

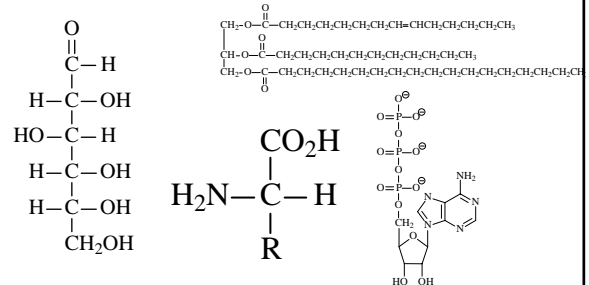
Introduction to Biochemistry

- “The chemistry of life”
- “organic chemistry with a purpose”

Biochemistry- Study of the structure, properties and changes of biomatter

Biochemistry is Based on Organic Chemistry

- Four classes of biomolecules



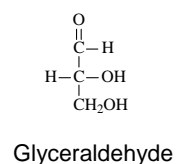
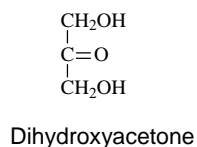
Functions of Carbohydrates

1. Energy storage molecules
2. Structural elements of cells (cell wall of plants)
3. Source of carbon for synthesizing other molecules
4. Recognition molecules

Carbohydrates

Carbohydrates are polyhydroxy aldehydes or ketones (monosaccharides) or, molecules that can be broken down into polyhydroxy aldehydes or ketones (disaccharides, oligosaccharides and polysaccharides)
 -ose ending indicates carbohydrate (glucose)

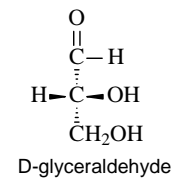
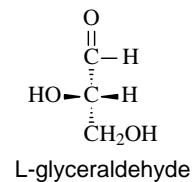
Simplest Carbohydrates



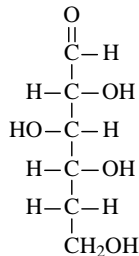
Chiral Carbons

A chiral carbon is one that has 4 different R groups attached to it.

Chiral carbons result in stereoisomers



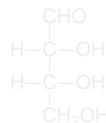
Identify the Chiral Carbons in this Molecule



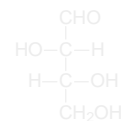
Carbons with double bonds can never be chiral

Carbons with two of the same of anything can never be chiral

Moving Up



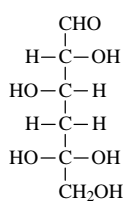
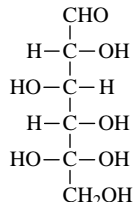
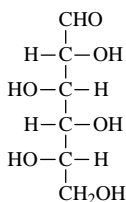
Erythrose
D



Threose
D or L?

The D and L designation of sugars with $n > 3$ are taken from the chiral carbon furthest from the carbonyl carbon.

Indicate Whether the Following Are D- or L- Sugars



Stereoisomers

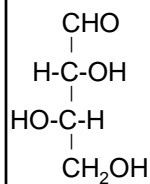
1. enantiomers- mirror images of each other, but not superimposable in 3D space.

D- and L-sugars are enantiomers

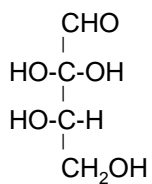
2. diastereomers- not mirror images, not superimposable in 3D space.

Practice Stereoisomer Problem

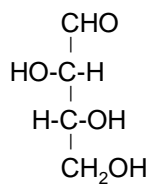
1. In the following examples, identify the enantiomers and the diastereomers



A

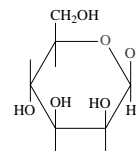
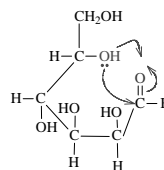
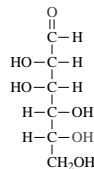


B



C

Very Little Sugar is Present in Open-chain Form Physiologically



Very Little Sugar is Present in Open-chain Form Physiologically

1. Converting open-chain to closed-chain form
2. OH on carbon 1 can be up or down
3. Anomers- term applies only to closed chain sugars

α - C6 and C1 OH point in opposite directions

β - C6 and C1 OH point in same directions

Anomers- sugars which differ in their stereochemistry at the *anomeric carbon*

Anomeric carbon- the new chiral center which is formed when carbohydrates form ring structure

Converting Open-chain to Closed-chain Form (Fischer projection to Haworth Projection)

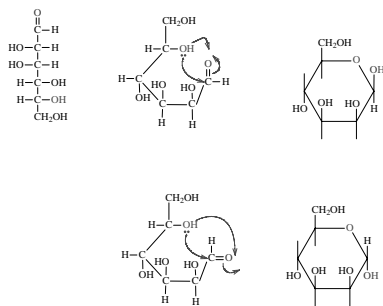
1. Aldohexose forms *pyranose* ring
2. D sugars have C6 pointing up, L sugars down
3. Other -OH groups: right down and left up
4. OH on carbon 1 can be up or down

Anomeric carbon- term applies only to closed chain sugars. A new chiral center is formed when ring structure forms

α - C6 and C1 OH point in opposite directions

β - C6 and C1 OH point in same directions

α - and β -anomers



Other Important Terminology

Furanose- sugar shaped like furan

Pyranose- sugar shaped like pyran

Hexose- 6 carbon sugar

Pentose- 5 carbon sugar

Epimer- chiral carbons, other than the anomeric carbon, which differ in orientation of alcohol groups



Pyran



Furan



Pyranose



Furanose

Mop-up of Other Sugars

- Aldopentose: furanose (ribose)
- Ketohexose: furanose (fructose)
- Smaller sugars will not form ring
- Larger sugars can form rings, for example sialic acid is a 9 carbon pyranose, but for the most part only 5- and 6-carbons sugars are physiologically relevant

Sugars You Must Know

- Ribose
- Glucose
- Galactose
- Mannose
- Fructose

Other Important Sugars

- Deoxyribose
- N-AcetylGlucose (GlcNAc)
- N-AcetylGalactose (GalNAc)

Reactions of Monosaccharides

1. Open chain \leftrightarrow closed chain equilibrium (mutarotation)
2. Reducing sugars
3. Reduction to polyols (open-chain only)
4. Esterification
5. Acetal (Ketal) formation

Important Disaccharides

1. Sucrose (glucose-fructose)
2. Maltose (glucose-glucose)
3. Lactose (galactose-glucose)

Sample Test Question

1. Draw the Haworth projection of a molecule of β -D-Glucose (β 1 \rightarrow 2) Ribose.

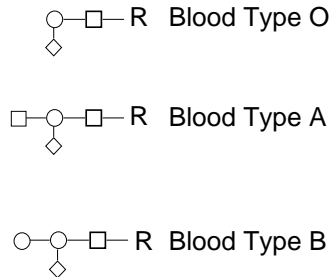
Important Polysaccharides

1. Cellulose
2. Glycogen/Starch
3. Chitin

Sample Test Questions

1. List two differences in structure of chitin and starch.
2. Draw a segment of cellulose.

Glycoproteins and Recognition



Lipids

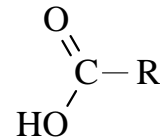
Lipids are water-insoluble molecules which are soluble in non-polar solvents such as methylene chloride.

Functions of Lipids

1. Energy storage molecules
2. Structural elements of cells (plasma membrane)
3. Sleep-inducing lipids have been identified
4. Signal-transduction molecules

Fatty acids

General form



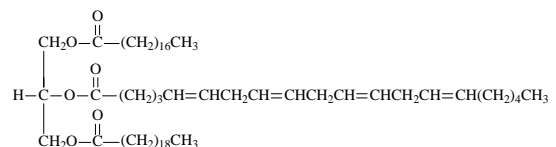
16- and 18-carbons long most common unbranched molecules _____

Fatty Acids You Must Know

- Palmitic
- Stearic
- Palmitoleic
- Oleic

Sample Test Questions

1. Draw the formula of a triglyceride composed of palmitic acid, stearic acid and oleic acid.
2. Predict the structures of the products resulting if the following triglyceride is saponified in KOH

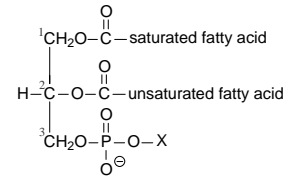


Reactions to Study Fats

- Iodine Number
iodine number = $\text{g I}_2/100 \text{ g fat}$
tells us _____
- Saponification
saponification number = mg KOH/g fat
tells us _____
- Catalytic hydrogenation used commercially
– this is very bad

Phospholipids are Important Structural Lipids

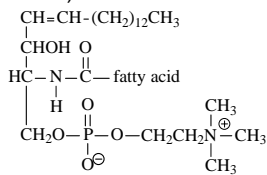
- Esters containing phosphorous and a second alcohol (glycerol is the 1st alcohol).



- The alcohol (X in figure) is polar.
- Typically, C1 has a saturated fatty acid and C2 has an unsaturated fatty acid.

Sphingolipids are Derivatives of Sphingosine Instead of Glycerol

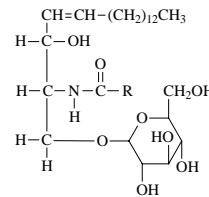
- Compare sphingosine to glycerol
- Fatty acid attached to N
- Alcohol can be phosphorous-linked or something else (next slide)



Cerebrosides and Gangliosides are Complicated

Remember that the cerebrosides have simple sugar residues on C1 OH

But *nota bena*, no phosphoester linkage



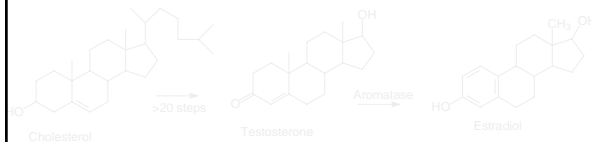
The *gangliosides* have more sugars that are branched

All Steroids are Cholesterol Derivatives

- Cholesterol is essential to life of mammals
- Body produces 0.5 g/d
- Eat about 0.5 g/d
- If you eat less, your body makes more (but will not make 1 g/d)

Know and be able to draw cholesterol
cholesterol → testosterone → estrogen

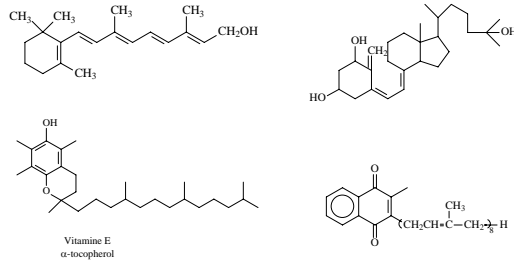
cholesterol → testosterone → estrogen



Fats vs. Oils

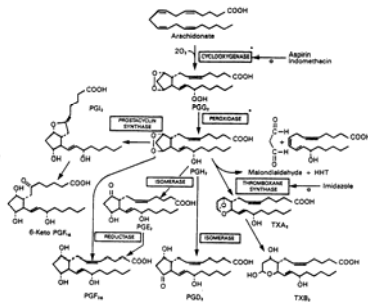
- | | |
|---|--|
| Fat | Oil |
| <ul style="list-style-type: none"> • Solid at room temp. • Animal derived | <ul style="list-style-type: none"> • Liquid at room temp • Plant derived |
- There are two ways to make oil instead of fat:
 - Decreased "tail" length in oil
 - Increased number double bonds in oil

Other Important Lipids Include the Fat-Soluble Vitamins (Vitamins A, D, E, and K)



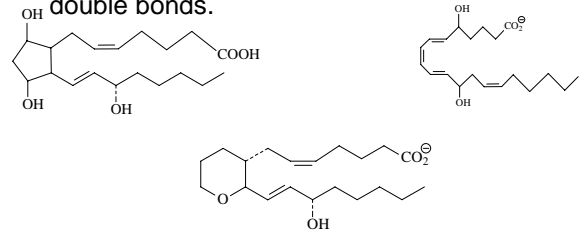
Other Important Lipids Include the "eicosanoids"

2. Prostagandins (PGs), thromboxanes (TXs) and leukotrienes (LTs), which are made from arachidonic acid. There are many of them.



Other Important Lipids Include the Eicosanoids

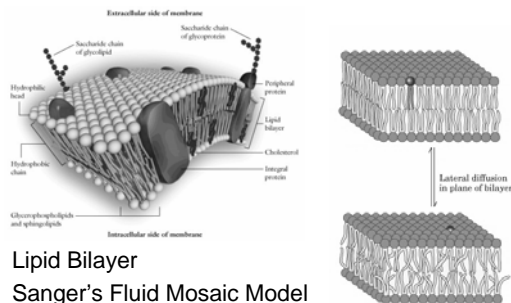
PGs all have a 5-membered ring in the "middle" of the molecule, TXs all have a 6-membered ether ring and LTs have three double bonds.



Cell Membranes

Fig. 19.6 Blei and Odian;

Fig. 12-6 Lehninger POB 3rd Ed.



1. Lipid Bilayer
2. Sanger's Fluid Mosaic Model

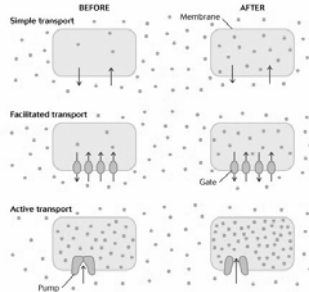
Membrane Permeability

- Polar on each side of bilayer, therefore nonpolar molecules can't go through
- Nonpolar core in the bilayer, therefore polar molecules can't go through
- BUT, we must get glucose and other molecules in.
- Membranes are selectively permeable to important things because of proteins.

Active vs. Passive transport

Fig. 19.7 Blei and Odian

- Passive allows concentration to be equal on both sides of cell
- Active transport allows concentration to be higher inside the cell (or *vice versa*), but energy is needed to do this (ATP hydrolysis)



Sample Test Question Energy From Classes of Biomolecules

- Carbohydrate 4 Cal/g
 - Protein 4 Cal/g
 - Lipid 9 Cal/g
 - Alcohol 7 Cal/g
- A person eats 100 g carbohydrate, 20 g protein, and 40 g of fat daily. How many Calories (kcal) does this person consume?

Proteins

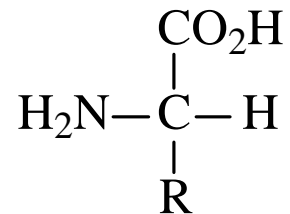
Protein- polymer (polypeptide) of amino acids.

All of the properties of proteins depend on the sequence of the amino acids they contain.

Be able to draw the structure of the 20 naturally occurring amino acids and list their three-letter abbreviations.

Amino Acids

General structure



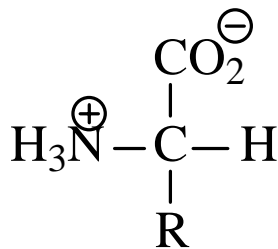
Optically active: L- form present physiologically. R group determines which amino acid.

Charge on Amino Acids and pH

pK- pH at which proton is donated/accepted.

There is a pK for the carboxyl group, the amino group, and the R group for some amino acids.

pI- isoelectric pH. The pH at which the amino acid is a zwitterion and has no net charge. Different for each amino acid.



Essential Amino Acids

Essential amino acid- amino acid that cannot be synthesized by our body and therefore must be obtained in our diet.

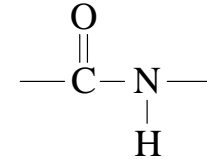
Essential Amino Acids

- PVT TIM HALL
*rapid growth only
- Arg* } basic
 - His } basic
 - Lys } basic
 - Trp } aromatic
 - Phe } aromatic
 - Ile } branched-chain
 - Leu } branched-chain
 - Val } branched-chain
 - Met (sulfur)
 - Thr (alcohol)

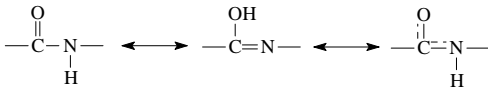
Protein Primary Structure

Primary structure- the sequence of amino acids in a protein.

Amino acids joined by a peptide bond. (an amide bond)

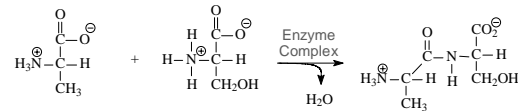


Peptide Bonds Have Partial Double Bond Character



- Makes the peptide bond rigid and flat: extremely important in determining protein shape

Peptide Bond Formation

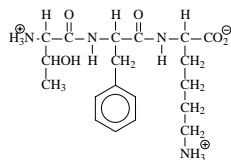


- Condensation reaction

Naming Peptides

Named:

1. From *amino terminus* to *carboxy terminus*.
2. Remove the *ine* ending from the name of the first amino acid and add *yl*.
3. The carboxy terminus name ends with the *ine*.



Secondary Structure

The way in which sections of primary structure arrange themselves based on the sequence of amino acids. Two major types:

Alpha (α) helix

Beta (β) sheet or β pleated sheet

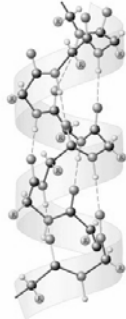
The α -helix

Fig. 20.6 Blei and Odian

Dimensions

Stabilized by h-bonds
parallel to axis of helix

Location of R groups



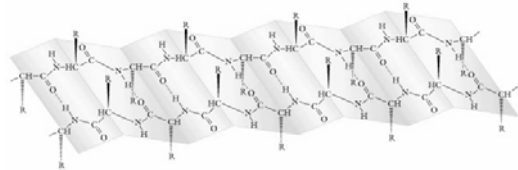
The β -sheet

Fig. 20.7 Blei and Odian

"Dimensions"

Stabilized by h-bonds perpendicular to backbone

Location of R groups



Tertiary Structure

- How the secondary structures arrange themselves in 3D space (many possible ways)
- *All* proteins have primary, secondary and tertiary structures.
- Rasmol demonstration

Classification of Proteins

- Globular vs. fibrous- based on the shape of the protein
- simple vs. conjugated- based on whether the protein is made up of anything but amino acids

Quaternary Structure

- Some proteins have two or more peptides held together by *noncovalent* forces.
- Quaternary structure is how these peptides lay in relation to one another.

Denaturation

Denaturation is a change in a proteins' secondary, tertiary and quaternary structure, based on disruption of bonds (except peptide bond).

Bonds:	strong	Peptide bonds
	strong	Disulfide bonds
	weak	Hydrogen Bonds
	weak	van der Waal Forces
	weak	Salt Bridges
	weak	hydrophobic interactions

Denaturants

Heat	disrupts all of the weak bonds
Acids/Bases	Disrupt salt bridges
Reducing agents	Break disulfide bonds
alcohol	disrupt H bonds
detergents	disrupt hydrophobic interactions
Heavy metals	bind to -SH groups
Vigorous shaking	disrupts all of the weak bonds

Important Proteins

- There are no unimportant proteins.
- Protein means 'of first importance'

Types of Proteins

- a. transport and storage of molecules
- b. mechanical functions
- c. movement
- d. protection
- e. information processing
- f. ENZYMES

Catalysts

There are three general ways to speed up a chemical reaction:

1. Increase the temperature,
2. adjust the concentration of product or reactant, or
3. add a catalyst.

Catalyst- something that changes the speed of a reaction without being changed itself. It is not a reactant, not a product, and does not change the equilibrium. It only lowers the *activation energy* of the reaction.

Activation Energy

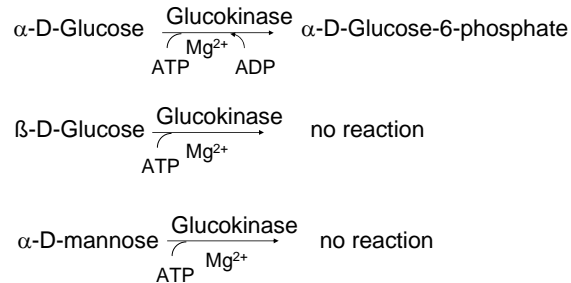
Activation Energy- the minimum energy required for a reaction to occur.

Enzymes are Protein Catalysts

Enzymes are proteins which catalyze the conversion of a specific reactant (called a *substrate*) to a specific product.

Enzymes are very efficient. A slow enzyme-catalyzed reaction will convert 250 substrate molecules to products per second, a fast one 600,000/sec.

Enzymes are Very Specific



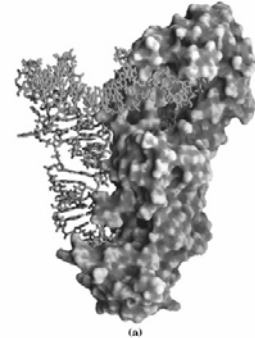
Models of Enzyme Specificity

Fig. 27-19 Lehninger POB 3rd Ed.

Lock-and-Key Model-

says that, just like not being able to open any lock with a key, only one substrate will fit in the *active site* of an enzyme.

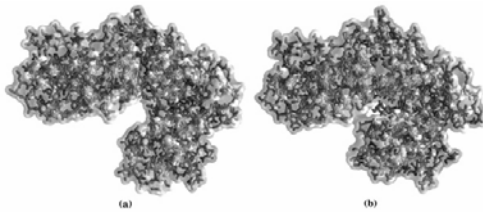
Active Site- region of the protein where the substrate binds and is converted to product.



Models of Enzyme Specificity

Fig. 8-21 Lehninger POB 3rd Ed.

Induced-fit-Model- says that when the correct substrate enters the active site, it causes the protein to change shape around the substrate, so



Coenzymes and Cofactors

Most enzymes require a molecule other than the substrate molecule to carry out a reaction.

Cofactor- non-protein inorganic substances that are required to carry out the reaction.

Coenzyme- organic substances (usually *vitamins* or vitamin derivatives) that are required to carry out the reaction.

Cofactors

Cofactor- non-protein inorganic substances.

Fe ²⁺	Protease, aconitase
Mg ²⁺	Glucokinase, stabilize charge on ATP
Mn ²⁺	PEPCK
Cu ²⁺	lysyl oxidase
Zn ²⁺	Zinc fingers
K ⁺	pyruvate kinase

Have in common a positive charge, pull electrons away to lower the activation energy.

Coenzymes and Cofactors

Table 22-3 Blei and Odian

Coenzyme- organic substances. (Table 20.1 is a *partial list*)

Don't have to draw or recognize, but know some of the names and where they are used.

TABLE 22.3 Vitamins and Corresponding Coenzymes Serving as Group Transfer Carriers

Vitamin	Coenzyme	Group Transferred
biotin	biotin	carbon dioxide
folic acid	tetrahydrofolate	other one-carbon groups
pantothenic acid	coenzyme A	acyl groups
cobalamin (vitamin B ₁₂)	5'-deoxyadenosylcobalamin	alkyl groups, hydrogen atoms
riboflavin	flavin adenine dinucleotide	hydrogen atoms
niacin (nicotinic acid)	nicotinamide adenine dinucleotide	hydride ion (H ⁻)
pyridoxine (vitamin B ₆)	pyridoxal phosphate	amino groups
thiamine	thiamine pyrophosphate	aldehydes

Vitamins

Vitamin- organic substance which cannot be synthesized and must be obtained from diet.

Vitamins are present in all foods in small amounts. There are two broad classes: water soluble and fat soluble.

Water soluble: C and the "B complex"

Fat soluble: A, D, E and K

There is a disease for every vitamin deficiency and many vitamins cause problems when taken in too large of amounts.

Vitamin Deficiencies and Excesses

Water soluble vitamins do not have toxic effects.

Vitamin	Deficiency	Excess
B ₁ (Thiamin)	Beriberi	none
B ₂ (Riboflavin)	skin lesions	none
B ₅ (niacin)	Pellagra	none
B ₆ (3 forms)	several- anemia, e.g.	none
Folic acid	anemia	none
C (ascorbic acid)	Scurvy	none

Vitamin Deficiencies and Excesses

Fat-soluble vitamins accumulate and cause toxicity.

Vitamin	Deficiency	Excess
A	night blindness	yellow pigmentation
D	Rickets	hypercalcemia
E	sterility, abortions	unstudied
K	hemorrhage	hemolytic anemia

Enzyme Nomenclature

Common names end in -ase, e.g. glucokinase

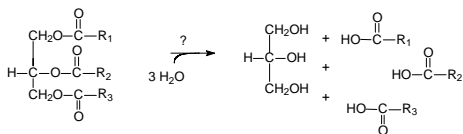
Six classes by Enzyme Commission nomenclature:

4.1.1.32 Phosphoenolpyruvate Carboxykinase (PEPCK)

1. Oxidoreductases- redox reactions
2. Transferases- transfer something
3. Hydrolases- split with water
4. Lyases- remove group from substrate without hydrolysis- usually leave a double bond
5. Isomerases- form isomers
6. Ligases- join together

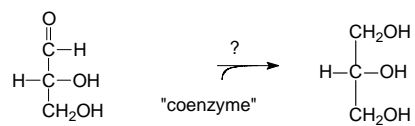
Sample Test Question

- Selfridge and associates decide to go into business raising sunflowers as a source of glycerol, since sunflower oil is a source of glycerol by the reaction below. What class of enzyme is responsible for this reaction?



Sample Test Question

- McConnel and associates decide to compete with Selfridge and associates, but to get around the patent issue pursue the following reaction. What class of enzyme is responsible for this reaction?



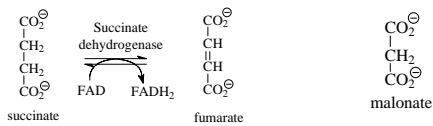
Rates of Enzyme-catalyzed Reactions

1. Substrate concentration- 2 shapes
hyperbolic- most enzymes
sigmoidal (S-shaped)- allosteric enzymes
allosteric means "other site"
2. Temperature- composite of 2 slopes
all reactions go faster at higher temperatures
high temperatures denature proteins

Rates Continued

3. pH- optimum depends on function (normal environment) and substrate characteristics
4. Inhibitors, natural and artificial

4a. Competitive Enzyme Inhibitors Bind at the Active Site



Succinate = normal substrate
Malonate = competitive inhibitor

Enzyme Inhibitors

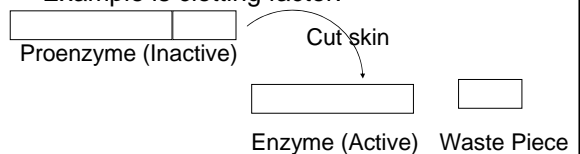
- 4b. Noncompetitive- binds somewhere besides the active site
- 4c. Uncompetitive- binds somewhere besides the active site, but only binds when substrate is in the active site

Regulation of Enzyme Activity

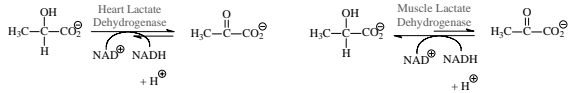
- Most enzymes are either on or off- there is no fast/slow
- There are 5 major ways that the body has found to keep enzymes in an inactive state so they can be quickly converted into an active state:

1. Proenzymes (Zymogens)

- Enzymes are made in a longer than usual form. When needed, the protein is cut into an active piece and a waste piece.
- Example is clotting factor.



2. Isoenzymes



- Iso means “something same, something different”
- Example is lactate dehydrogenase- there is a muscle isoenzyme and a heart isoenzyme.
 - same reaction
 - different direction

3. Covalent Modification

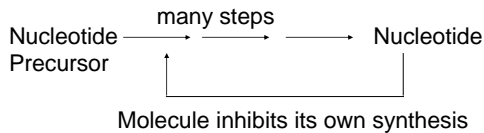
Something is covalently attached to the enzyme which affect the activity.

Example is phosphorylation- glycogen synthesizing enzyme and glycogen degrading enzyme.

	Dephosphorylated	Phosphorylated
synthesizing	active	inactive
degrading	inactive	active

4. Feedback inhibition

- This is an example of an allosteric enzyme. Functions in many places in the body, but one example is nucleotide synthesis.



5. Enzyme Repression

PEPCK- Insulin blocks, or represses, the synthesis of PEPCK. When insulin levels go down, PEPCK is made.



Two Major Types of Nucleic Acids

DNA deoxyribonucleic acid

RNA ribonucleic acid

Both are polymers of nucleotides linked to sugars through phosphodiester linkages.

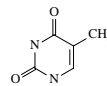
Pyrimidine Bases



pyrimidine



Cytosine
4-amino-2-oxypyrimidine

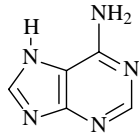


Thymine
5-methyluracil
DNA only

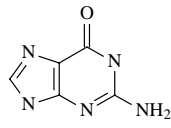


Uracil
2,4-dioxypyrimidine
RNA only

Purine Bases (Adenine and Guanine)



Adenine
6-aminopurine

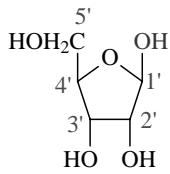


Guanine
2-amino-6-oxypurine

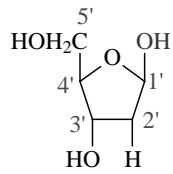
Bases, Nucleosides and Nucleotides

Base	Nucleoside (Base + Sugar)	Nucleotide (Base+Sugar+Phosphate)
Adenine	Adenosine	Mono, Di, TriPhosphate AMP, ADP, ATP
Thymine	Thymidine	TMP, TDP, TTP
Cytosine	Cytidine	Etc.
Guanine	Guanosine	
Uracil	Uridine	

Ribose and Deoxyribose

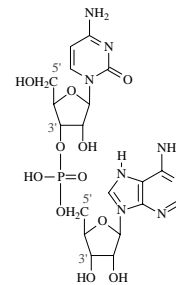


β-D-ribose



β-D-deoxyribose

Nucleotides are Polymerized by 3'-5'Phosphodiester Linkages

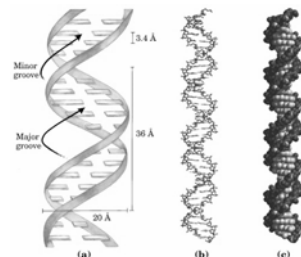


DNA Structure

Lehninger POB 3rd Ed.

See Fig. 24.4 your book

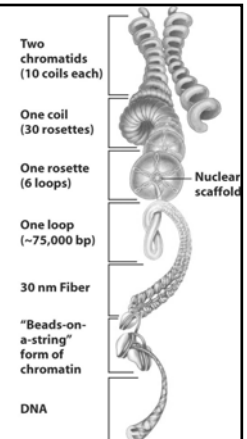
1. Double stranded
2. Antiparallel
3. phosphodiester backbone outside
4. hydrogen bonded base-pairs (A=T, G≡C) inside
5. α-helix- 10 bp/turn



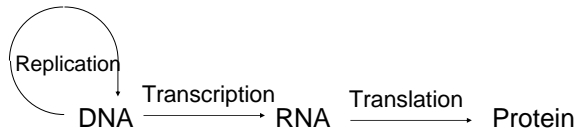
Higher Levels of DNA Structure

Fig 24-33 Lehninger POB 4th Ed.

- See Fig. 24.7 Denniston



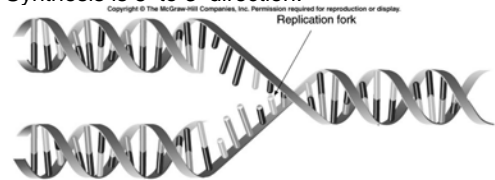
Central Dogma of Information Flow



Replication

Fig. 24.9 Denniston

1. Synthesis is *semiconservative*- two molecules result (daughter molecules) each of which contain one parent strand and one newly synthesized strand.
2. Synthesis is 5' to 3' direction.

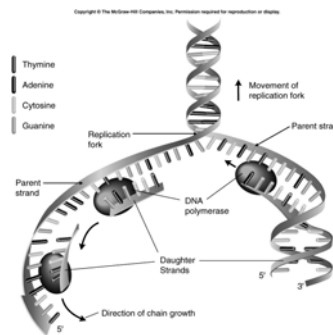


1. Initiation

Fig. 24.9 Denniston

Begins at origin of replication (Ori)

1. strands separate
2. DNA polymerase binds
3. Replication fork
Okazaki fragments



2. Elongation

1. Phosphodiester formed
2. Inorganic pyrophosphate (PPi) is given off
3. Cofactor is Mg^{2+}
4. Substrate: all 4 NTPs

3. Termination

1. Incompletely known
2. Okazaki fragments must be ligated together
cleave RNA primer (one enzyme activity)
fill gaps (second enzyme activity)
ligate together (third enzyme activity)

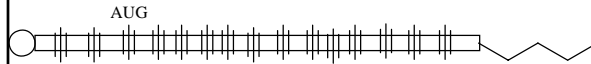
RNA

Single stranded instead of double
not α -helix
U instead of T
3 major types: mRNA, rRNA, and tRNA

mRNA

3 major types:

<u>type</u>	<u>shape</u>	<u>size</u>	<u>function</u>
mRNA	linear	variable	code for protein

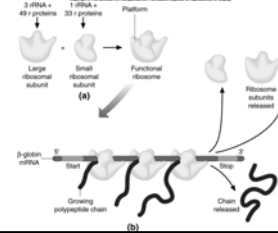


rRNA

Fig. 24.17(a) Denniston

3 major types:

<u>type</u>	<u>shape</u>	<u>size</u>	<u>function</u>
mRNA	linear	variable	code for protein
rRNA	globular	2 sizes	polymerize protein

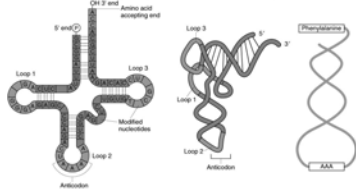


tRNA

Fig. 24.10 Denniston

3 major types:

<u>type</u>	<u>shape</u>	<u>size</u>	<u>function</u>
mRNA	linear	variable	code for protein
rRNA	globular	2 sizes	polymerize protein
tRNA	"cloverleaf"	~75 nt	adapter



RNA Synthesis (Transcription)

1. DNA must unwind
2. Elongation reaction is ribose-dependent
3. Begins with polymerase binding *promoter*
4. All RNA is synthesized longer than necessary

mRNA Processing

1. Capping- mGppp-mRNA
2. Splicing- cut out introns (eukaryotes)
3. Polyadenylating- adding 100-1,000 A to end

Protein Synthesis

mRNA carries code (Universal Genetic Code)

gene (DNA) → mRNA → processed mRNA

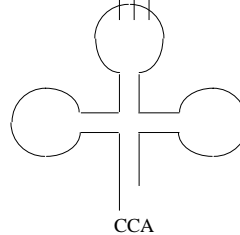
Universal Genetic Code

- Universal- used in all species
- Degenerate- more than one amino acid per codon (Wobble)
- Unambiguous- one codon does not mean more than one thing
- Not Punctuated

Protein Synthesis

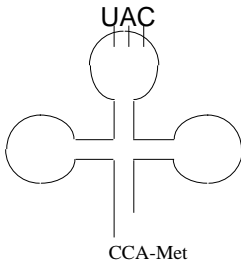
tRNA *anticodon* binds *codon* of mRNA

mRNA: AUG CCC CAG GAU
tRNA: UAC GGG GUC CUA



Protein Synthesis

tRNA carries an amino acid esterified to 3' A
(charged tRNA)



Protein Synthesis

rRNA complexes with tRNA and mRNA,
along with many proteins.

Peptide bond is formed between adjacent
amino acids by a peptidyl transferase of
this complex.

Mutations

AUG CCC CAG GAU AAG
Met Pro Gln Asp Lys

Insertion mutation:

AUG CCC CCA GGA UAA G
Met Pro Pro Gly Stop

Missense mutation: Pro #2 instead of
Gln

Nonsense mutation: Stop instead of Lys