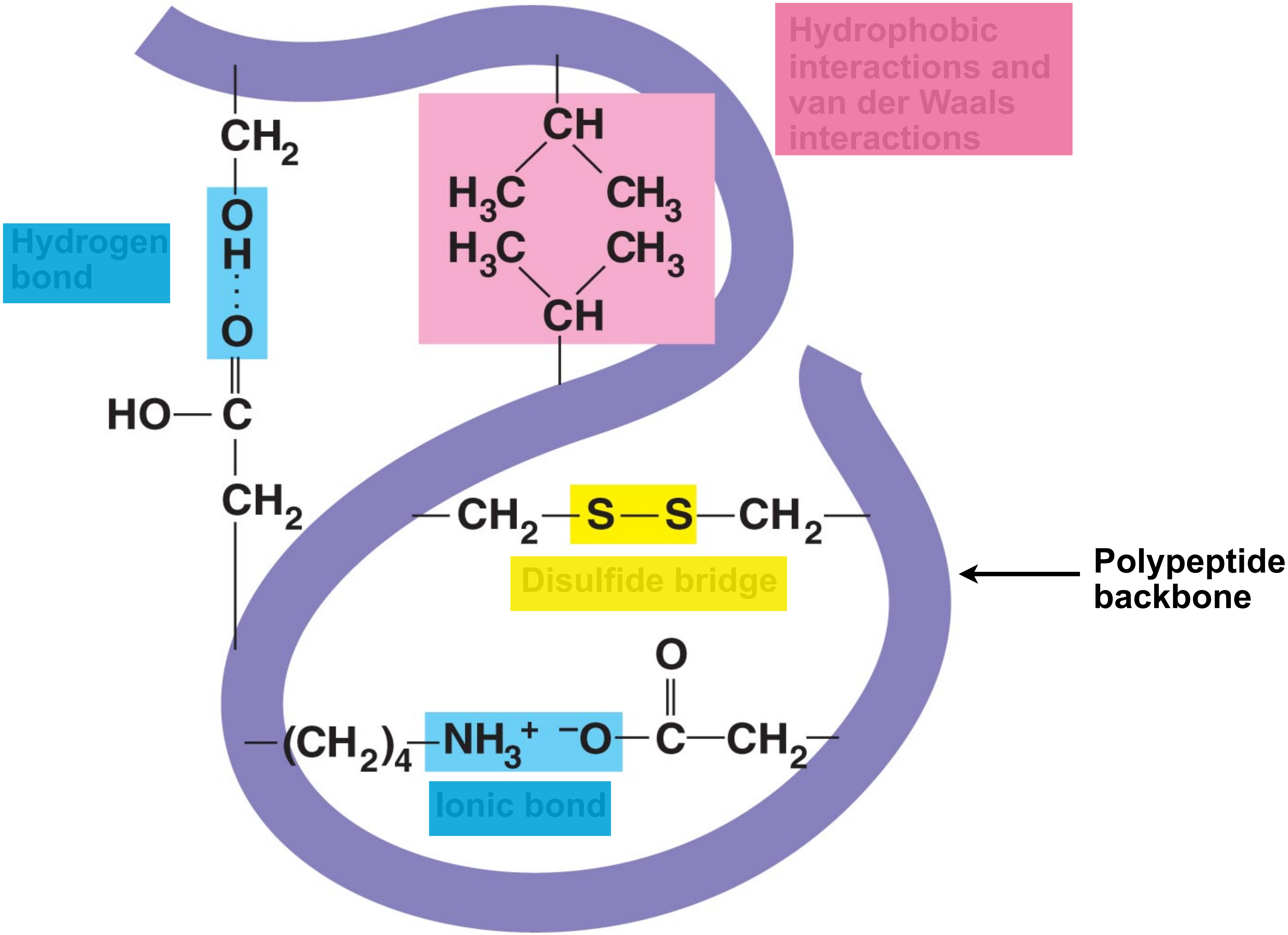
Large "R" groups help to capture crystals which in turn decrease the pleated sheets ability to expand

Small "R" groups cannot capture crystals which in turn allows the pleated sheets to expand and have flexibility

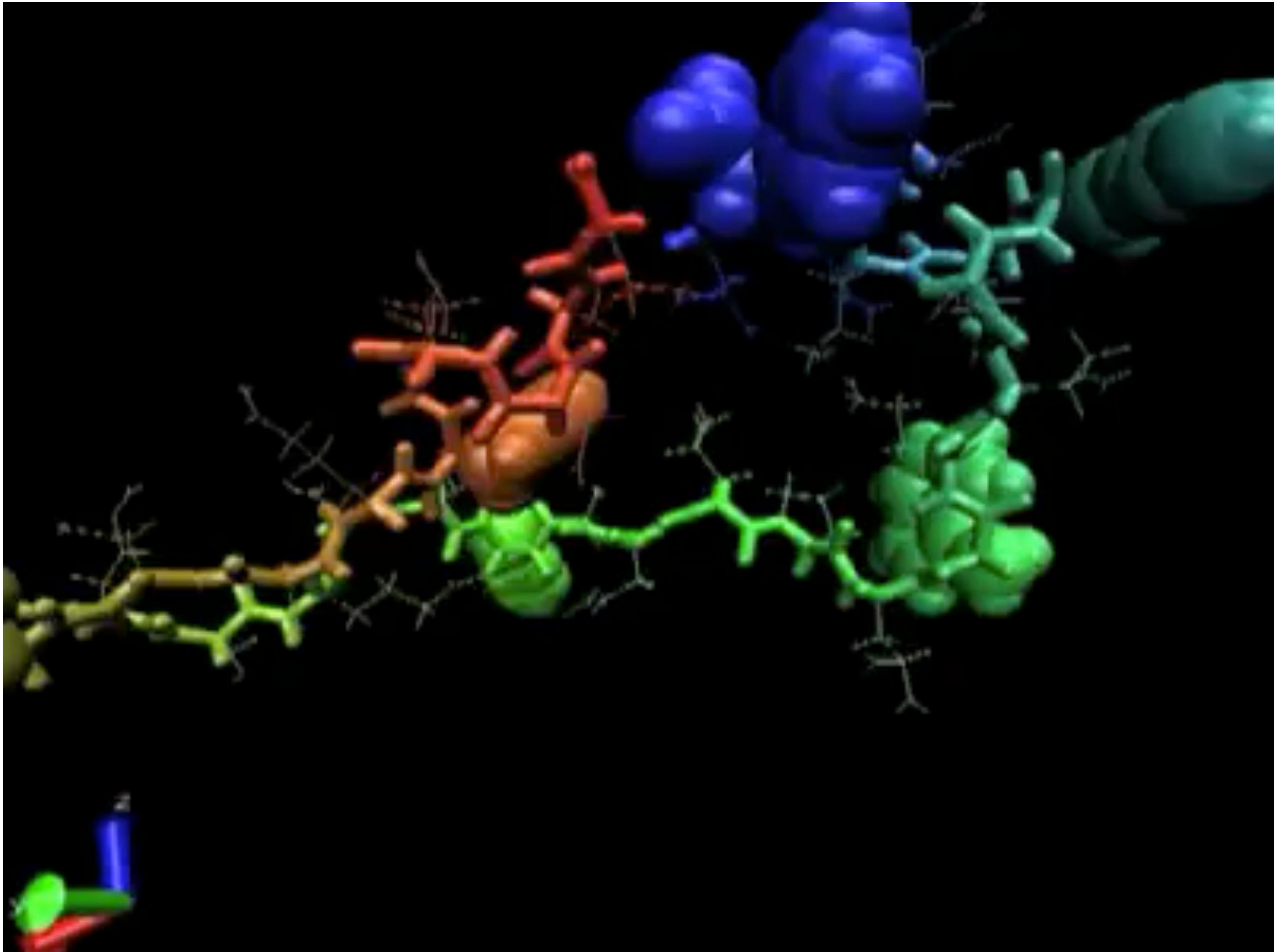
If these webs were 3 cm diameter, it could stop in 747 during flight.

Tertiary Structure

Overall 3-D Shape

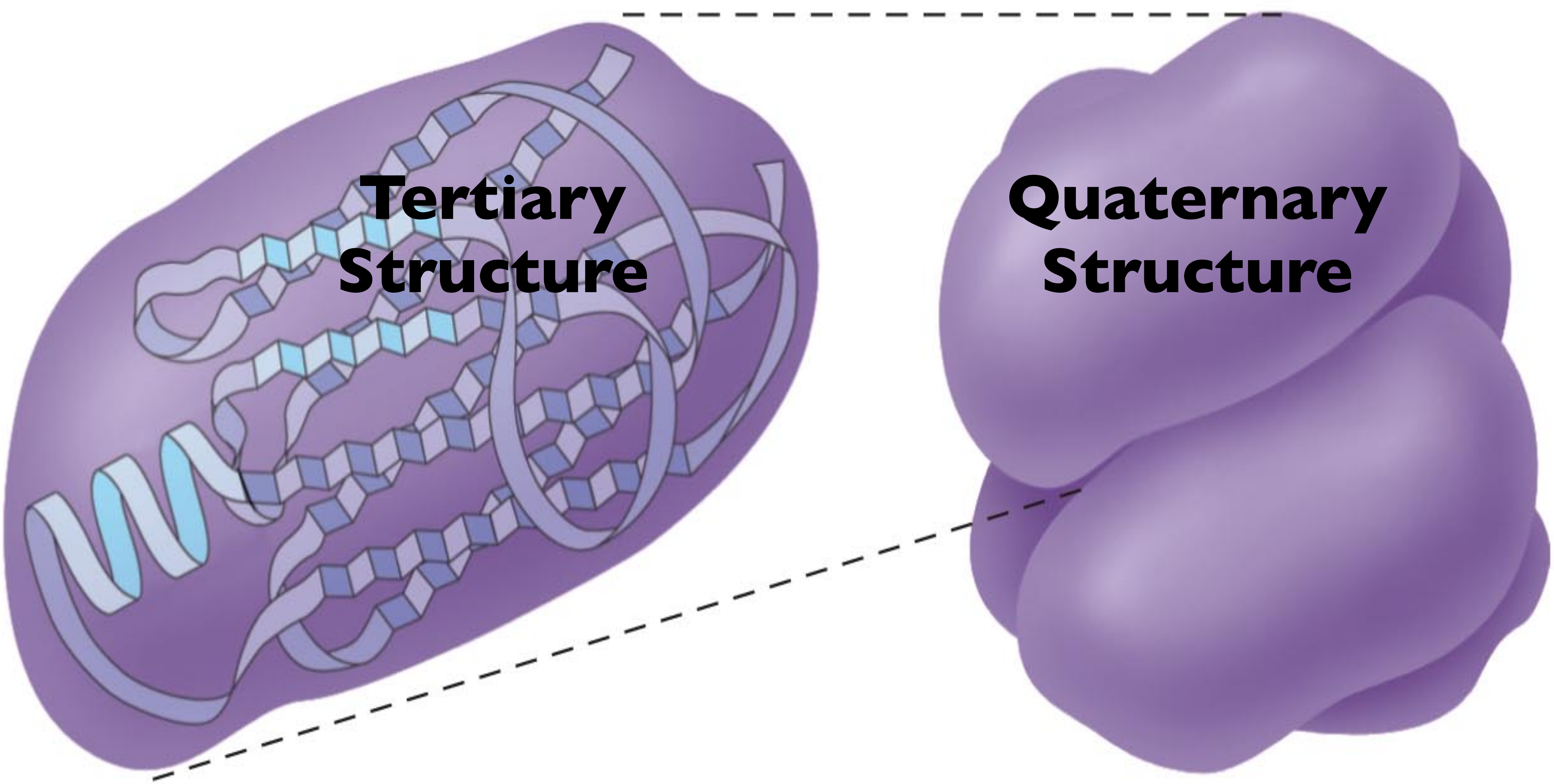


Another Look at Protein Folding



Tertiary Structure

Some tertiary proteins come together and form larger proteins



Quaternary Structure

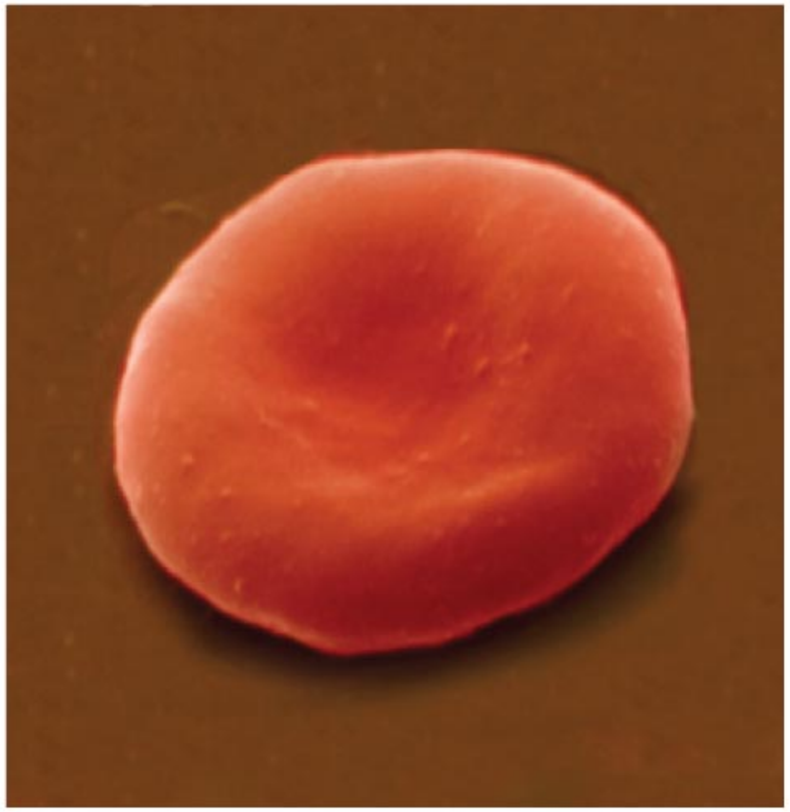
Association of multiple polypeptides forming a functional protein

Polypeptide chains

Collagen

In almost every case the function of a protein depends on its ability to recognize and bind with some other molecule.

2. Sickle Cell Disease: Change Primary Structure



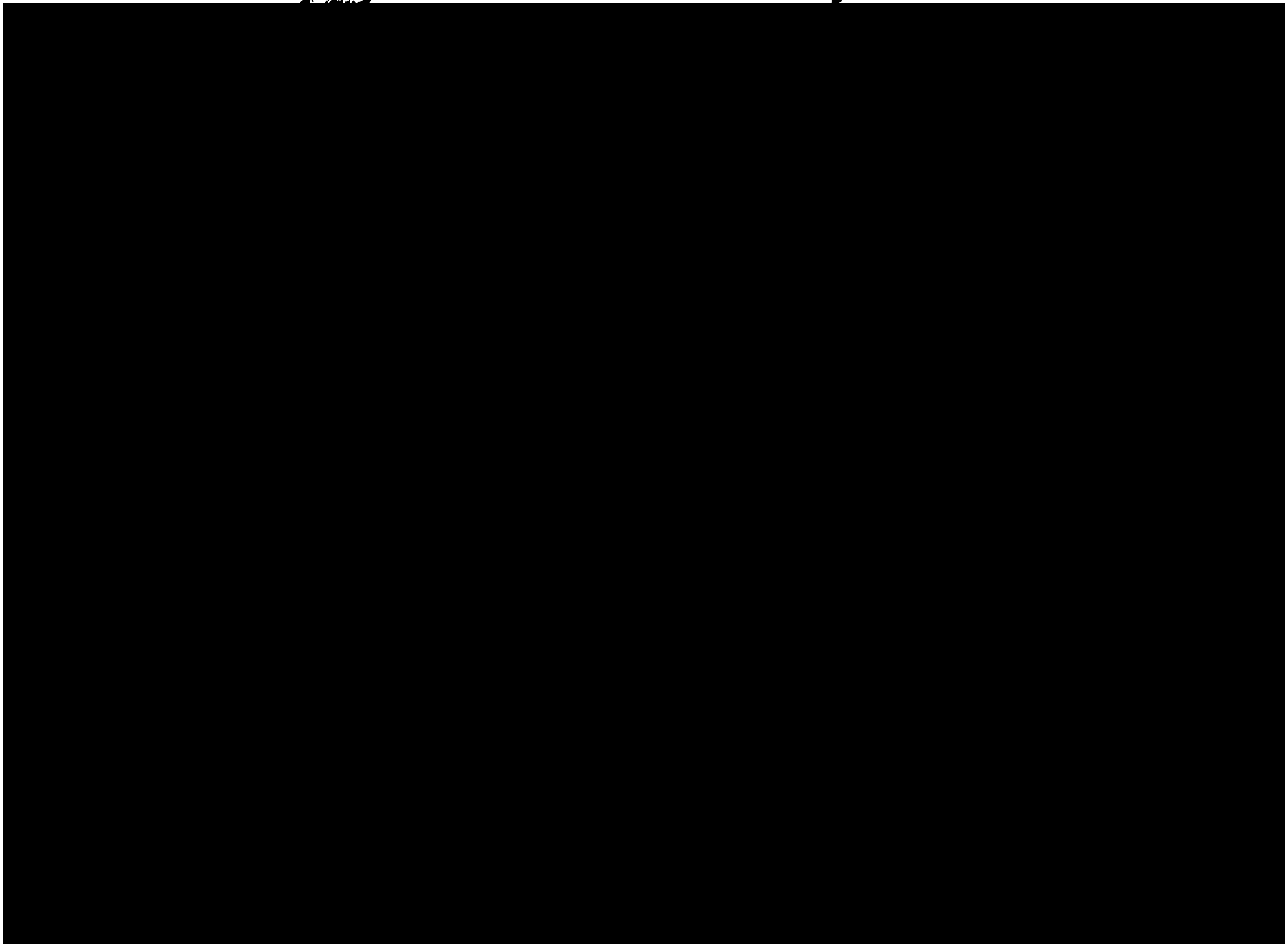
Normal red blood cells are full of individual hemoglobin molecules, each carrying oxygen.

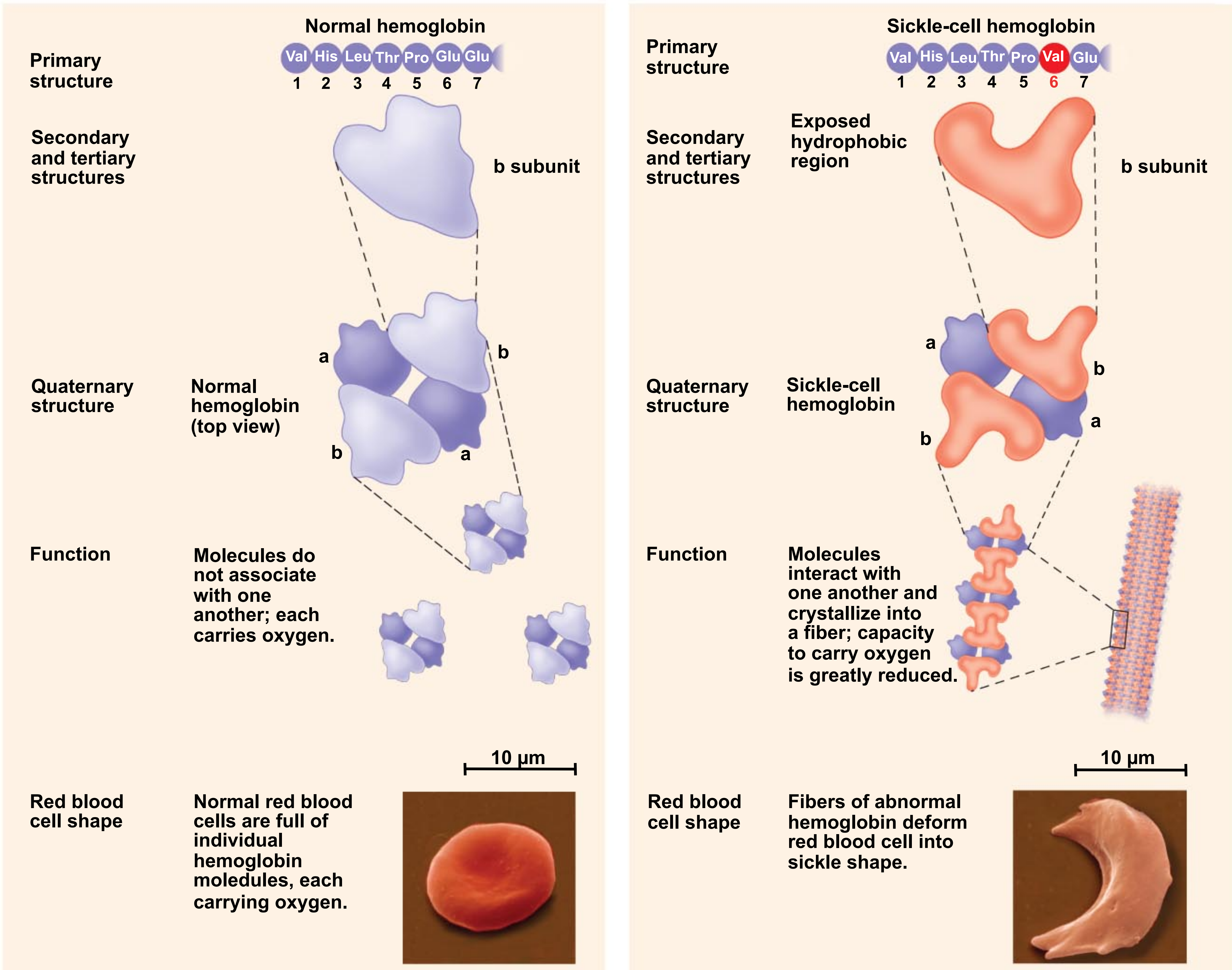
Fibers of abnormal hemoglobin deform red blood cell into sickle shape.

Haemoglobin - structure and function

Red blood cells are responsible for much of the gaseous exchange which occurs through the human respiratory system.

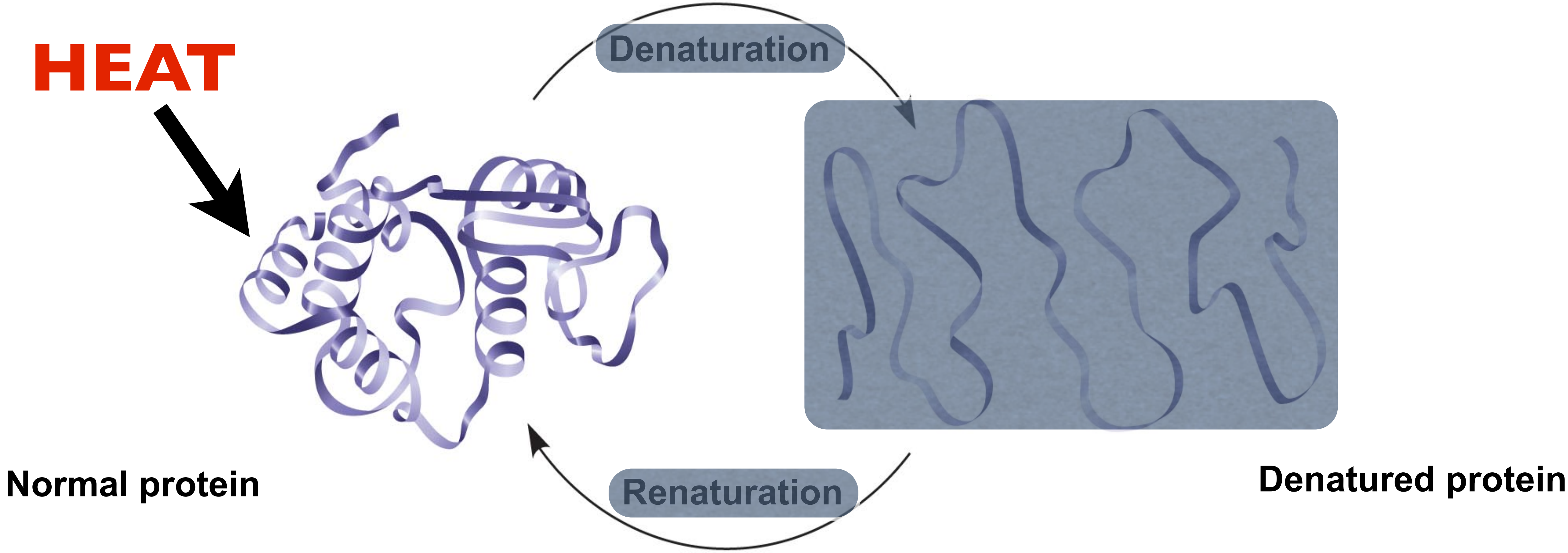
Oxygen Transport



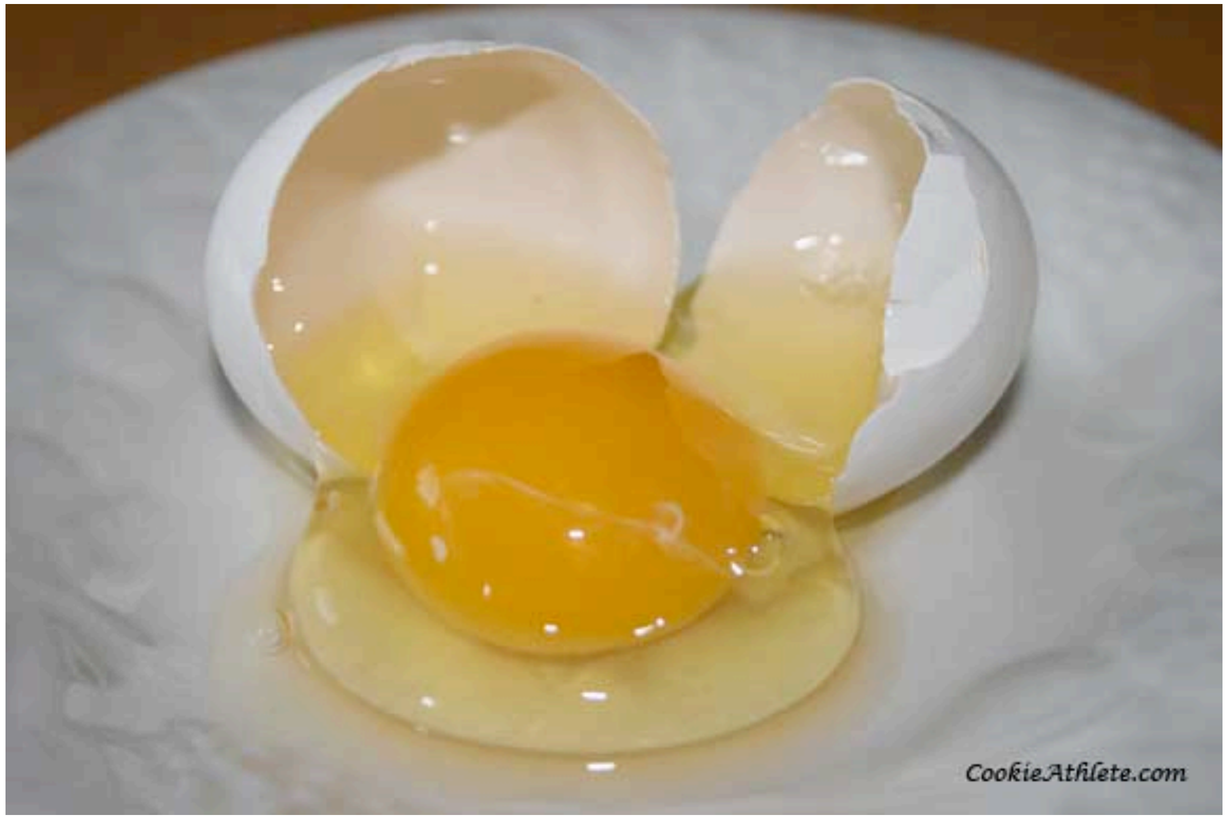

Normal hemoglobin
Primary structure
Val His Leu Thr Pro Glu Glu
1 2 3 4 5 6 7
Secondary and tertiary structures
b subunit
Quaternary structure
Normal hemoglobin (top view)
a
b
b
a
Function
Molecules do not associate with one another; each carries oxygen.
10 µm
Red blood cell shape
Normal red blood cells are full of individual hemoglobin moledules, each carrying oxygen.
Sickle-cell hemoglobin
Primary structure
Val His Leu Thr Pro Val Glu
1 2 3 4 5 6 7
Secondary and tertiary structures
Exposed hydrophobic region
b subunit
Quaternary structure
Sickle-cell hemoglobin
a
b
a
b
Function
Molecules interact with one another and crystallize into a fiber; capacity to carry oxygen is greatly reduced.
10 µm
Red blood cell shape
Fibers of abnormal hemoglobin deform red blood cell into sickle shape.

3. What Determines Protein Structure?

- The blueprints for proteins are found in DNA.
  - Protein synthesis involves both DNA and is aided by other proteins.
- Aside from this above, the physical and chemical environment can also effect a proteins structure.
- An alteration in any of the following conditions can result in an alteration of protein structure, they include...
  - pH, salt concentration, temperature and others

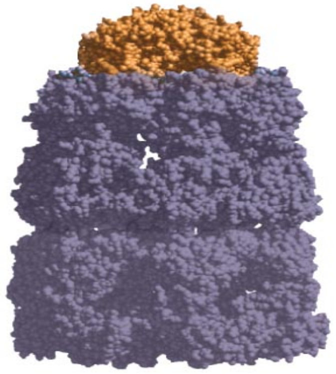


Not all proteins will renature after they have denatured



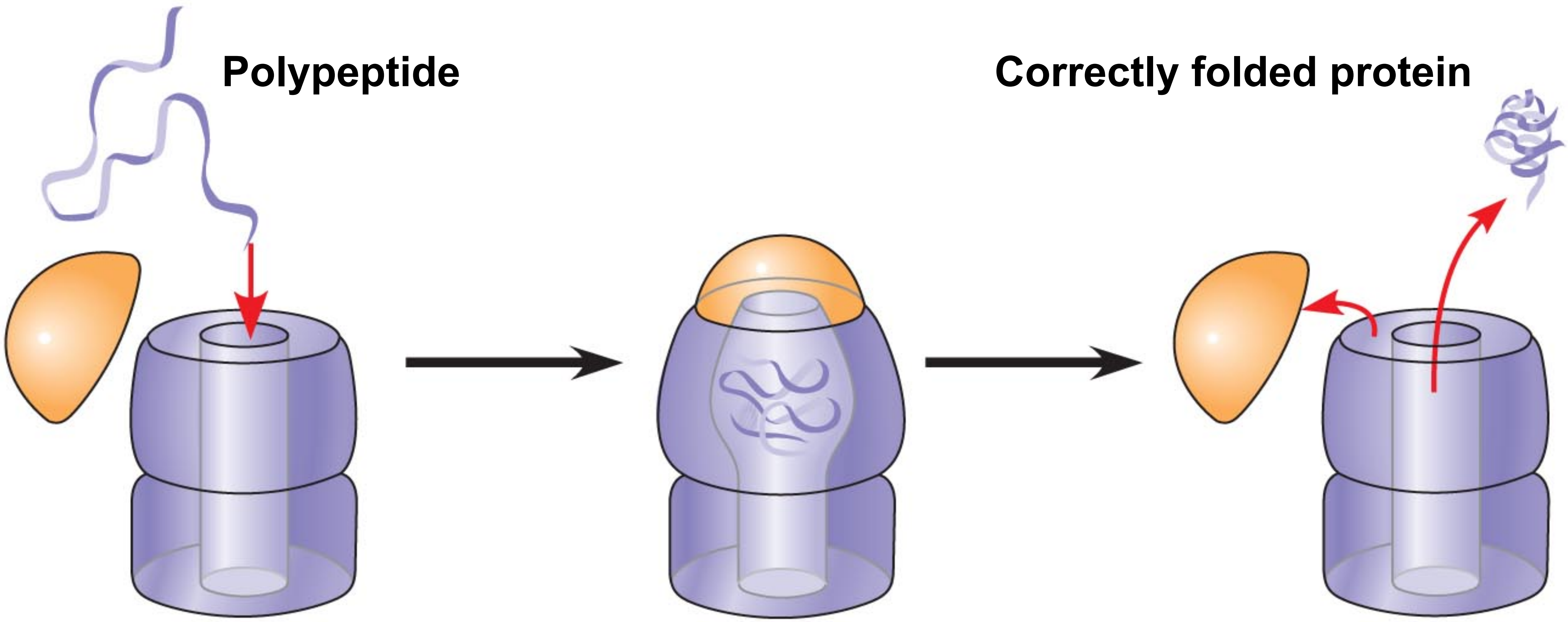
4. Protein Folding in the Cell

- **Biochemists have the primary structure of more than 10 million proteins and the 3-D structure of more than 20,000.**
- **Finding a correlation between the amino acid sequence and overall shape is not easy.**
- **Biochemists have identified *chaperone proteins*, they assist other proteins in their proper folding**
  - **These giant hollow protein complexes provide a favorable environment for other proteins to fold properly.**



- **Proper folding is important, many diseases result from misfolded proteins. (Alzheimer's, Parkinson's, mad cow)**

Steps of Chaperonin Action:



An unfolded poly-peptide enters the cylinder from one end.

The cap attaches, causing the cylinder to change shape in such a way that it creates a hydrophilic environment for the folding of the polypeptide.

The cap comes off, and the properly folded protein is released.

Functions of Proteins

Table 5.1 An Overview of Protein Functions

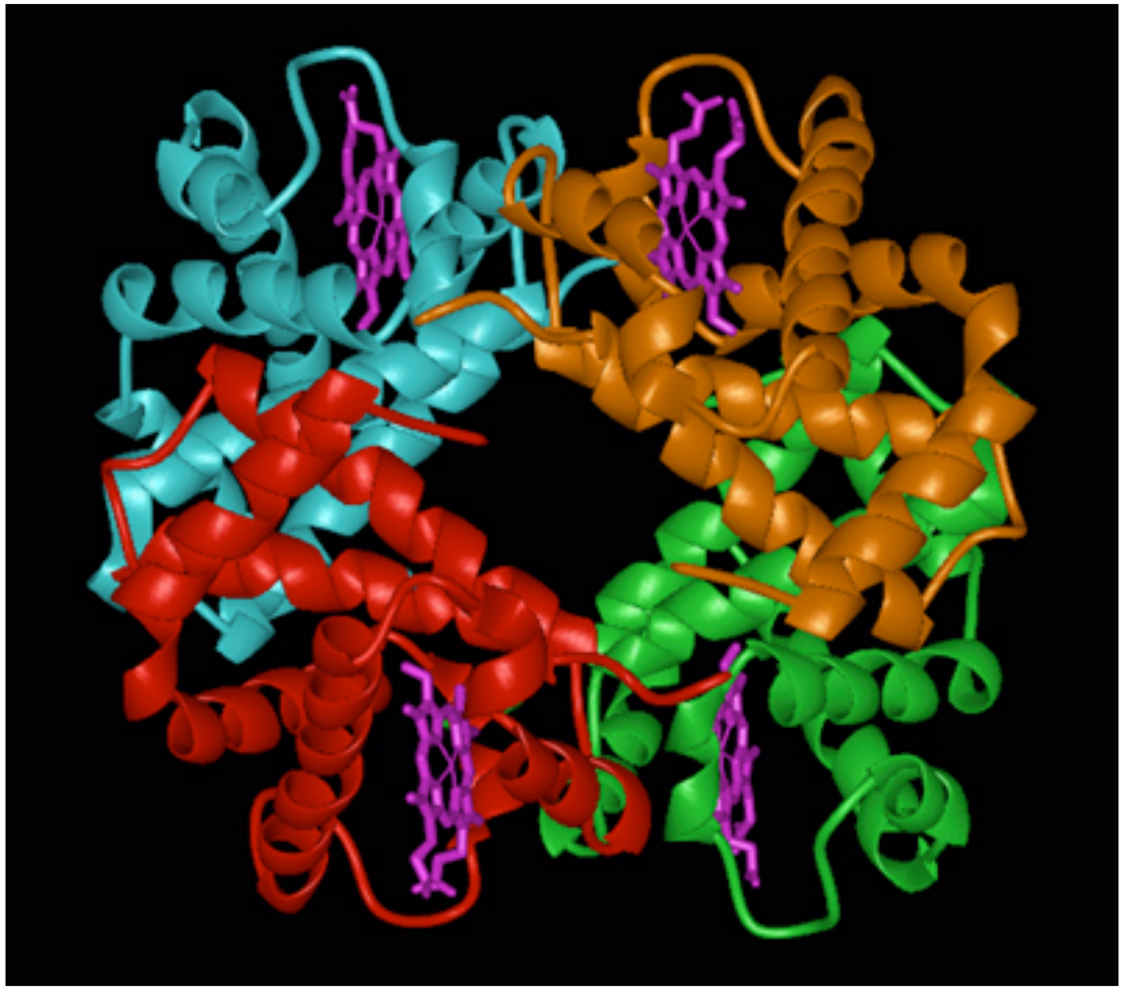
Type of Protein	Function	Examples
Enzymatic proteins	Selective acceleration of chemical reactions	Digestive enzymes
Structural proteins	Support	Silk fibers; collagen and elastin in animal connective tissues; keratin in hair, horns, feathers, and other skin appendages
Storage proteins	Storage of amino acids	Ovalbumin in egg white; casein, the protein of milk; storage proteins in plant seeds
Transport proteins	Transport of other substances	Hemoglobin, transport proteins
Hormonal proteins	Coordination of an organism's activities	Insulin, a hormone secreted by the pancreas
Receptor proteins	Response of cell to chemical stimuli	Receptors in nerve cell membranes
Contractile and motor proteins	Movement	Actin and myosin in muscles, proteins in cilia and flagella
Defensive proteins	Protection against disease	Antibodies combat bacteria and viruses.

(5) Biochemistry

V.

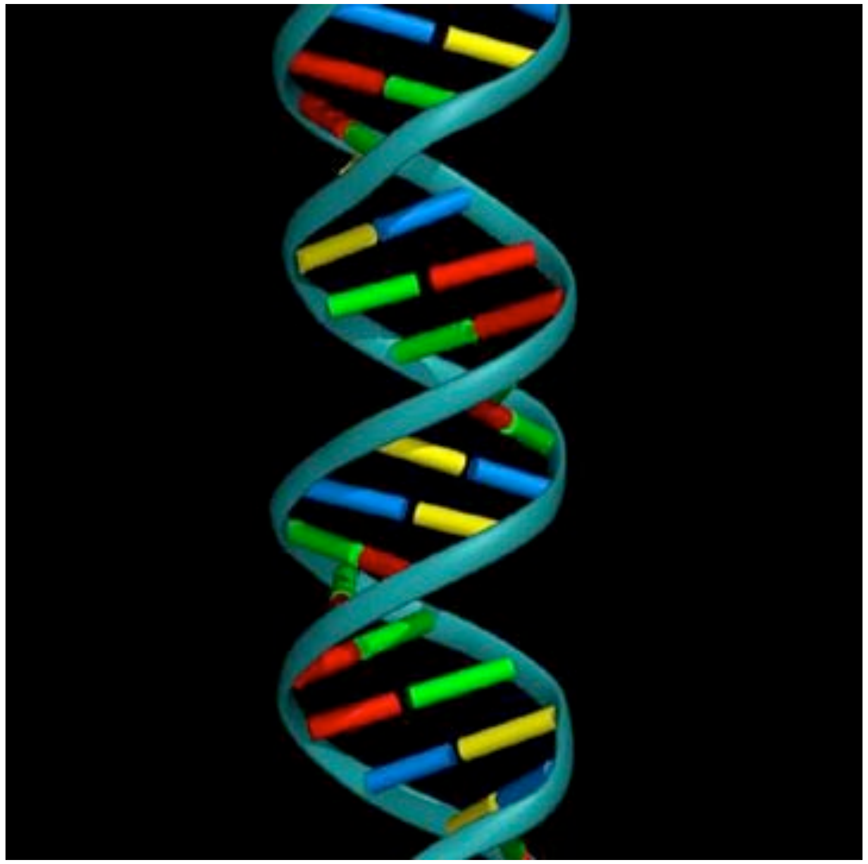
Main Idea: Nucleic acid polymers are built from monomers called nucleotides.

Main Idea: Nucleic acid polymers contain the information to build the primary structure of proteins.

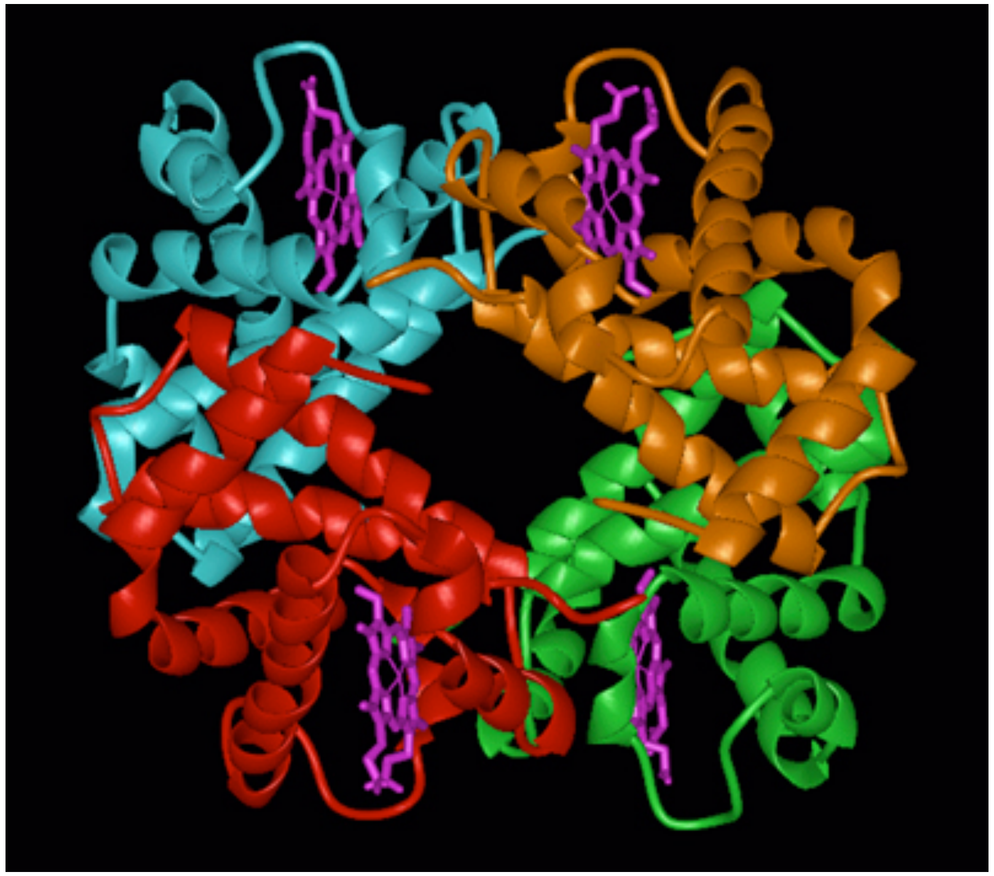


NUCLEIC ACIDS STORE, TRANSMIT, AND HELP EXPRESS HEREDITARY INFORMATION

- Nucleic acids contain genes.
- Genes contain the information to build proteins.



→



A. The Roles of Nucleic Acids

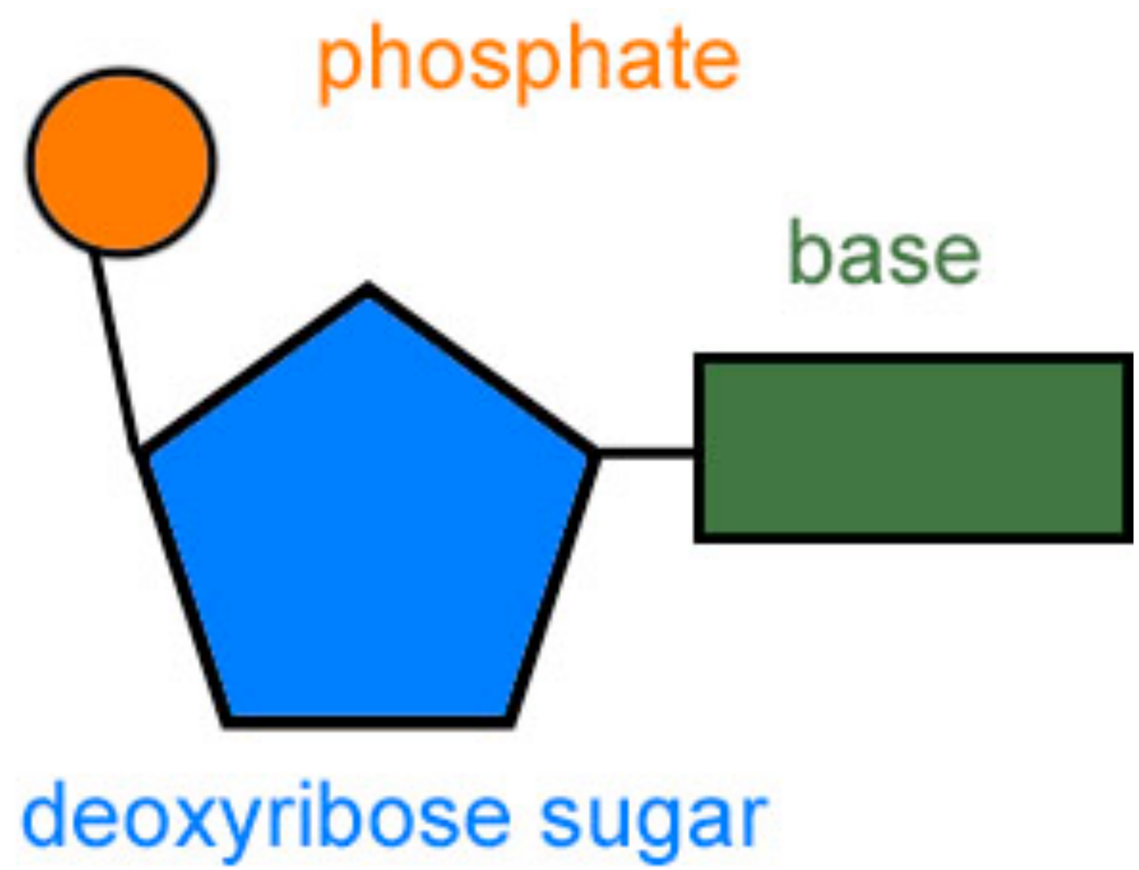
- DNA and RNA allow organisms to produce their complex components from one generation to the next.
  - DNA is material that we inherit from our parents.
  - DNA contains the blueprint for cell structures and the information for cellular activities.
- Think of DNA as the computer's software and PROTEINS as the hardware.

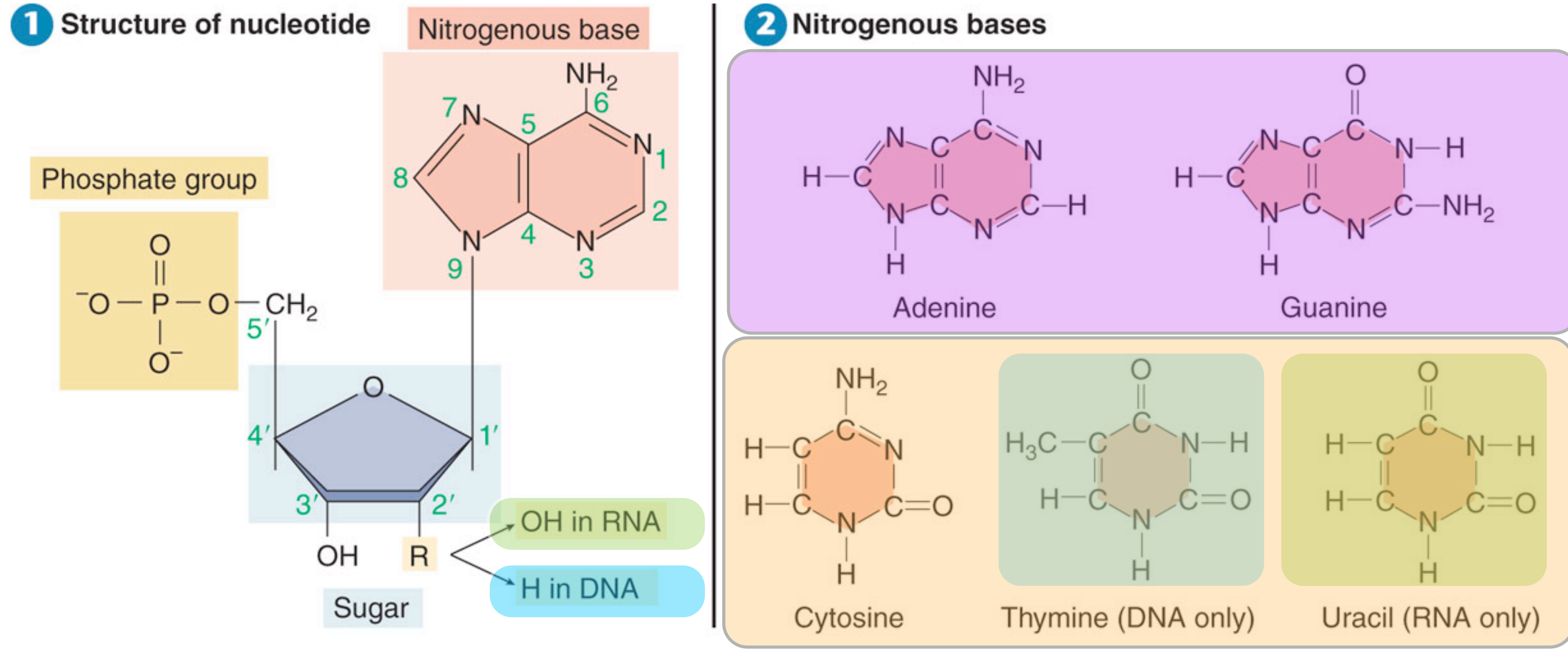
<u>The Global Flow of Information...</u>

DNA → **RNA** → **PROTEINS**

B. The Components of Nucleic Acids

- Nucleic acids are true polymers.
- <u>Polynucleotides</u> (polymers) are made from <u>nucleotides</u> (monomers)



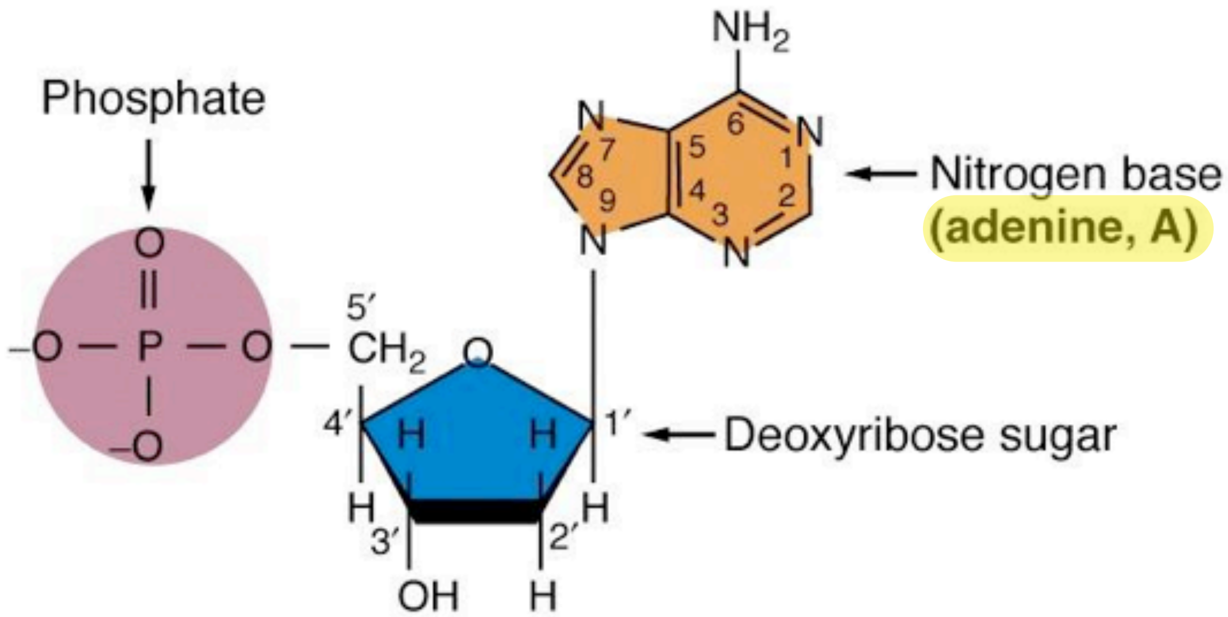


Counter Intuitive Mnemonic

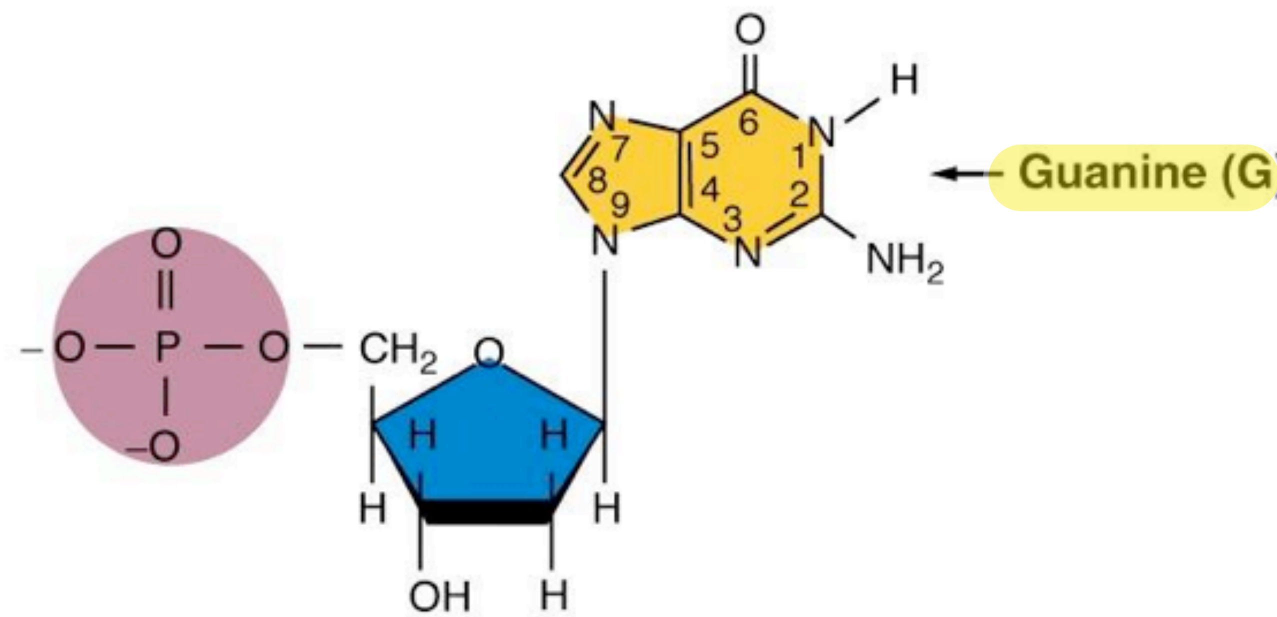
Purine (small word) BIG MOLECULE

PYRIMIDINE (BIG WORD) small molecule

Purine nucleotides

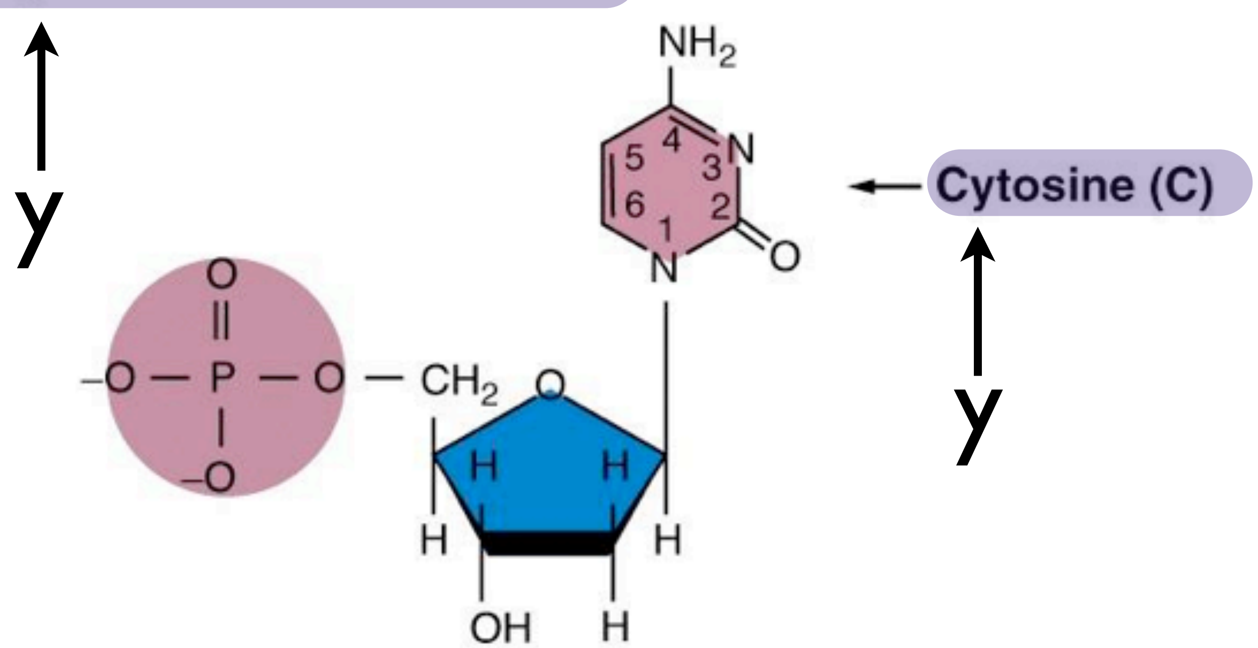


Deoxyadenosine 5′-phosphate (dAMP)

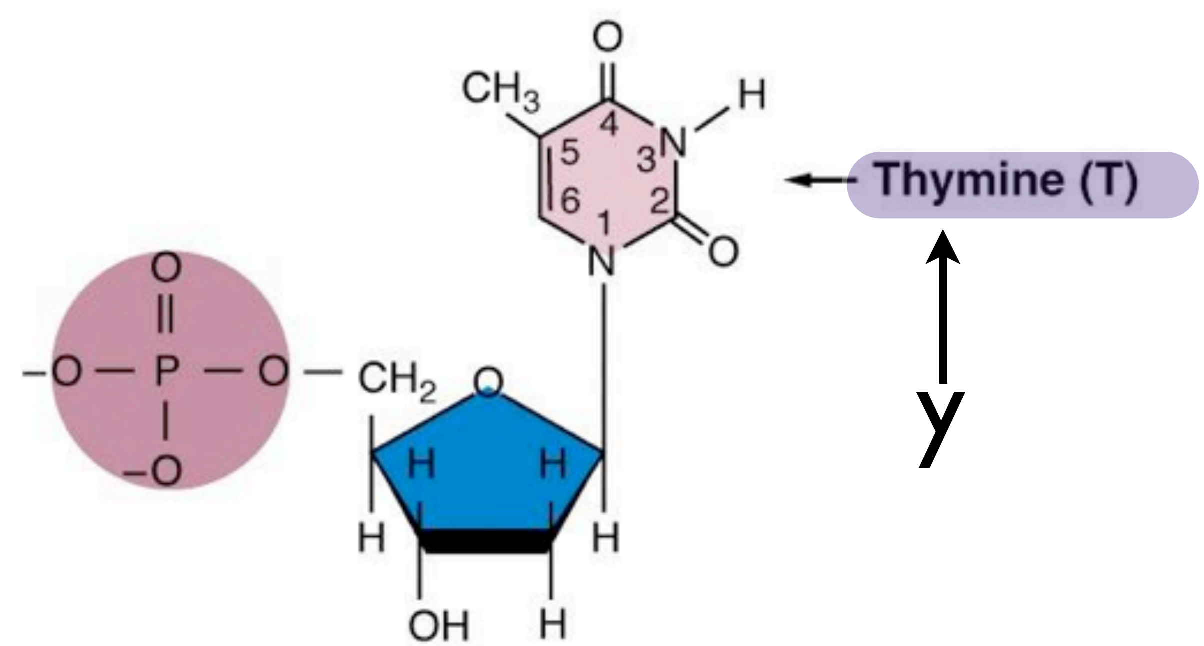


Deoxyguanosine 5′-phosphate (dGMP)

Pyrimidine nucleotides



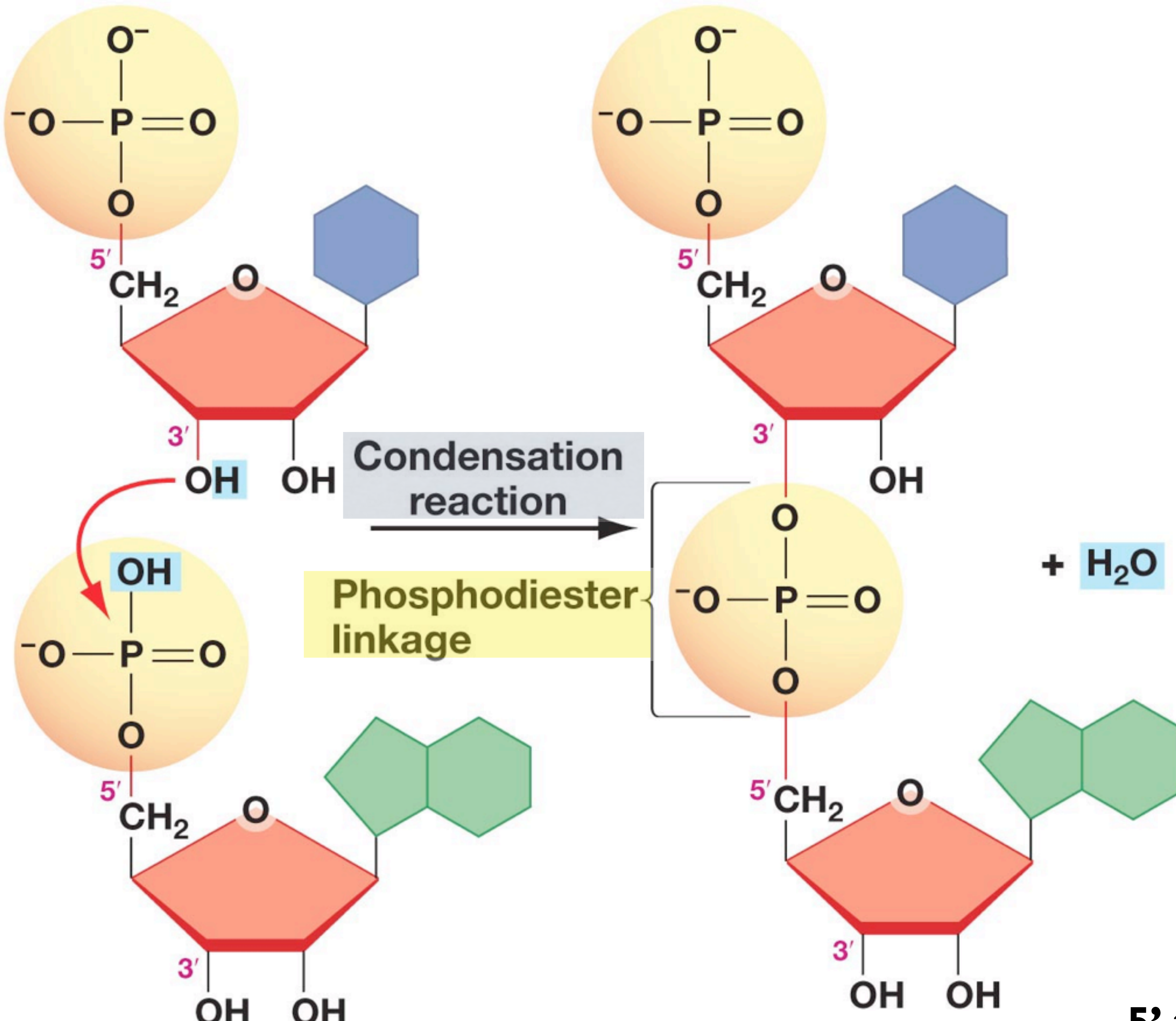
Deoxycytidine 5′-phosphate (dCMP)



Deoxythymidine 5′-phosphate (dTMP)

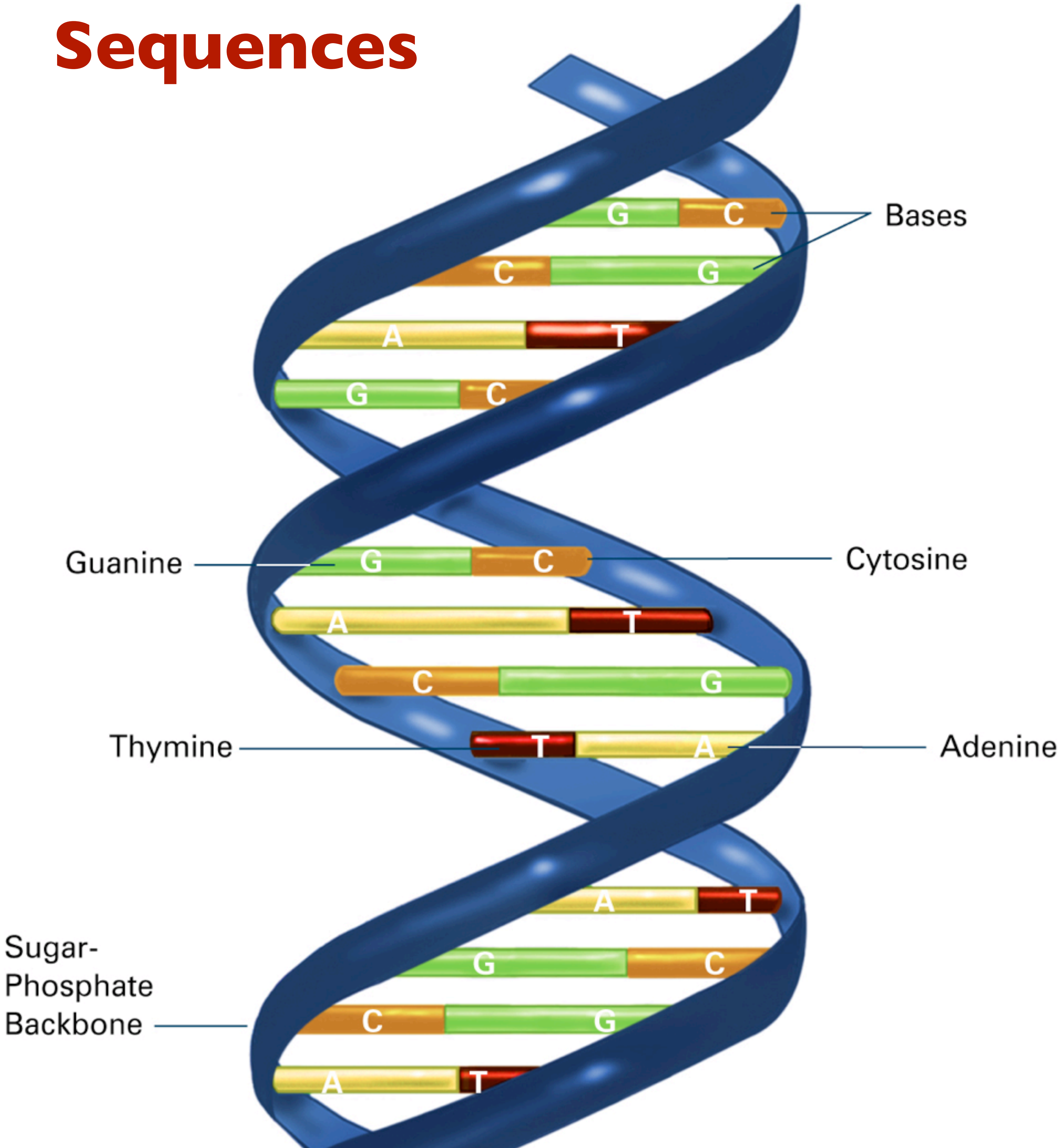
C. Nucleotide Polymers

DNA, has directionality



Built in the 5' to 3' direction

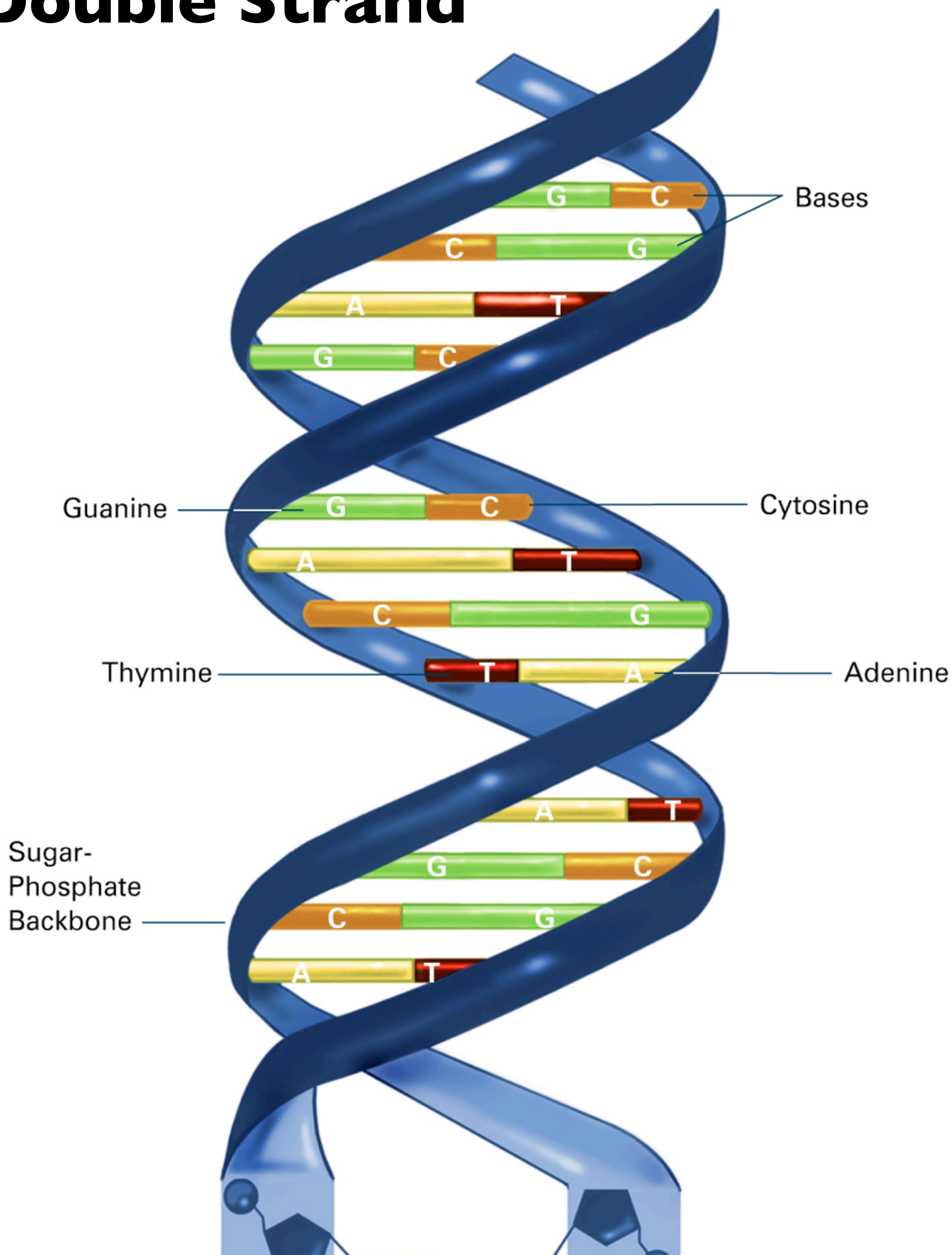
Base Sequences



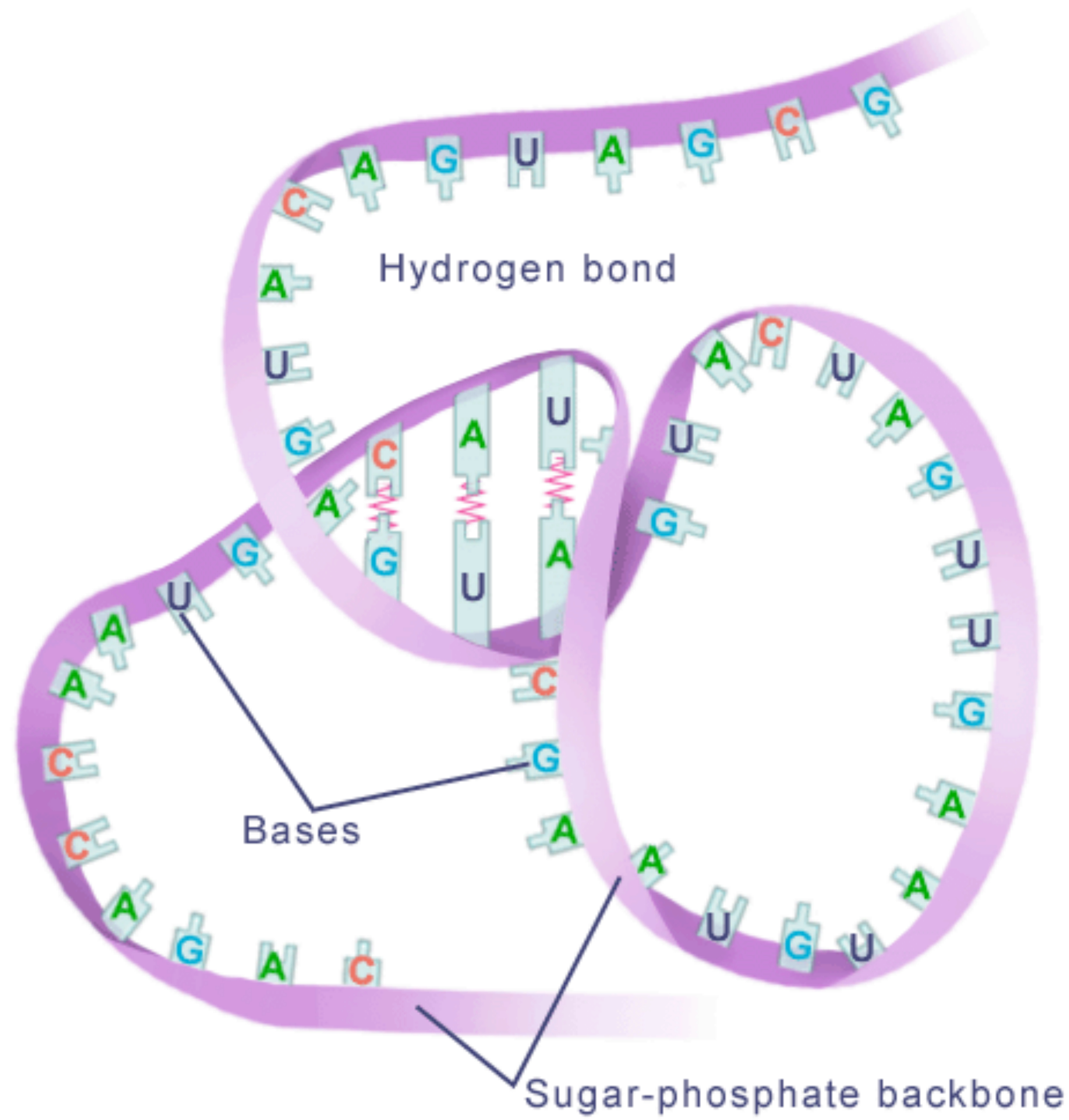
- The sequence of bases along DNA is unique for each gene.
- Genes provide specific information to the cell.
- Genes are 100's to 1000's of nucleotides long.
- A gene's meaning is in encoded in its specific sequence of the four DNA bases

D. The Structures of DNA and RNA

Double Strand

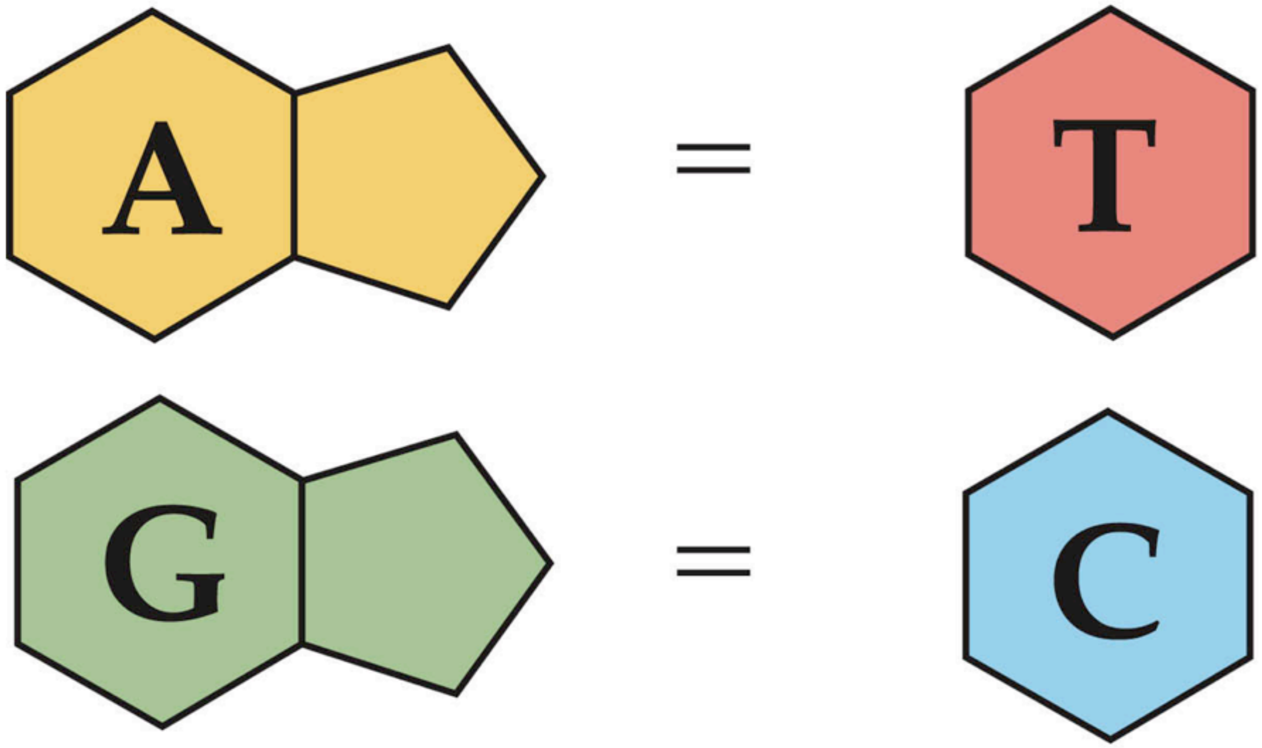


Single Strand, but the strand can and does fold

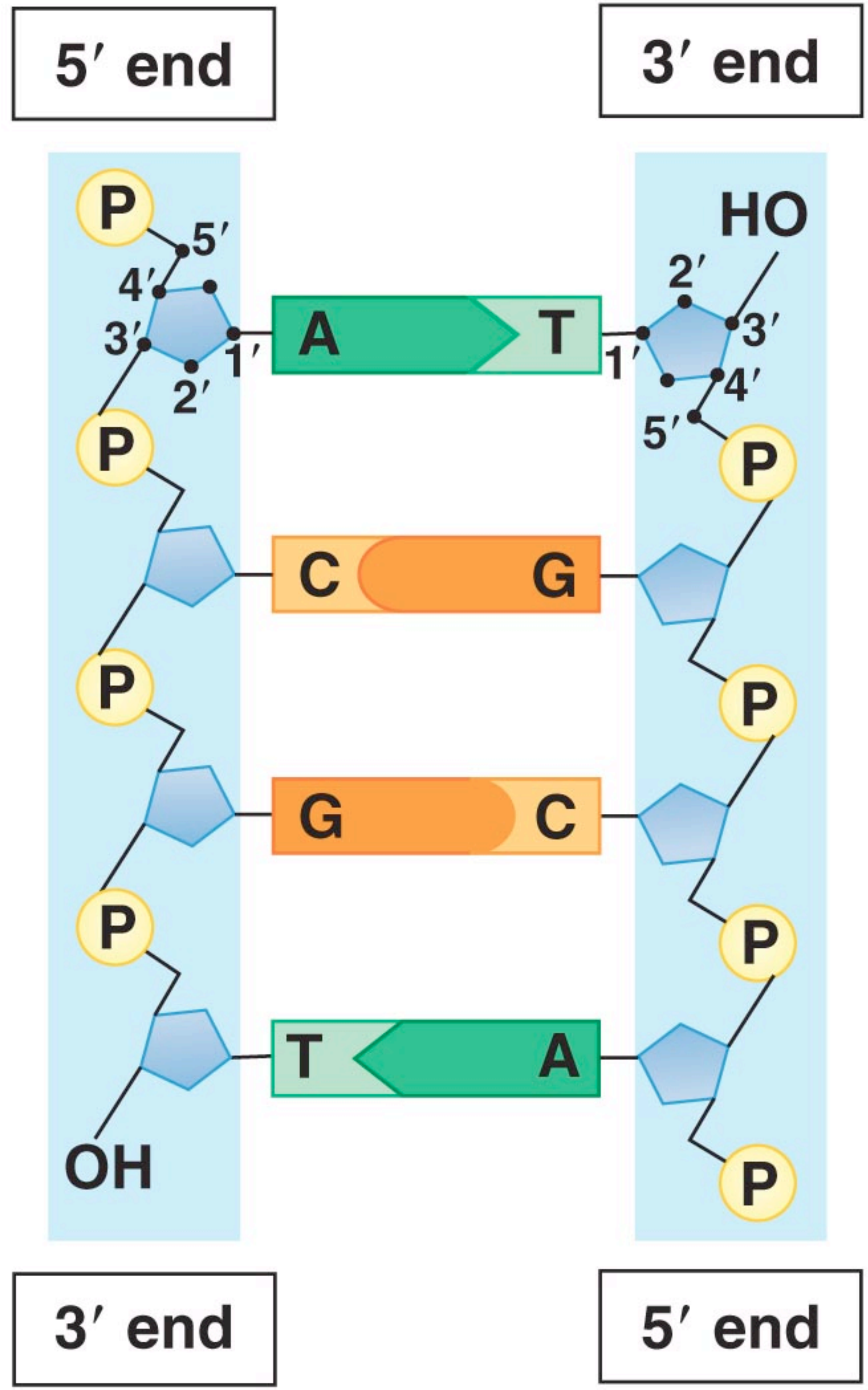


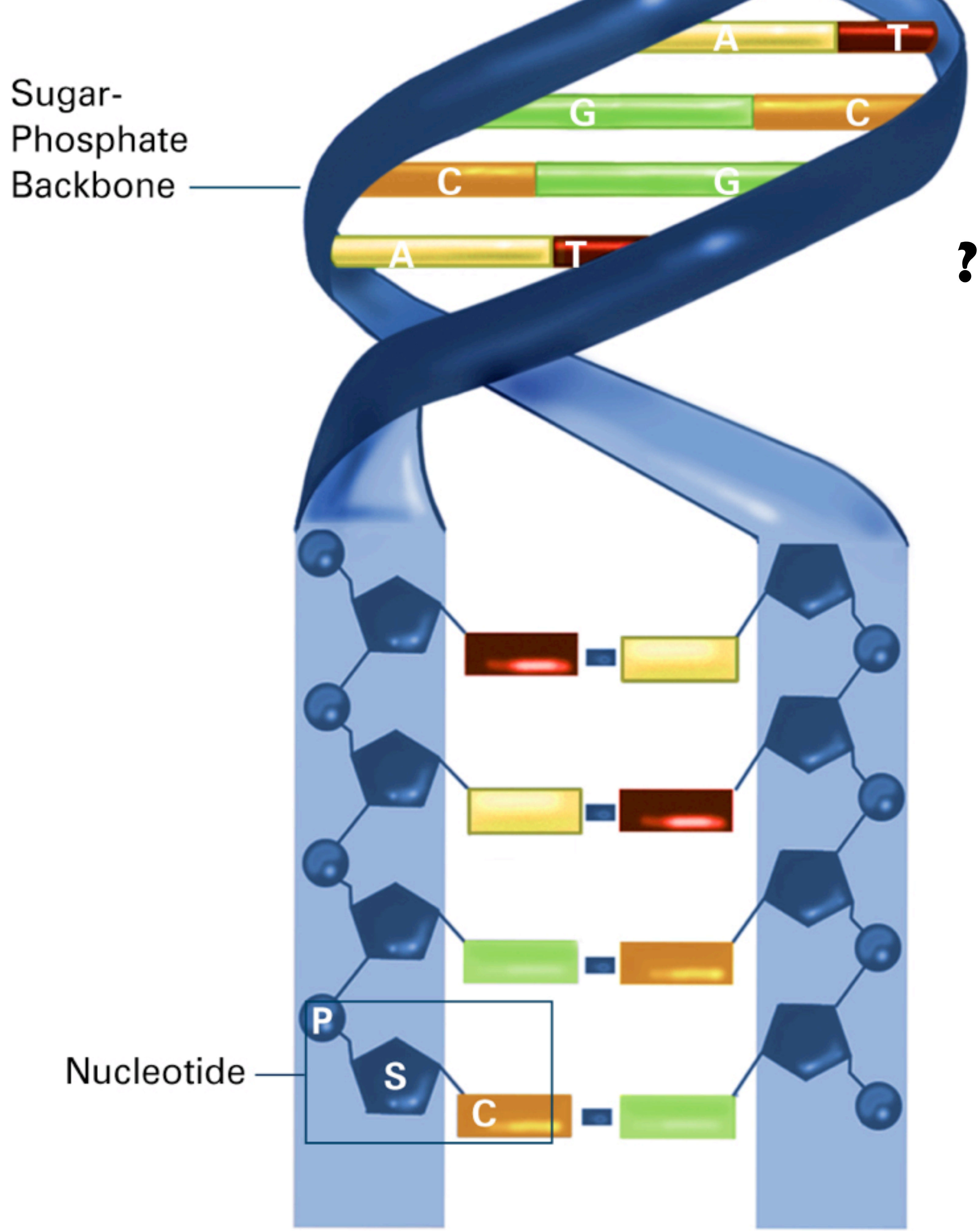
Antiparallel Strands

Base Pair Rules



Purines = Pyrimidines





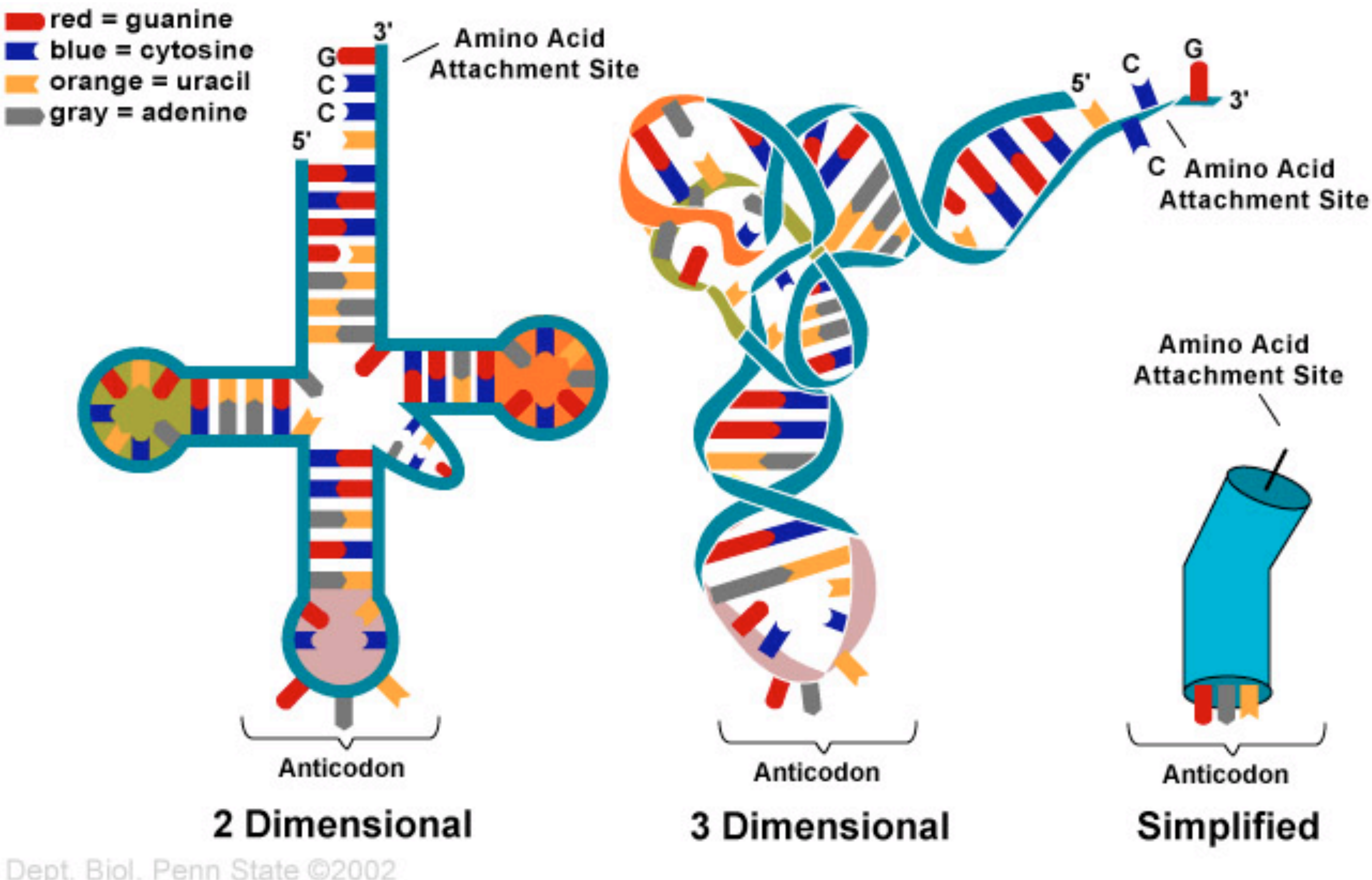
Complimentary

5’-AGGTCCG-3’

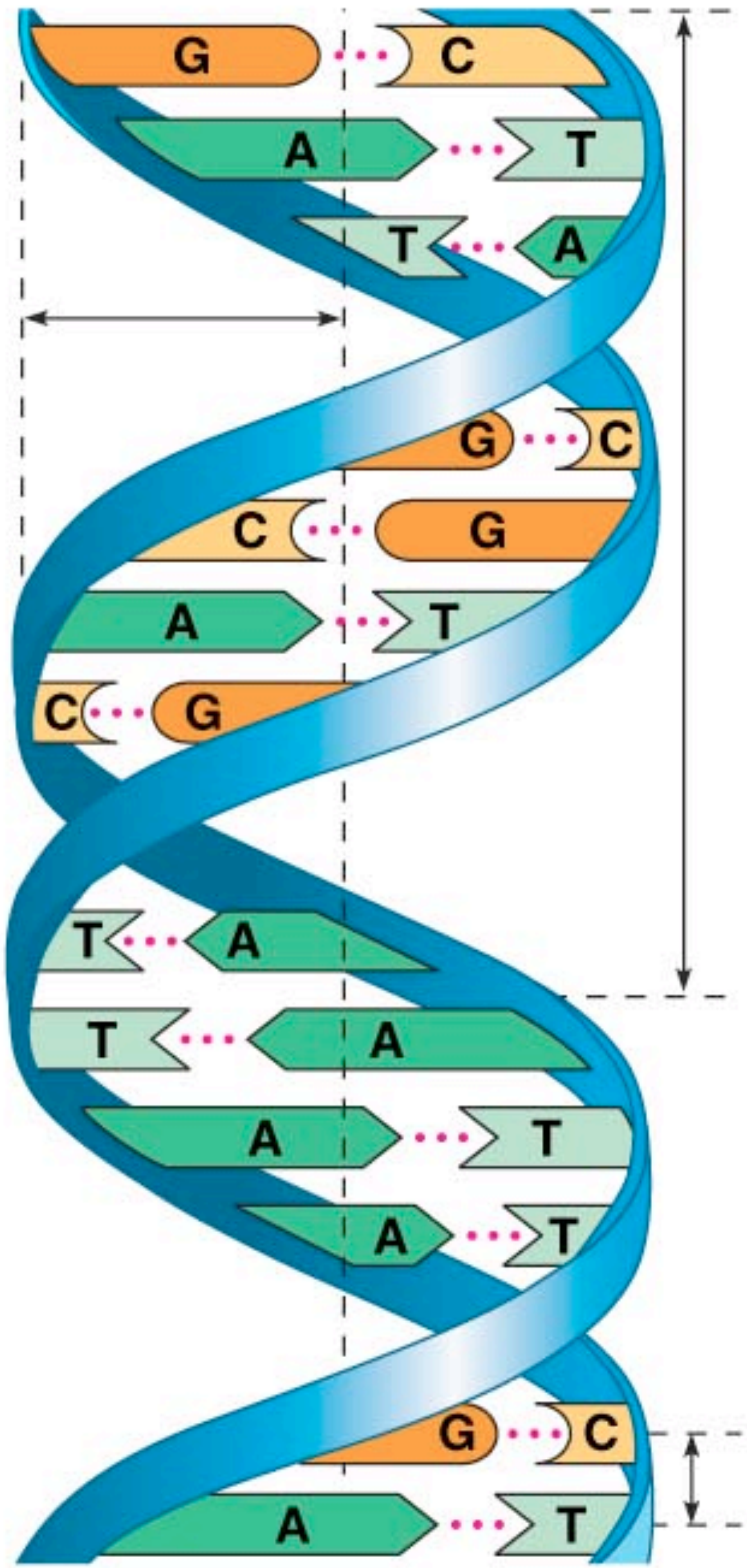
? 3’-TCCAGGC-5’

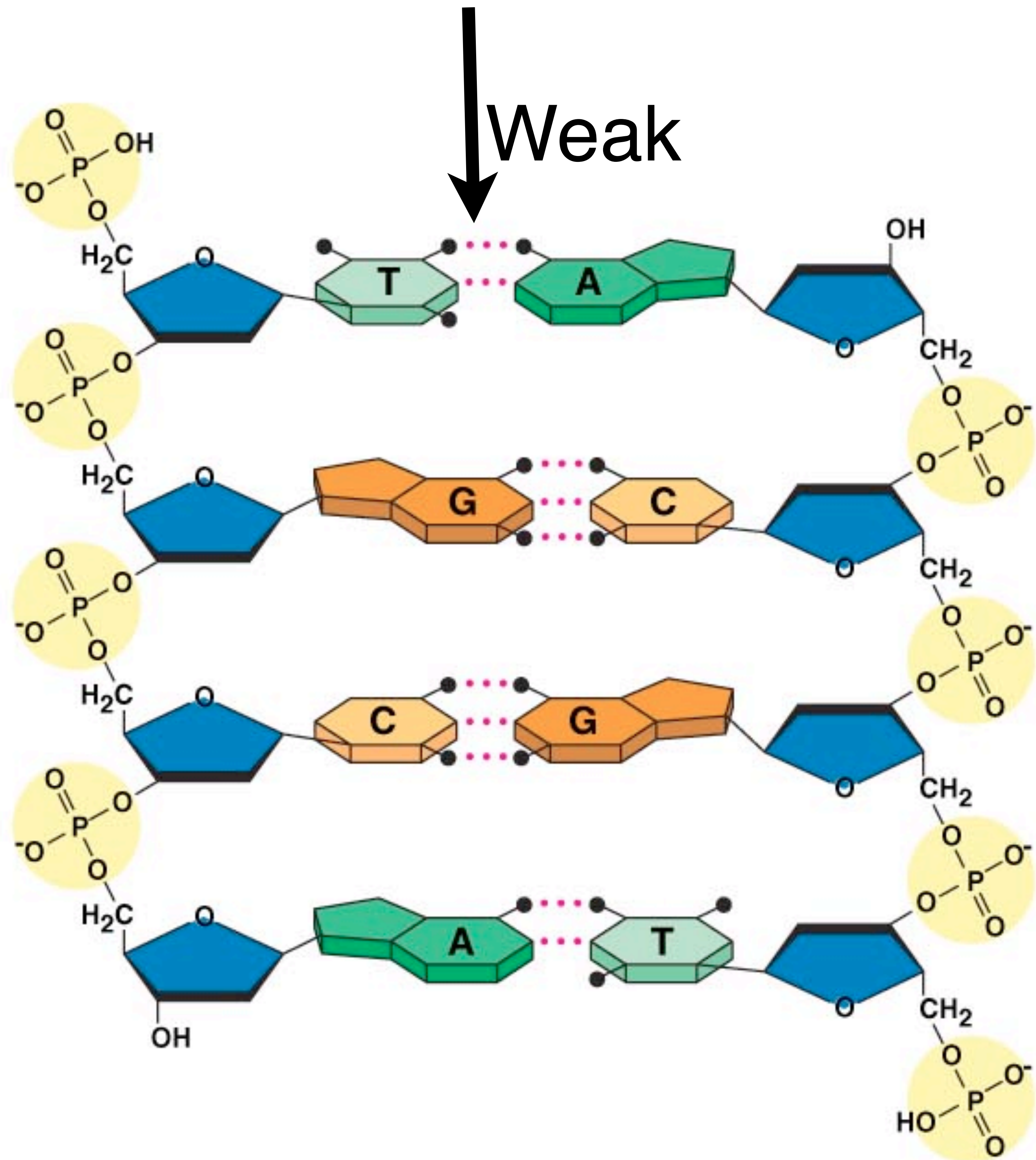
this property allows DNA make exact replicas of each DNA molecule

Complimentary Base Pairing



Hydrogen Bonds

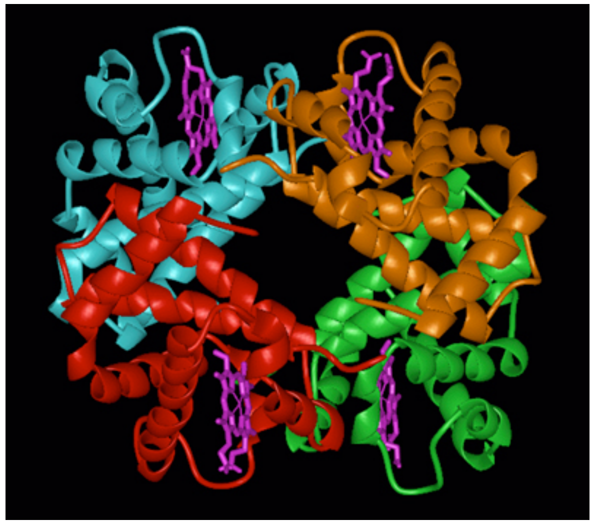




E. DNA and Proteins as Tape Measures of Evolution

- DNA carries heritable information in the form of genes.
  - DNA is passed from parent to offspring.
- Nucleotide sequence determines amino acid sequence.
- The amount of corresponding bases in the DNA of two separate species is directly correlated with their relatedness.
  - Two species with very similar DNA sequences share a more recent common ancestor than two species with dissimilar DNA sequences.

Hemoglobin



:one subunit has 146 amino acids

Humans and Gorillas differ by 1 amino acid

Humans and Frogs differ by 67 amino acids