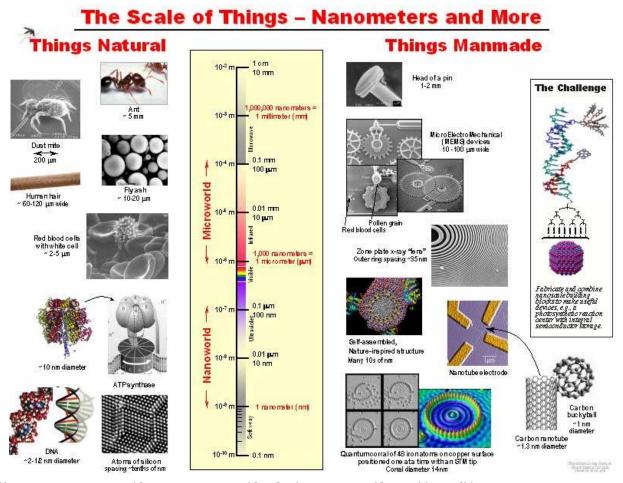
What is nano?



http://cohesion.rice.edu/CentersAndInst/CNST/emplibrary/Scale%20of%20Nanotechnology.jpg

Nanosciences and Nanotechnology

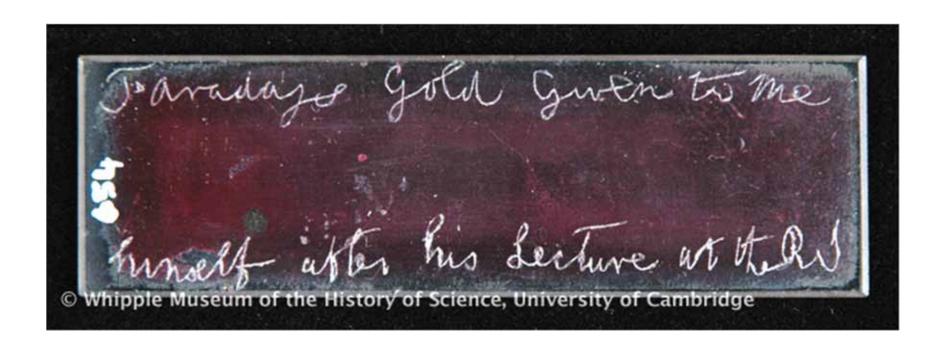
- Science
 - Theory
 - Experiment
- Technology
 - Development
 - Applications
 - Commercialization

Nanotechnolgy

- Top-Down Approach
- Lithographic, Manipulation, Industrial process

- Bottom-Up
- Self-assembly, natural process

Faraday's Gold Sol



1856 20-40 nm gold



Plenty of Room at the Bottom

Richard P. Feynman, December 1959

How do we *write* it? We have no standard technique to do this now. But let me argue that it is not as difficult as it first appears to be. We can reverse the lenses of the electron microscope in order to demagnify as well as magnify. A source of ions, sent through the microscope lenses in reverse, could be focused to a very small spot. We could write with that spot like we write in a TV cathode ray oscilloscope, by going across in lines, and having an adjustment which determines the amount of material which is going to be deposited as we scan in lines. This method might be very slow because of space charge limitations. There will be more rapid methods. We could first make, perhaps by some photo process, a screen which has holes in it in the form of the letters. Then we would strike an arc behind the holes and draw metallic ions through the holes; then we could again use our system of lenses and make a small image in the form of ions, which would deposit the metal on the pin.



Plenty of Room at the Bottom

Richard P. Feynman, December 1959

A simpler way might be this (though I am not sure it would work): We take light and, through an optical microscope running backwards, we focus it onto a very small photoelectric screen. Then electrons come away from the screen where the light is shining. These electrons are focused down in size by the electron microscope lenses to impinge directly upon the surface of the metal. Will such a beam etch away the metal if it is run long enough? I don't know. If it doesn't work for a metal surface, it must be possible to find some surface with which to coat the original pin so that, where the electrons bombard, a change is made which we could recognize later.



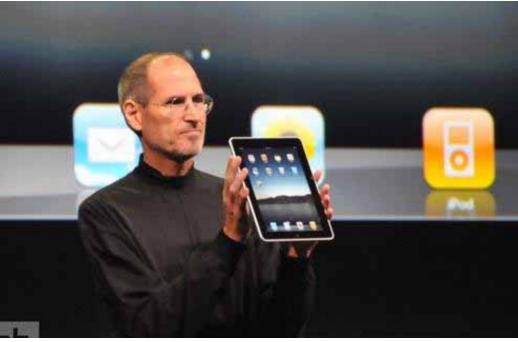
Plenty of Room at the Bottom

Richard P. Feynman, December 1959

There is no intensity problem in these devices—not what you are used to in magnification, where you have to take a few electrons and spread them over a bigger and bigger screen; it is just the opposite. The light which we get from a page is concentrated onto a very small area so it is very intense. The few electrons which come from the photoelectric screen are demagnified down to a very tiny area so that, again, they are very intense. I don't know why this hasn't been done yet!

Consumer Electronics



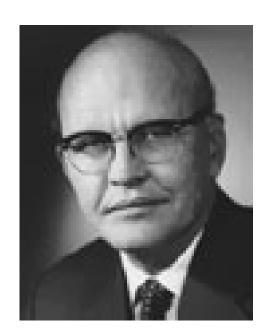








First Integrated Circuit

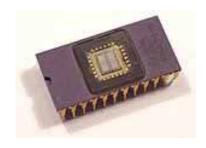




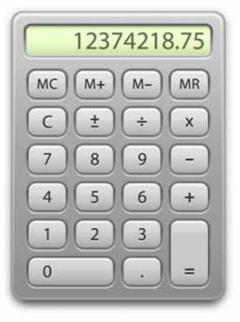


"What we didn't realize then was that the integrated circuit would reduce the cost of electronic functions by a factor of a million to one, nothing had ever done that for anything before" - Jack Kilby 2000 Nobel Prize

1958 Texas Instruments



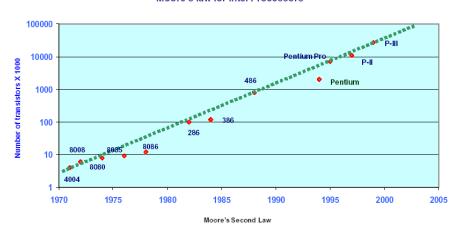






Moore's Law

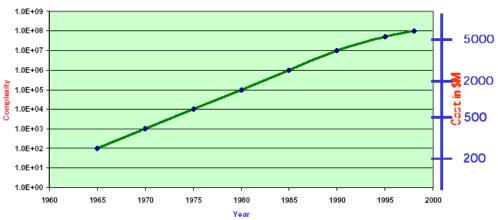
Moore's law for Intel Processors



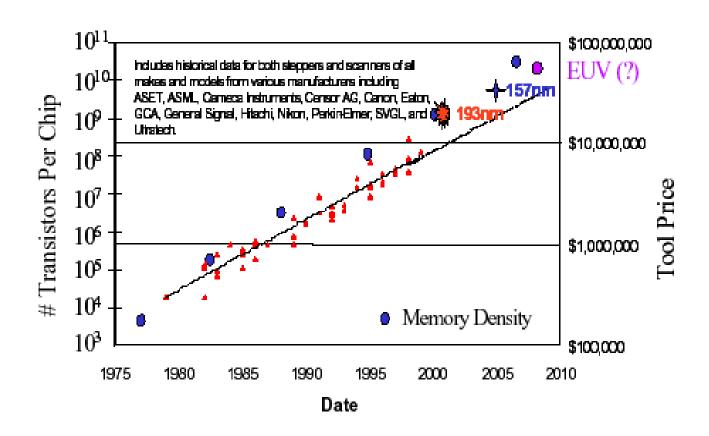
Moore's Laws

First Law: Number of components in a chip (IC) will double roughly every 18 months (1965, in *Electronics*). This has held true more or less since then.

Second Law: Facility costs increase on a semilog scale (terminology due to Eugene Meieran, Intel Fellow). Fab costs double approximately every four years.

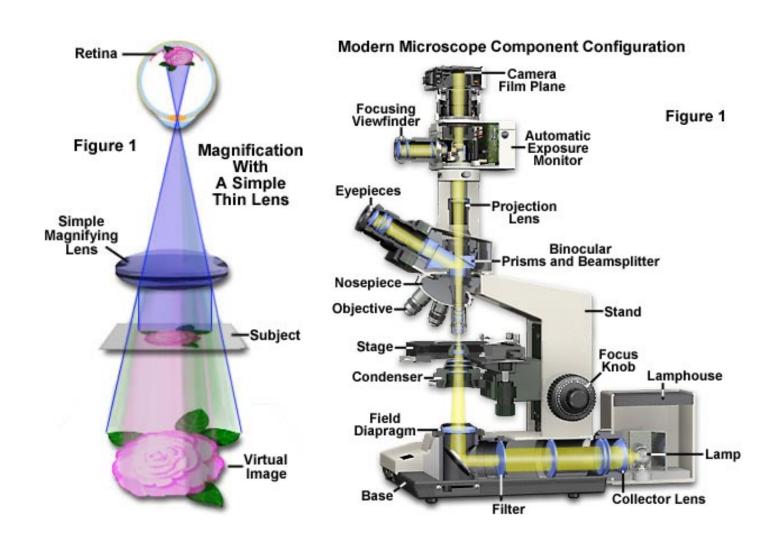


Tool Cost

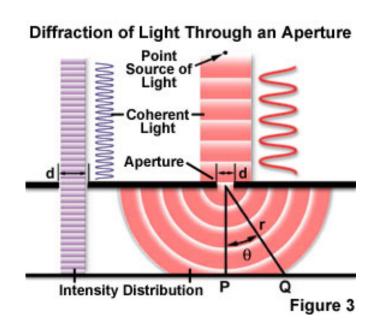


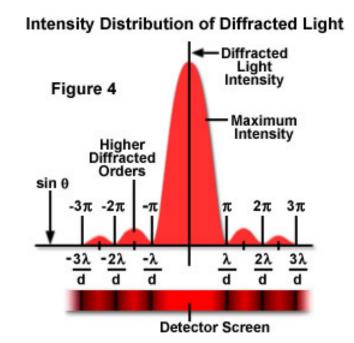
Visible Light Quantum Devices Transistor Gates Colloidal Particles Polymers **MEMS Devices** Atoms Proteins Bacteria Liquid Drops Molecules Cells 10⁴ 0.1 100 and a condition of the Optical Lithography E-Beam Lithography Masked Deposition Scanning Probe Techniques Molding and Embossing Contact Printing Edge Lithography

Optical Microscope



Limit of Photolithography

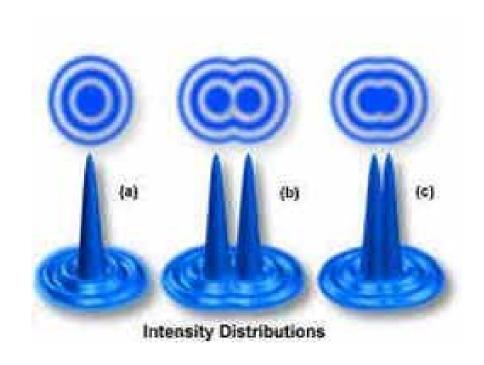




$$r = 1.22 \times \lambda/(2 \times N.A.)$$

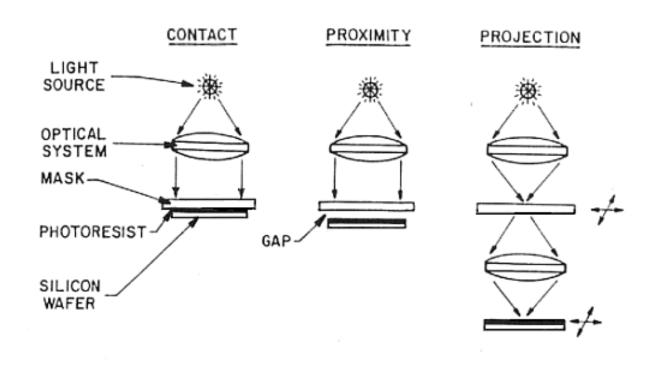
N.A. = n x sin(θ)

Diffraction Limit



Resolution = K x
$$\lambda$$
/(N.A.)
Depth of Focus = λ /(N.A.)²
K = 0.61

Methods of Photolithography



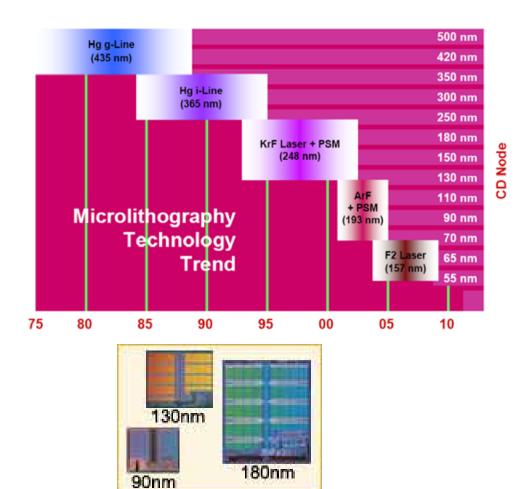
$$W_{min} = k_1 \operatorname{sqrt}(\lambda d)$$

$$W_{min} = k_1 \lambda / NA$$

Photolithography







UV Wavelength (nm)	Wavelength Name	UV Emission Source				
436	g-line	Mercury arc lamp				
405	h-line	Mercury arc lamp				
365	i-line	Mercury arc lamp				
248	Deep UV (DUV)	Mercury arc lamp or Krypton Fluoride (KrF) excimer laser				
193	Deep UV (DUV)	Argon Fluoride (ArF) excimer laser				
157	Vacuum UV (VUV)	Fluorine (F ₂) excimer laser				

Year	Linewidth (nm)	Wavelength (nm)		
1986	1,200	436		
1988	800	436/365		
1991	500	365		
1994	350	365/248		
1997	250	248		
1999	180	248		
2001	130	248		
2003	90	248/193		
2005 (fcst)	65	193		
2007 (fcst)	45	193		



PRESIDENT CLINTON'S ADDRESS TO CALTECH ON SCIENCE AND TECHNOLOGY

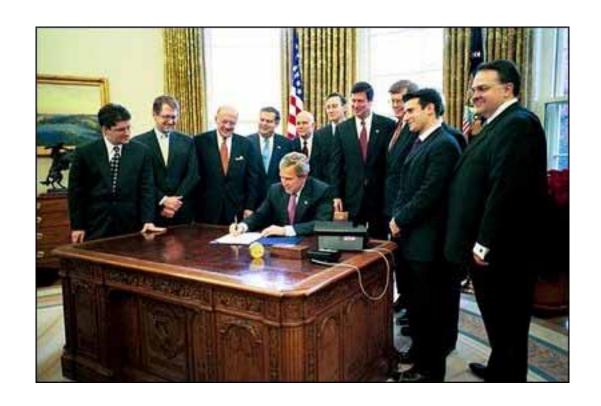


Speaking at the California Institute of Technology, in Pasadena, California, President Bill Clinton said that a strong America requires strong investments in science and technology. In his speech, the president announced that his fiscal budget for 2001 will include a \$2.8 billion increase in the "Twenty-First Century Research Fund"—investments that will support advances in biomedical research, information technology, nanotechnology, university- based research, and cleaner energy. Hailing the "critical role that science and technology have played in bringing America to this remarkable moment," Clinton emphasized how such research furthers American prosperity, improves health, and preserves the environment. He called for enhanced efforts to raise public awareness of the benefits that flow from a continuing commitment to the scientific enterprise.









President Bush signs the 21st Century Nanotechnology Research and Development Act in the Oval Office Dec. 3, 2003. Nanotechnology offers the promise of breakthroughs that will revolutionize the way we detect and treat disease, monitor and protect the environment, produce and store energy, and build complex structures as small as an electronic circuit or as large as an airplane.

What is nanobiotechnology

- Nano + Bio
- Nano-fabrication => nanopatterning,
 NEMs
- Nano-manipulation => optical, electrical, acoustic, thermal, magnetic, mechanical
- Nanomaterials => Q-dots, SERS, Plasmon, Magnetic
- Nano-imaging => SPM, optical tool, EM

What is nanobiotechnology

- Bio + nano
- DNA assembly
- Cell factory
- Molecular motor
- Energy

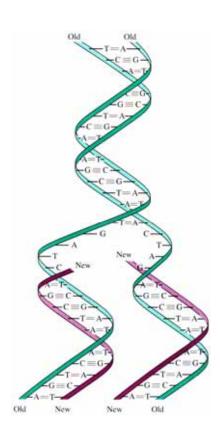
Building Block

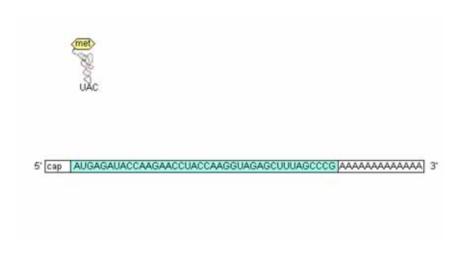
- Log, Brick
- High energy physicist –quark
- Physicist-proton, neutron, electron
- periodic table
- Chemist- molecule
- Biologist- cells

How to assemble them

- Thermodynamic
- Chemical bond
- Hydrogen bond
- Electrostatic
- Van der Waals interaction
- Other interactions

Self-Assembly Process in Nature





Topics

Fundamental Knowledge and Current Literatures

- Analytical Chemistry
- Spectroscopic tools
- Microarray
- Cell-surface interaction
 Ultrasensitive detection
- Physical Chemistry
- Single molecular behavior (Optical and AFM)
- Optical properties of Q-dot
- SERS
- Surface plasmon
- Material Chemistry:
- Nanomaterials: Q-dot, nanoparticle, DNA assembly
- Surface functionalization
- Drug delivery
- DNA, Protein, Cell interactions

•

Review of Biochemistry

Review of Cell Biology

Synthesis of Nanoparticles and Surface Modifications

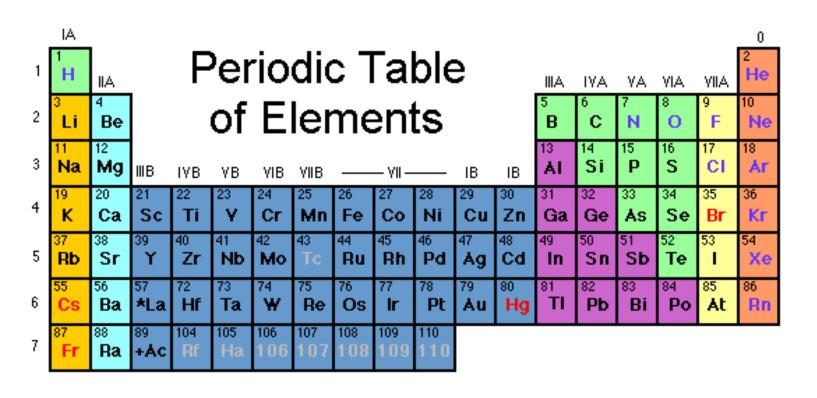
Nanomaterials for Biodiagnostic

Nanomaterials for Biomedical Applications

Nanomedicine

Bioimaging

Review of Biochemistry





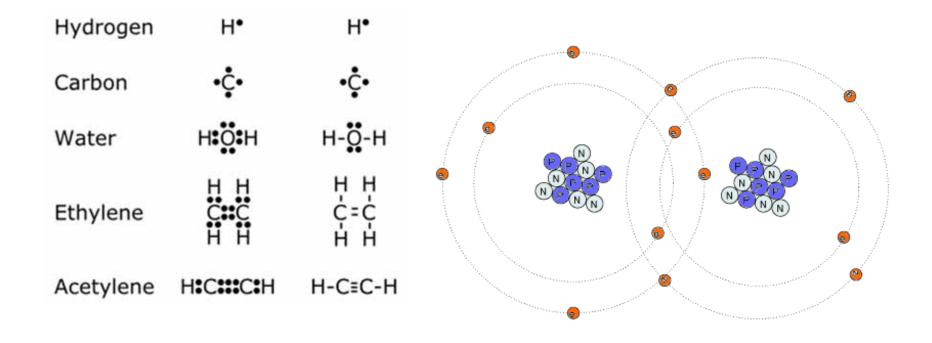
+ Actinide Series

58	59	60	61	62	63	64	65	66	67	68	69	70	71
C (Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
90	91	92	93	94	95	96	97	98	99	100	101	102	103
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Legend - click to find out more... -



Chemical bond

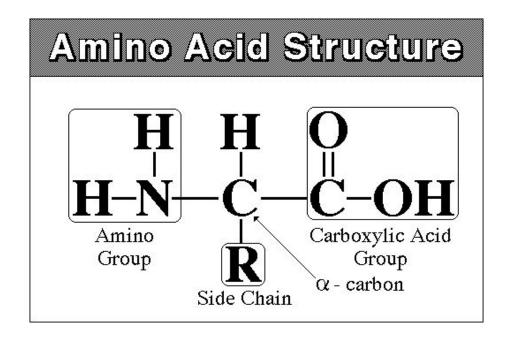


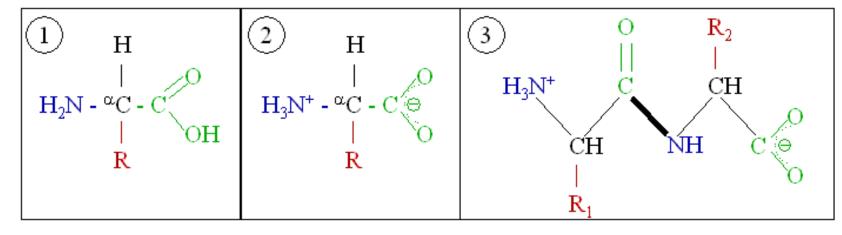
Functional Groups

TABLE 18.1 Functional Groups of Importance in Biochemical Molecules

Functional Group	Structure	Type of Biomolecule Amino acids and proteins (Sections 18.3, 18.7)	
Amino group	-NH ₃ +, -NH ₂		
Hydroxyl group	-ОН	Monosaccharides (carbohydrates) and glycerol: a component of triacylglycerols (lipids) (Sections 22.4, 24.2)	
Carbonyl group	-c-	Monosaccharides (carbohydrates); in acetyl group (CH ₃ CO) used to transfer carbon atoms during catabolism (Sections 22.4, 21.4, 21.8)	
Carboxyl group	о -с-он, -с-о	Amino acids, proteins, and fatty acids (lipids) (Sections 18.3, 18.7, 24.2)	
Amide group	-c-N-	Links amino acids in proteins; formed by reaction of amino group and carboxyl group (Section 18.7)	
Carboxylic acid ester	O -C−O−R	Triacylglycerols (and other lipids); formed by reaction of carboxyl group and hydroxyl group (Section 24.2)	
Phosphates, mono-, di-, tri-	-c-0-r-0-	ATP and many metabolism intermediates (Sections 17.8, 21.5, and throughout metabolism sections)	
	-ç-o-p-o-p-o-		
	-c-o-p-o-p-o-		
Hemiacetal group	-с-он or	Cyclic forms of monosaccharides; formed by a reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.4)	
Acetal group	−C−OR OR	Connects monosaccharides in disaccharides and larger carbohydrates; formed by reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.7, 22.9)	

Amino Acid





COO ⁻ H ₃ N [‡] -C-H CH ₃ Alanine A	COOT H ₃ N-C-H CH H ₃ C CH ₃ Valine V	COO ⁻ H ₃ N-C-H CH ₂ CH H ₃ C CH ₃ Leucine L	ÇOO ⁻ H ₃ N-Ç-H H ₃ C-ÇH CH ₂ CH ₃ Isoleucine	COOT HN-C-H 2HC CH2 CH2 Proline P
COOTH ₃ N-C-H CH ₂ CH ₂ S CH ₃	COO- H ₃ N-C-H CH ₂	Ç00⁻ H ₃ H-Ç-H ÇH ₂ C C C	COOT H ₃ N-C-H H Glycine G	ÇOO ⁻ H ₃ N-C-H CH ₂ OH Serine S
Methionine M COOT H ₃ N-C-H HC-OH CH ₃ Threonine	Phenylalar COOT H ₃ N-C-H CH ₂ SH Cysteine	COO- H3N-C-H CH2	COO ⁻ H ₃ N ⁻ C-H CH ₂ CH ₂ CH ₂ O ^C NH ₂ Glutamine Q	COOTH3N-C-H CH2 OH Tyrosine Y
COOTH ₃ N-C-H CH ₂ OOOTOT	COOTH3N-C-H CH2 CH2 CH2 CH2 CH2 CH2 CH2 CH2 CH2 CH	COOTH3N-C-H CH2 CH2 CH2 CH2 CH2 CH2 CH2 CH2 TNH3	COOTH ₃ N-C-H CH ₂ CH ₂ CH ₂ NH	H ₃ N-C-H CH ₂ HC=C HN NH
D	E	Lysine K	Arginine R	Histidine H

Small

Nucleophilic

Glycine (Gly, G) MW: 57.05

Alanine (Ala, A) MW: 71.09

Serine (Ser, S) MW: 87.08, pK a ~ 16

Threonine (Thr, T) MW: 101.11, pK_a ~ 16

Cysteine (Cys, C) MW: 103.15, $pK_a = 8.35$

Hydrophobic

Valine (Val, V) MW: 99.14

Leucine (Leu, L) MW: 113.16

Isoleucine (IIe, I) MW: 113.16

Methionine (Met, M) MW: 131.19

Proline (Pro, P) MW: 97.12

Aromatic

Phenylalanine (Phe, F) MW: 147.18

Tyrosine (Tyr, Y) MW: 163.18

H₂N

Tryptophan (Trp, W) MW: 186.21

ΗN

Acidic

Aspartic Acid (Asp, D) MW: 115.09, pK a = 3.9

Glutamic Acid (Glu, E) MW: 129.12, pK a = 4.07

Amide

Asparagine (Asn, N) MW: 114.11

 H_2N COOH

Glutamine (Gln, Q)

MW: 128.14

 H_2N COOH. Histidine (His, H)

MW: 137.14, $pK_a = 6.04$

Basic

 NH_3 + COOH H_2N

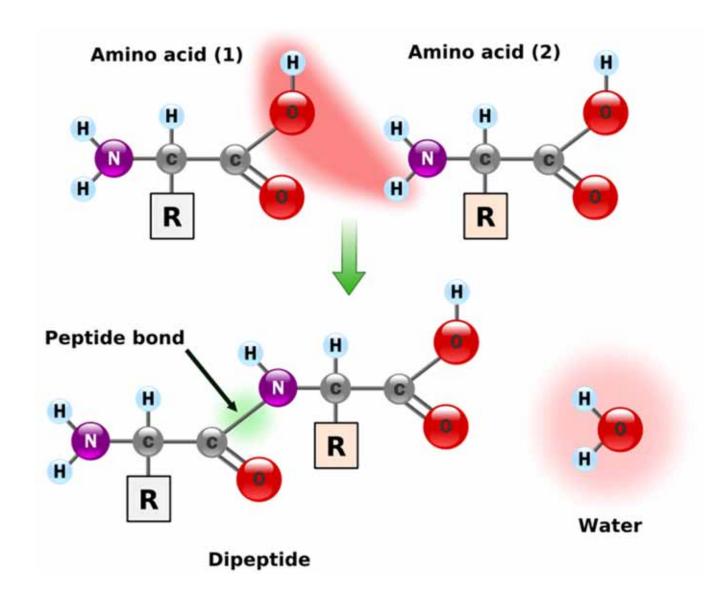
Lysine (Lys, K) MW: 128.17, pK a = 10.79

Arginine (Arg, R) MW: 156.19, $pK_a = 12.48$

Protein Structure and Function

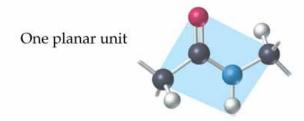
- Proteins are polymers of amino acids.
- Each amino acids in a protein contains a amino group, -NH₂, a carboxyl group, -COOH, and an R group, all bonded to the central carbon atom. The R group may be a hydrocarbon or they may contain functional group.
- All amino acids present in a proteins are α -amino acids in which the amino group is bonded to the carbon next to the carboxyl group.
- Two or more amino acids can join together by forming amide bond, which is known as a *peptide bond* when they occur in proteins.

Peptide bond



Primary Protein Structure

• Primary structure of a proteins is the sequence of amino acids connected by peptide bonds. Along the backbone of the proteins is a chain of alternating peptide bonds and α-carbons and the amino acid side chains are connected to these Planar units along a protein chain



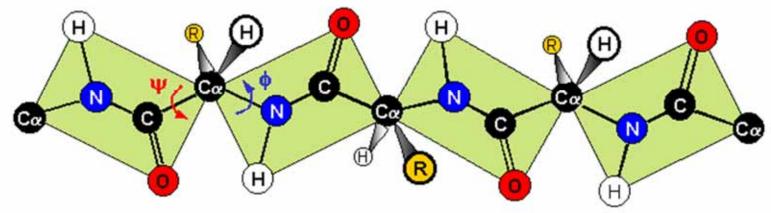
 By convention, peptides and proteins are always written with the amino terminal amino acid (Nterminal) on the left and carboxylterminal amino acid (C-terminal) on the right.

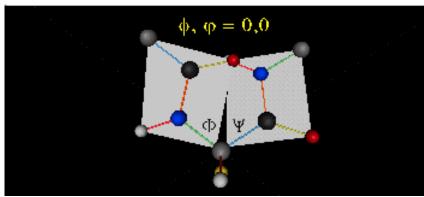
 $N \longrightarrow C$

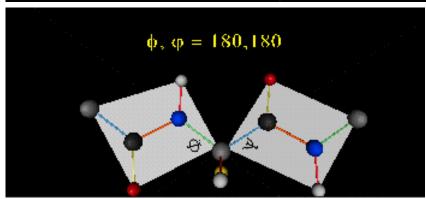
Secondary Protein Structure

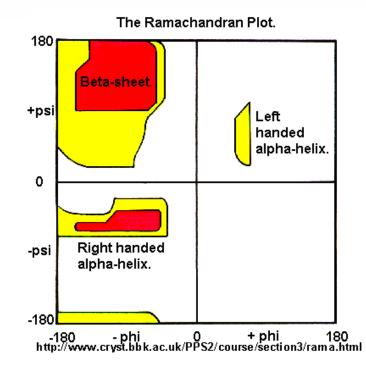
- Secondary structure of a protein is the arrangement of polypeptide backbone of the protein in space. The secondary structure includes two kinds of repeating pattern known as the α -helix and β -sheet.
- Hydrogen bonding between backbone atoms are responsible for both of these secondary structures.

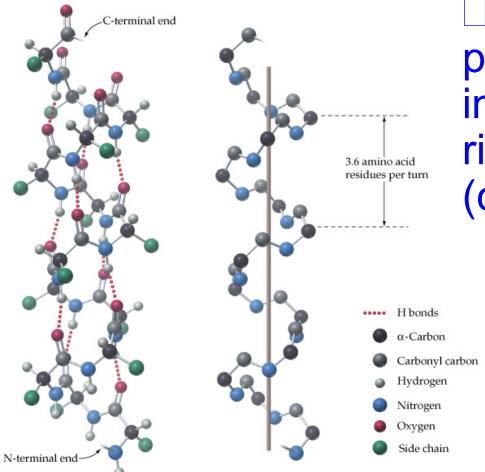
FULLY EXTENDED POLYPEPTIDE CHAIN





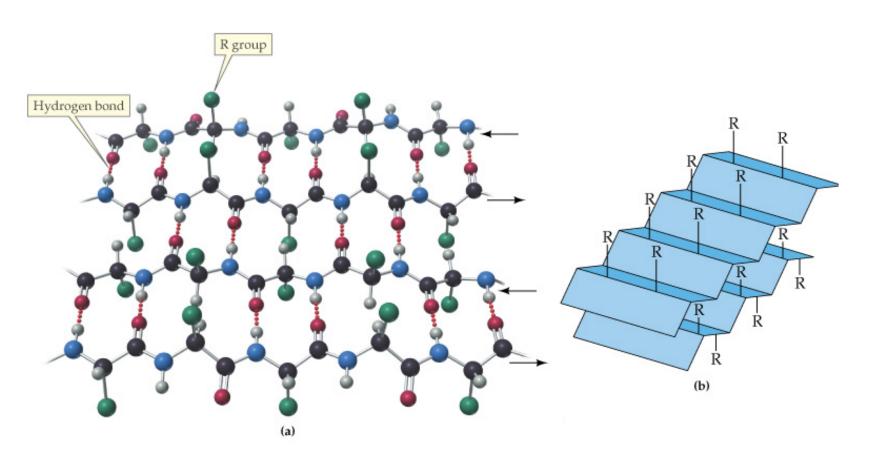


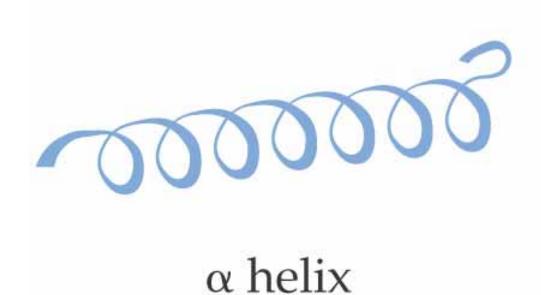


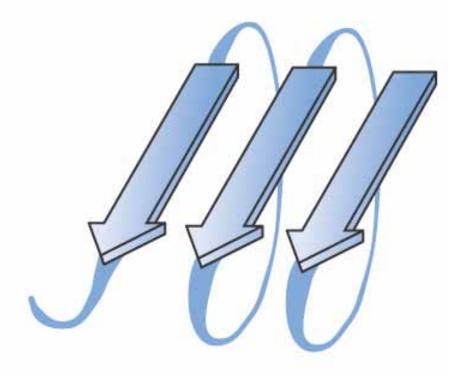


□α-Helix: A single protein chain coiled in a spiral with a right-handed (clockwise) twist.

 $\Box \beta$ -Sheet: The polypeptide chain is held in place by hydrogen bonds between pairs of peptide units along neighboring backbone segments.







β sheet

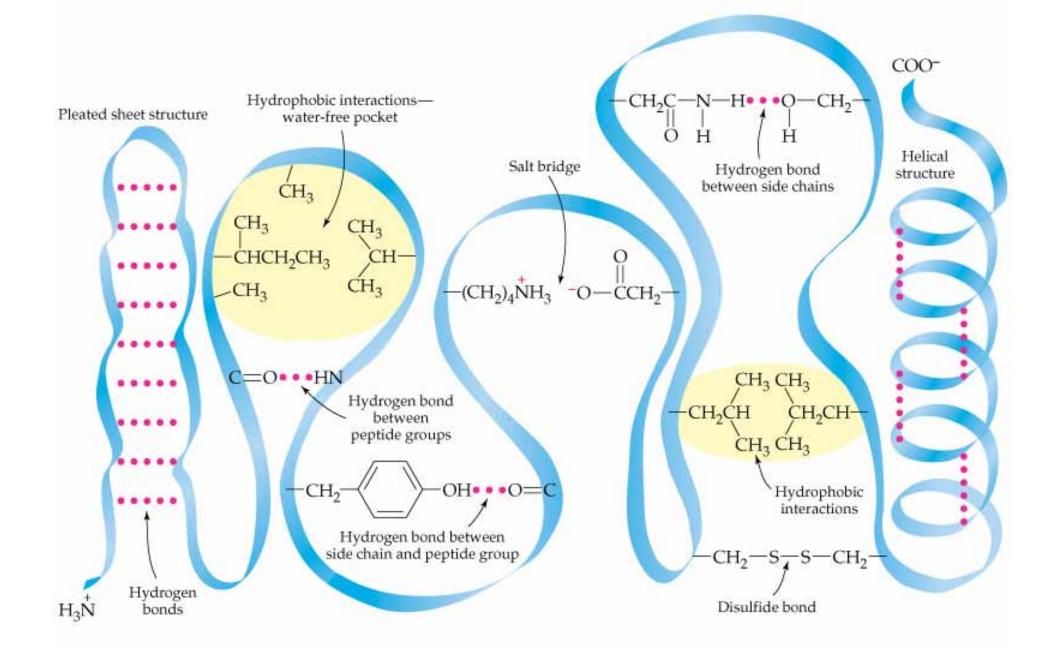
Tertiary Protein Structure

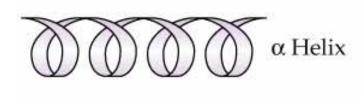
- Tertiary Structure of a proteins The overall three dimensional shape that results from the folding of a protein chain. Tertiary structure depends mainly on attractions of amino acid side chains that are far apart along the same backbone. Non-covalent interactions and disulfide covalent bonds govern tertiary structure.
- •A protein with the shape in which it exist naturally in living organisms is known as a native protein.

Shape-Determining Interactions in Proteins

•The essential structure-function relationship for each protein depends on the polypeptide chain being held in its necessary shape by the interactions of atoms in the side chains.

- Protein shape determining interactions are summarized below:
- Hydrogen bond between neighboring backbone segments.
- Hydrogen bonds of side chains with each other or with backbone atoms.
- lonic attractions between side chain groups or salt bridge.
- Hydrophobic interactions between side chain groups.
- Covalent sulfur-sulfur bonds.

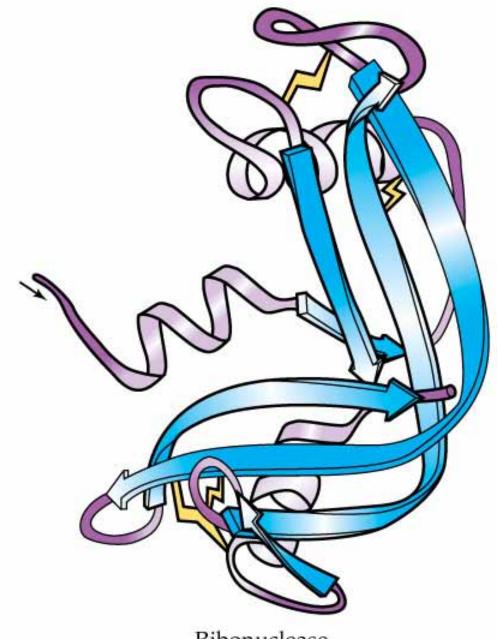




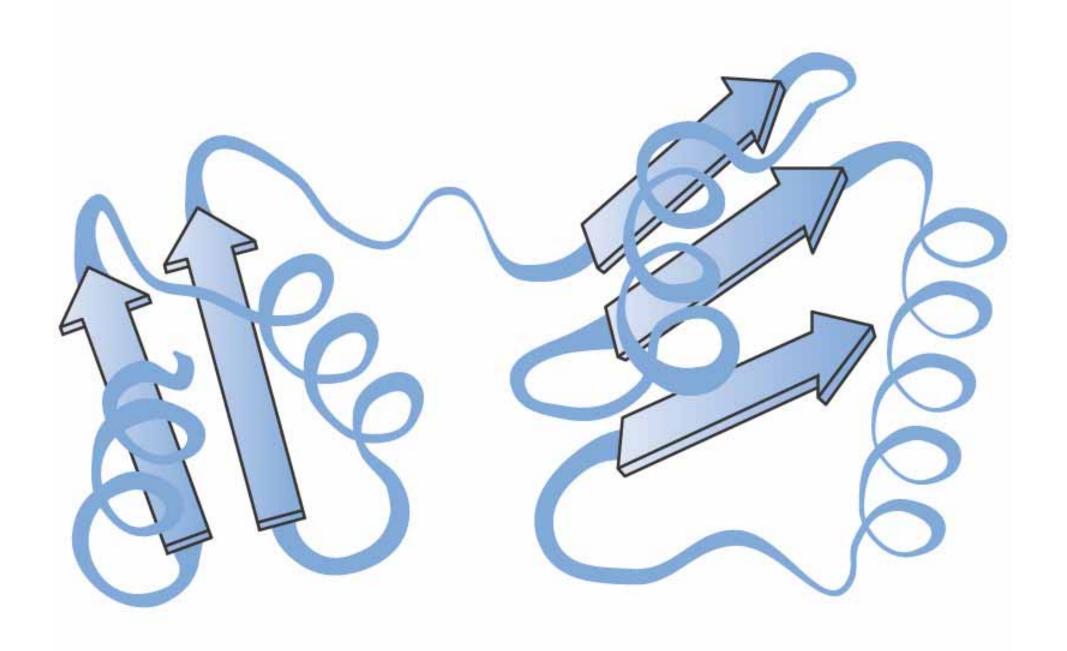


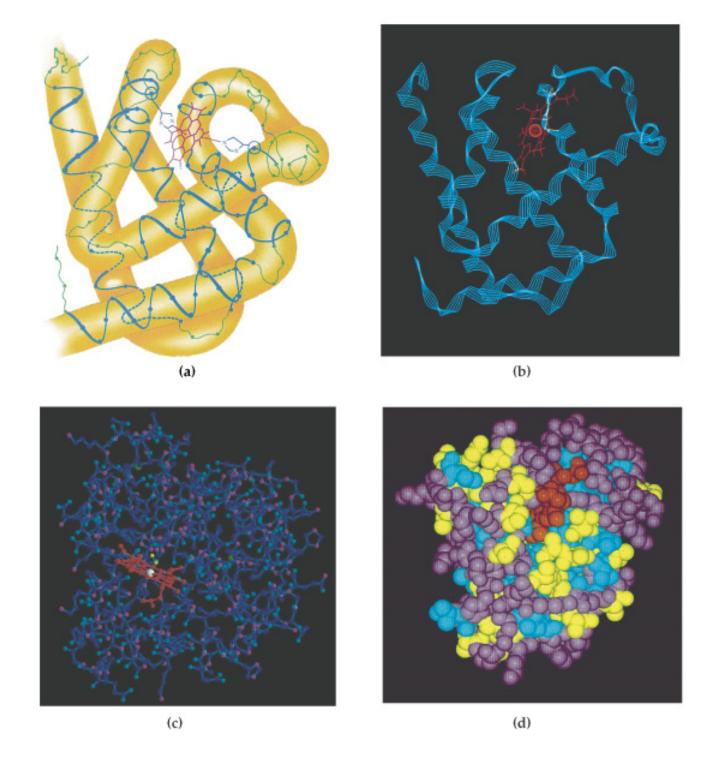






Ribonuclease

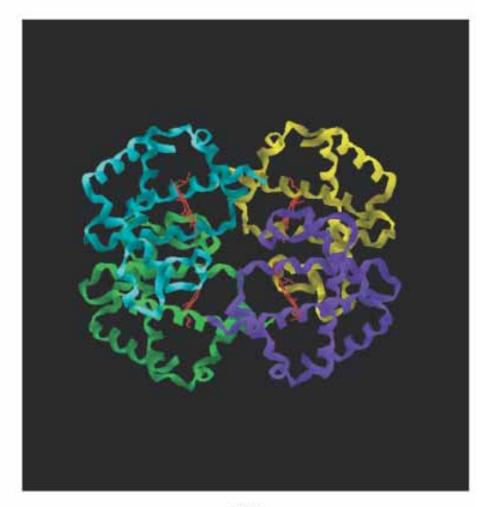




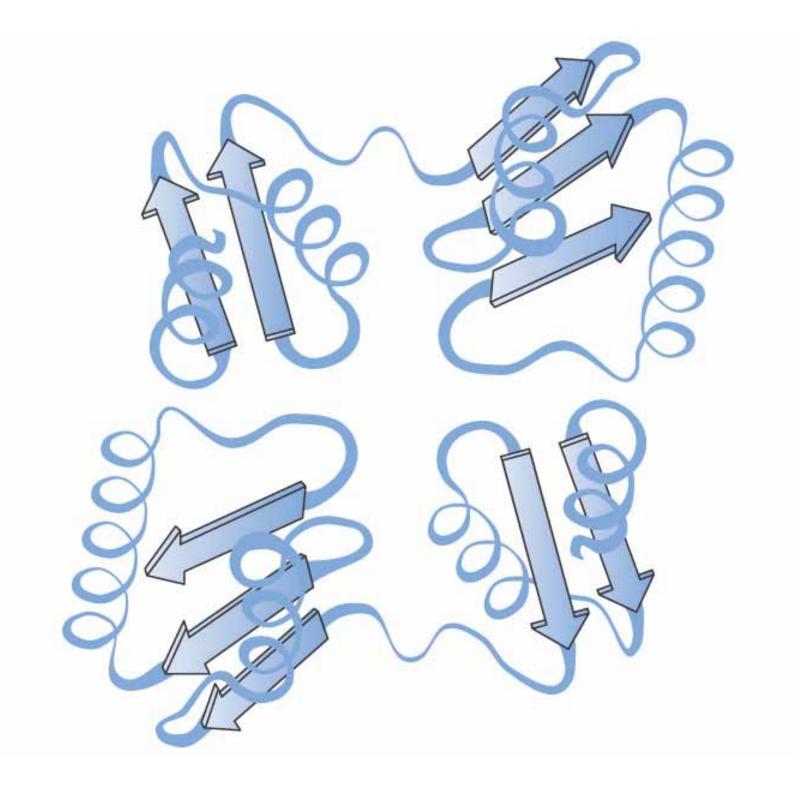
Quaternary Protein Structure

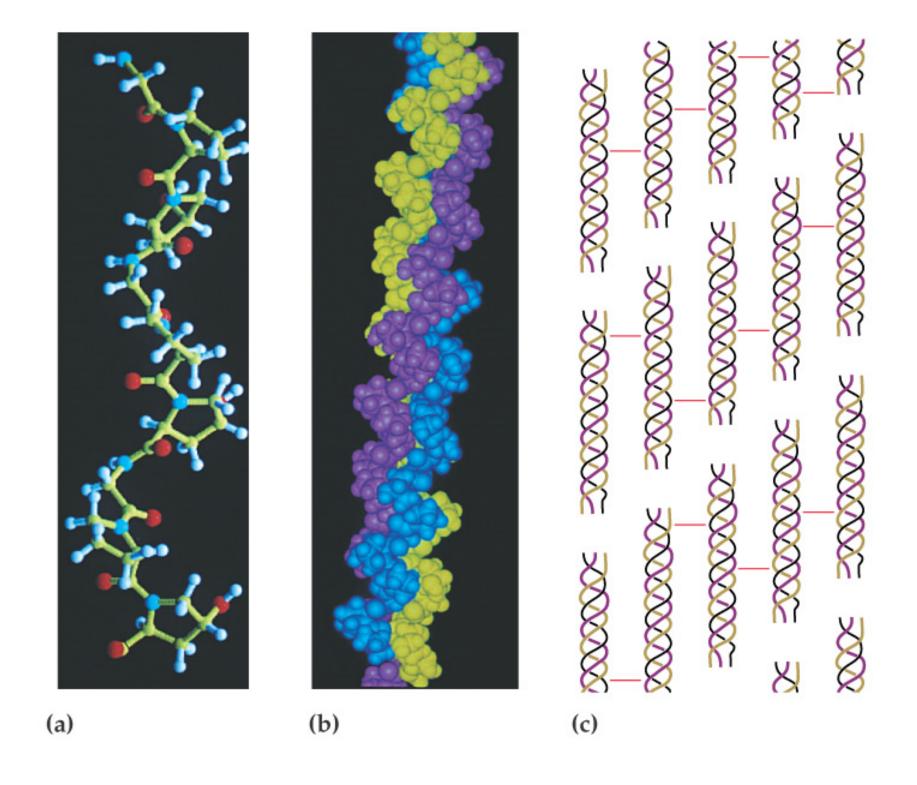
• Quaternary protein structure: The way in which two or more polypeptide sub-units associate to form a single three-dimensional protein unit. Non-covalent forces are responsible for quaternary structure essential to the function of proteins.

$$H_2C=CH$$
 CH_3
 H_3C
 N
 N
 CH_2
 CH_2
 CH_2COOH
 CH_2COOH
(a)



(b)





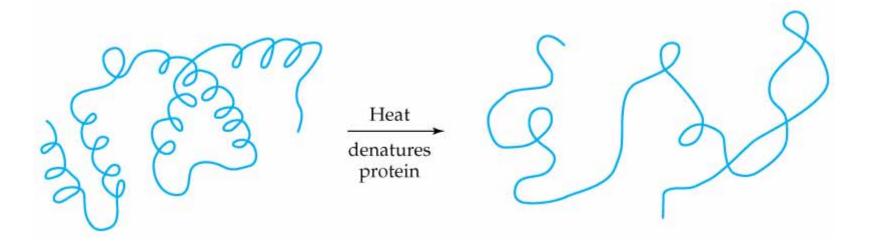
Chemical Properties of Proteins

 Protein hydrolysis: In protein hydrolysis, peptide bonds are hydrolyzed to yield amino acids. This is reverse of protein formation.



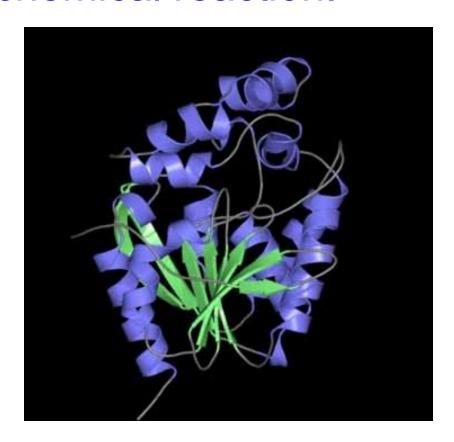


 Protein denaturation: The loss of secondary, tertiary, or quaternary protein structure due to disruption of non-covalent interactions and or disulfide bonds that leaves peptide bonds and primary

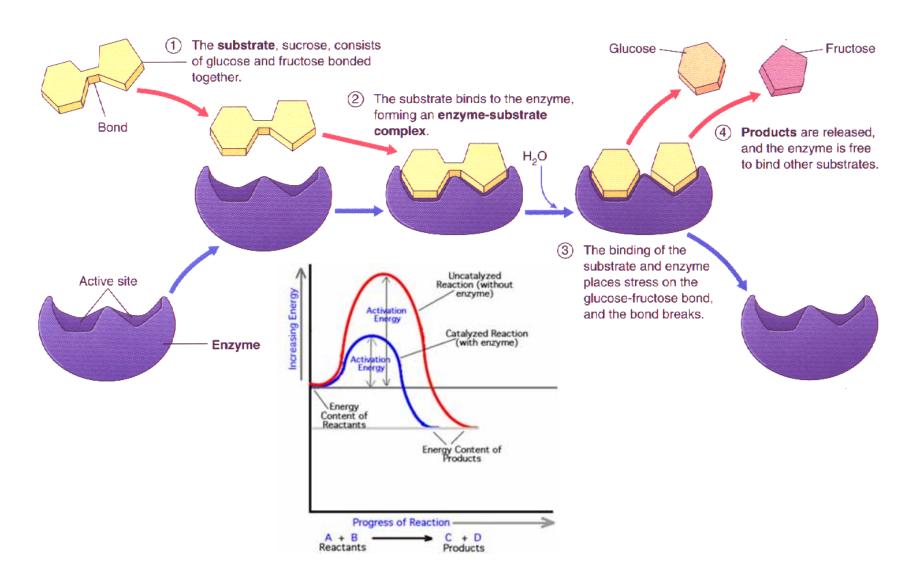


Catalysis by Enzymes

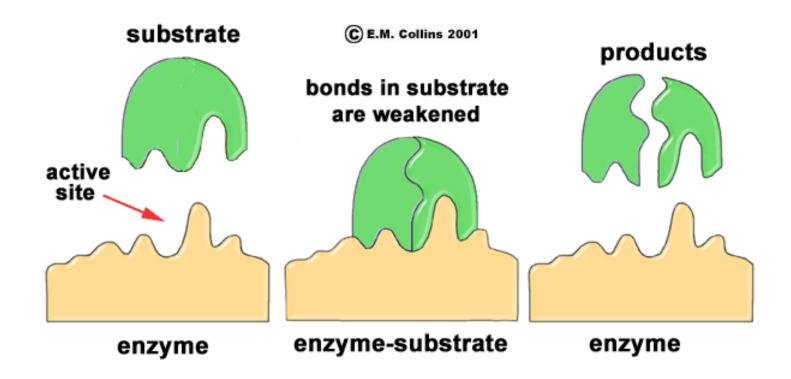
 Enzyme A protein that acts as a catalyst for a biochemical reaction.



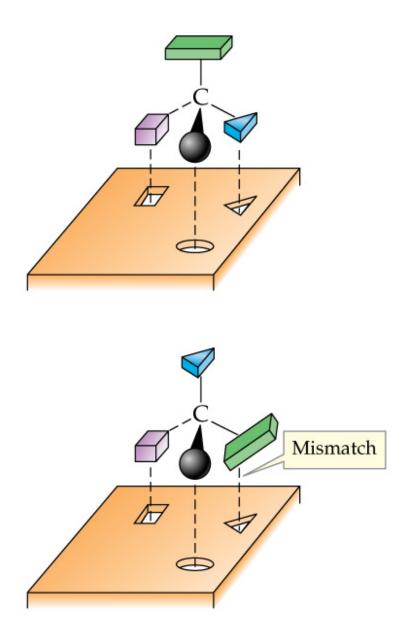
Enzymatic Reaction



Specificity



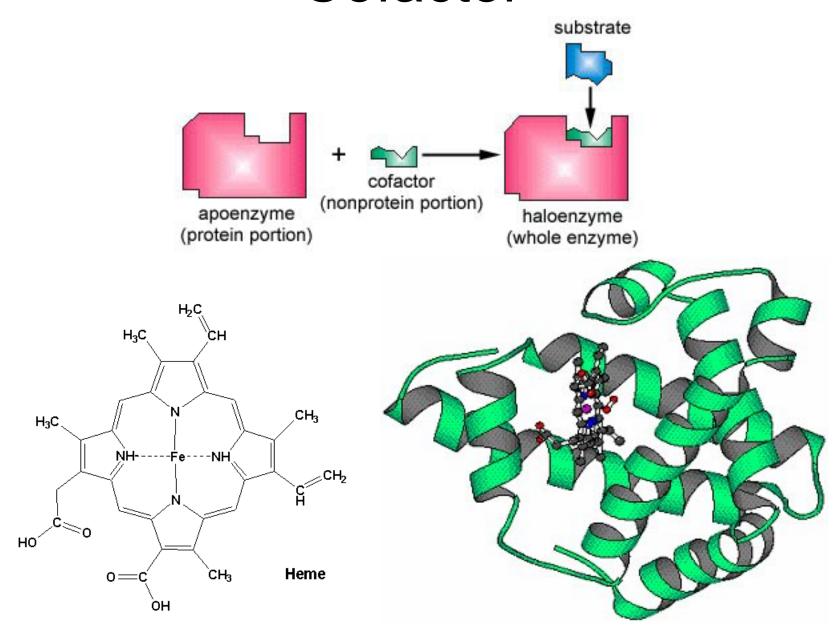
The specificity of an enzyme for one of two enantiomers is a matter of fit. One enantiomer fits better into the active site of the enzyme than the other enantiomer. Enzyme catalyzes reaction of the enantiomer that fits better into the active site of the enzyme.



Enzyme Cofactors

- Many enzymes are conjugated proteins that require nonprotein portions known as cofactors.
- Some cofactors are metal ions, others are nonprotein organic molecules called coenzymes.
- An enzyme may require a metal-ion, a coenzyme, or both to function.

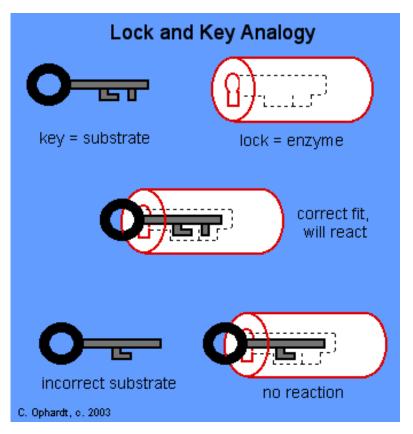
Cofactor

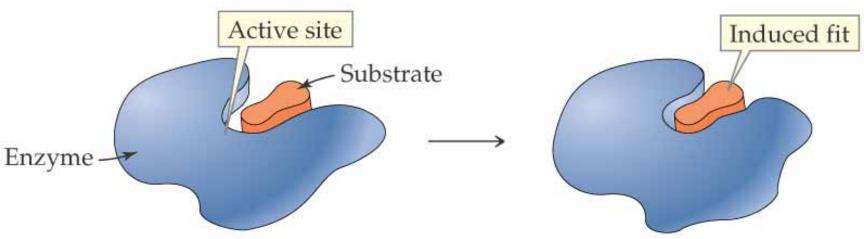


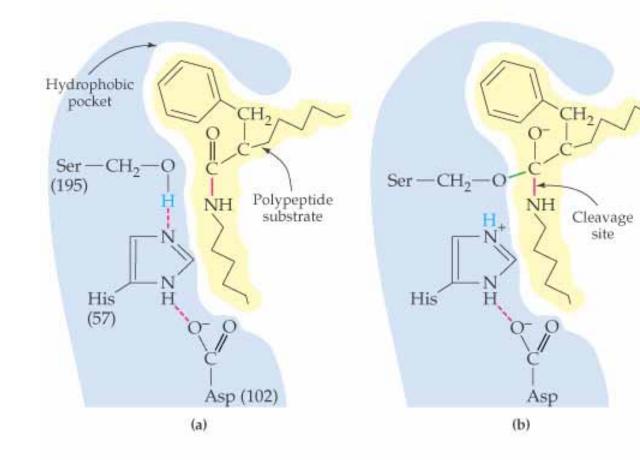
- Cofactors provide additional chemically active functional groups which are not present in the side chains of amino acids that made up the enzyme.
- Metal ions may anchor a substrate in the active site or may participate in the catalyzed reaction.

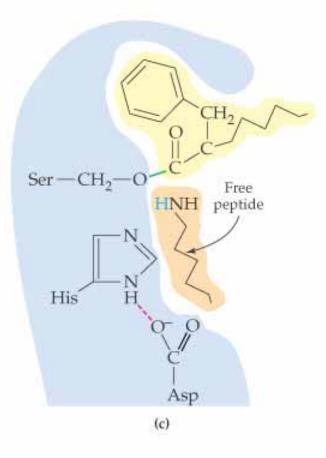
How Enzyme Work

- Two modes are invoked to represent the interaction between substrate and enzymes. These are:
- Lock-and-key model: The substrate is described as fitting into the active site as a key fit into a lock.
- Induced-fit-model: The enzyme has a flexible active site that changes shape to accommodate the substrate and facilitate the reaction.









19.5 Effect of Concentration on Enzyme Activity

- •Variation in concentration of enzyme or substrate alters the rate of enzyme catalyzed reactions.
- Substrate concentration: At low substrate concentration, the reaction rate is directly proportional to the substrate concentration. With increasing substrate concentration, the rate drops off as more of the active sites are occupied.

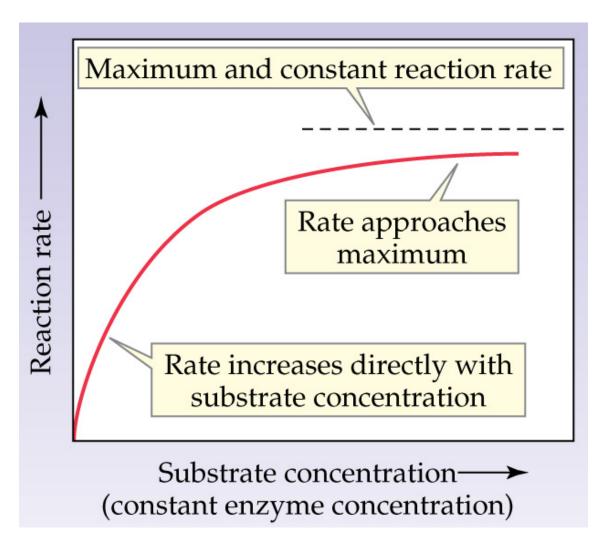
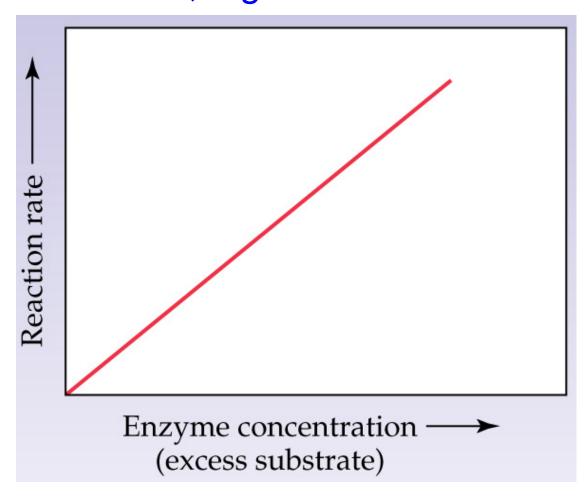


Fig 19.5 Change of reaction rate with substrate concentration when enzyme concentration is constant.

• Enzyme concentration: The reaction rate varies directly with the enzyme concentration as long as the substrate concentration does not become a limitation, Fig 19.6 below.



19.6 Effect of Temperature and pH on Enzyme Activity

- •Enzymes maximum catalytic activity is highly dependent on temperature and pH.
- Increase in temperature increases the rate of enzyme catalyzed reactions. The rates reach a maximum and then begins to decrease. The decrease in rate at higher temperature is due to denaturation of enzymes.

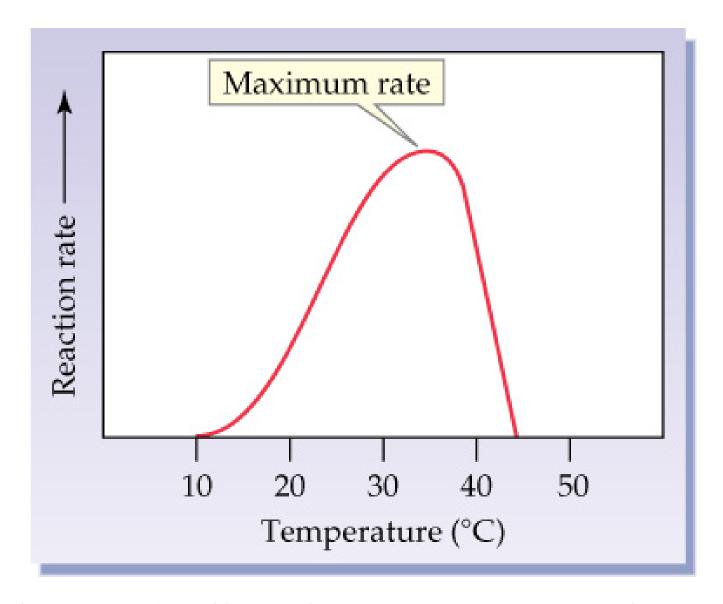
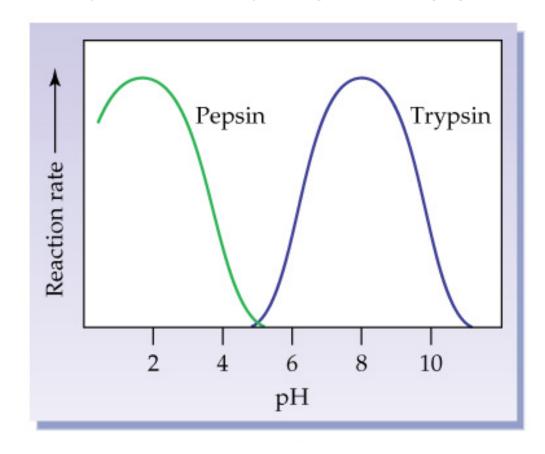


Fig 19.7 (a) Effect of temperature on reaction rate

• Effect of pH on Enzyme activity: The catalytic activity of enzymes depends on pH and usually has a well defined optimum point for maximum catalytic activity Fig 19.7 (b) below.



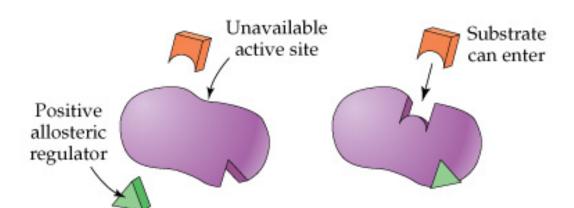
19.7 Enzyme Regulation: Feedback and Allosteric Control

- •Concentration of thousands of different chemicals vary continuously in living organisms which requires regulation of enzyme activity.
- •Any process that starts or increase the activity of an enzyme is *activation*.
- •Any process that stops or slows the activity of an enzyme is *inhibition*.

Two of the mechanism

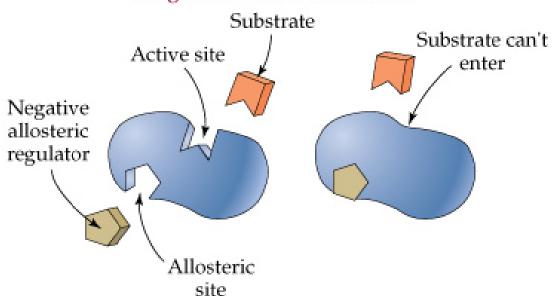
- Feedback control: Regulation of an enzyme's activity by the product of a reaction later in a pathway.
- Allosteric control: Activity of an enzyme is controlled by the binding of an activator or inhibitor at a location other than the active site. Allosteric controls are further classified as positive or negative.
 - A positive regulator changes the activity site so that the enzyme becomes a better catalyst and rate accelerates.
 - A negative regulator changes the activity site so that the enzyme becomes less effective catalyst and rate slows down.

Positive allosteric control



A positive regulator changes the activity site so that the enzyme becomes a better catalyst and rate accelerates.

Negative allosteric control



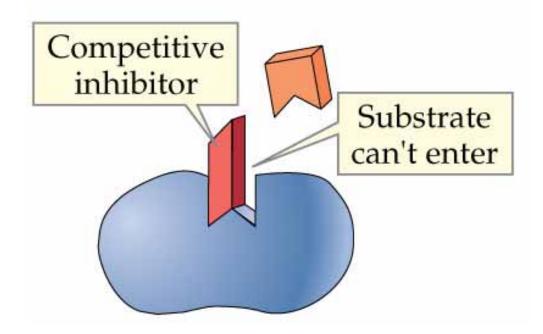
A negative regulator changes the activity site so that the enzyme becomes less effective catalyst and rate slows down.

19.8 Enzyme Regulation: Inhibition

- The inhibition of an enzyme can be reversible or irreversible.
- In reversible inhibition, the inhibitor can leave, restoring the enzyme to its uninhibited level of activity.
- In *irreversible inhibition*, the inhibitor remains permanently bound to the enzyme and the enzyme is permanently inhibited.

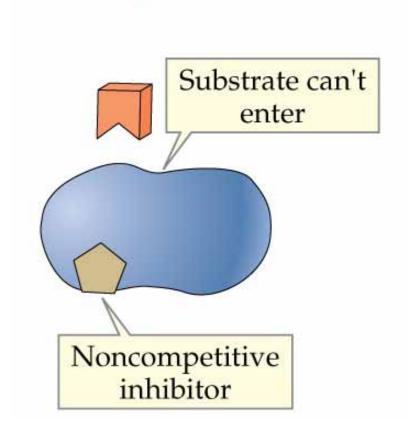
- Inhibitions are further classified as:
- Competitive inhibition if the inhibitor binds to the active site.

Competitive inhibition

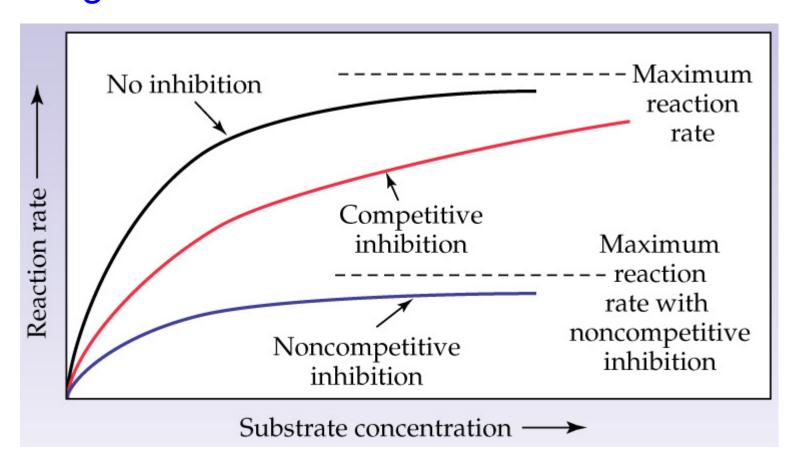


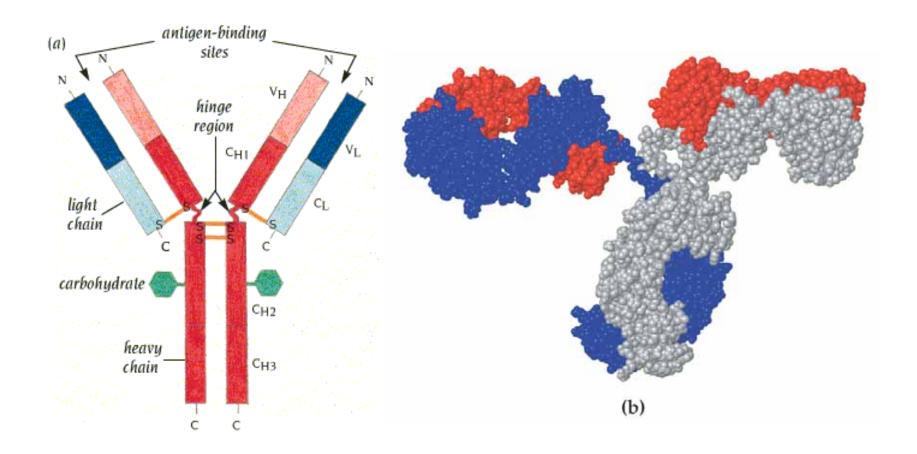
 Noncompetitive inhibition, if the inhibitor binds elsewhere and not to the active site.

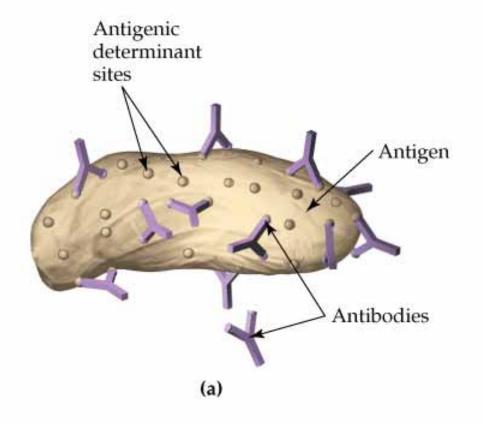
Noncompetitive inhibition

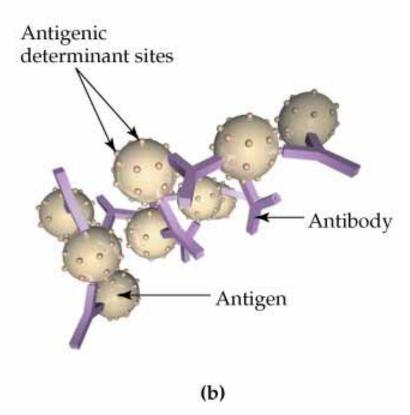


•The rates of enzyme catalyzed reactions with or without a competitive inhibitor are shown in the Fig 19.9 below.





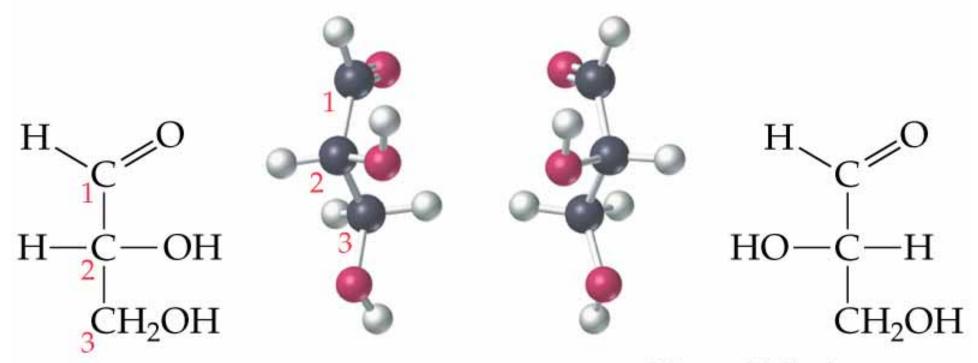




An Introduction to Carbohydrates

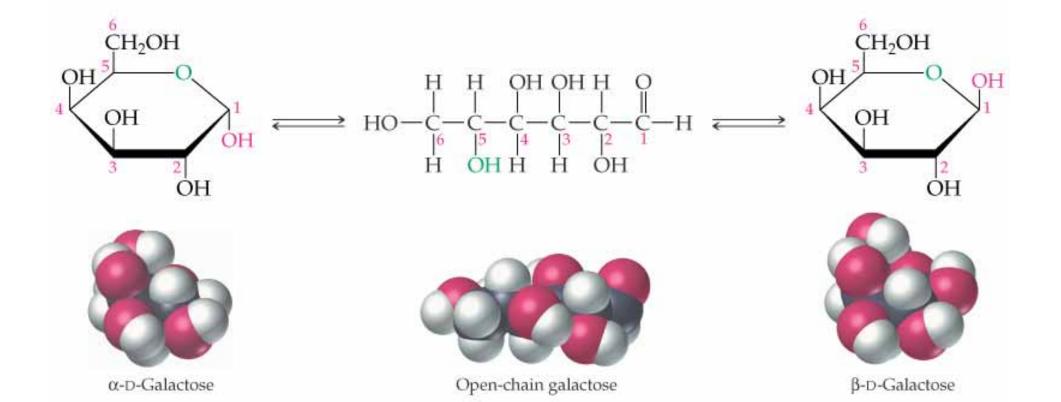
- Carbohydrates are a large class of naturally occurring polyhydroxy aldehydes and ketones.
- Monosaccharides also known as simple sugars, are the simplest carbohydrates containing 3-7 carbon atoms.
- sugar containing an aldehydes is known as an aldose.
- sugar containing a ketones is known as a ketose.

- The number of carbon atoms in an aldose or ketose may be specified as by tri, tetr, pent, hex, or hept. For example, glucose is aldohexose and fructose is ketohexose.
- Monosaccharides react with each other to form disaccharides and polysaccharides.
- Monosaccharides are chiral molecules and exist mainly in cyclic forms rather than the straight chain.

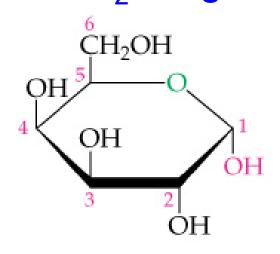


D-Glyceraldehyde Right-handed

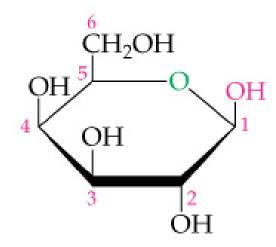
L-Glyceraldehyde Left-handed



• Anomers: Cyclic sugars that differs only in positions of substituents at the hemiacetal carbon; the α -form has the –OH group on the opposite side from the –CH₂OH; the β -form the –OH group on the same side as the –CH₂OH group.



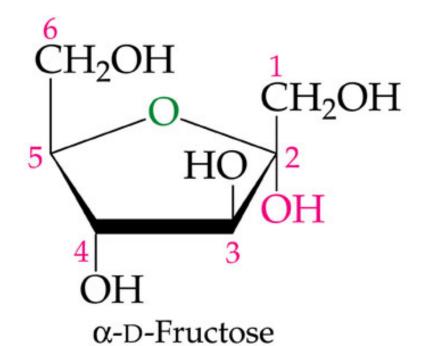
α-D-Galactose

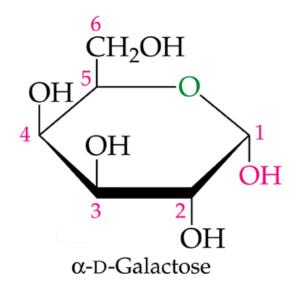


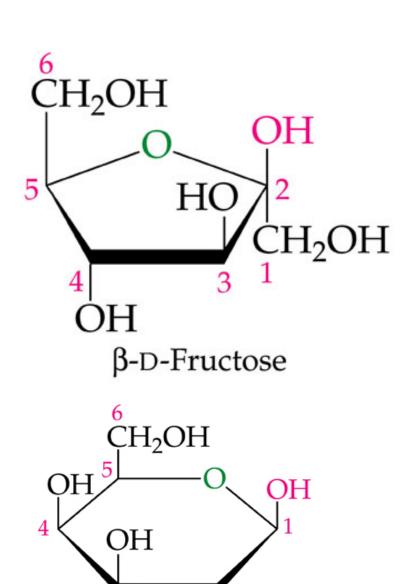
β-D-Galactose

Some Important Monosaccharides

Monosaccharides are generally high-melting, white, crystalline solids that are soluble in water and insoluble in nonpolar solvents. Most monosaccharides are sweet tasting, digestible, and nontoxic.



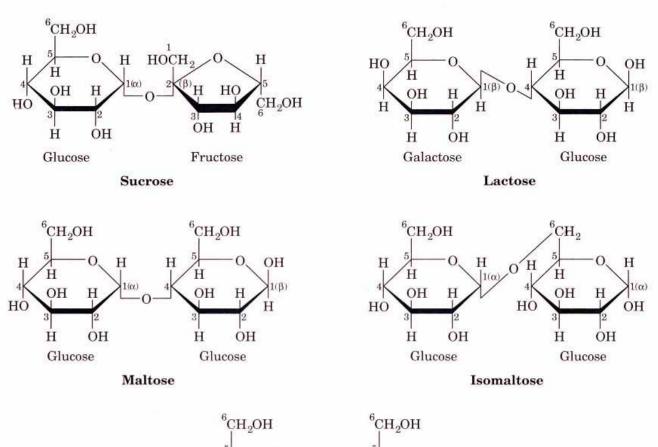




ÓН

 β -D-Galactose

Some Common Disaccharides



Cellobiose

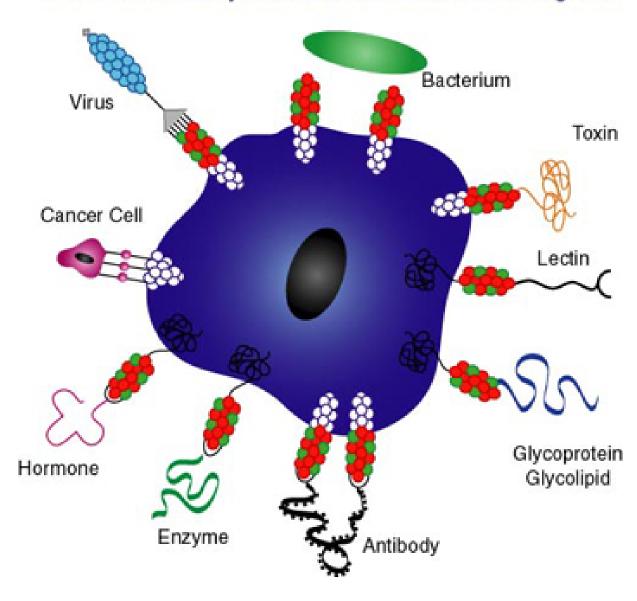
Polysaccharides

Sometimes shown as

Cellulose

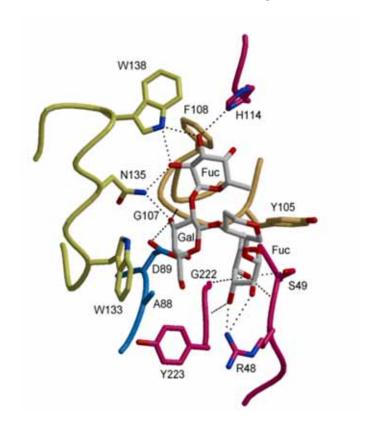
Reducing end

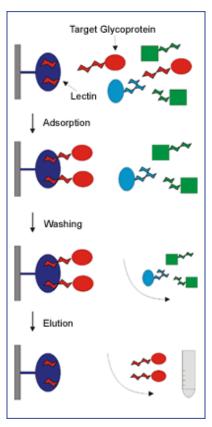
Cell-Surface Carbohydrates Involved in Molecular Recognition



Lectin

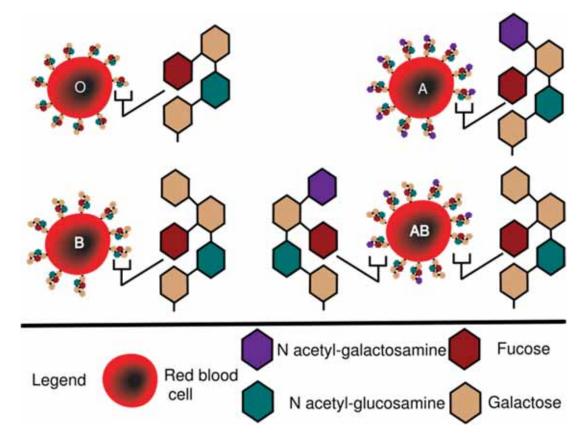
Lectins are sugar-binding proteins which are highly specific for their sugar moieties. They typically play a role in biological recognition phenomena involving cells and proteins. For example, some bacteria use lectins to attach themselves to the cells of the host organism during infection.



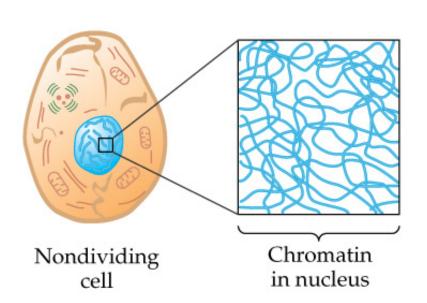


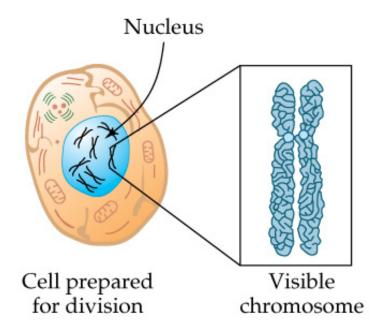
Blood Type

I				
	Group A	Group B	Group AB	Group O
Red blood cell type	P		AB	
Antibodie present	s Anti-B	Anti-A	None	Anti-A and Anti-B
Antigens present	A antigen	† B antigen	A and B antigens	No antigens

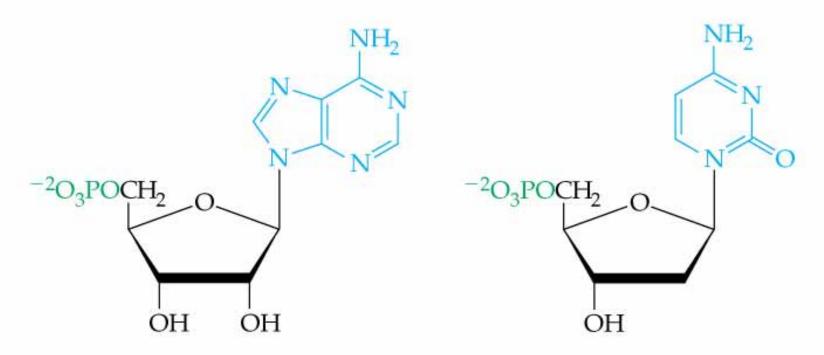


DNA





- •In RNA, the sugar is ribose.
- •In DNA, the sugar is deoxyribose.



Adenosine 5'-monophosphate (AMP) (a ribonucleotide)

Deoxycytidine 5'-monophosphate (dCMP) (a deoxyribonucleotide)

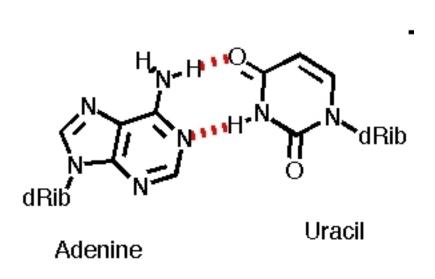
Base

cytosine

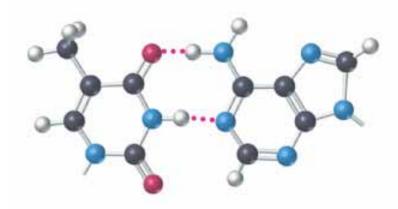
Purines

Pyrimidines

thymine



Thymine-Adenine



$$\begin{array}{c|c}
 & H \\
 & O.29 \text{ nm} \\
 & O.29$$

Cytosine-Guanine

