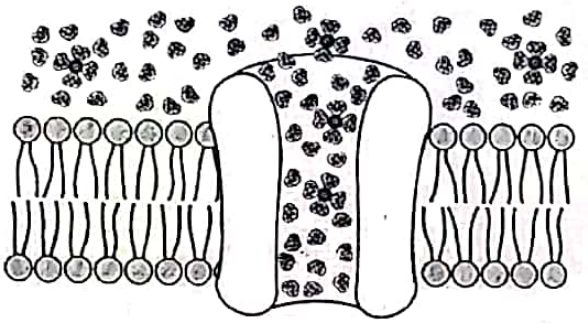
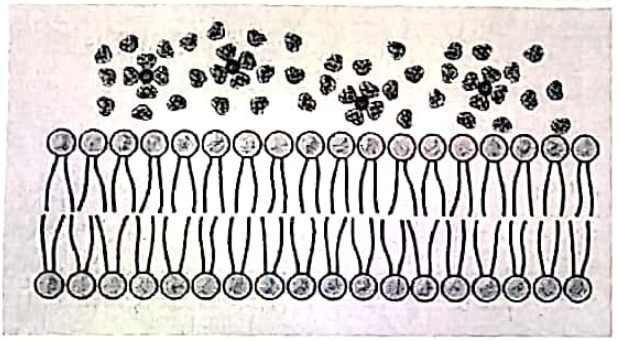
Ion channel structure and gating function

Ion Channels Provide a Polar Environment for Diffusion of Ions Across the Membrane



Ions Cannot Diffuse Across the Hydrophobic Barrier of the Lipid B



- Mediate the generation, conduction and transmission of electrical signals in the nervous system
- Control the release of neurotransmitters and hormones
- Initiate muscle contraction
- Transfer small molecules between cells (gap junctions)
- Mediate fluid transport in secretory cells
- Control motility of growing and migrating cells
- Provide selective permeability properties important for various

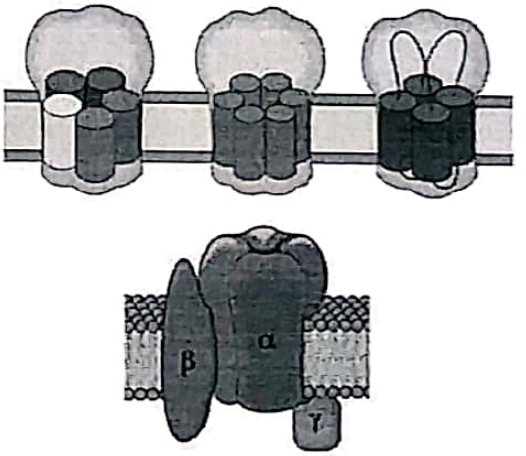
Conduction

❖Ion channels conduct up to 10^8 Ions/sec

❖Ion Channels Act As Catalysts

- Speed up fluxes
- Do not impart energy
- Driving force is provided by electrochemical potential

Channels are Made Up of Subunits



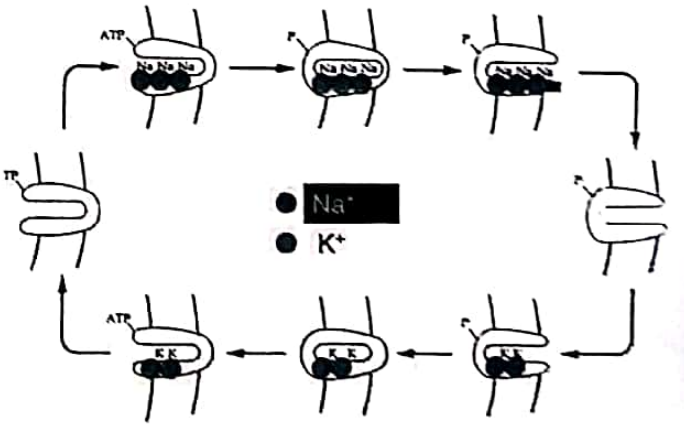
Conduction

❖Ion channels conduct up to 10^8 Ions/sec

❖Ion Channels Act As Catalysts

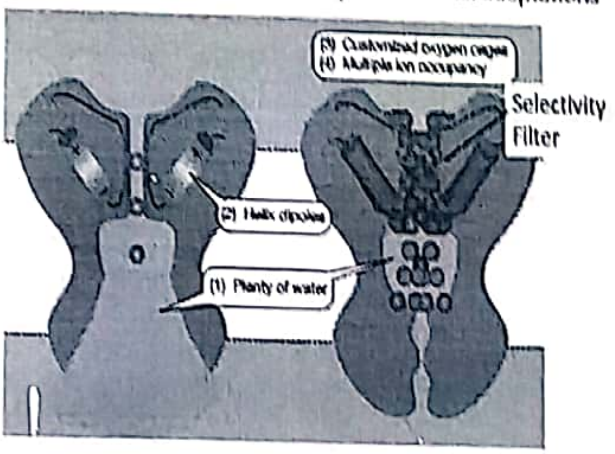
- Speed up fluxes
- Do not impart energy
- Driving force is provided by electrochemical potential

Unlike Channels, Ion Pumps Do Not Provide a Continuous Pathway Through the Membrane



Ion Channels are Selectively Permeable

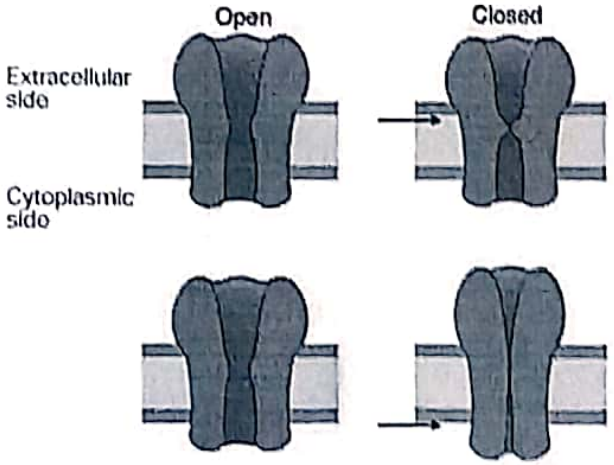
Structure of K^+ channel has multiple functional adaptations



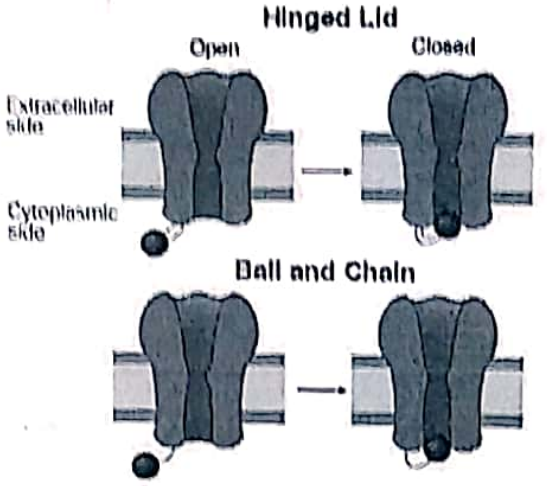
There are two major types of gating actions

1. **Conformational Changes Along the Channel Walls**
2. **Involve Plugging the Channel**

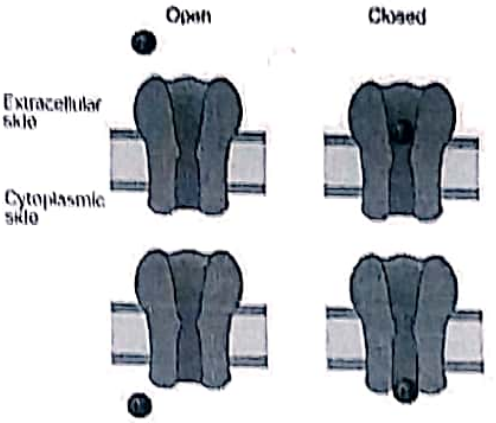
Gating Can Involve Conformational Changes Along the Channel Walls



Gating Can Involve Plugging the Channel

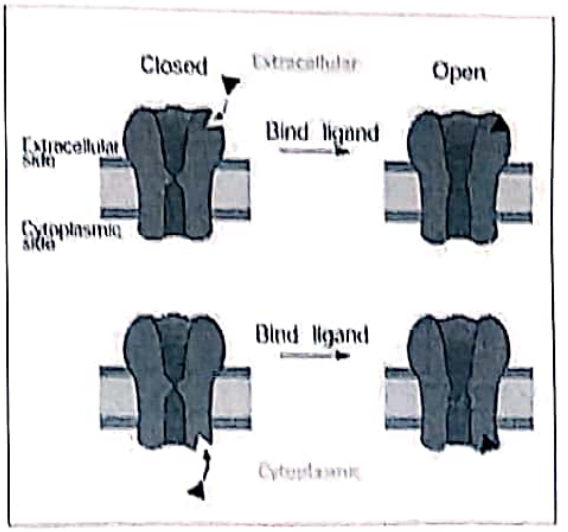


Gating Can Result from Plugging by Cytoplasmic or Extracellular Gating Particles

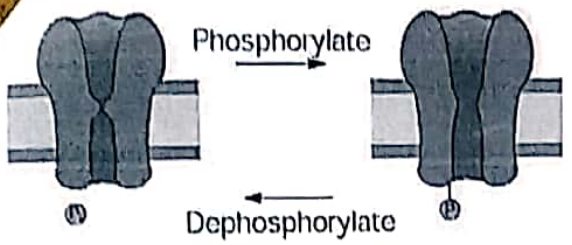


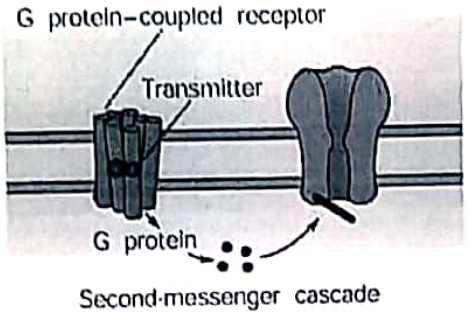
There are Five Types of Gating Controls

a) Ligand Binding

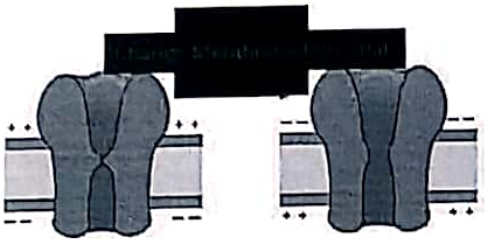


Phosphorylation

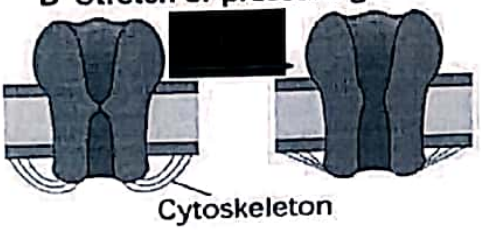




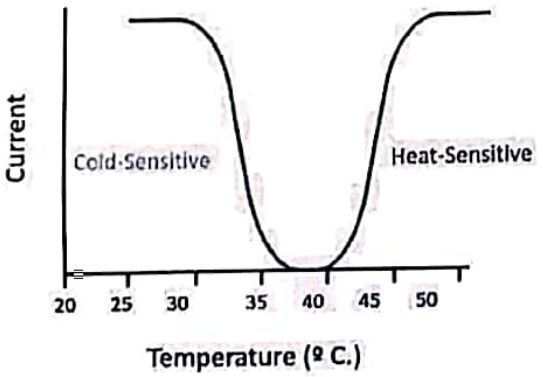
C Voltage-gated



D Stretch or pressure-gated

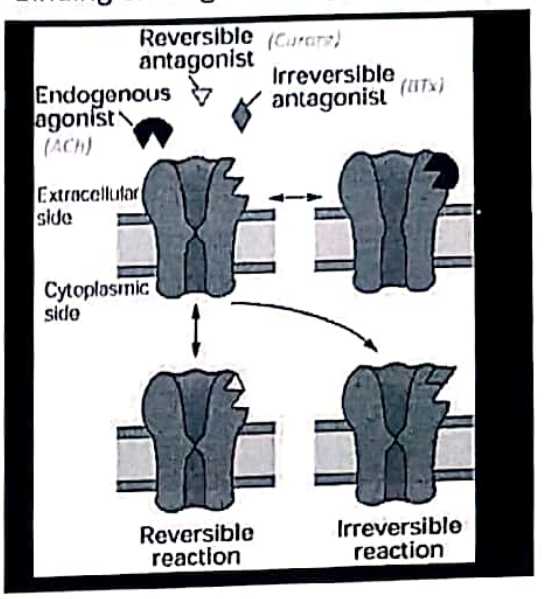


e) Temperature Gated

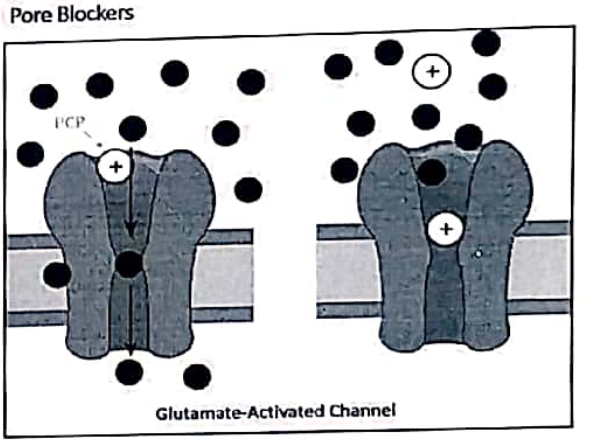


Modifiers of Channel Gating

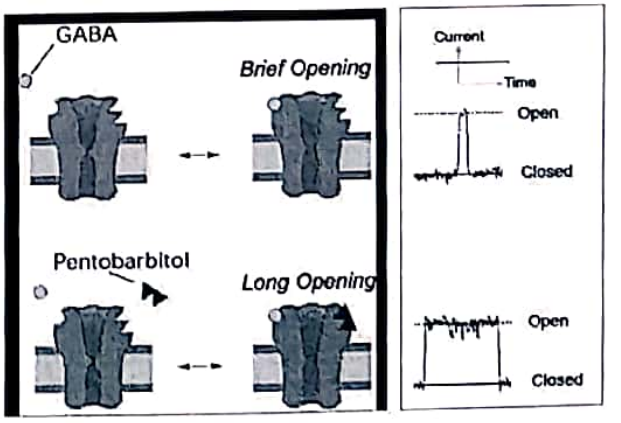
Binding of Exogenous Ligands Can Block Gating



Ion Permeation Can be Prevented by Pore Blockers



Exogenous Modulators Can Modify the Action of Endogenous Regulators



Ion channels have three basic functional properties

- ➢Conduct
- ➢Select
- ➢Gate

❖Evolutionary relationships between ion channels

❖Various factors contribute to ion channel diversity

Ion Channel Gene Superfamilies

I) Channels Activated by Neurotransmitter-Binding (pentameric channel structure):

- •Acetylcholine
- •GABA
- •Glycine
- •Serotonin

II) Channels Activated by ATP or Purine Nucleotide-Binding (quatrameric or trimeric channel structure)

III) Channels With Quatrameric Structure Related to Voltage-Gated, Cation-Permeant Channels:

A) Voltage-gated:
- •K^+ permeant
- •Na^+ permeant
- •Ca^{++} permeant
- •Cation non-specific-permeant

B) Cyclic Nucleotide-Gated (Cation non-specific-permeant)

C) TRP Family (Cation Non-specific). Gated by:
- • Osmolarity
- • pH
- • mechanical force (hearing, etc.)
- • ligand binding
- • temperature

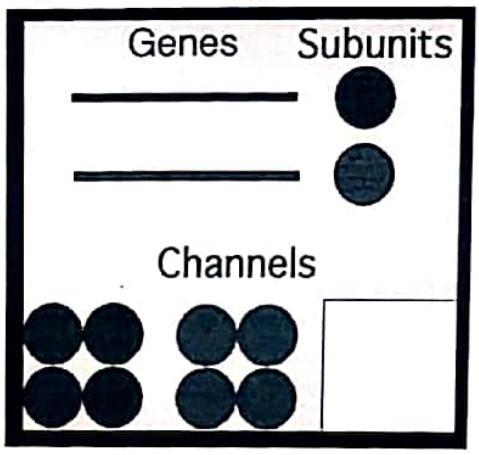
D) Channels Activated by Glutamate-Binding
- -quatrameric channel structure
- -cation non-specific permeability

IV) "CLC" Family of Cl^--Permeant Channels (dimeric structure):

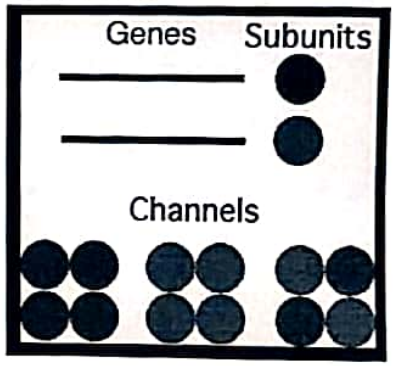
Gated by:
- •Voltage
- •Cell Swelling
- •pH

V) Gap Junction Channels (non-specific permeability; hexameric structure)

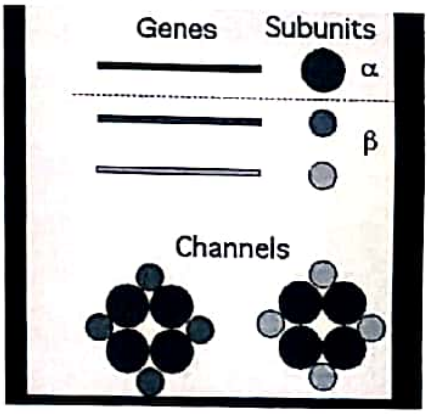
Different Genes Encode Different Pore-Forming Subunits

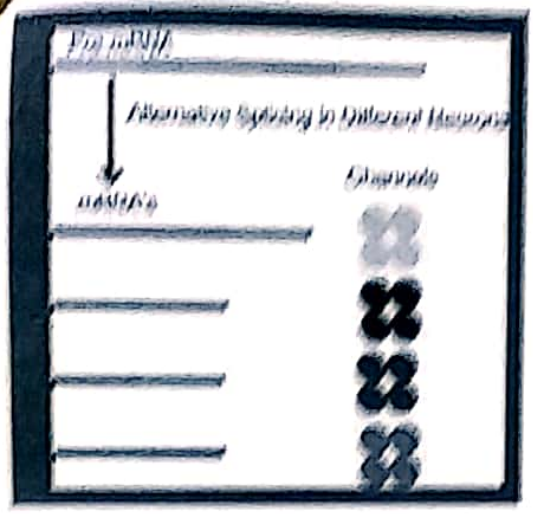


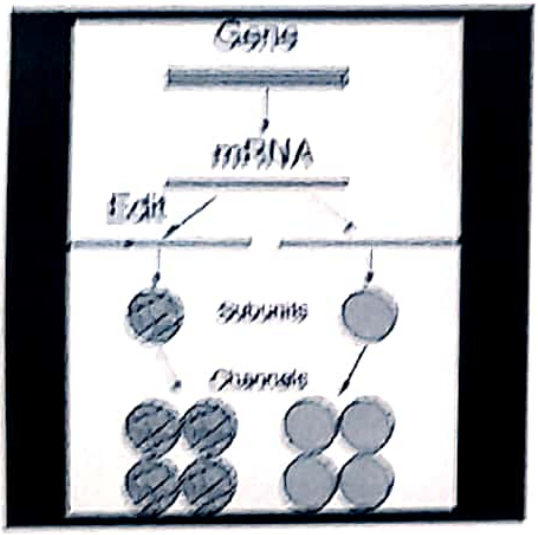
Different Pore-Forming Subunits Combine in Various Combinations

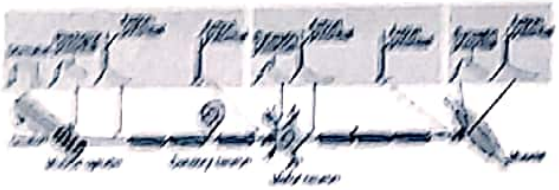


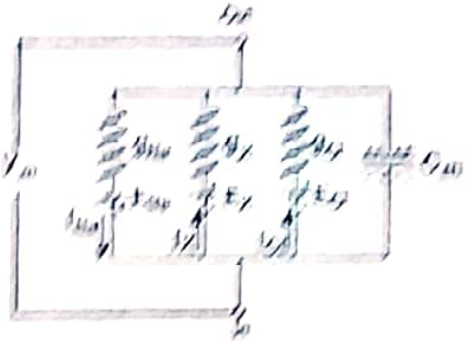
The Same Pore-Forming Subunits Can Combine with Different Accessory Subunits



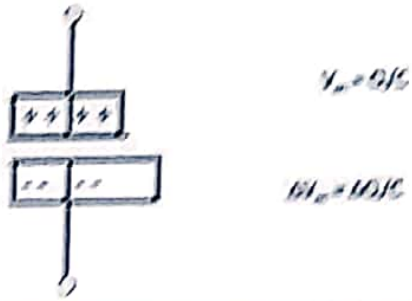


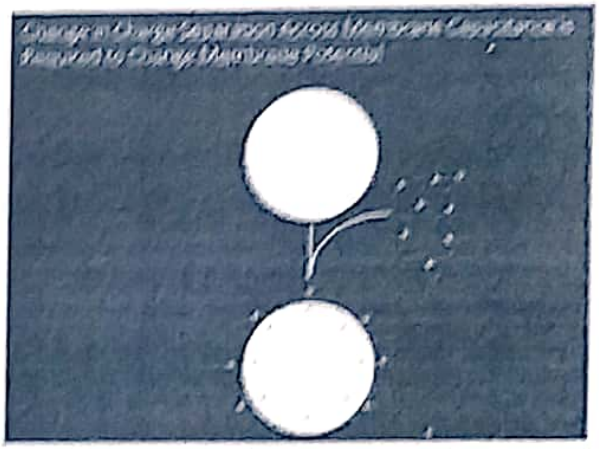


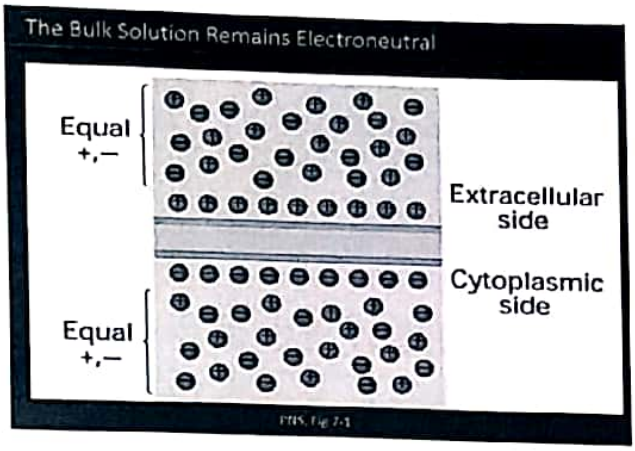


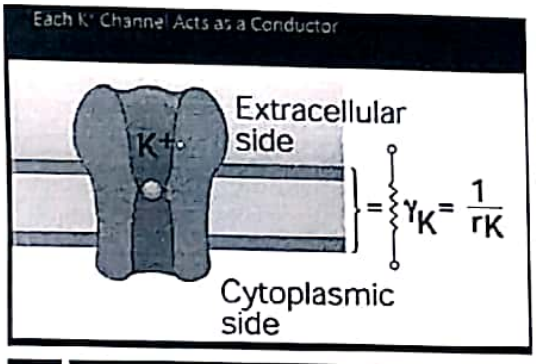


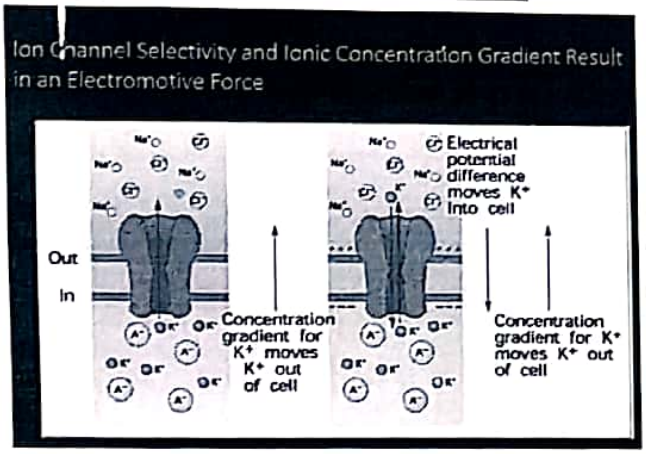
The Lipid Bilayer has Like a Capacitor

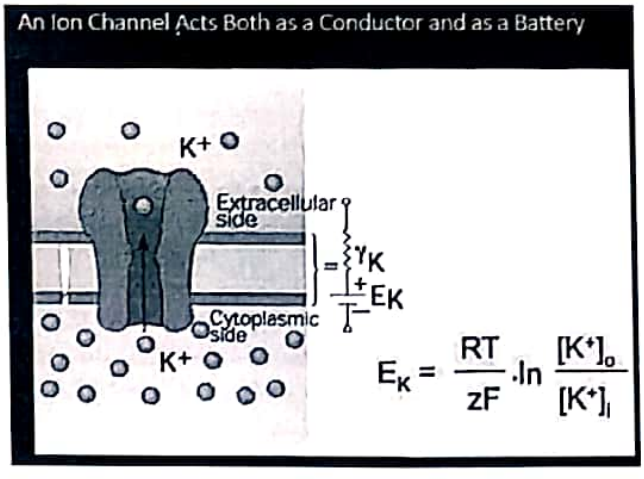




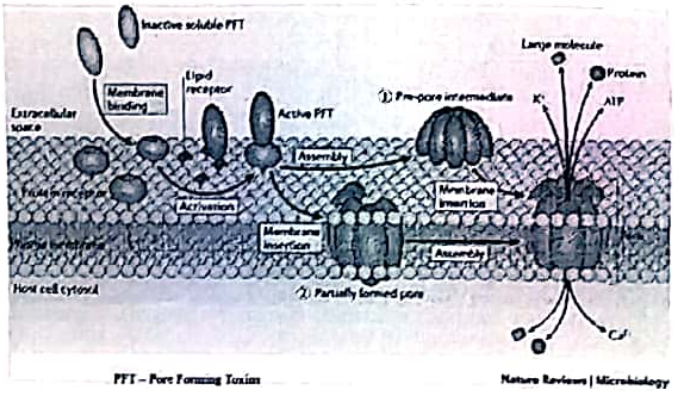








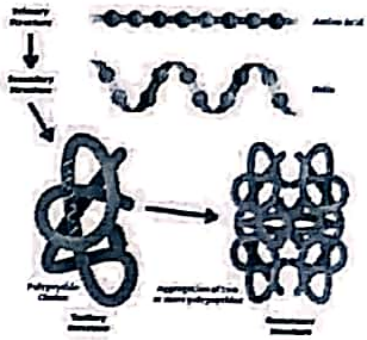
PORE FORMATION



Protein Structure

Protein structure is the three-dimensional arrangement of atoms in an amino acid chain molecule.

Proteins are polymers – specifically polypeptides – formed from sequences of amino acids, the monomers of the polymer.



Importance of Proteins

- Muscle structure depends on protein-protein interactions
- Transport across membranes involves protein-solute interactions
- Nerve activity requires transmitter substance-protein interactions
- Immune protection requires antibody-antigen interactions

Types of Protein structure

Primary Structure

Secondary Structure

Tertiary Structure

Quaternary Structure

Primary Structure

Polypeptide chains → Amino Acids

Largest polypeptide chain approx has 5000AA but most have less than 2000AA

Amino Acid Basic Structure $H_2N\text{-}CH\text{-}COOH$

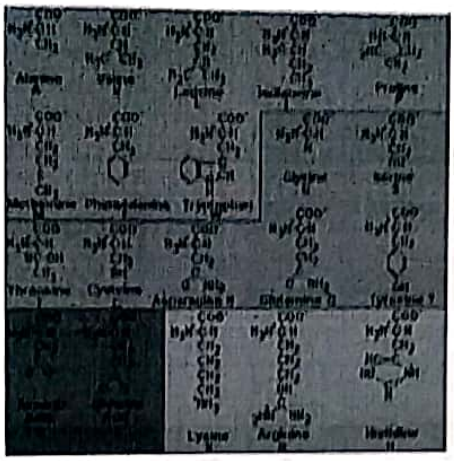
Arrangement of the 20 amino acids in the polypeptide is the amino acid sequence which composes the primary structure of the protein

20 Amino Acids

Nonpolar, hydrophobic

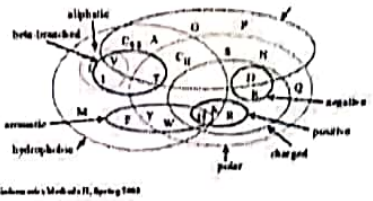
Polar, uncharged

Polar, charged



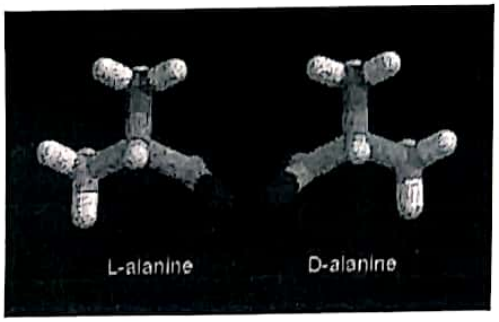
http://www.people.virginia.edu/~rjh9u/aminacid.html

Amino Acid Classification



A Venn diagram showing the relationship of the 20 naturally occurring amino acids to a selection of physio-chemical properties thought to be important in the determination of protein structure.

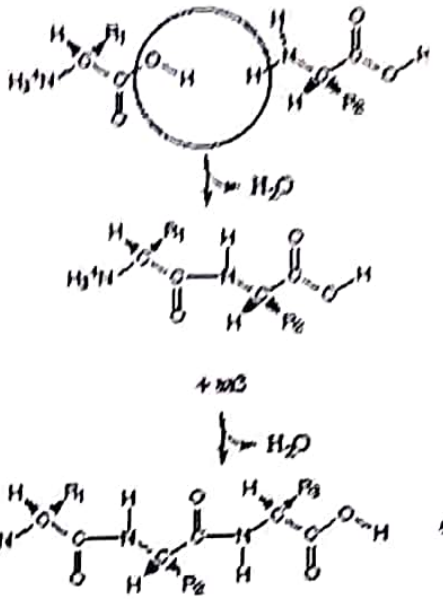
Stereochemistry (Configuration of amino acids in proteins)



Bond Formation

Linking two amino acids together

Definitions (N-terminal, C-terminal, polypeptide backbone, amino acid residue, side chains)



http://web.mit.edu/esgbio/www/lm/proteins/peptidebond.html

Primary Structure

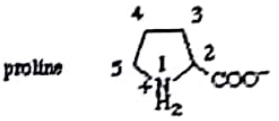
What is a native protein?

Protein conformation & problem of protein folding

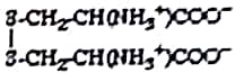
- Hydrophobic, hydrophilic
- Charge
- Chaperones

Special Purpose Amino Acids

Proline



Cysteine



Protein Secondary Structure

Introduction

Peptide bond geometry

Ramachandran plot

Structures

Peptide Bond

Peptide Bond

Resonance

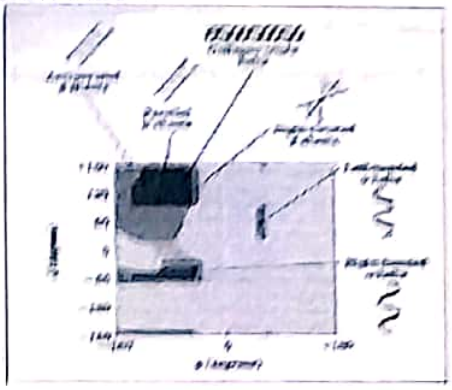
C-N bond length of the peptide is 132% shorter than that found in usual C-N amin

Peptide bond planar

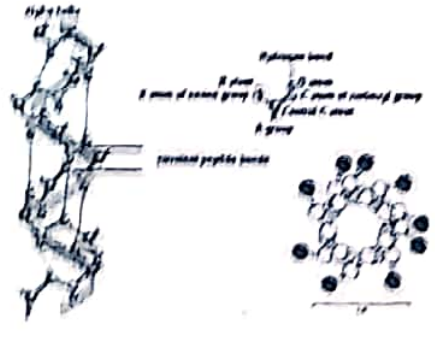
ω, angle around peptide bond,

0° for cis, 180° for trans

Ramachandran Plot



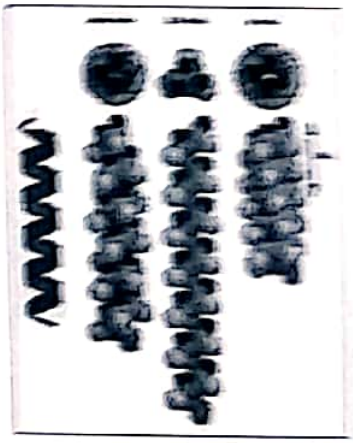
Alpha Helix



Alpha Helix

Alpha Structure Features

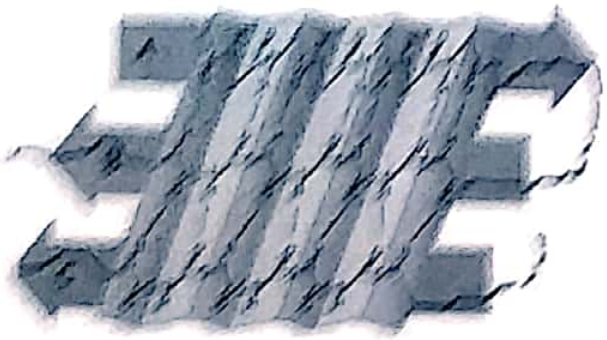
Helix Structures



More Helix Structures

Type	Φ	ψ	comments
Collagen	-51	153	Fibrous proteins Three left-handed helicies (Gly-X-Y)n, X = Pro / Lys
Type II helices	-75	150	left-handed helicies formed by polyglycine

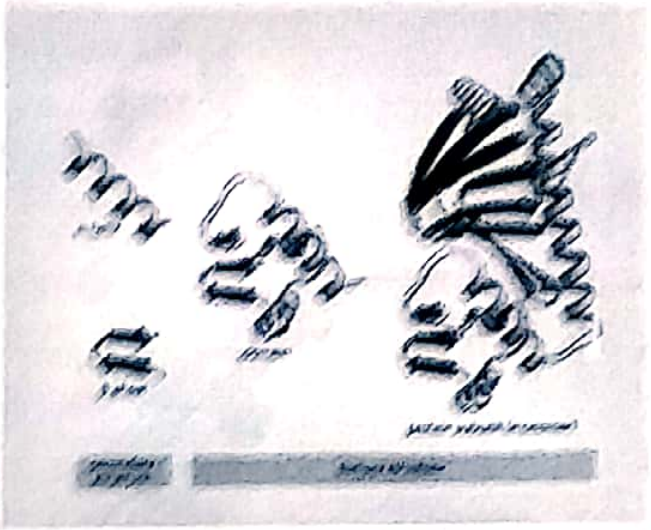
Beta Sheet



Beta Sheet Features

More Beta Structures

Tertiary Protein Structure



Quaternary Structure

Not all proteins have a quaternary structure

A composite of multiple poly-peptide chains is called an oligomer or multimeric

Hemoglobin is an example of a tetramer

Globular vs. Fibrous