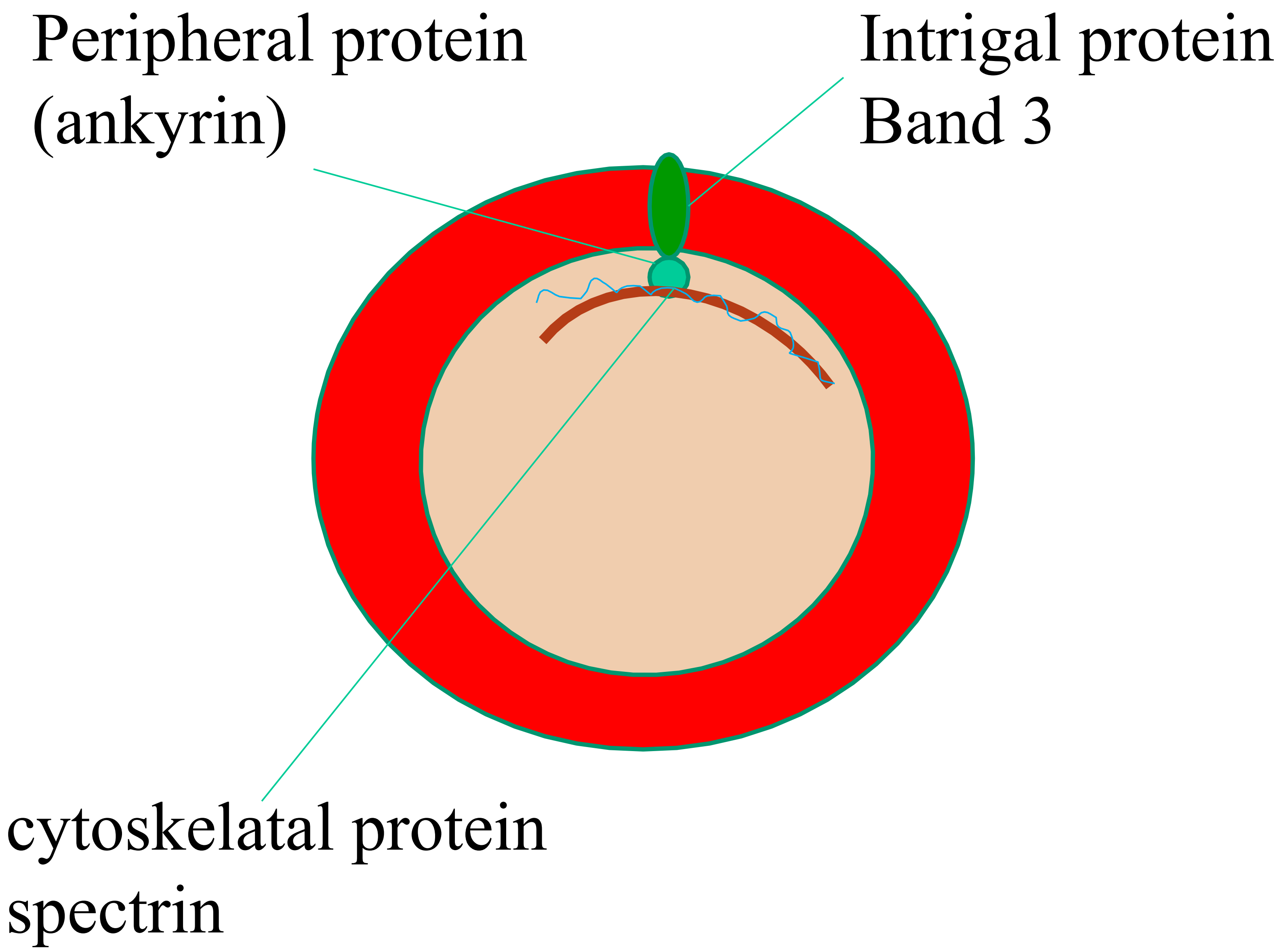
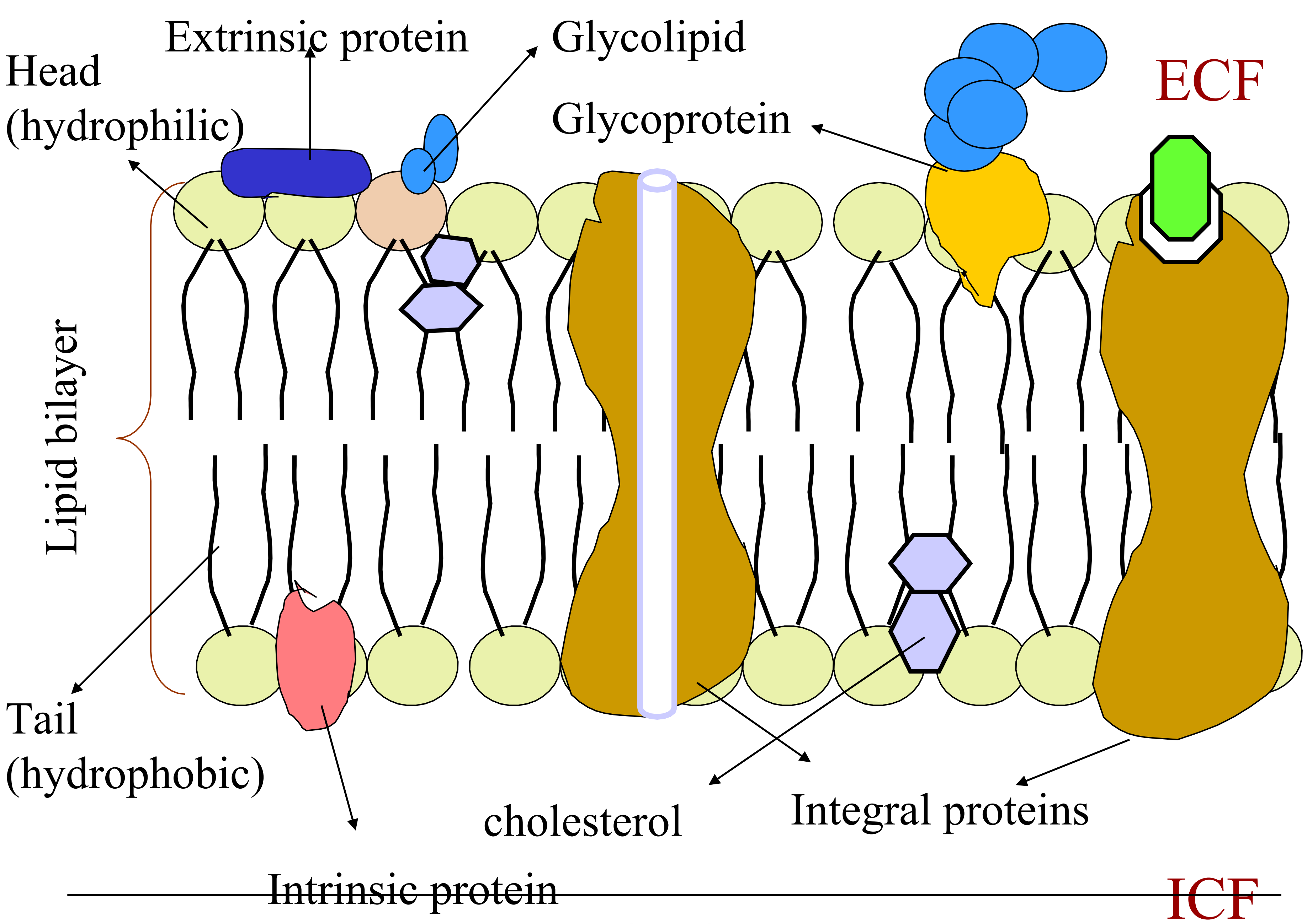
Substances transported for

- chemical reactions
- electrical potentials at the membrane
- Elimination from the cells

Cell Membrane

- surrounds entire cell and cell organelles
- Fluid in nature – movement of molecules
- Phospholipid bilayer – head – polar/hydrophilic
  tail – nonpolar/hydrophobic
- Proteins → Integral –carrier & channel
  → Peripheral-receptors & antigen


Peripheral protein
(ankyrin)
Intrigal protein
Band 3
cytoskelatal protein
spectrin


Extrinsic protein
Glycolipid
Head
(hydrophilic)
Glycoprotein
ECF
Lipid bilayer
Tail
(hydrophobic)
cholesterol
Integral proteins
Intrinsic protein
ICF

Functions of cell membrane

- Acts as semi permeable barrier –(selective)
  - Maintains difference in composition of ICF & ECF & fluid in various organelles
  - Protects cell from toxic substances
  - Excretion of waste products
  - Transport of nutrients

- Receives signals from the outside
  - Chemical signals
  - Electrical signals

- Site for attachment to the neighboring cells

Transport across cell membrane

Transport Mechanisms

Passive

- Simple diffusion
- Facilitated diffusion
- Filtration
- Osmosis
- dialysis

Active

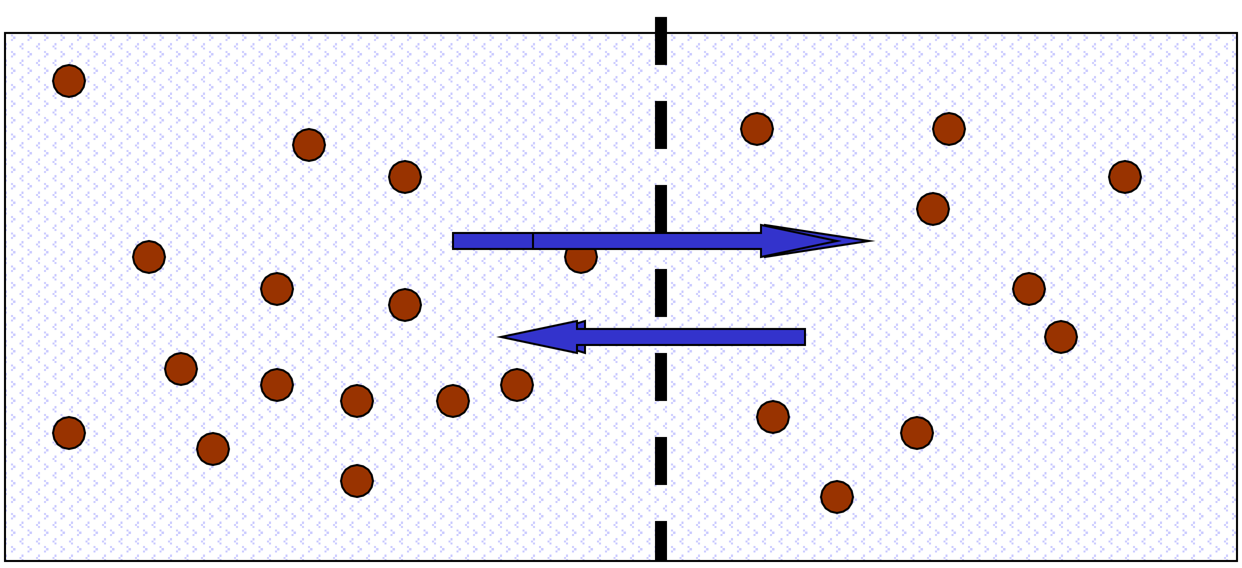
- Primary active transport
- Secondary active transport
- Endo/Exocytosis

Methods of transport

- **Passive**
  - Diffusion
    - Simple
      - Lipid bilayer
      - Protein channels
        - Leaky channels
        - Gated channels
          - voltage gated
          - Ligand gated
    - facilitated
  - Osmosis
  - Filtration
  - Dialysis
- **Active**

Simple diffusion -

Movement of molecules from higher concentration to lower concentration till equilibrium is reached



.Diffusion can takes place through:

a) Lipid bilayer

i) Lipid soluble substances-
O2,Co2,alcohol, steriods etc

ii) Lipid insoluble – water (through spaces bet lipid mol) urea, sugar
(less or no permeability)

iii) Electrolytes – impermeable
– charge on fatty acid chain
- Hydrated forms are larger

.

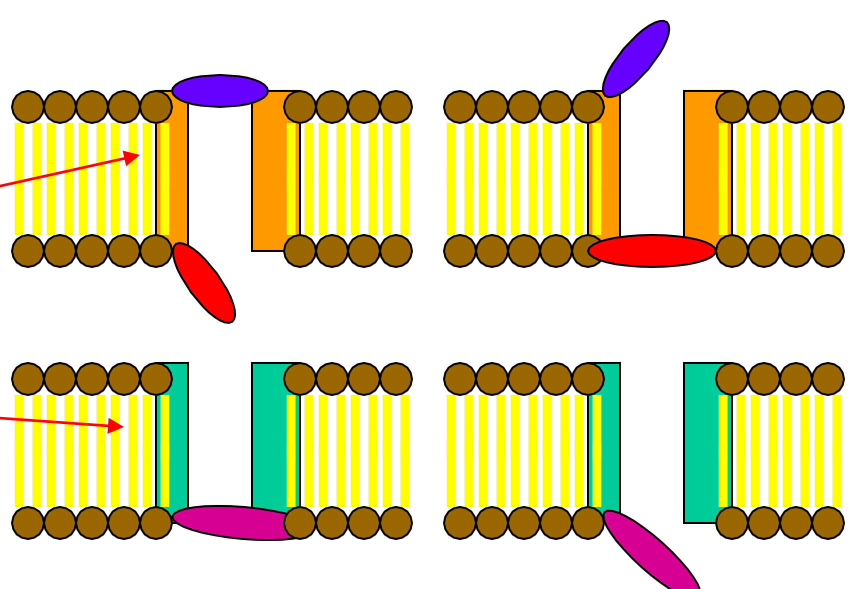
b) Protein Channels → Open/leaky – Na+ channels,
K+ channels

↓

Gated –channels open under specific conditions

Ligand gated
Na+
K+

Voltage gated
Na+,
K+
Ca++,



Mutation of ionic channels produce channelopathies –affecting muscle and brain – paralysis or convulsions

Factors affecting rate of diffusion

- Lipid solubility
- Molecular size & wt.
- Temperature

} **Molecular**

- Thickness of membrane
- Surface area

} **Membrane related**

- Concentration gradient
- Pressure gradient
- Electrical gradient

} Gradients

Imp.

Fick's law of diffusion –

$$Q \;\alpha\; \frac{\Delta C \cdot P \cdot A}{MW \cdot \Delta X}$$

Q = net rate of diffusion

ΔC = conc. gradient of a substance

P = permeability of membrane to the sub.

A = surface area of a membrane

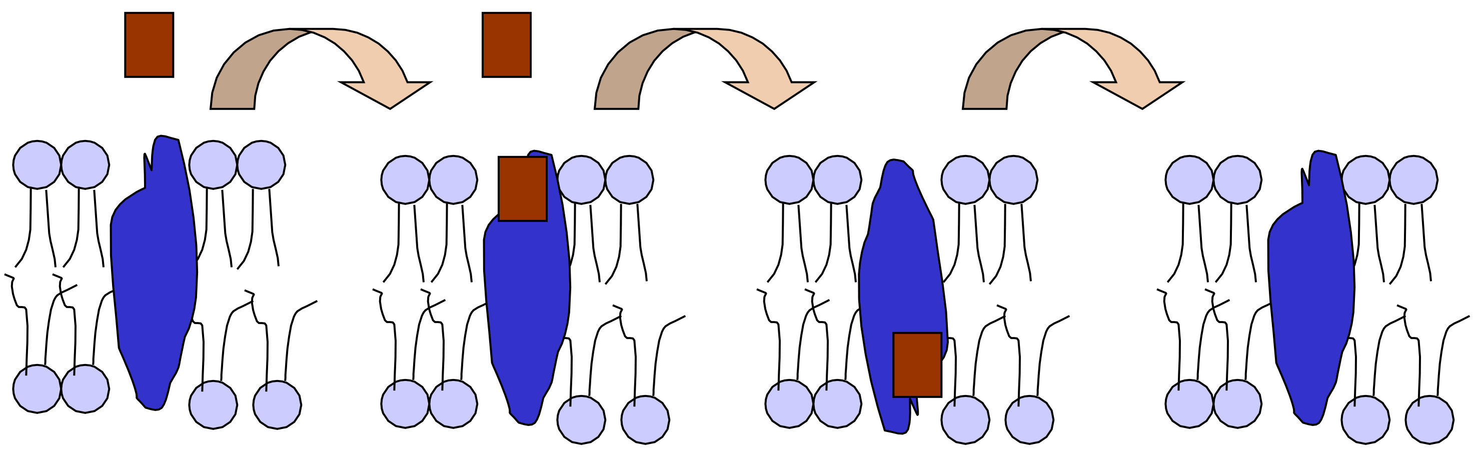
MW = molecular wt. of sub.

ΔX = thickness or distance

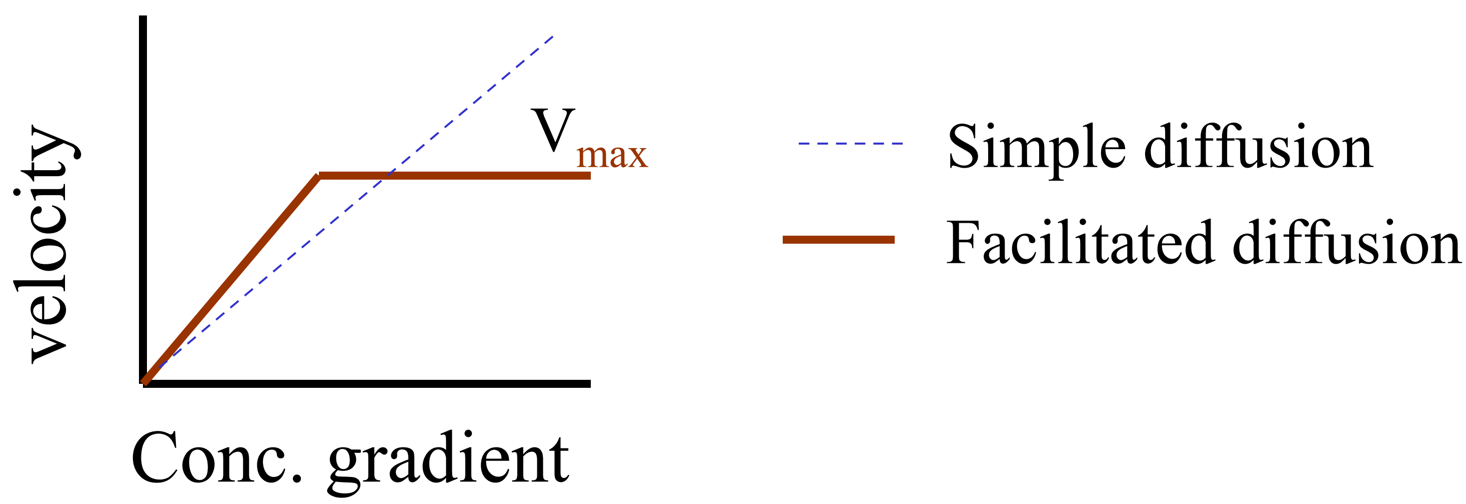
II. Facilitated diffusion :

- for larger water soluble mols.
- type of passive transport
- along the conc. Gradient
- carrier mediated transport
- receptor site on one side

Mechanism



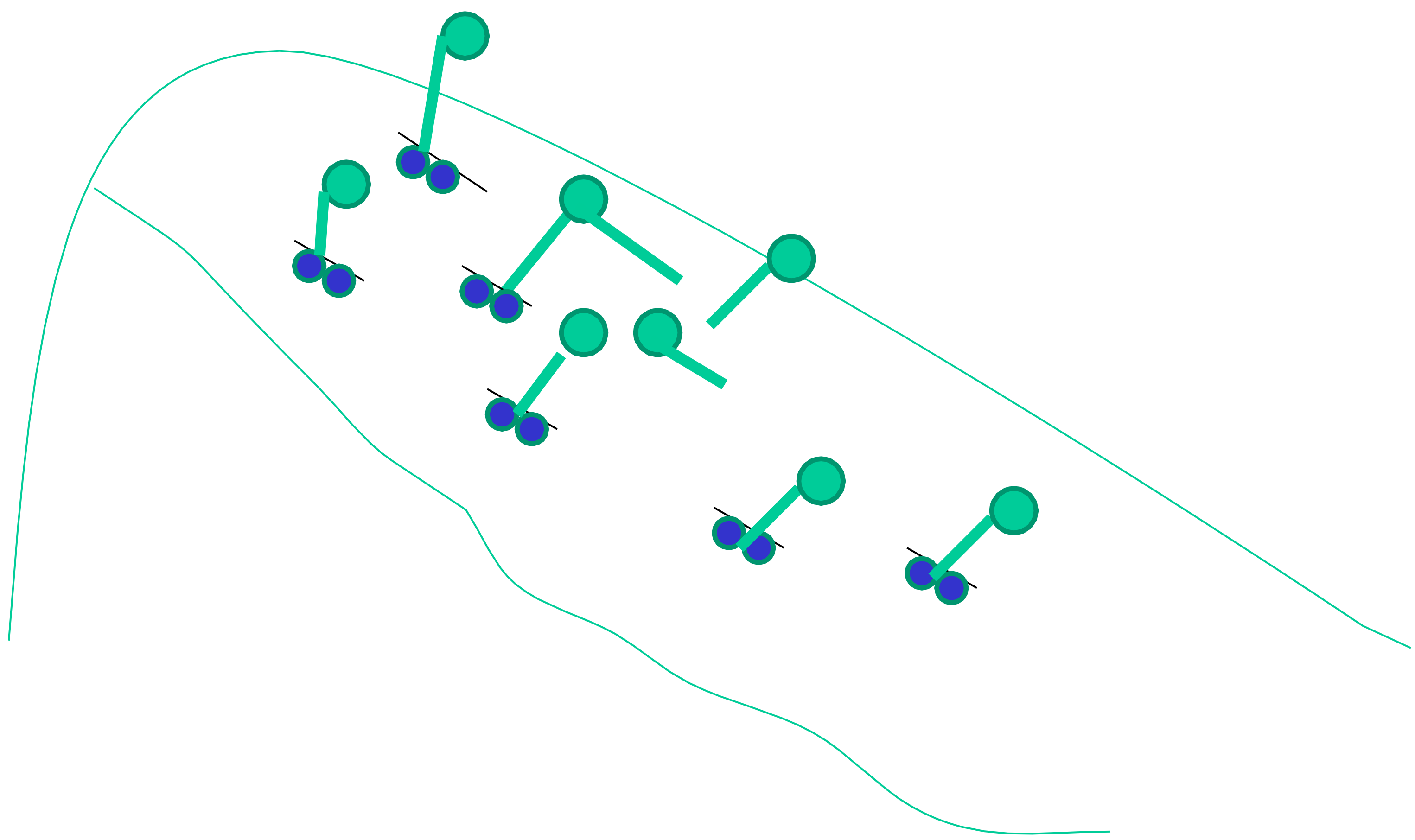
- Rate of transport – V_{max}



Initially, rate is directly proportional to conc. gradient

Till it reaches V_{max} (limitation because of no. of carrier mols. & rate of conformational change)

Hormonal regulation by changing #of carriers.



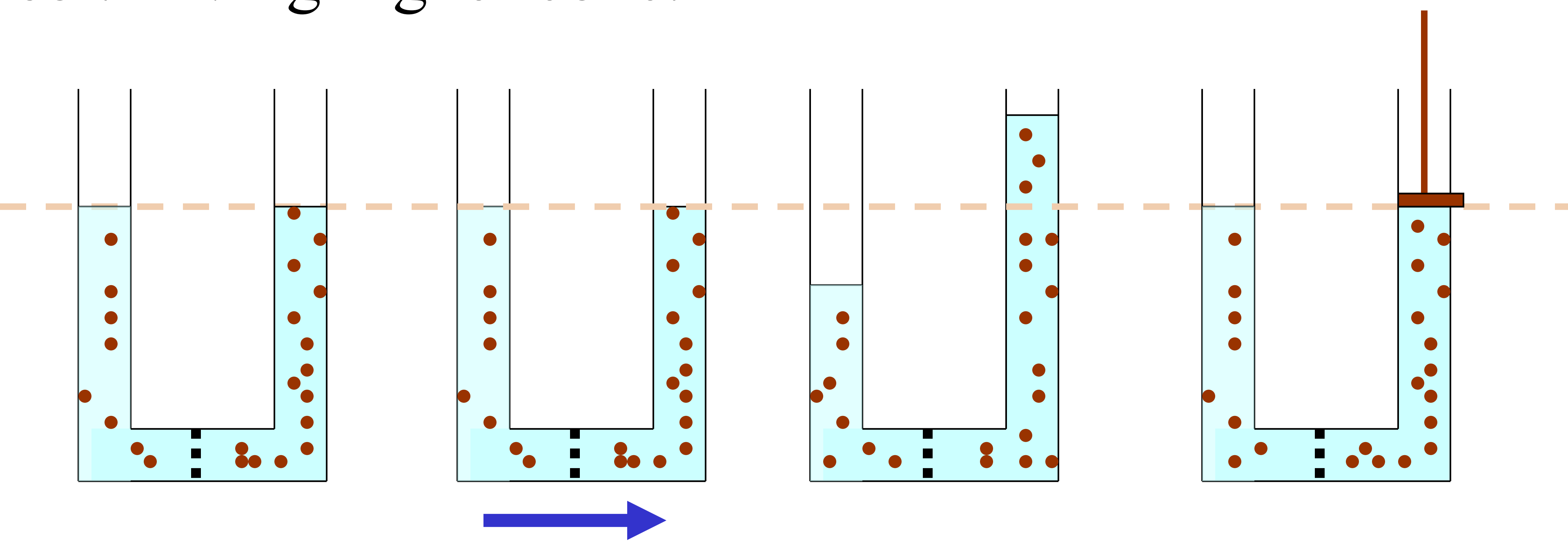
- Peculiarities of carrier mediated transport –

- specificity,
- competitive or noncompetitive inhibition – phloridzin for glucose
- saturation,
- blocking of receptor
- V_{max}

-Examples – transport of glucose, amino acids, galactose, etc. in the peripheral cells or counter transport of Ci and HCO3 in renal tubules

III. Osmosis & osmotic pressure–

when two solutions of different concentrations are separated by a semi permeable membrane (impermeable to solute and permeable to water) water mols. diffuse from solution having less conc. To the sol. having higher conc.



Osmotic pressure is the minimum pressure applied on the solution with high conc. which prevents osmosis.

- depends upon total no. of particles of dissolved solutes rather than type of the particles

Osmols or mOsmols – expresses conc. of osmotically active particles

$$1 \text{ osmol} = \frac{\text{total no. of particles in gram molecular}}{\text{wt. of non diffusible substance per kg. of water}}$$

Applied -

Isotonic, hypotonic & hypertonic solutions

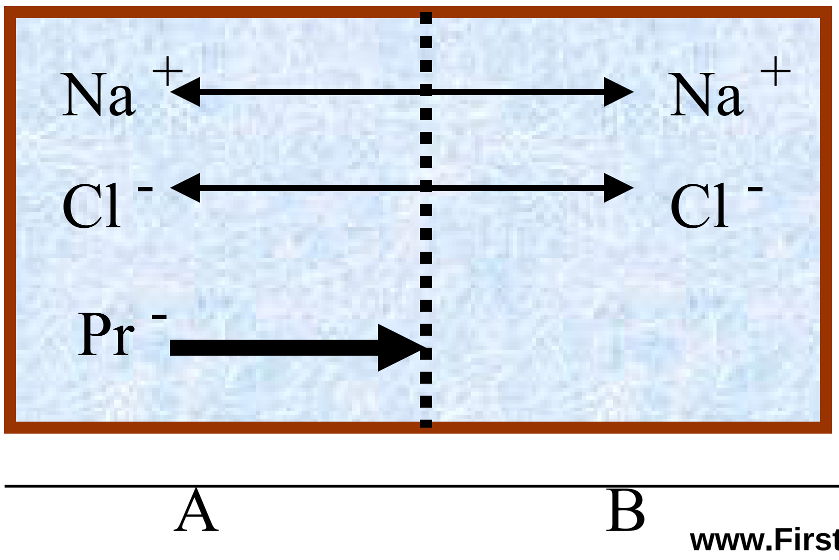
Isotonic solution – fluids having osmolarity same as that of plasma (290 mOsmols) . Red cells suspended in such solution do not shrink or swell. (0.9 % NaCl, 5% glucose)

In Hypotonic soln. RBCs swell and hemolysis may occur.

In hypertonic solution RBCs shrink because water moves out.

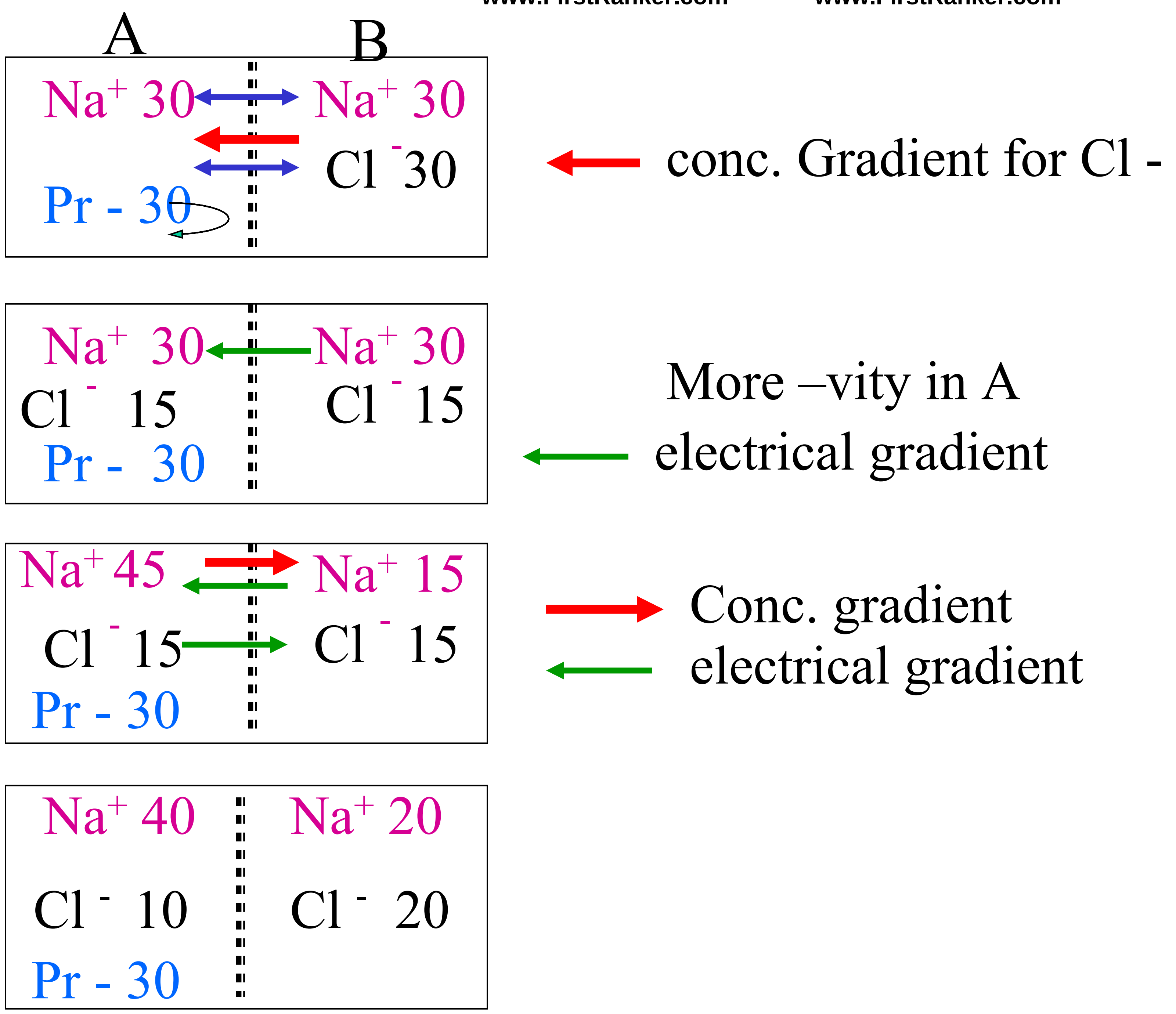
Gibbs – Donnan Equilibrium

Explains difference in the conc. of diffusible ions in two compartments separated by semi permeable membrane, when one compartment **contains non diffusible ions**



Proteins are non diffusible anions in A

Conc. Of Na^+ is more in A as compared to B



Explaination –

1) All the solutions are electrically neutral.

(total no. of anions = total no. of cations)

2) Product of diffusible cations and an anions in both the compartment is equal.

$$(Na^+_A \times Cl^-_A = Na^+_B \times Cl^-_B)$$

Applied –

In ICF conc. of diffusible K^+ is more because of presence of non diffusible Pr^- and PO_4^-

Diffusion potential or Equilibrium potential - E

Potential generated across the cell membrane in the presence of non diffusible ions in one compartment.

Magnitude of potential developed can be calculated by Nernst equation.

Nernst equation -

Equilibrium potential or diffusion potential (E)

$$= \underline{+}\,61 \log \frac{\text{Conc. inside}}{\text{Conc. outside}}$$

$$E_K = -94 \text{ mV}$$

$$E_{Na} = +61 \text{ mV}$$

$$E_{Cl} = -90 \text{ mV}$$

Goldmann-Hodgkin's equation =

$$-61 \log \frac{C_{Nai}.P_{Na} + C_{Ki}.P_{Na} + C_{Clo}.P_{Clo}}{C_{Nao}.P_{Na} + C_{Ko}.P_{Na} + C_{Clo}.P_{Cli}}$$

IV. Filtration

Filtration is a process in which fluid along with solutes passes through a membrane due to difference in pressures on both sides.

e.g. Filtration at capillary

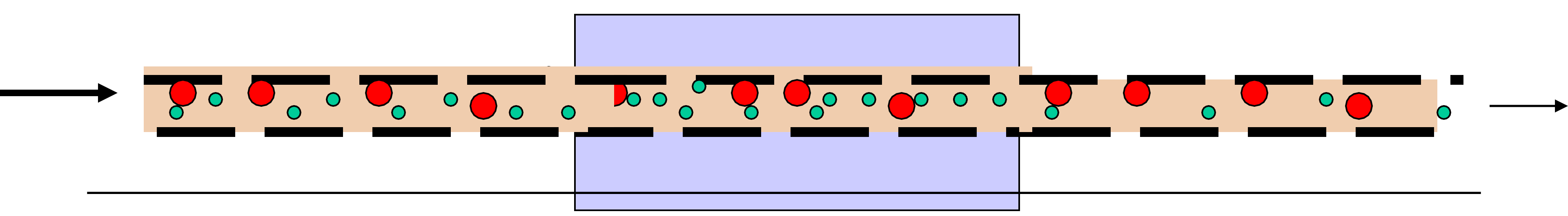
Capillary hydrostatic pressure –	28mm Hg
Interstitial fluid hydrostatic pressure -	-2mm Hg
Colloidal osmotic pressure -	25mm Hg

Net Filtration pressure = 28 - (- 2 + 25) = 5 mm Hg

V. Dialysis –

separation of larger dissolved particles from smaller particles

It is used for elimination of waste products in the blood in case of renal failure.



Active transport

- Primary active transport
- Secondary active transport
- Endocytosis
  - Pinocytosis
  - Phagocytosis
- Exocytosis

Peculiarities of active transport

1) Carrier mediated transport
2) Rapid rate of transport
3) Transport takes place against electrochemical gradient (uphill)
4) Expenditure of energy by transport protein which incorporates ATPase activity

5) Carrier protein shows specificity, saturation competitive inhibition, blocking

6) Substances transported – Na^+ , K^+, H^+, Cl^-, I^- , Glucose, Amino acids

I. Primary active transport –

Examples - Na^+ - K^+ pump, Ca^{++} pump

H^+-K^+ pump

- Inner surface of carrier mol. has ATPase which is activated by attachment of specific ions and causes hydrolysis of ATP molecule
- Energy released from ATP causes conformational change in the carrier which transports ions to the opposite side.

a) Na^+ -K^+ pump- electrogenic pump

- Attachment of $2K^+$ on outer side & 3 Na^+ on inner side

↓

Activation of ATPase

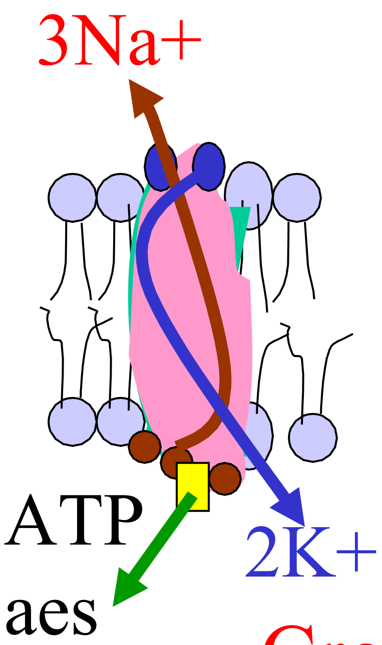
↓

Conformational change

↓

Efflux of 3 Na^+ & influx of $2K^+$

↓



Creates high K^+ conc. & - vity inside the cell

Helps in maintaining cell volume

Na-K pump is one of the major energy using process in the body & accounts for a large part of basal metabolism.

Regulators of Na-K pump –

- Incraesed amount of cellular Na conc.
- Thyroid hormones increase pump activity by more # of Na-K ATPase mol
- Aldosterone also increases # of pumps
- DOPamine inhibits pump
- Insulin increases pump activity
- Oubain or Digitalis inhibits ATPase (used when weakness of cardiac muscle –maintains Ca conc. In ICF of cardiac muscle

- Ca++ pump –

present in the membrane of ER, mitochondria and cell membrane

- involves uniport carrier

- helps to maintain low Ca++conc. in ICF

II. Secondary active transport

Active transport depending upon conc.

gradient of Na+ from ECF to ICF created by

utilization of energy

_ carrier does not have ATPase activity

Substance is transported along with Na+

(Na increases affinity of carrier for gl.)

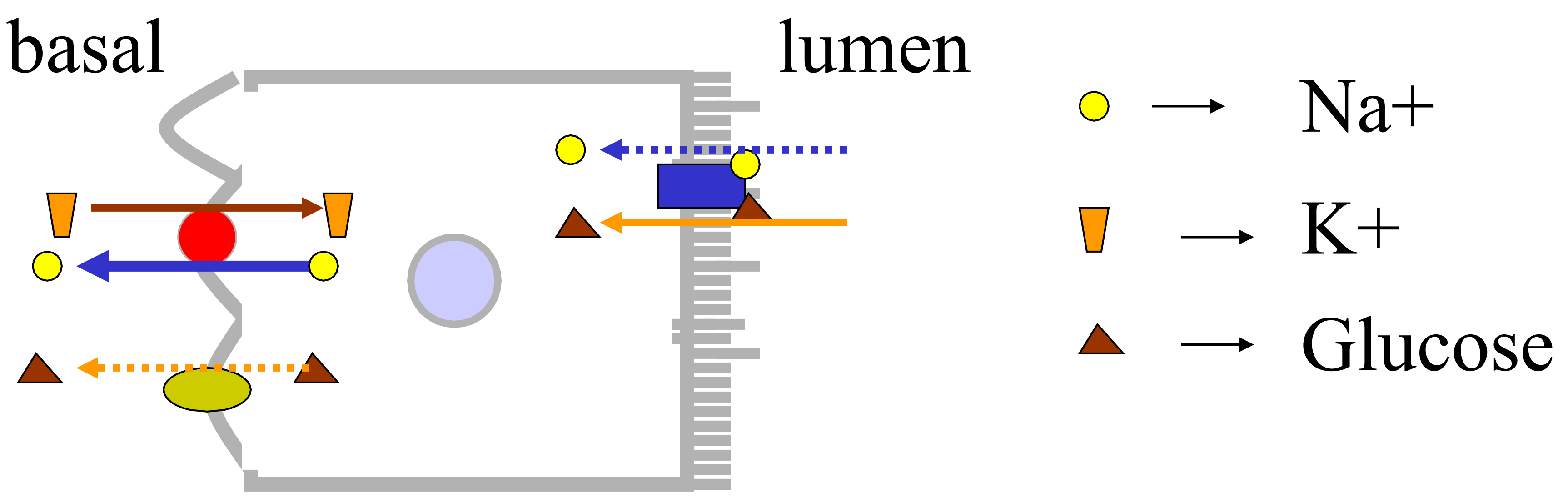
Na+ is transported only when glucose mol. is

attached

Examples – a) Reabsorption of glucose & amino acids in PCT & Intestinal mucosa – Co-transport mechanism

b) H+ secretion by tubular epithelium – counter transport mechanism

c)In heart Na-K ATPase indirectly affects Ca transport. –antiport in the membrane of cardiac muscle exchanges intracellular Ca for extracellular Na



- Na + – K + pump on basal side
- Electrochemical gradient for Na + on luminal side
- Carrier mediated transport (SGLT-1)of Na+ along with glucose (or amino acid) through the apical membrane
- Transport of glucose by facilitated diffusion (GLUT-2) through basal side

Types of transporters

- Uniport
- Synport
- Antiport

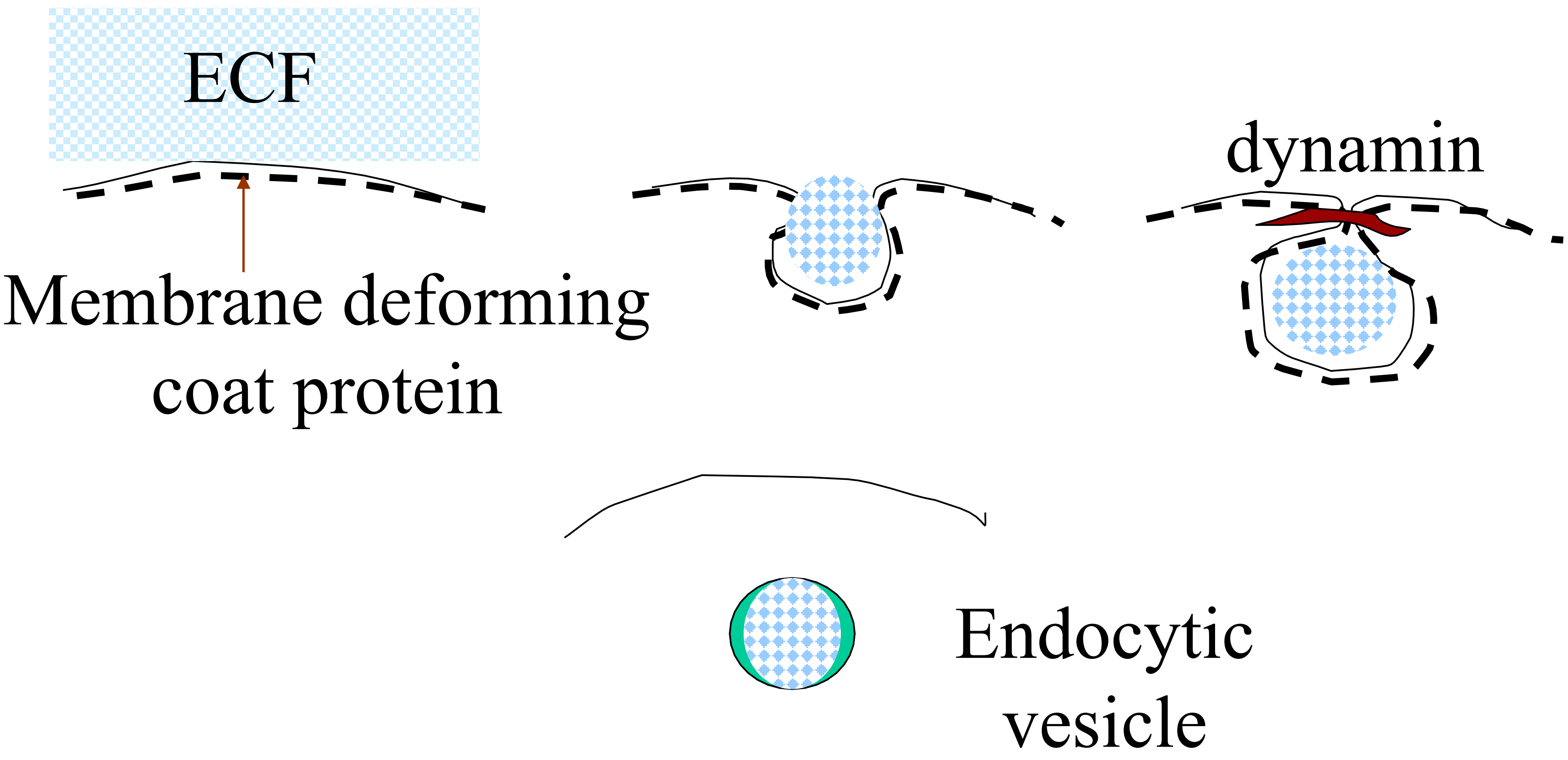
Extracellular material to be tackled by lysosomes is brought into the cell by **endocytosis**

3 types

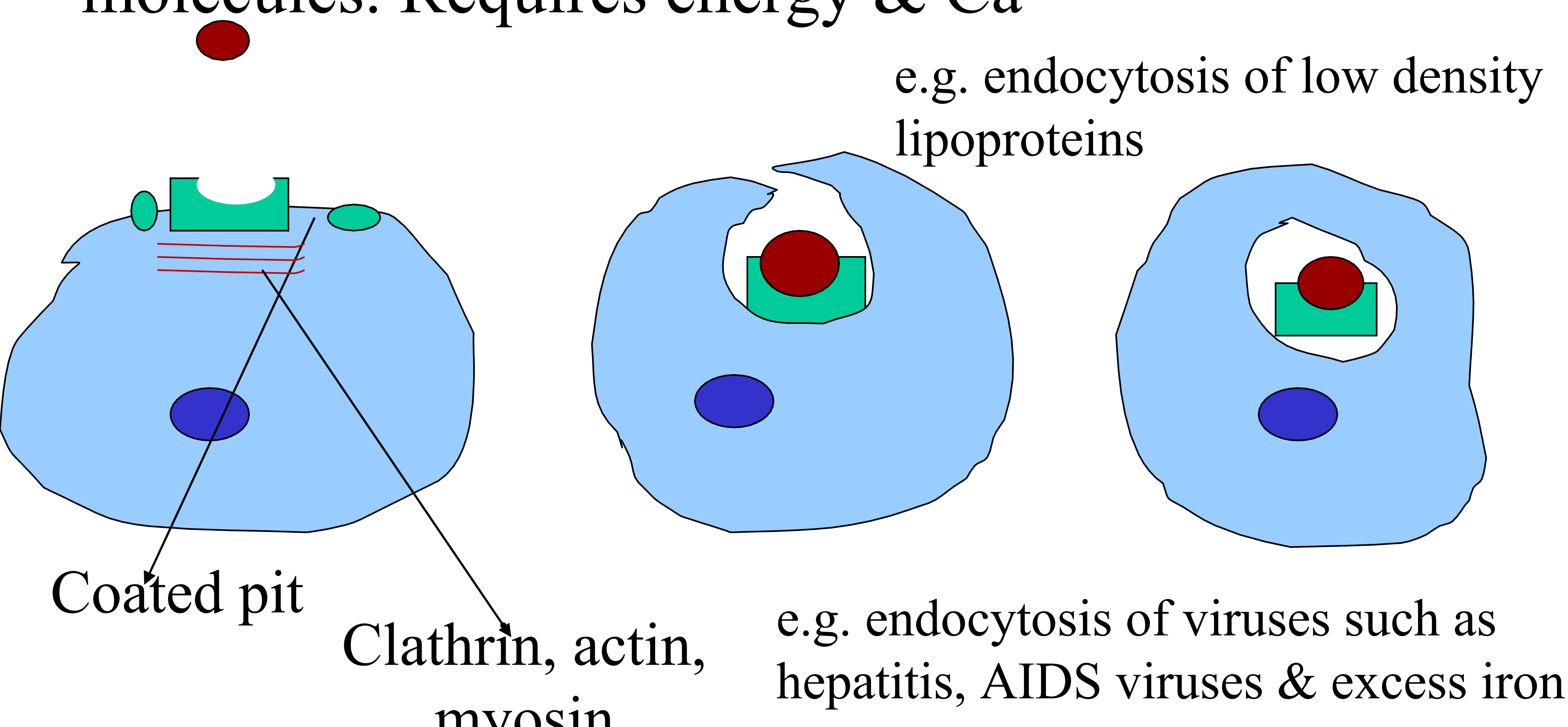
- **pinocytosis** — All cells
- **Receptor mediated endocytosis**
- **phagocytosis** — Specialised cells

Requires ATPase, Ca, microfilaments

Pinocytosis

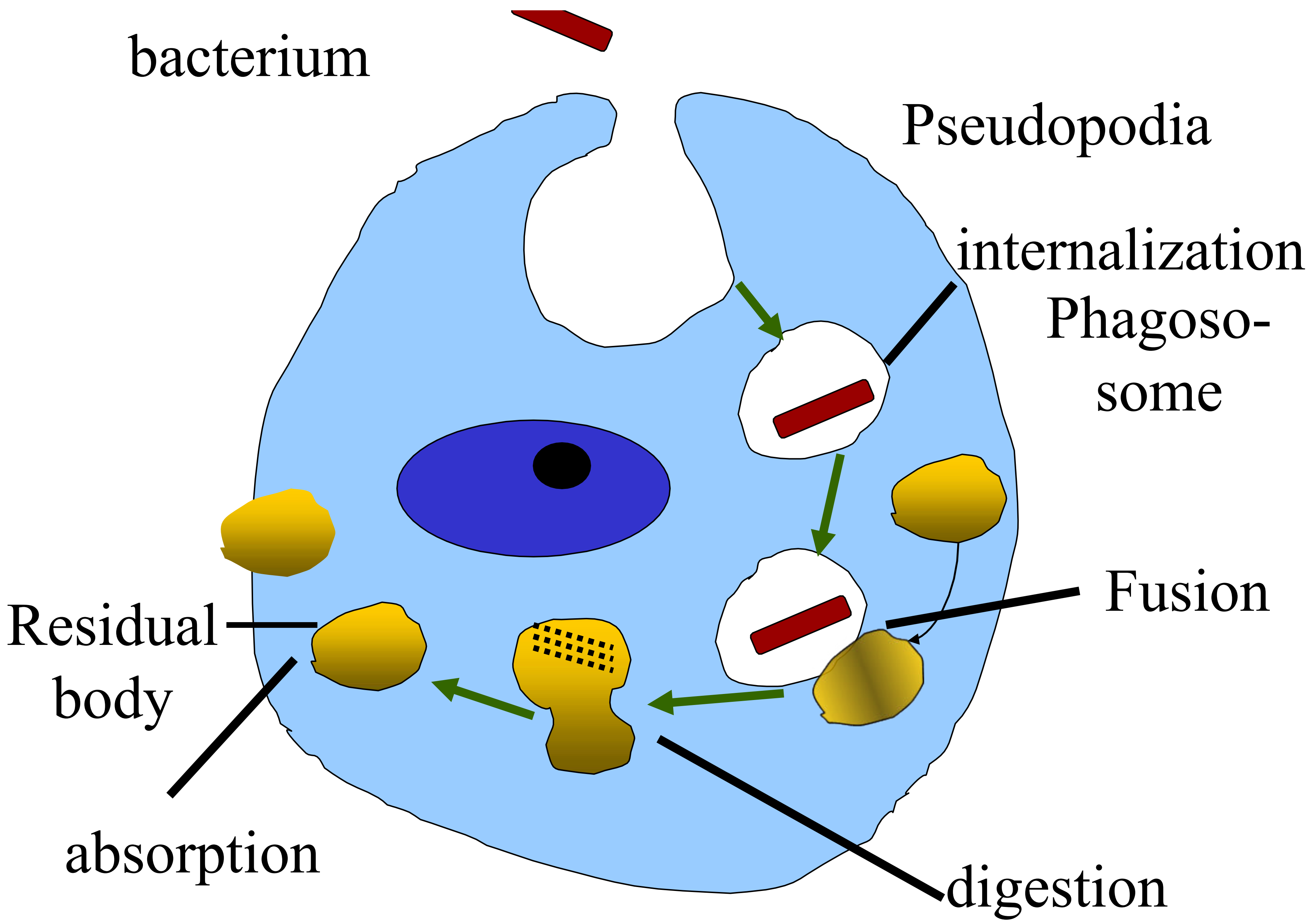


B. Receptor mediated endocytosis – highly selective process to import imp. specific large molecules. Requires energy & Ca^{++}.



C. Phagocytosis

- Internalization of large multimolecular particles, bacteria, dead tissues by specialized cells e.g. certain types of w.b.c.s (Professional phagocytes)
- The material makes contact with the cell membrane which then invaginates.



Phagocytosis

Passive transport

- No expenditure of energy molecules
- Takes place along conc., electrical, & pressure gradient
- Carrier may or may not be required
- Rate is proportional to conc. difference

Active transport

- Expenditure of energy mol. (ATP)
- Can take place against conc. Gradient
- Carrier is always required
- Rate is proportional to availability of carrier & energy. (V_{max})

Simple Diffusion

- Passive transport
- For small molecules
- No carrier required
- Rate of transport is directly proportional to conc. gradient
- Examples –
  - Lipid soluble –
    - O2, CO2, alcohol
  - Lipid insoluble –
    - urea, Na+, K+

Facilitated Diffusion

- Passive transport
- For large molecules
- Carrier mediated
- Initially rate is proportional to conc. gradient till V_{max} (saturation of carriers)
- Examples –
  - glucose, amino acids