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Receptor-1

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INTRODUCTION

- Drugs produce their therapeutic effects
- By producing biochemical/physical changes in the target tissues
- of the host
- of the organisms which invade the host.

- These changes are due to;
  - physical and chemical properties of drug.
  - action on the drug targets namely;
    - Receptors
    - Enzymes
    - Carrier molecules
    - Ion channels

To get drug action, it is essential that-

1. Sufficient concentration of drug reaches the site of action

2. Remains there for a sufficient duration

3. The tissue is susceptible for drug action

- Magnitude of drug action is proportional to the concentration of drug at the site of action.

- Receptor mechanism is very important to understand the action and effect of a drug.

Receptor

- component of a cell or organism
- interacts with a drug.
- initiates the chain of biochemical events leading to the drug's observed effects

- They have specific binding sites that are definite in size and shape.
- Most are present on or near the membrane.
- Some lie in the enzymes or genes.
- protein (polypeptide) in nature.

RECEPTOR?

- **Paul Ehrlich**

- **Specialized areas of cell to which drugs get bound.**

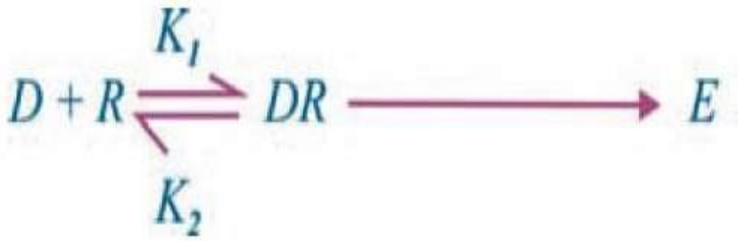
- **They are regulatory protein macro-molecules .**

- **drug should have –selectivity to a receptor ; receptor should have - ligand specificity to elicit action.**

Theories Proposed

Receptor occupancy theory:

- The interaction between the two molecular species, *viz.* drug (*D*) and receptor (*R*) to be governed by the law of mass action, and the effect (*E*) to be a direct function of the drug-receptor complex (*DR*) formed.



DRUG RECEPTOR INTERACTIONS

- Effect of drug attributed to two factors -

- Affinity : tendency of the drug to bind to receptor and form D-R complex .

- Efficacy or intrinsic activity (IA): ability of the drug to trigger pharmacological responses after forming D-R complex .

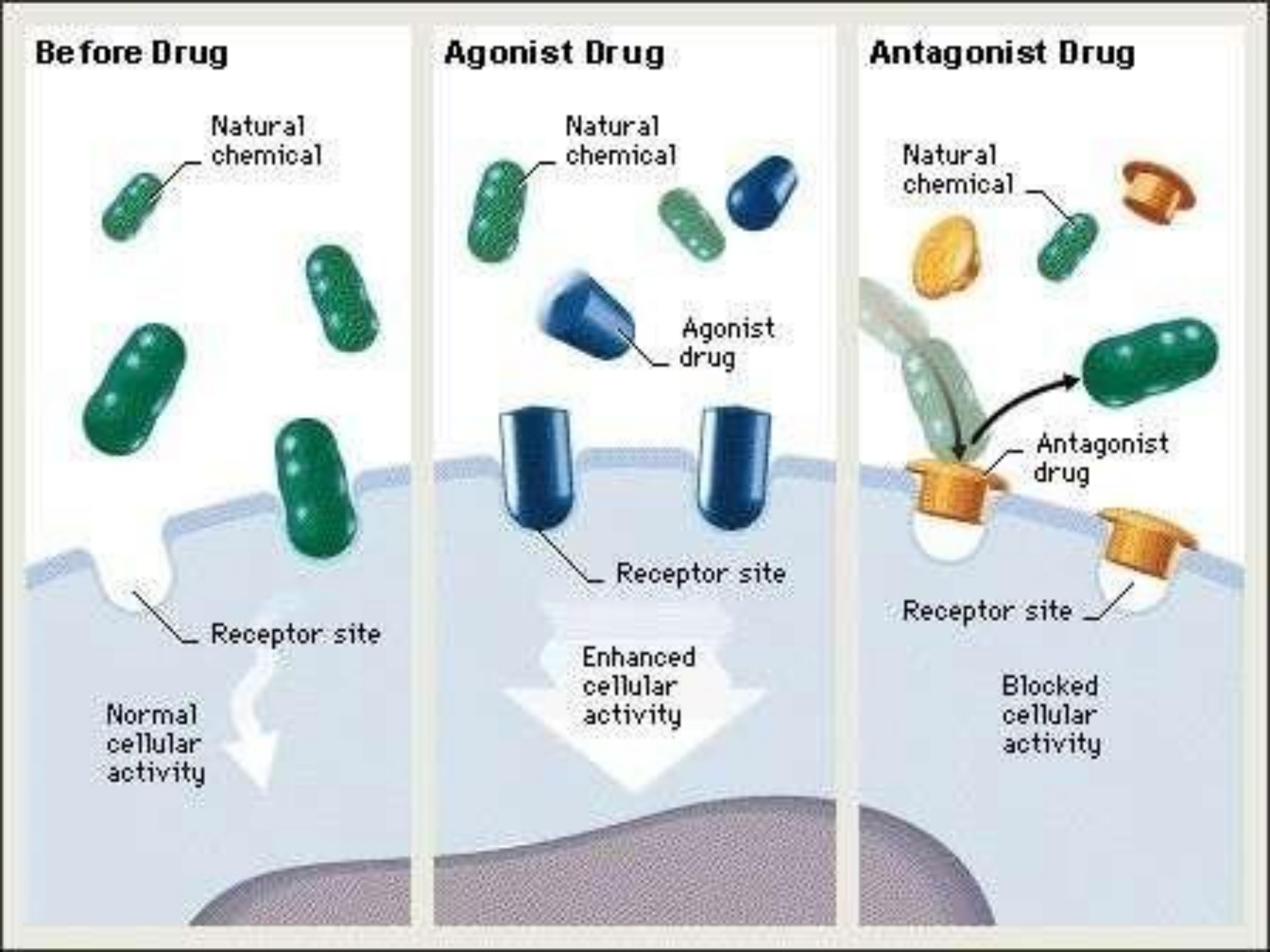
CONTD…

- **Based on affinity and intrinsic activity:**
  - **Full agonist : high affinity**
    high intrinsic activity(=1)

Eg. Methacholine on acetylcholine receptors

  - **Antagonist : only affinity**
    no intrinsic activity (=0)

Eg. Atropine on muscarinic –receptors


Before Drug
Natural chemical
Receptor site
Normal cellular activity
Agonist Drug
Natural chemical
Agonist drug
Receptor site
Enhanced cellular activity
Antagonist Drug
Natural chemical
Antagonist drug
Receptor site
Blocked cellular activity

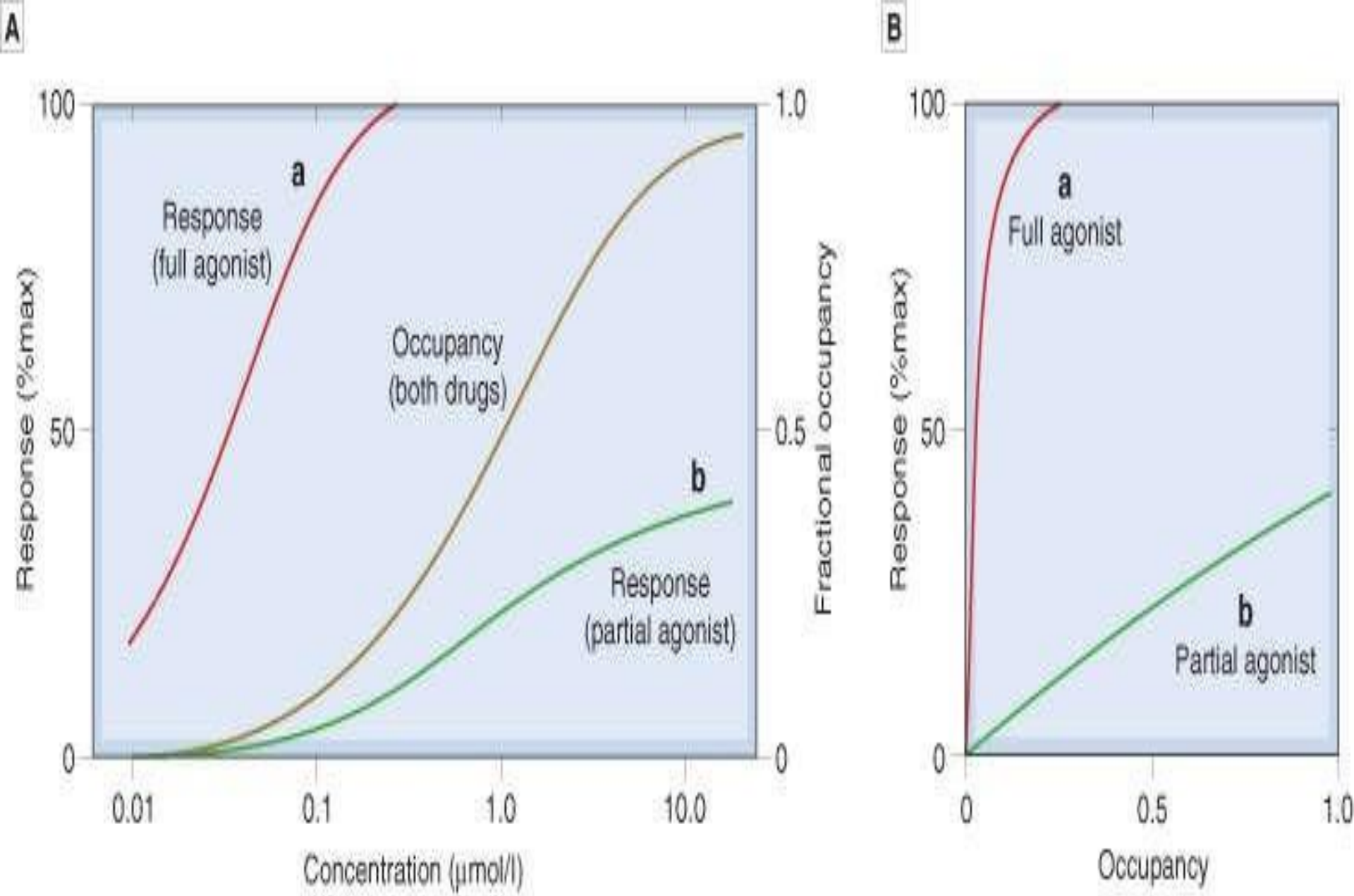
CONTD..

- **Partial agonist: full affinity**
  intrinsic activity <1 (0 to 1)

Eg. Naloxene on opioid receptors
saralasin on angiotensin receptors.

- **Inverse agonist: full affinity**
  intrinsic activity<0(0 to-1)

Eg. Beta carbolines on BZP receptor.



CLASSIFICATION -

IUPHAR

Cell surface

1. **Inotropic.**
3. **Metabotropic.**
5. **Ligand regulated trans membrane.**

Intracellular

1. **Nuclear receptors .**

Ligand Gated Ion Channels

- **Also called ionotropic receptors.**
- **involved mainly in fast synaptic transmission.**

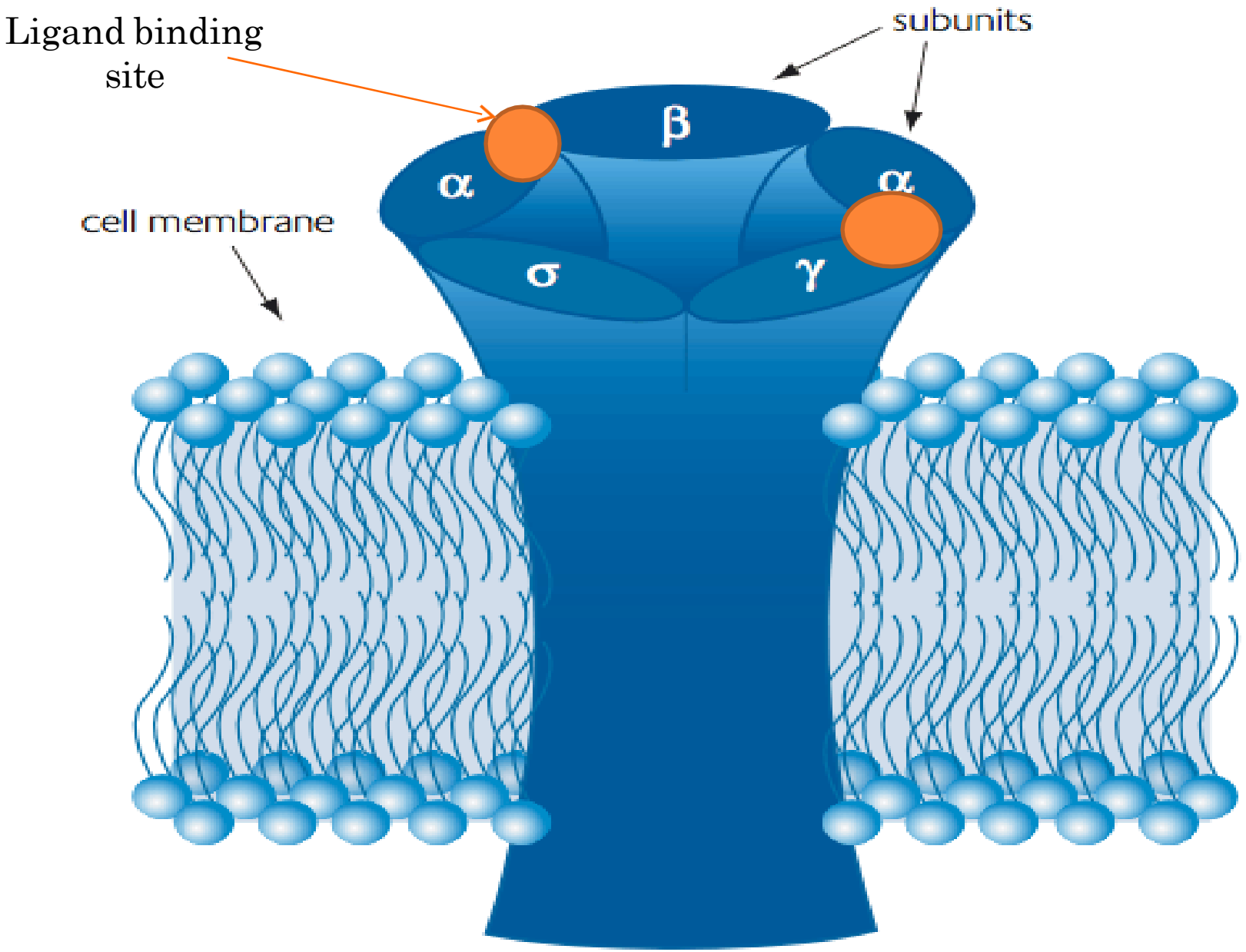
Eg: nAchR, $GABA_A$, and glutamate receptors of the NMDA, AMPA and kainate types.

FEATURES-ION CHANNELS

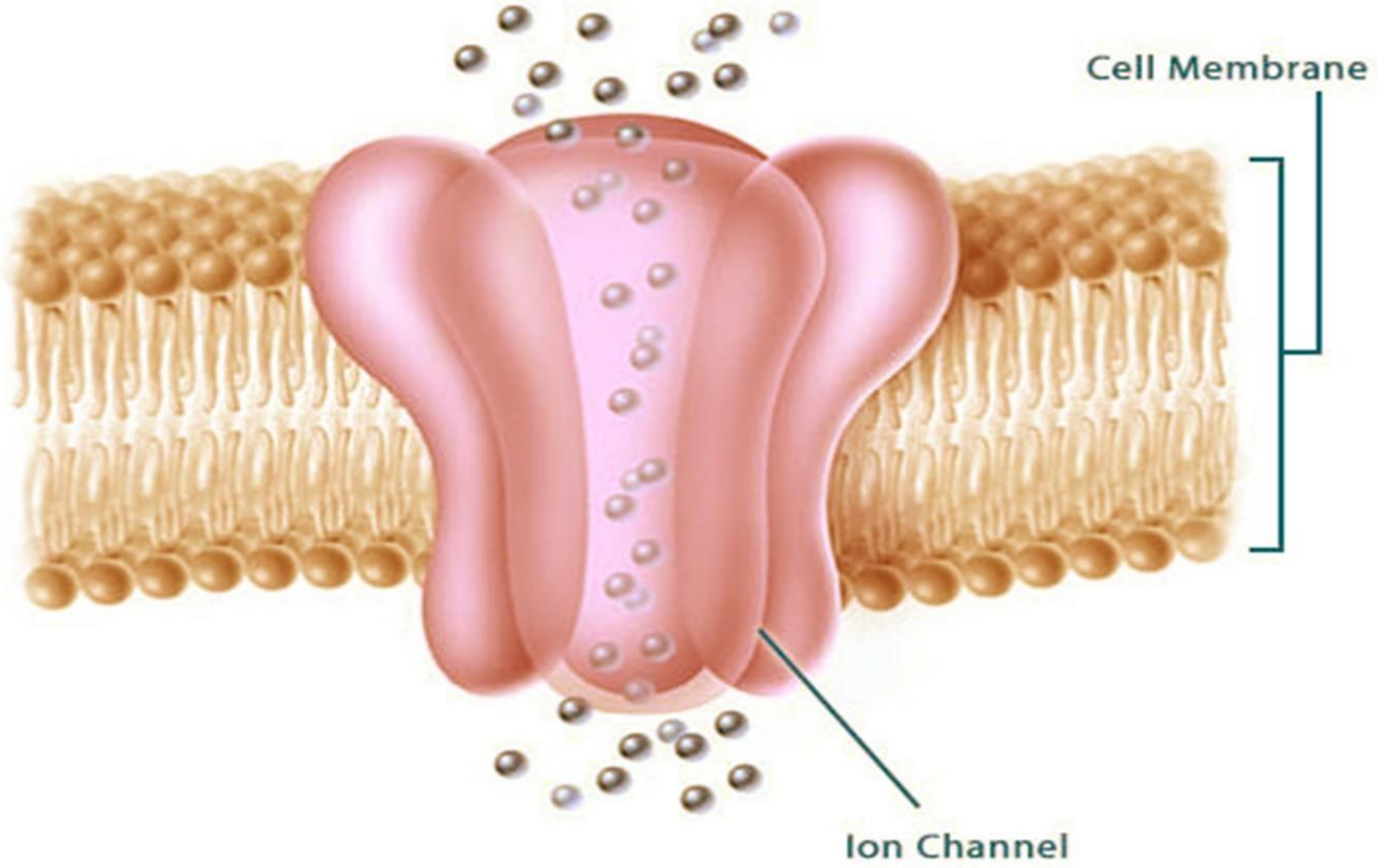
- **Protein molecules form water filled pores that span the membrane.**
- **Switch between open and closed states.**
- **Rate and Direction of movement depends on electrochemical gradient of the ions.**

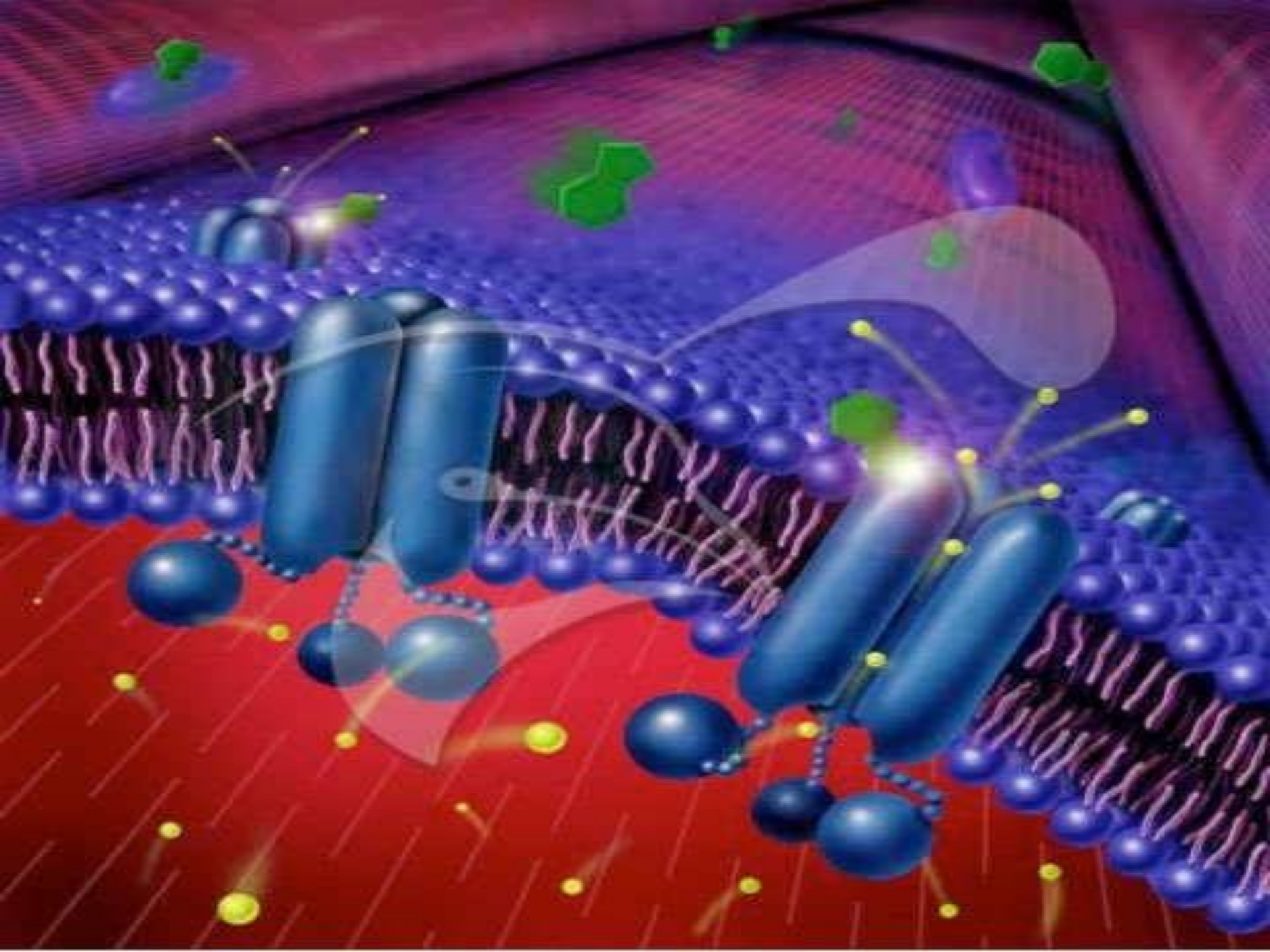
STRUCTURE

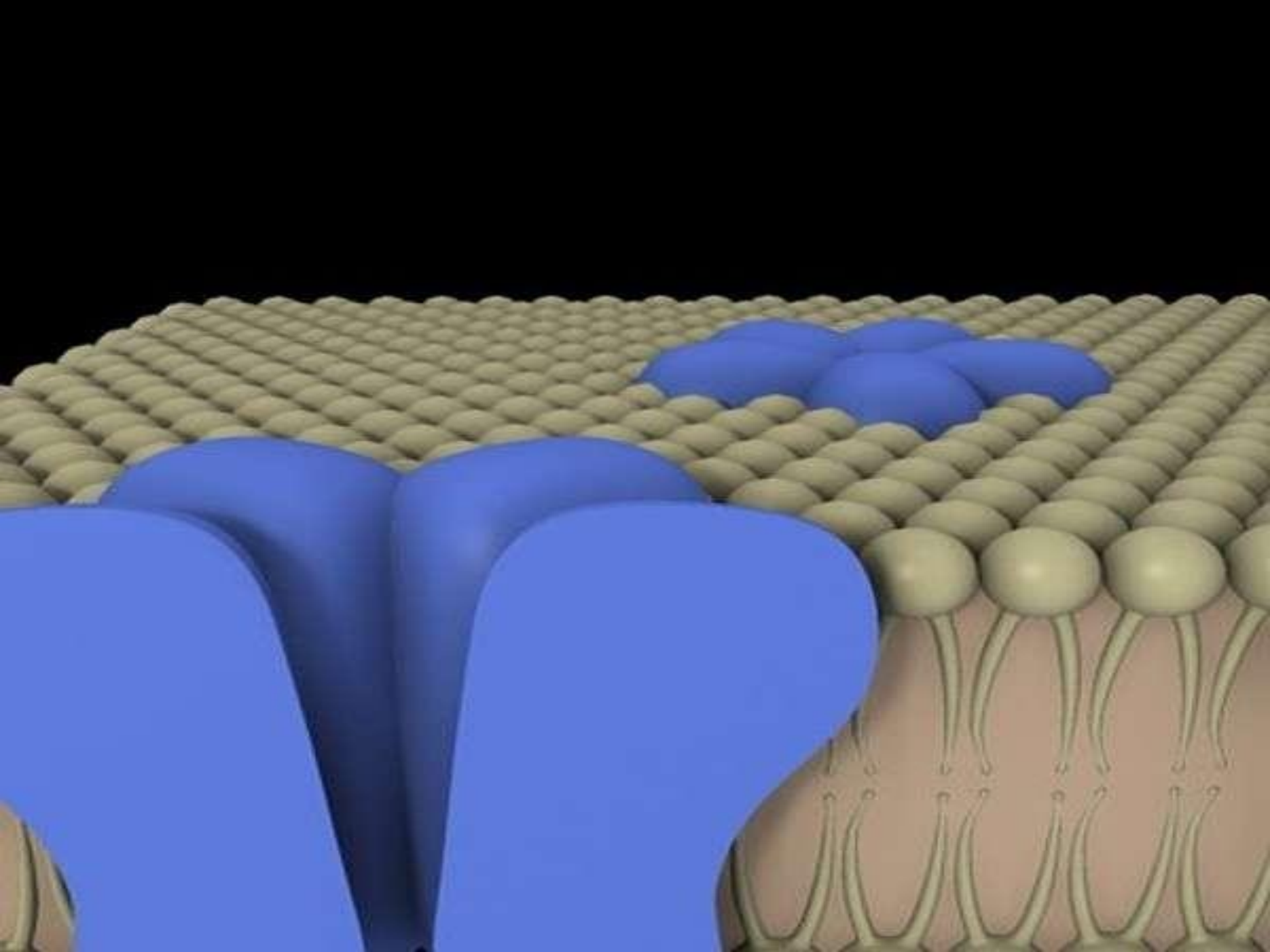
- ligand binding site in extracellular domain.
- 4 subunits α, β, γ and δ.
- α_2, β, γ - pentameric str - 2 ligand binding sites.
- Each subunit spans the membrane 4 times; all subunits form a central pore.



Representative Ion Channel


Cell Membrane
Ion Channel

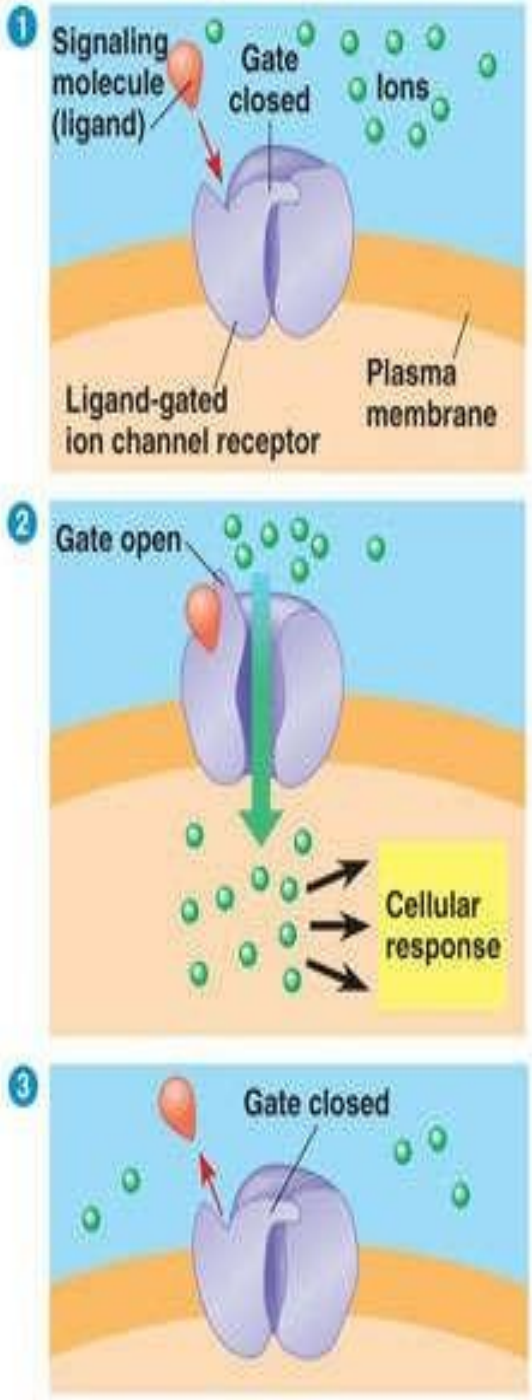




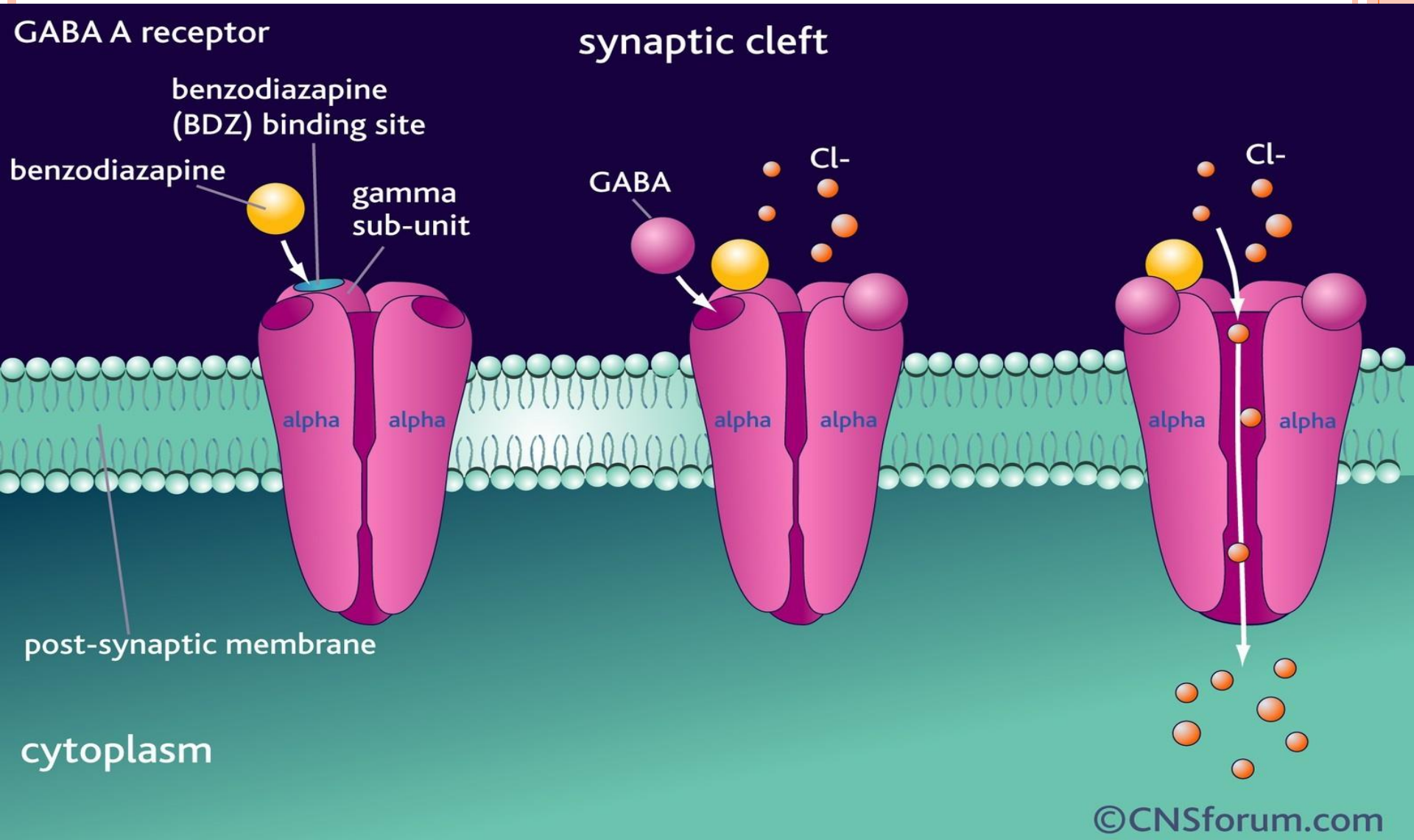
Signal molecule binds as a ligand at a specific site on the receptor

Conformational changes open the channel allowing ions to flow into the cell

The change in ion concentration within the cell triggers cellular responses



GATING MECHANISM IN $GABA_A$ RECEPTOR



CONTD.

- **Due to the concentration changes of different ions the following effects are seen.**
- **Increase in Na and Ca levels- excitatory**
- **Decrease in Na and Ca levels- inhibitory**

- **Increase in K levels – inhibitory**
- **Decrease in K levels – excitatory**

- **Increase in Cl levels – inhibitory**
- **Decrease in Cl levels- excitatory**

IMPORTANCE

- Generation , propagation of nerve impulse.
- Synaptic transmission of neurons.
- Muscle contraction.
- Salt balance.
- Hormone release.
- Muscle relaxants , anti-arrhythmatics ,anesthetics – act by blocking ion channels.


THANK YOU