Transport Across Plasma Membrane Lecture - 2

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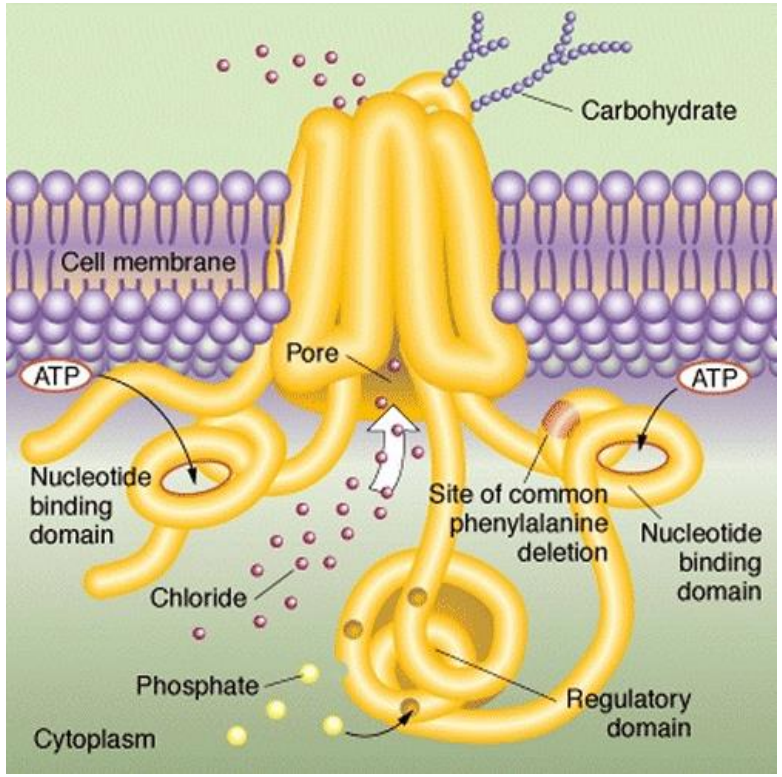
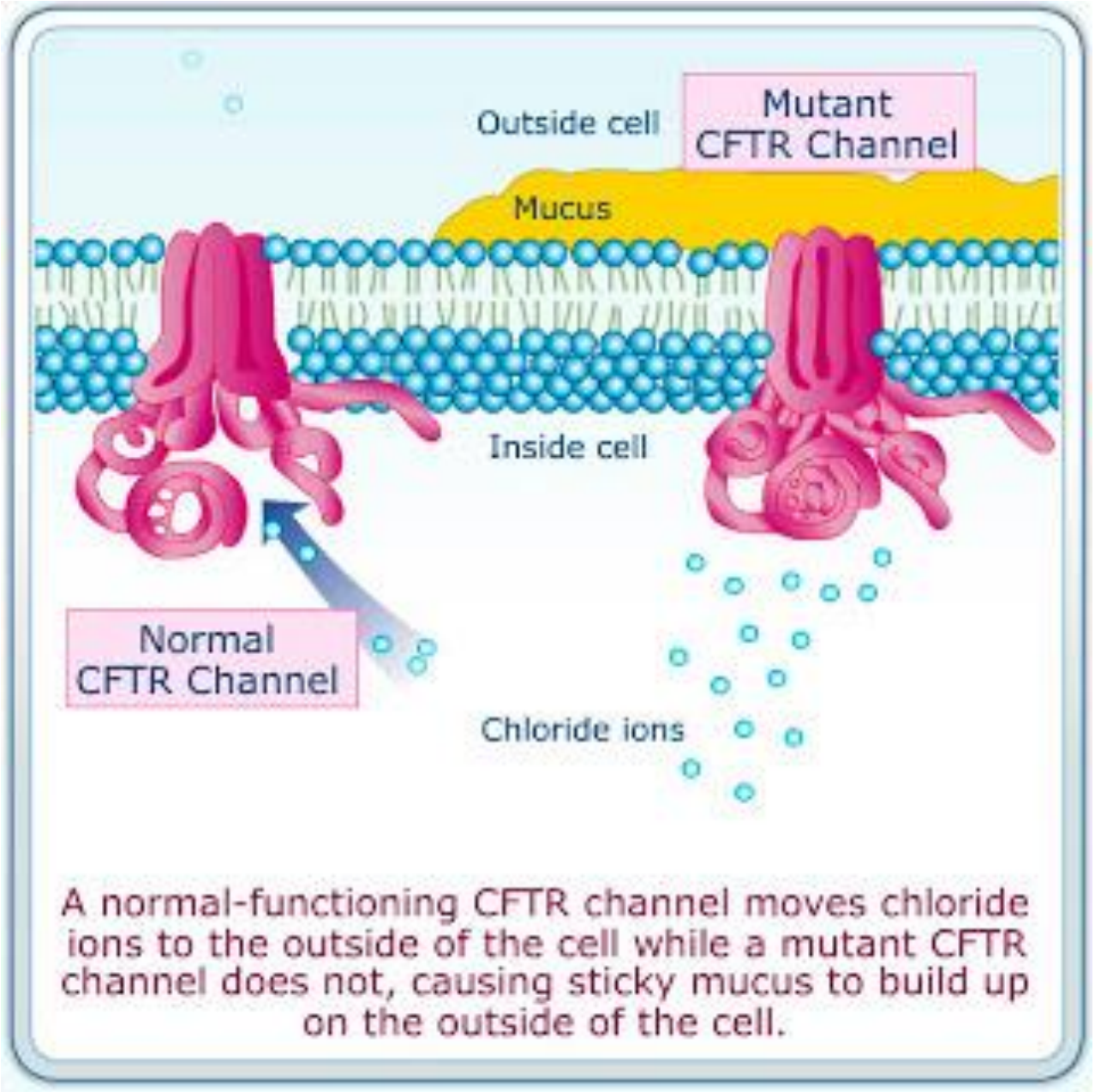
Cystic Fibrosis and ABC transporter

- It is an ion specific channel for transport of chloride ions.
- Its activity increases when Pi is transferred on the protein chains from ATP.
- But during cystic fibrosis, this transporter called as CFTR undergoes a mutation and fails to transport chloride ions.

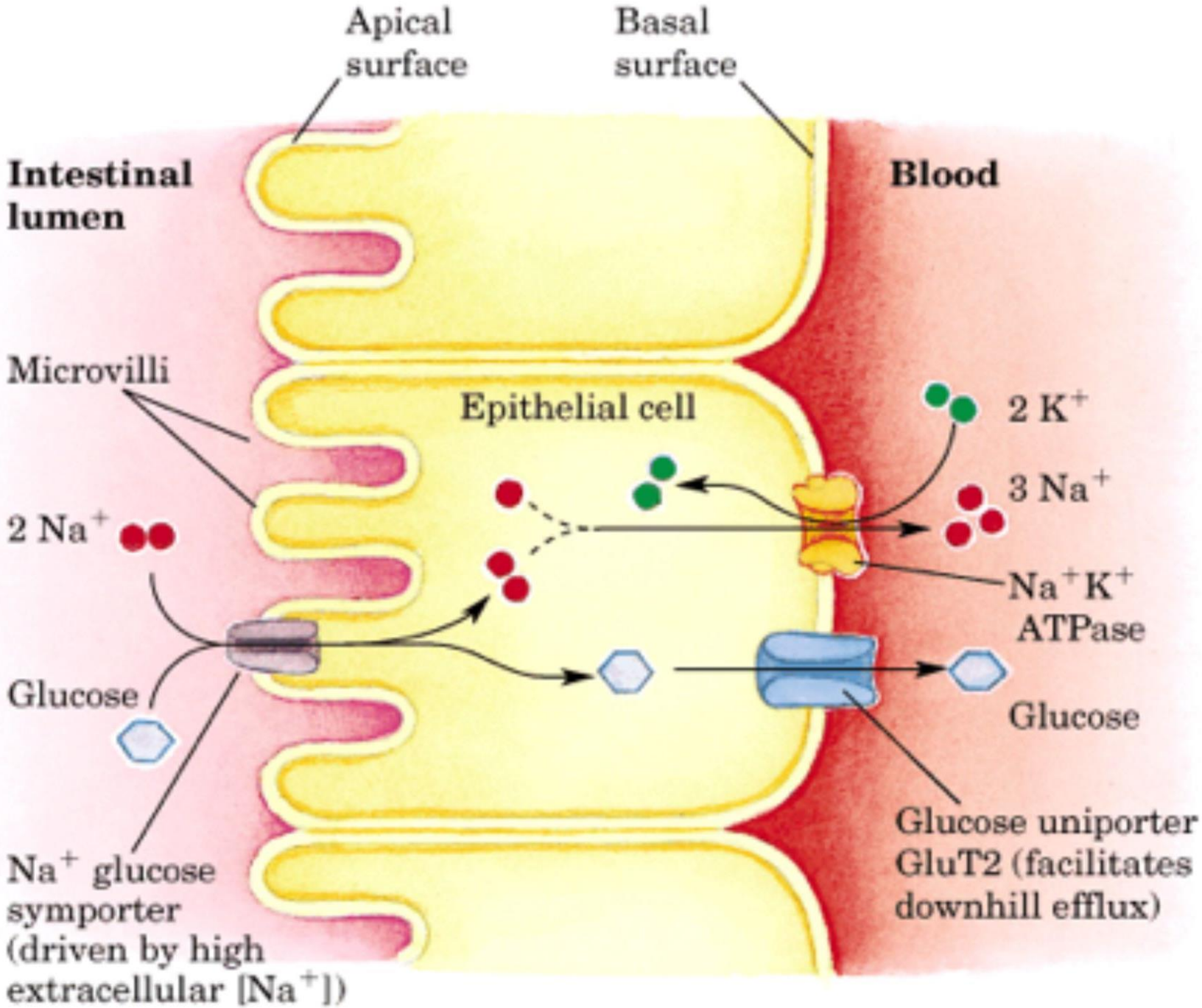
1. **CFTR = Cystic fibrosis transmembrane conductance regulator.**
2. **Most common mutation that leads to CFTR is deletion of a phenylalanine residue at position 508.**
3. **In diseased state, thin layer of mucus lining the respiratory pathway becomes very thick.**
4. **It blocks air flow and provides a suitable habitat for the growth of pathogenic bacteria such as *Staphylococcus aureus & Pseudomonas aeruginosa.***
5. **It is a recessive autosomal disorder.**


Carbohydrate
Cell membrane
Pore
ATP
ATP
Nucleotide binding domain
Site of common phenylalanine deletion
Nucleotide binding domain
Chloride
Phosphate
Regulatory domain
Cytoplasm


Outside cell
Mutant CFTR Channel
Mucus
Inside cell
Normal CFTR Channel
Chloride ions
A normal-functioning CFTR channel moves chloride ions to the outside of the cell while a mutant CFTR channel does not, causing sticky mucus to build up on the outside of the cell.

Secondary active transport and glucose absorption in small intestine

- In this, glucose is absorbed in the cells of small intestine by symport.
- This symport takes place along with sodium ions.
- The sodium ions move down the gradient that has been established by the activity of Sodium-Potassium ATPase pump.
- Glucose moves uphill or against the concentration gradient.
- Thus, a non-spontaneous process is coupled with spontaneous process.

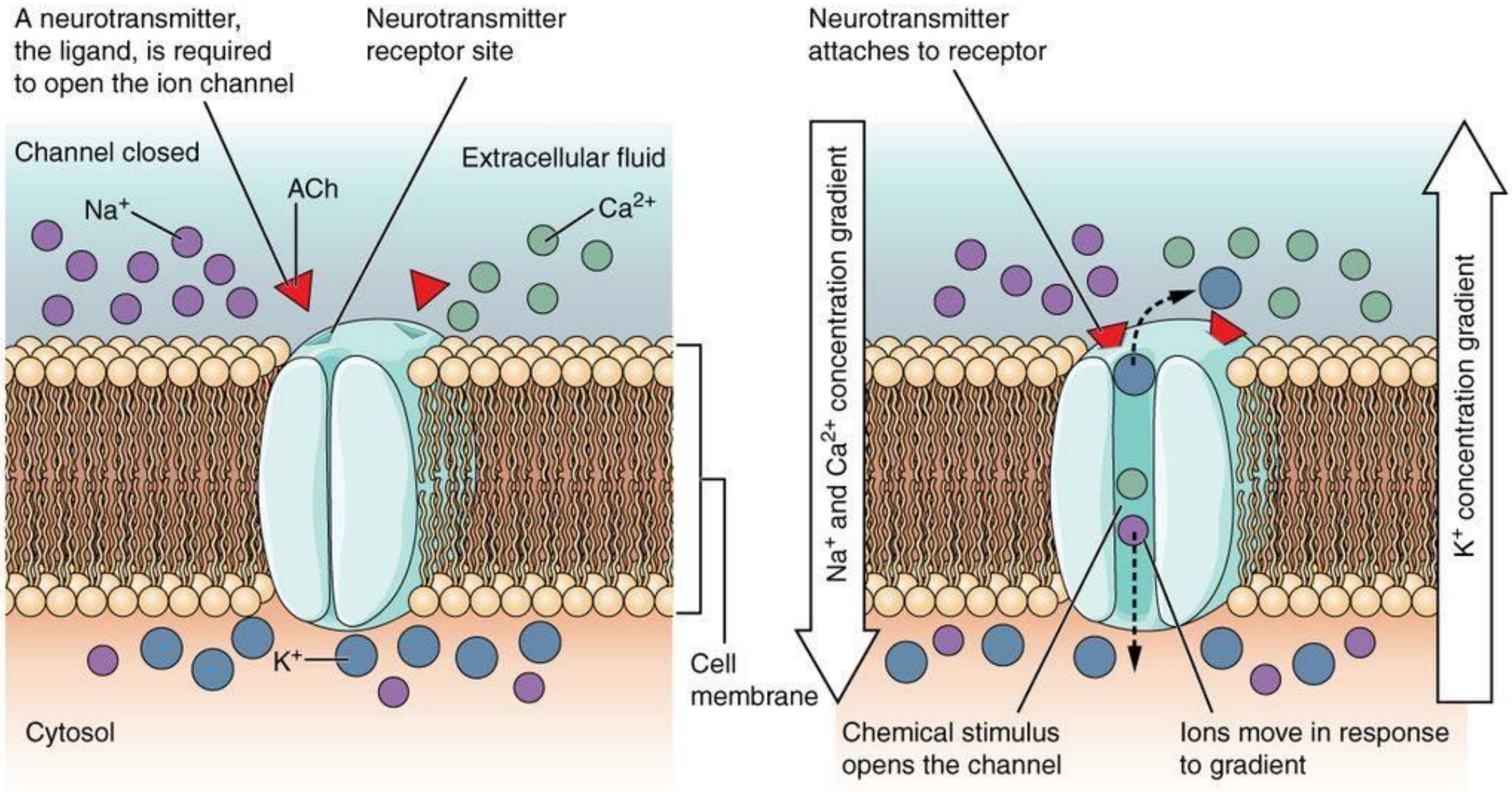

Apical surface
Basal surface
Intestinal lumen
Blood
Microvilli
Epithelial cell
2 K+
3 Na+
2 Na+
Na+K+ ATPase
Glucose
Glucose
Glucose uniporter GluT2 (facilitates downhill efflux)
Na+ glucose symporter (driven by high extracellular [Na+])

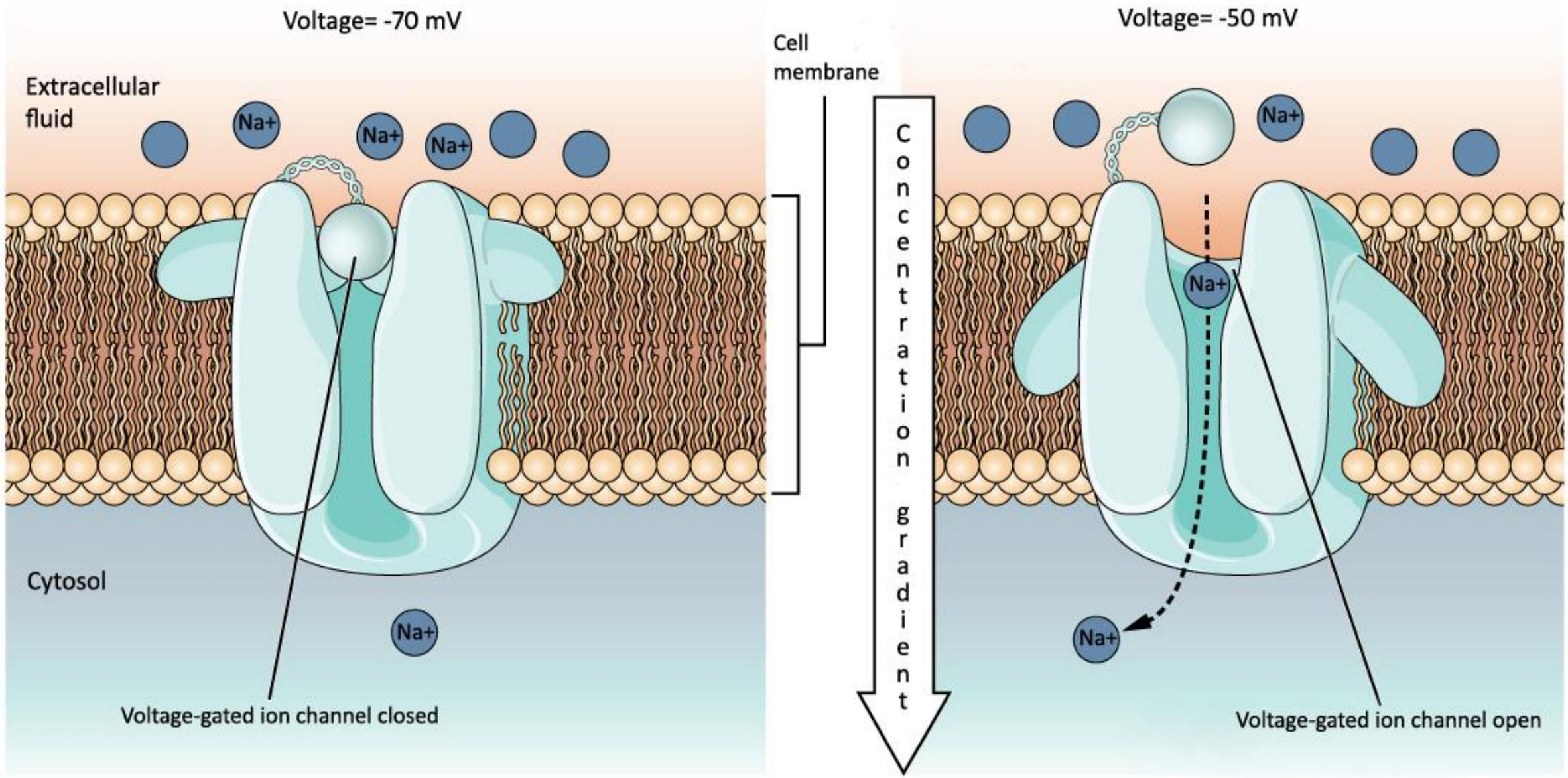
Ion selective channels

- Ion channels as discussed earlier have some peculiar features
  1. They have high rate of transport/ flux across them i.e. 10 million to 100 million ions/second.
  2. They are unsaturable.
  3. They are gated.

- **Why gated**??
- Because unregulated ion flow will disturb the normal charge and function of the cell.
- But introduction of gating provides for influx and efflux of ion channels only when a signal is given and signal has reached the ion channel to activate it.
- The signal can be a ligand or change in membrane voltage.

  - Channels responding to ligand are called as ligand –gated channel. E.g. Acetylcholine receptor and receptors of other neurotransmitters.
  - Channels responding to voltage changes are called as voltage gated channels. E.g. Sodium and potassium channels in neurons.


A neurotransmitter, the ligand, is required to open the ion channel
Neurotransmitter receptor site
Channel closed
ACh
Extracellular fluid
Na^+
Ca^{2+}
K^+
Cytosol
Cell membrane
Neurotransmitter attaches to receptor
Na^+ and Ca^{2+} concentration gradient
K^+ concentration gradient
Chemical stimulus opens the channel
Ions move in response to gradient


Voltage= -70 mV
Extracellular fluid
Na+
Na+
Na+
Cytosol
Na+
Voltage-gated ion channel closed
Cell membrane
Concentration gradient
Voltage= -50 mV
Na+
Na+
Na+
Voltage-gated ion channel open

Ionophores and ion channel toxins

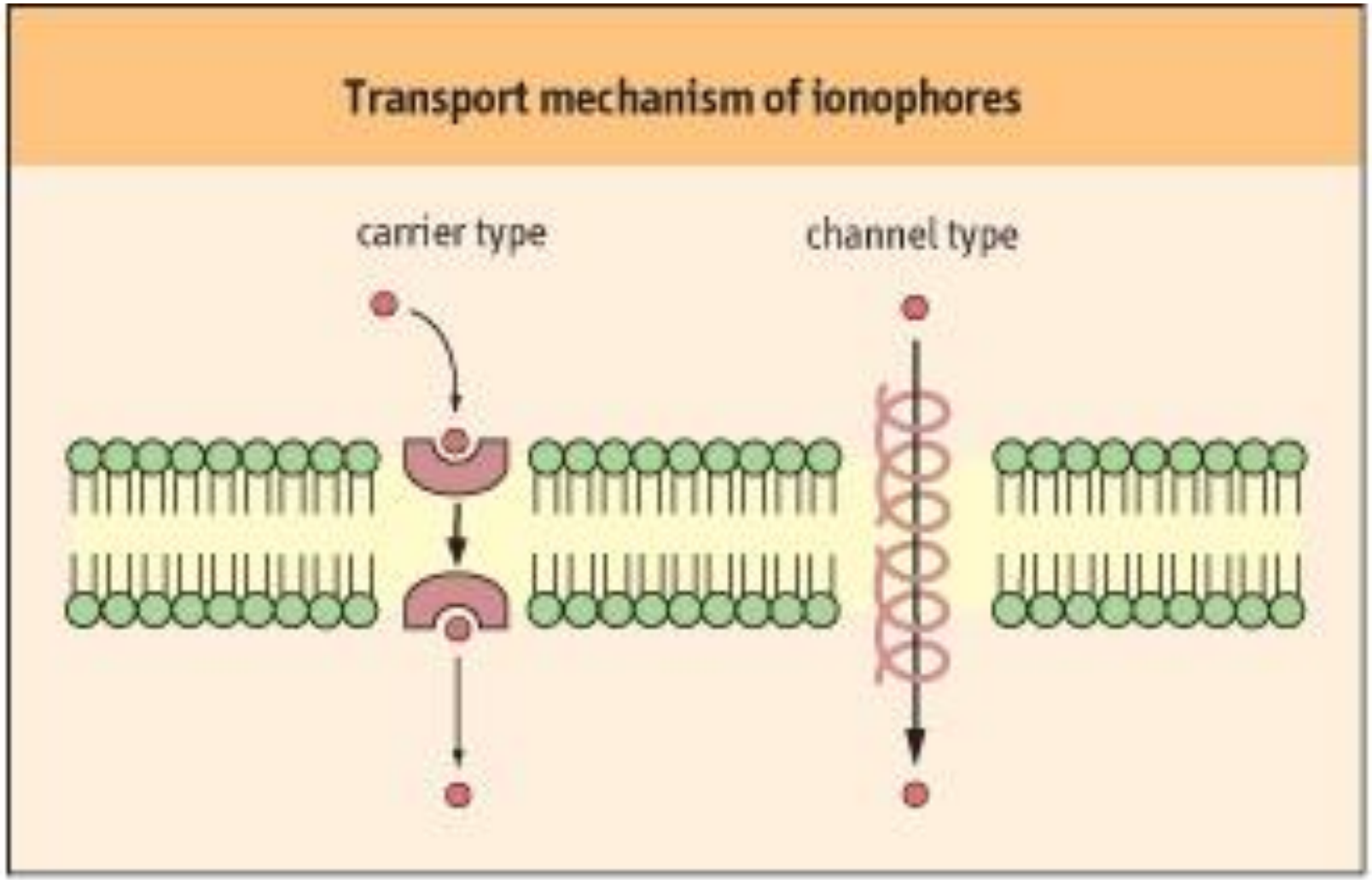
- **Ionophores:** These are compounds that are hydrophobic peptides and can bind to a particular ion.
- Once bound to the ion they can cross the plasma membrane due to their hydrophobicity.

- Thus, they can dissipate the ionic gradient for given ion.
- These molecules that can cross the PM from one side to the other are called as carrier ionophores.

- E.g. Valinomycin, a potassium ionophore and Monensin, a sodium ionophore are used as antibiotics.

- Some proteins can insert themselves in the plasma membrane and form a channel for dissipation of ionic gradients. These are called as channel forming ionophores.

- E.g. Gramicidin family of antibiotics.


Transport mechanism of ionophores
carrier type
channel type

- **Ion channel toxins:**

1. **Tetrodotoxin:** It blocks the voltage gated Sodium channels and prevents the generation of nerve action potential. Same effect is caused by Saxitoxin.

2. **Dendrotoxin:** It is the toxin of Black Mamba snake and interferes with voltage gated Potassium channels.

3. **Tubocurarine:** It is an arrow toxin used in Amazon. It acts by blocking the acetylcholine receptor. This causes loss of signal from nerves to muscles and leads to paralysis and death.

- Same effect is shown by snake venoms cobrotoxin and bungarotoxin.

Thank you