Cell membrane Transport across

Dr katek balapala

Substances transported for

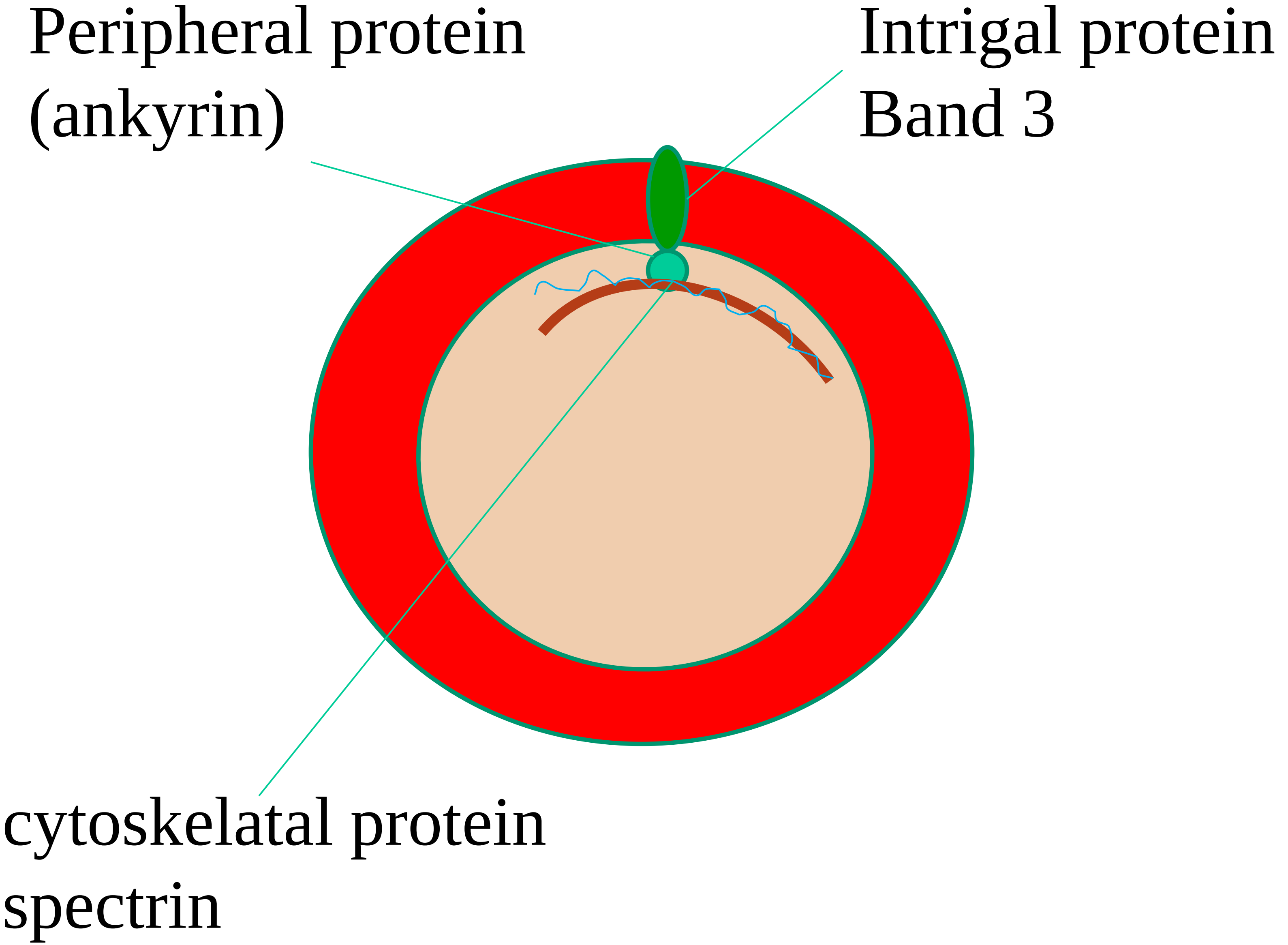
chemical reactions

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

Fluid mosiac – membrane proteins like iceberg in sea –floating in sea of phospholipids which also moves

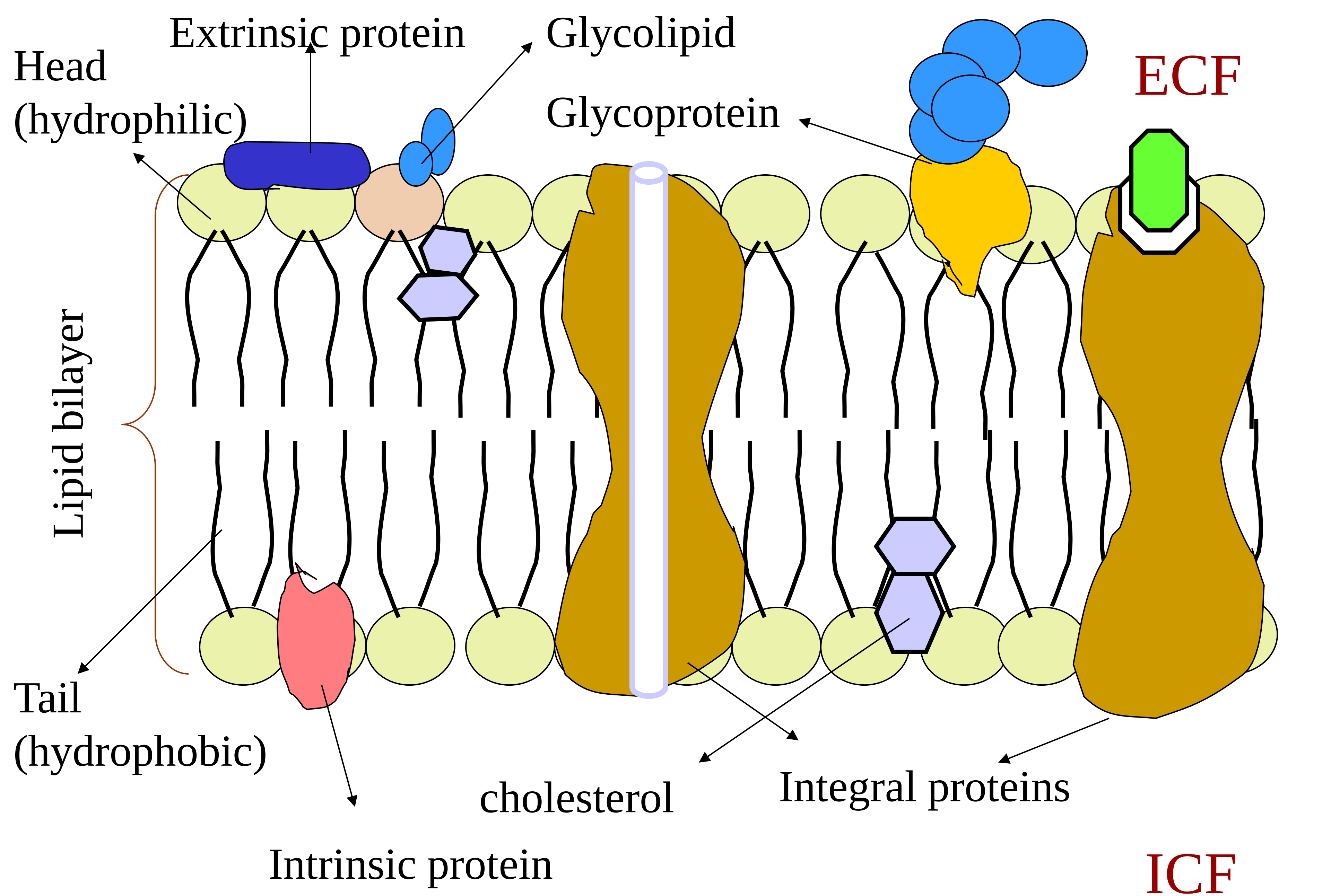
Translational diffusion –rate many micrometrs/sec.

Long chain & saturated fatty acids make membrane stiff. More kinks in unsaturated fatty acids-more fluidity

Cholesterol helps to maintain fluidity over wide range of temp.

Regional asymmetry of membrane

Transverse asymmetry


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

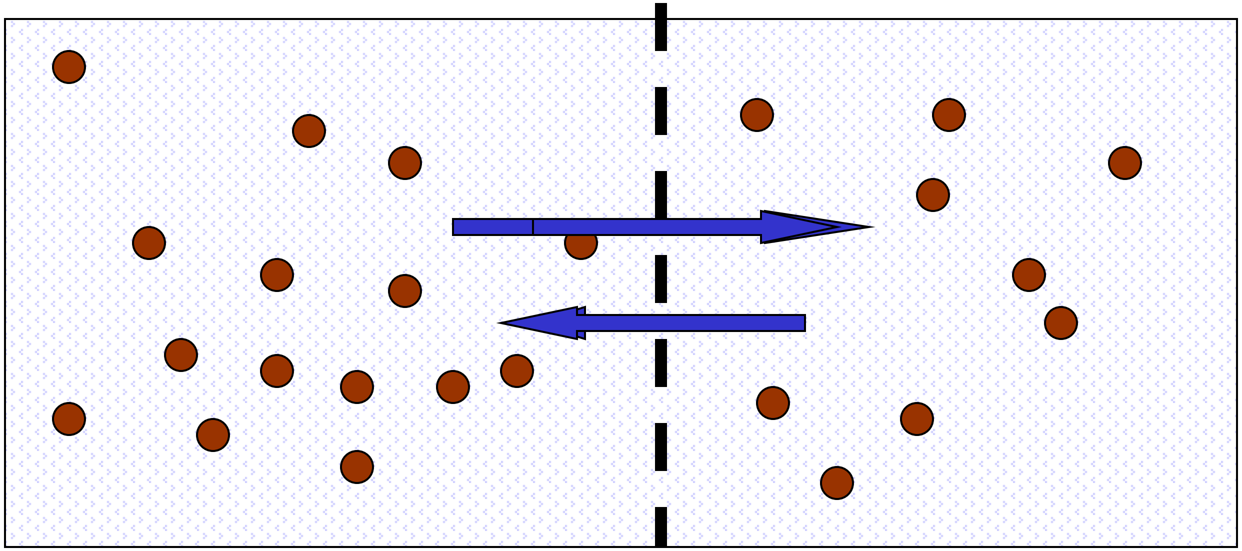
- Primary active transport
- Secondary active transport
- Endo/Exocytosis

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+

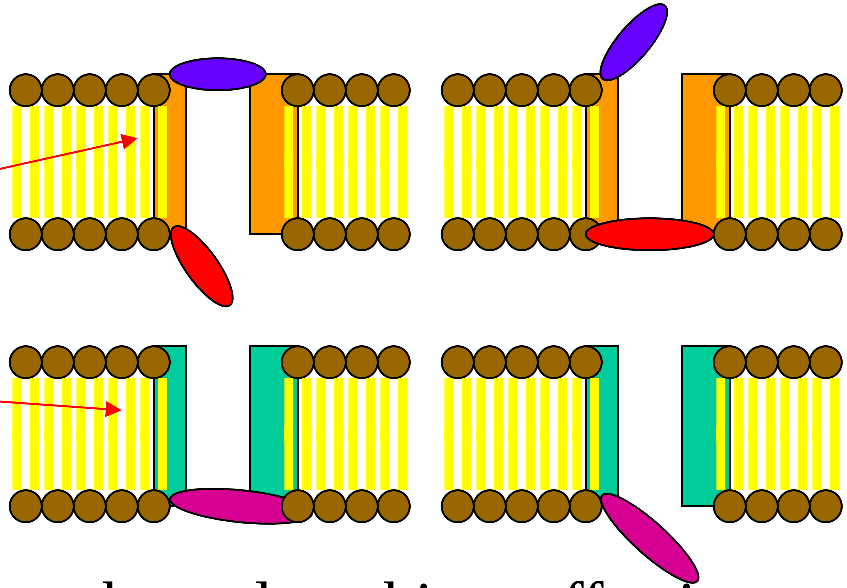
K+

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 –

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

Q = net rate of diffusion

ΔC = conc. gradient of a substance

P = permeability of membrane to the sub.

A = surface area of a membrane

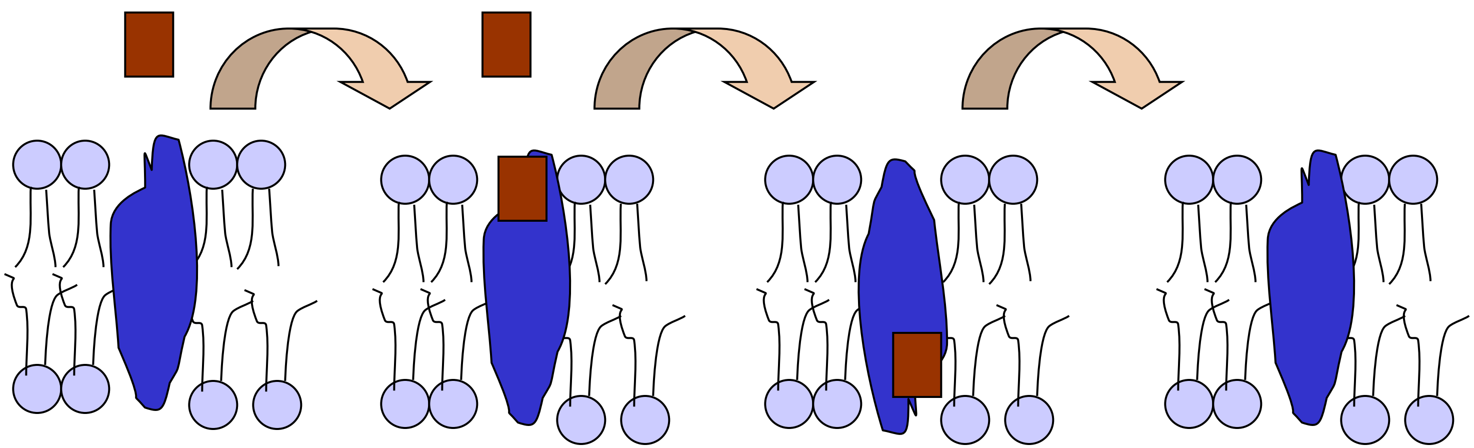
MW = molecular wt. of sub.

ΔX = thickness or distance

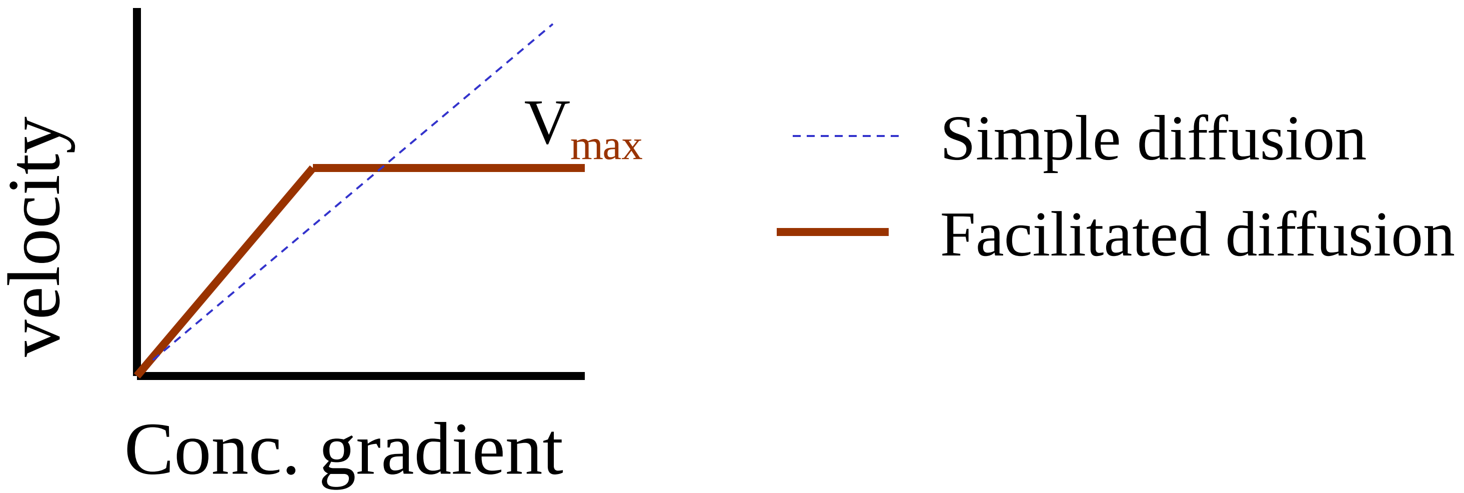
II. Facilitated diffusion :

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

Mechanism



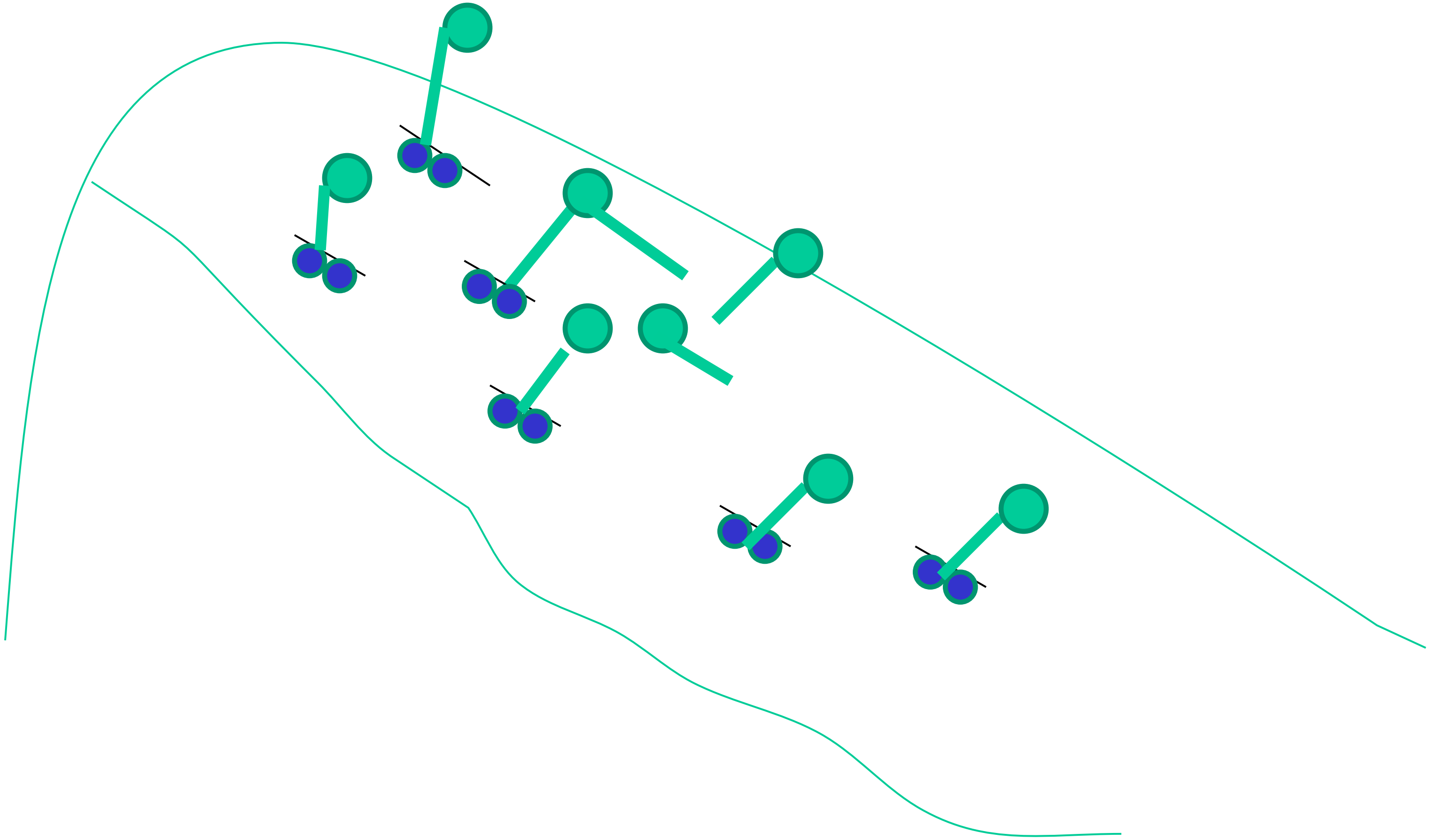
- Rate of transport – V_{max}



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.



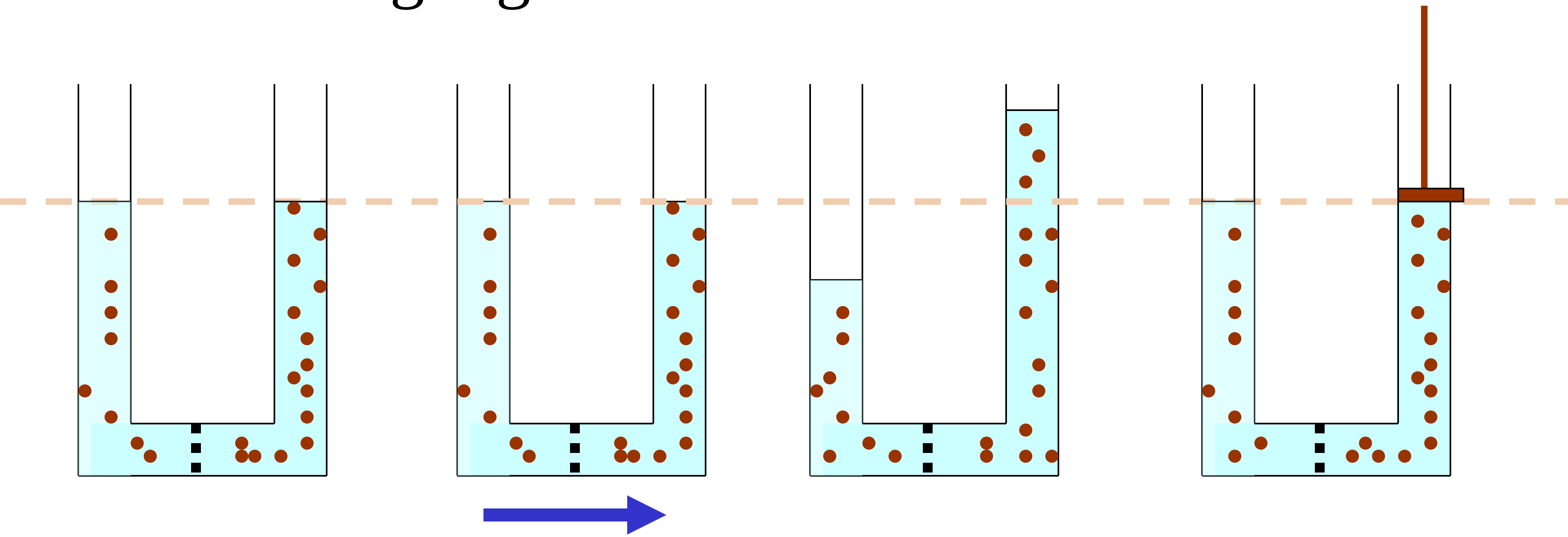
- Peculiarities of carrier mediated transport –

- 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 osmol = total no. of particles in gram molecular 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.

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 =

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

The Goldman-Hodgkin-Katz equation

$$V_m = \frac{RT}{F} \ln\left(\frac{p_K[K^+]_o + p_{Na}[Na^+]_o + p_{Cl}[Cl^-]_i}{p_K[K^+]_i + p_{Na}[Na^+]_i + p_{Cl}[Cl^-]_o}\right)$$

- ***Vm*** is the membrane potential. This equation is used to determine the resting membrane potential in real cells, in which K^+, Na^+, and Cl^- are the major contributors to the membrane potential. Note that the unit of V_m is the Volt. However, the membrane potential is typically reported in millivolts (mV). If the channels for a given ion (Na^+, K^+, or Cl^-) are closed, then the corresponding relative permeability values can be set to zero. For example, if all Na^+ channels are closed, $p_{Na} = 0$.
- ***R*** is the universal gas constant (8.314 $J.K^{-1}.mol^{-1}$).
- ***T*** is the temperature in Kelvin (K = °C + 273.15).
- ***F*** is the Faraday's constant (96485

https://www.physiologyweb.com/calculators/ghk_equation_calculator.html

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

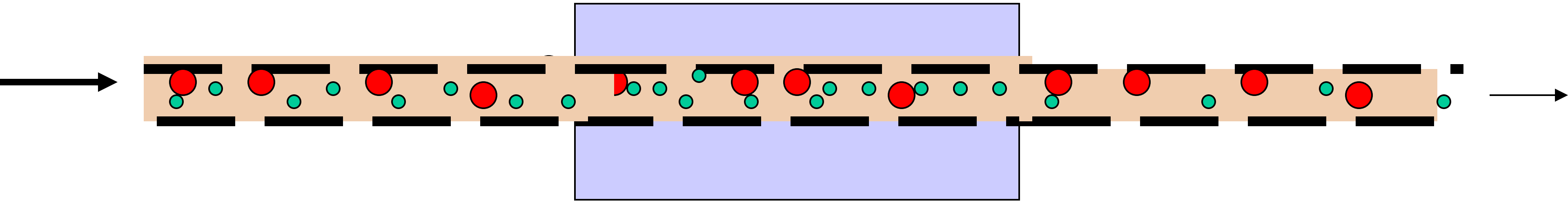
Colloidal osmotic pressure - 25mm Hg

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.

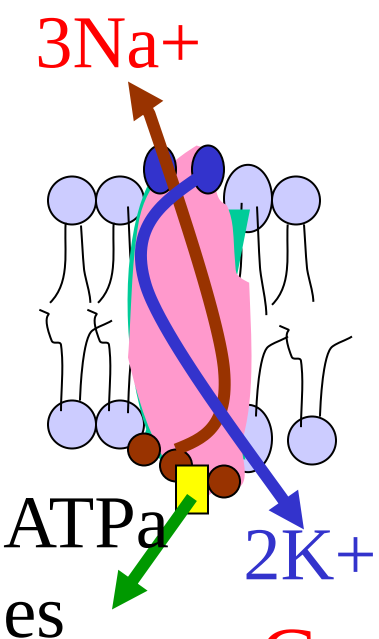
a) Na^+ -K^+ pump- electrogenic pump

- 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.)

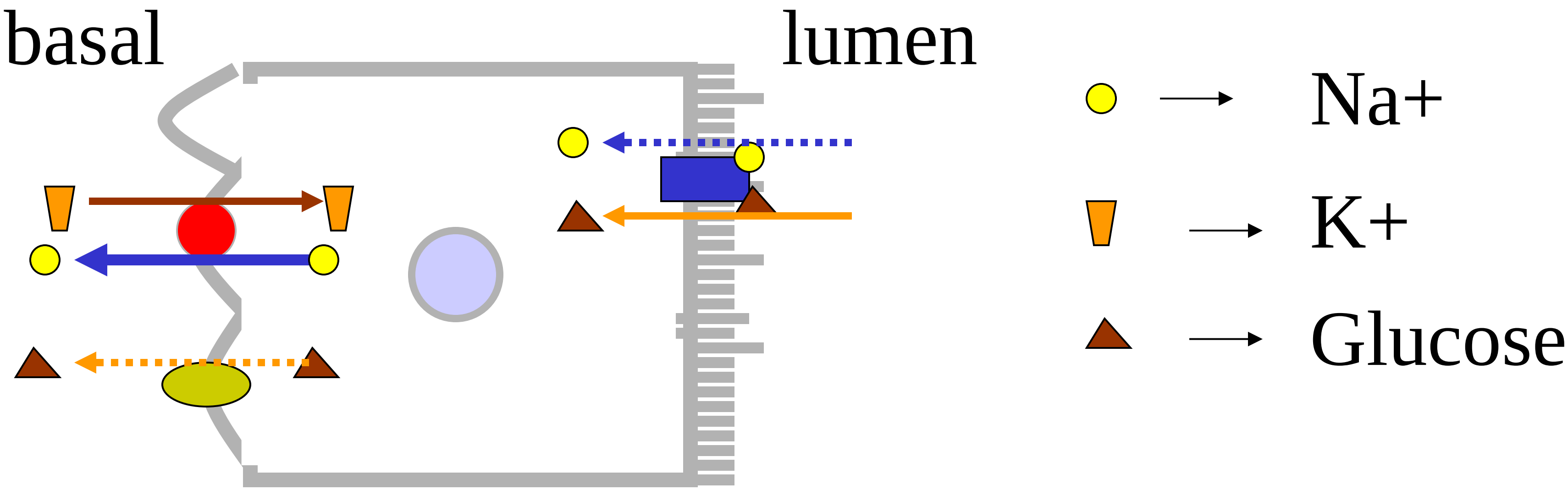
Na+ is transported only when glucose mol. is attached

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

uniporter is the glucose transporter (GLUT) in found in erythrocytes (referred to as GLUT1 to separate from other mammalian glucose transporters). This allows glucose to enter the cell via facilitated diffusion

Symport = the H^+/oligopeptide transporter (PepT), found in the small intestine, couples the downhill movement of H^+ across the plasma membrane to the uphill **transport** of dipeptides and tripeptides into the cell against a concentration gradient.

Antiport =

Na/Ca exchanger

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

3 types

pinocytosis

All cells

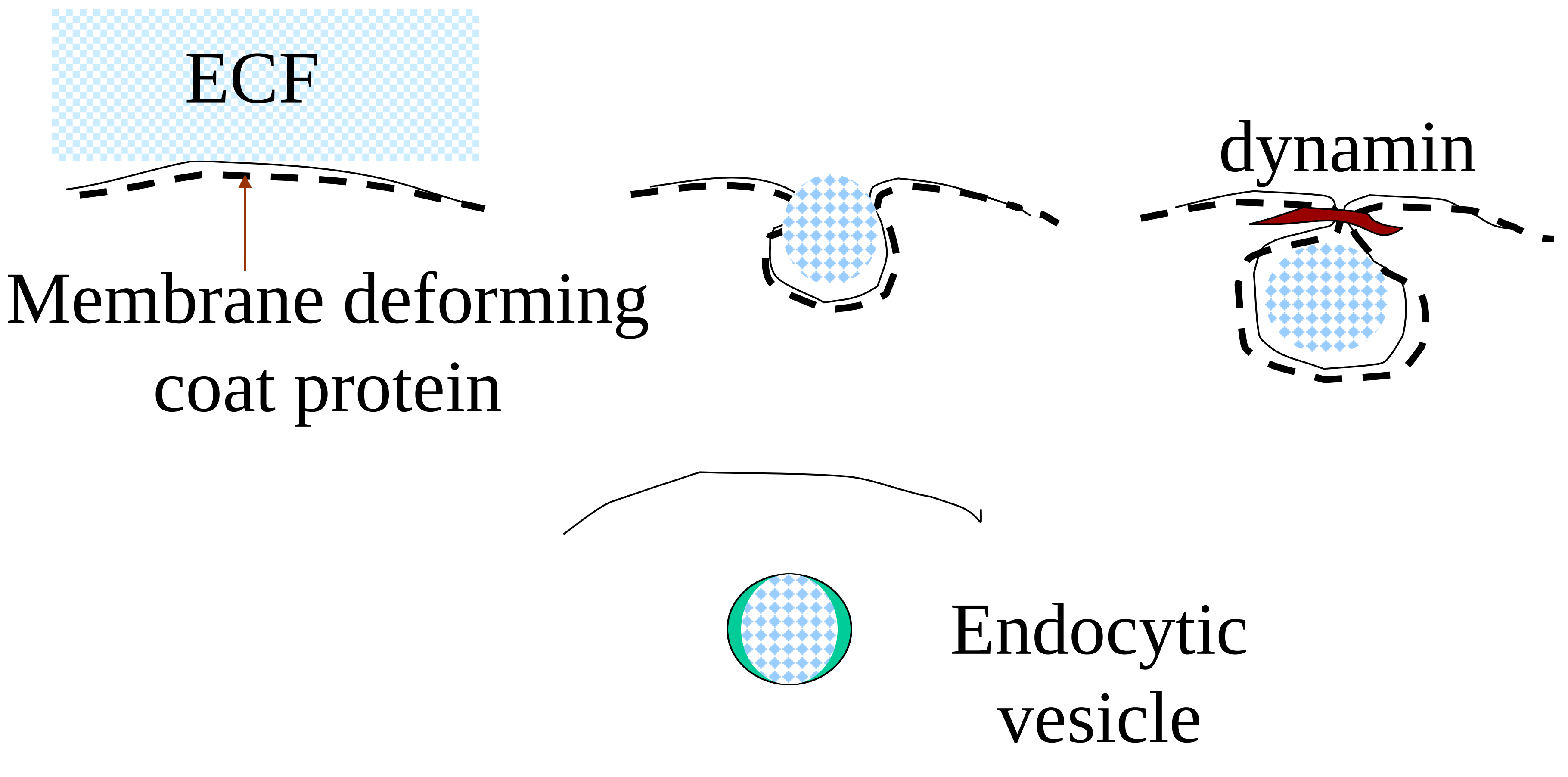
Receptor mediated endocytosis

phagocytosis

Specialised cells

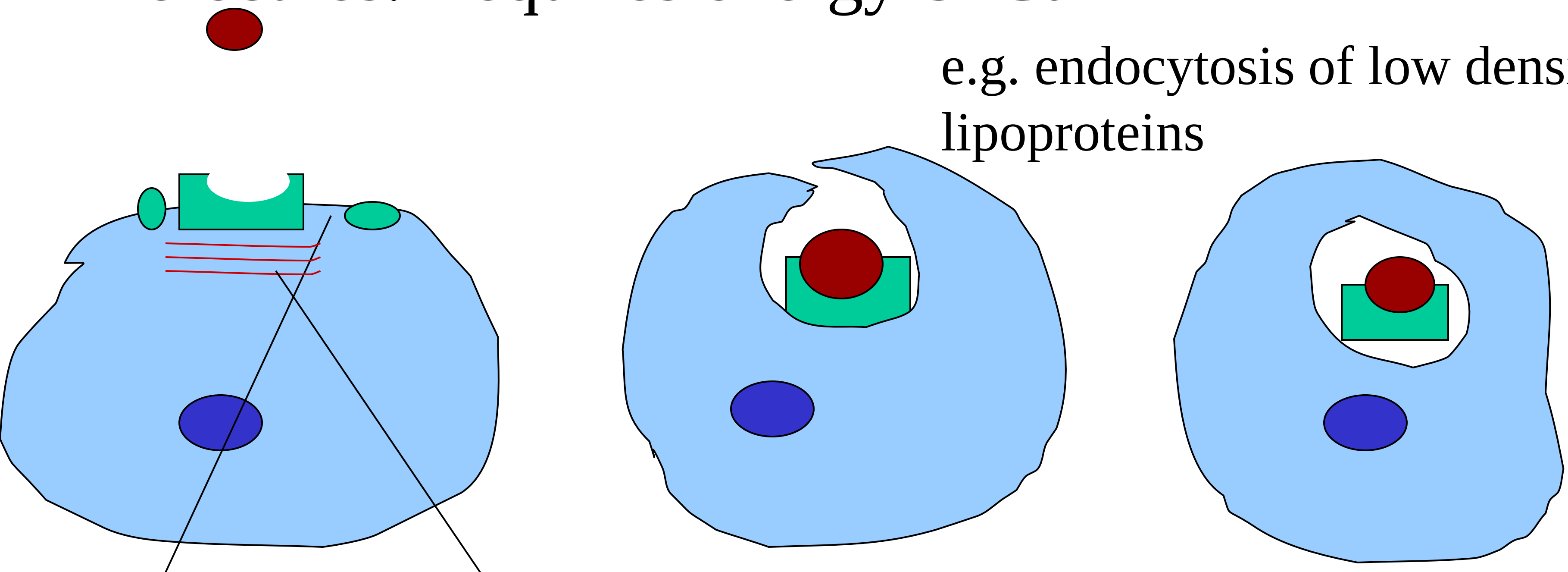
Requires ATPase, Ca, microfilaments

Pinocytosis



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

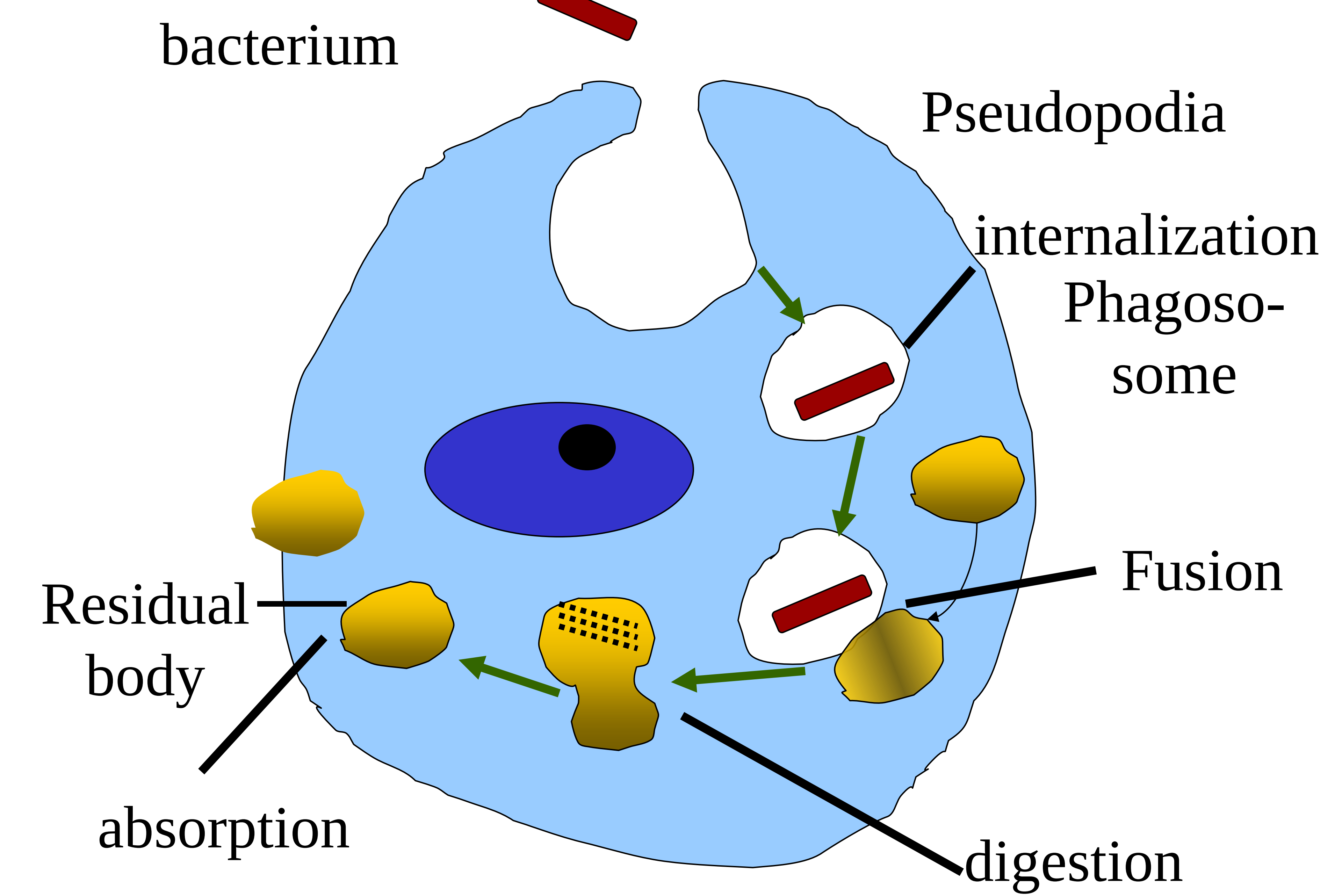
e.g. endocytosis of low density lipoproteins



e.g. endocytosis of viruses such as hepatitis, AIDS viruses & excess iron

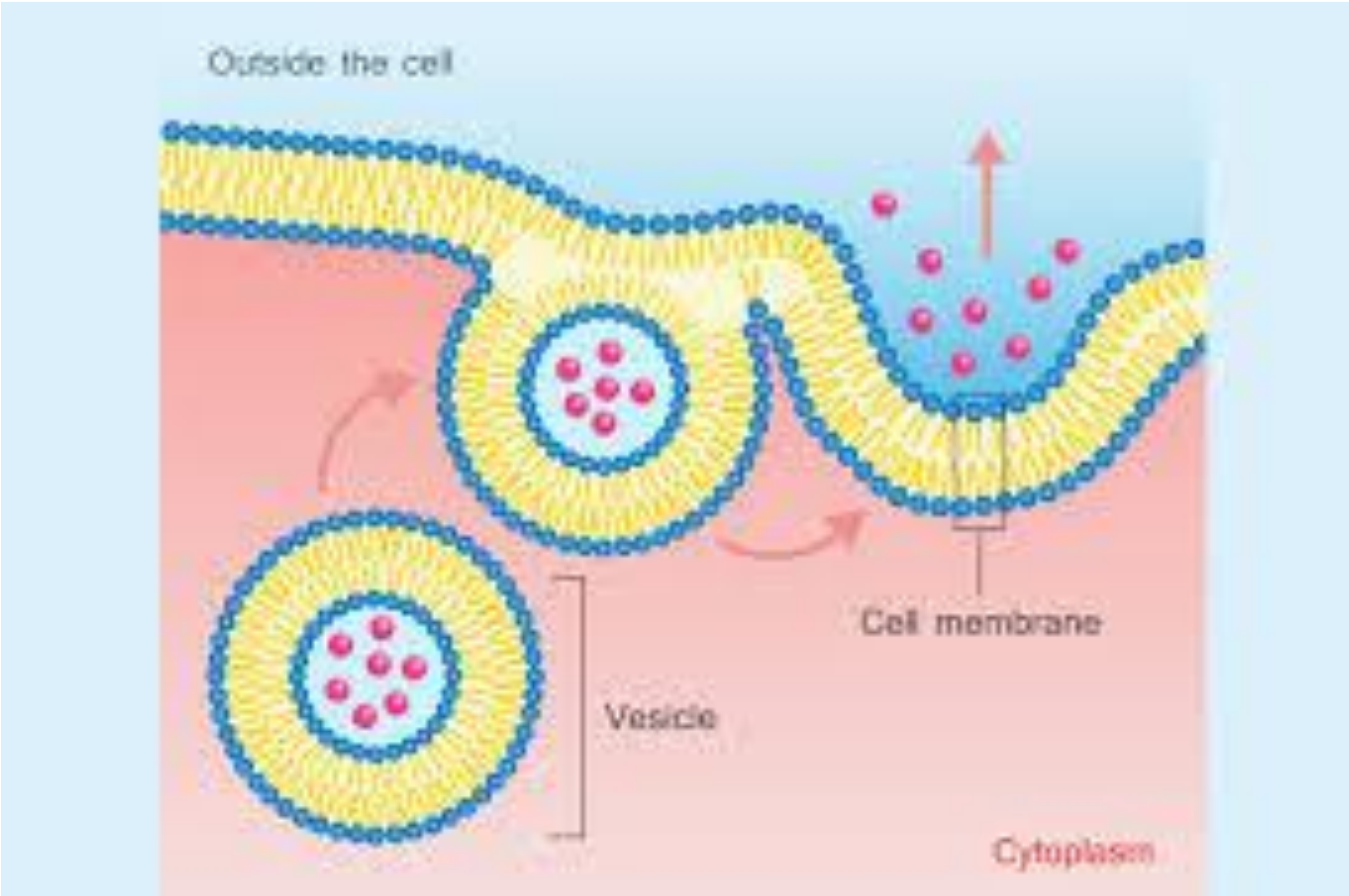
C. Phagocytosis

- 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

Exocytosis is a form of active transport and bulk transport in which a cell transports molecules out of the cell by secreting them through an energy-dependent process



Outside the cell
Cell membrane
Vesicle
Cytoplasm

Passive transport	Active transport
• No expenditure of energy molecules	• Expenditure of energy mol. (ATP)
• Takes place along conc., electrical, & pressure gradient	• Can take place against conc. Gradient
• Carrier may or may not be required	• Carrier is always required
• Rate is proportional to conc. difference	• 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 –

  O_2, CO_2, alcohol

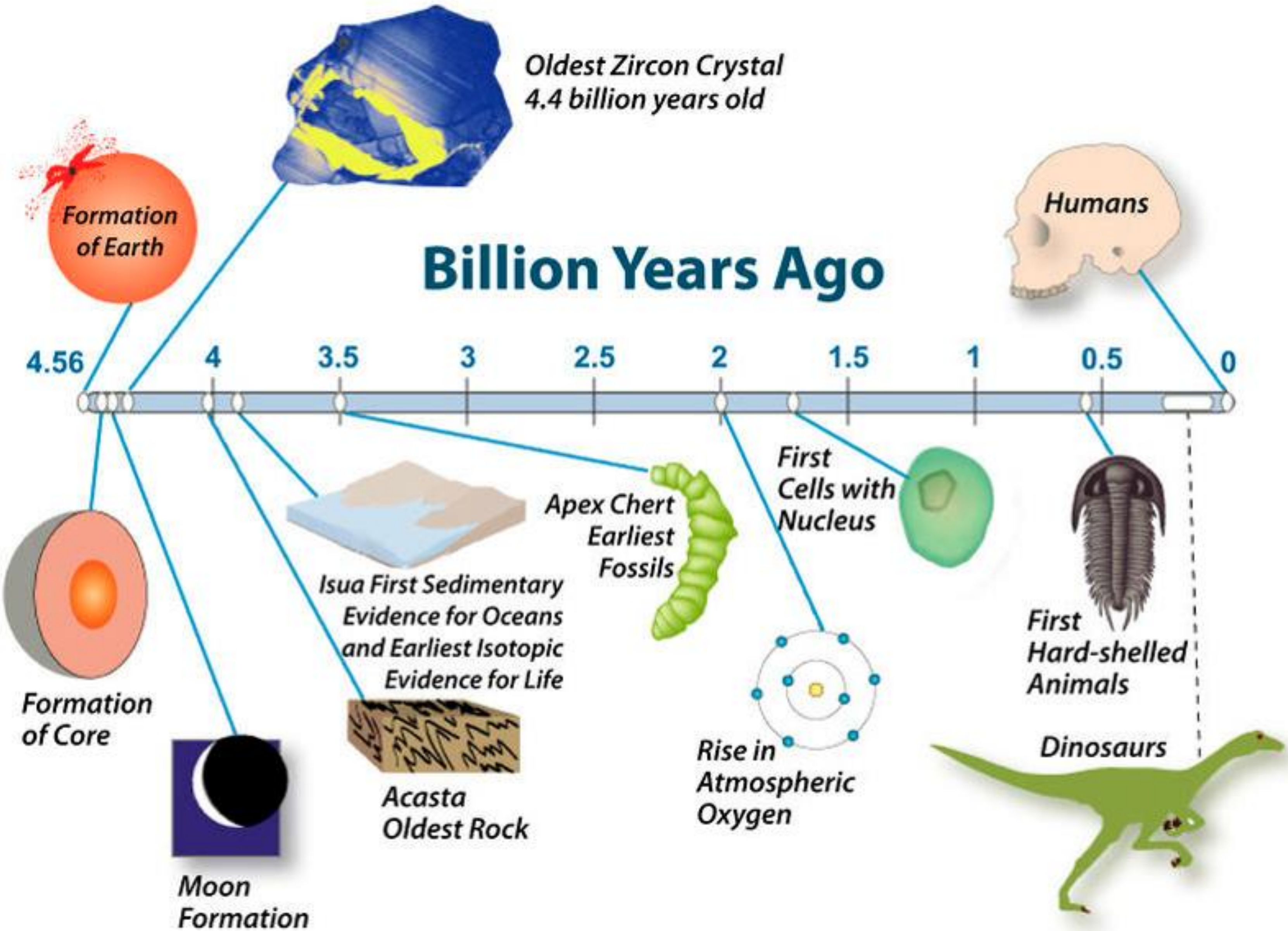
  Lipid insoluble –

  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


Oldest Zircon Crystal
4.4 billion years old
Formation of Earth
Humans
Billion Years Ago
4.56
4
3.5
3
2.5
2
1.5
1
0.5
0
First Cells with Nucleus
Apex Chert Earliest Fossils
Isua First Sedimentary Evidence for Oceans and Earliest Isotopic Evidence for Life
First Hard-shelled Animals
Formation of Core
Rise in Atmospheric Oxygen
Dinosaurs
Acasta Oldest Rock
Moon Formation


Thank
you