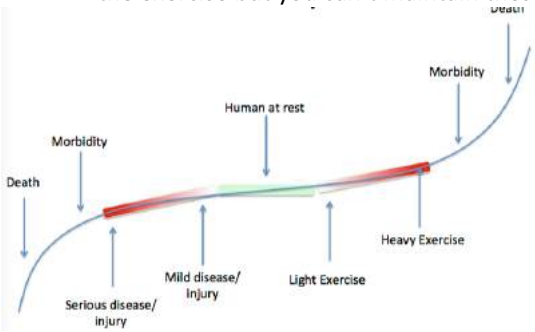
Integrated Physiology Notes

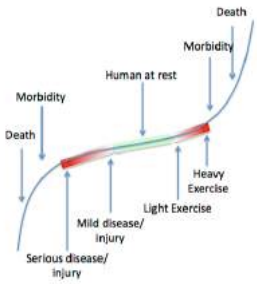
- Integrated processes by which organisms work
- Molecular → cellular → tissues → organs → systems → whole systems (organisms)

Physiology and Homeostasis

Homeostasis

- Effectively a *set of steady states* in which an organism operates 'comfortably'
- "Similar conditions"
- Energy input required to maintain
- When you do more exercise, you establish a separate set of steady states to allow you to stay doing the exercise but you can't maintain these steady states indefinitely

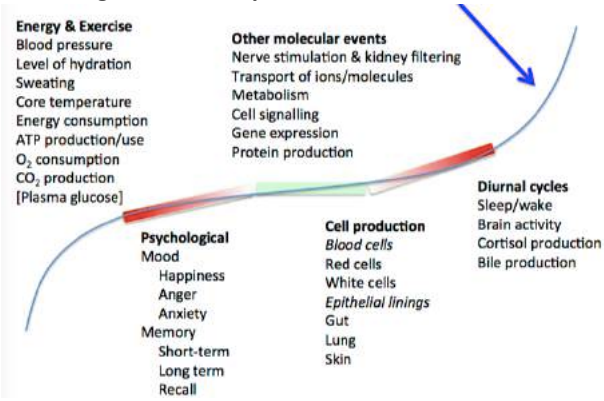




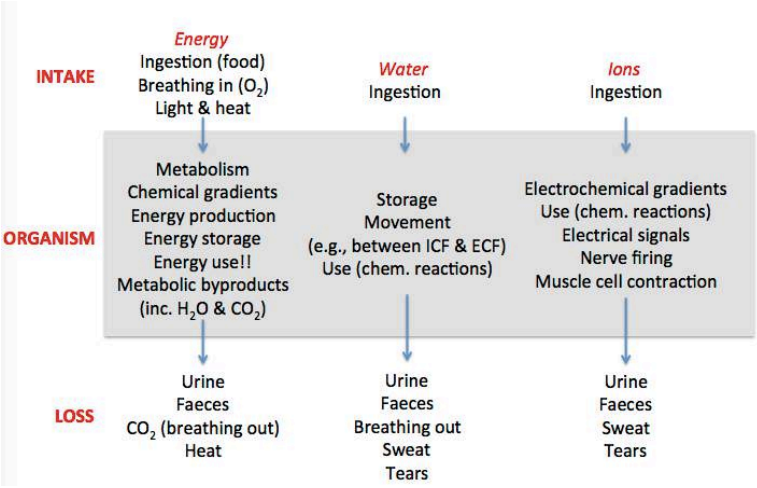
Athletes pushed to their limits – collapsed, can only sustain their set of steady states for so long
Parkinson's disease – off and on periods, can sometimes walk fine, sometimes not

Pathophysiology – precarious or no comfort zone, comfort zone is compressed, scope for being comfortable is smaller, difference for how you feel with mild exercise comes on quicker, more susceptible to things like disease, injury

What might the line represent?



Homeostasis – steady states require intakes and losses, intake, organism uses to maintain homeostasis, loss



ICF – intracellular fluid

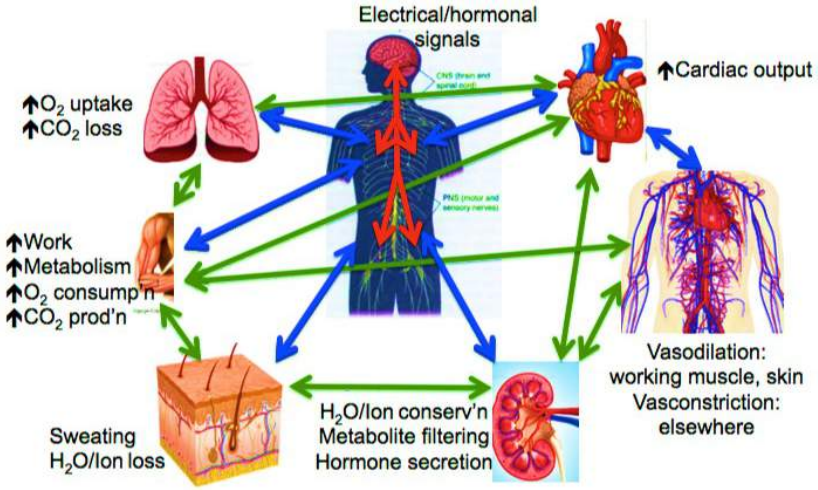
Other types of loss

- **Diarrhoea**
- **Vomiting**
- **Feeding your gut flora**
- **Diuresis** (e.g., diuretics, cholera)

- **Blood/tissue loss**
  - *Menstruation, ejaculation*
  - *Donation*
  - *Injury, amputation*

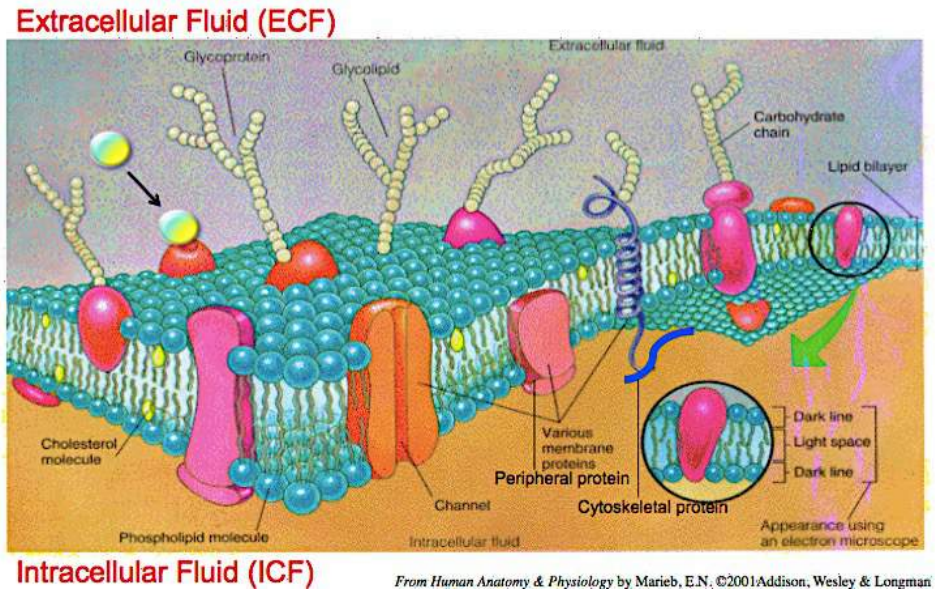
- **Disease**
  - *Muscle wasting (DMD, ALS)*
  - *Cachexia (cancer)*
  - *Nerve loss (Parkinson's, Alzheimer's, stroke)*
  - *Cardiomyopathy*

An example – dynamic exercise



- **GI tract** produces the energy

The plasma membrane



The plasma membrane: lipid bilayer

- Phospholipids
  - Hydrophilic head groups (face water)
  - Long hydrophobic tails (oily interaction)
  - Self-assembling, very little stability
- Permeable to small hydrophobic molecules
  - Naturally occurring, clinical drugs, toxins
- Barrier to:
  - Large hydrophobic molecules
  - Large molecules (e.g., proteins)
  - Atomic ions (e.g., Na, K, Cl)
  - Charged molecules (e.g., amino acids, sulphates)
  - Polar molecules (e.g., glucose, water)

Plasma membrane: a fluid mosaic

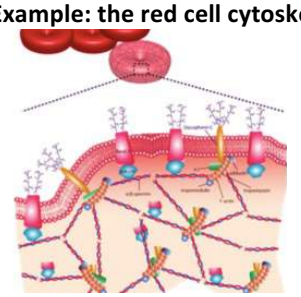
- Lipid bilayer is modified by addition of
  - **Specialised lipids** (e.g. cholesterol and glycolipids) which alter permeability to small hydrophobic molecules
  - **Membrane-attached proteins** e.g. cytoskeletal proteins, which provide stability
  - **Transmembrane proteins**
    - **Transporters –** which greatly and selectively modify barrier permeability
      - Allow selectively entry of molecules that normally can't get through
    - **Receptors –** receive and interpret signals (communication between cells near and far)

Membrane-attached proteins: cytoskeletons

- Essential support for lipid bilayers – every cell needs them
- **Allows for:**
  - Cells at rest to remain stable
  - Adoption of specialised shapes
  - Resistance to high shear stress
    - Red and white cells in circulation (really get a hammering)
  - Motility and shape change
    - Red cells squeezing through capillaries
    - White cells squeezing between cells
    - Movement to sites of infection
    - Swallowing invaders (phagocytosis)
  - Contraction and relaxation

        - Skeletal, cardiac and smooth muscle
    - Stretching and relaxation
        - Vasculature, heart, lungs, bladder, GIT, skin

Example: the red cell cytoskeleton

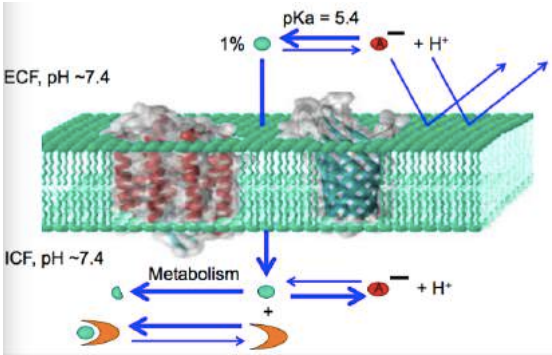


Cytoskeletal network on inside of membrane

Change shape readily, squished, need to streamline to reduce viscosity to make it easier on your heart to pump blood around

Lipid bilayer: penetration by small hydrophobic molecules

- Small hydrophobic molecules penetrate lipid bilayer



Hydrophobic molecule – green, because small and hydrophobic, can penetrate the membrane

A lot of molecules are charged acidic molecules – because they are charged, can't penetrate bilayer, so, join with proton to become a small, uncharged hydrophobic molecule – many drugs work this way

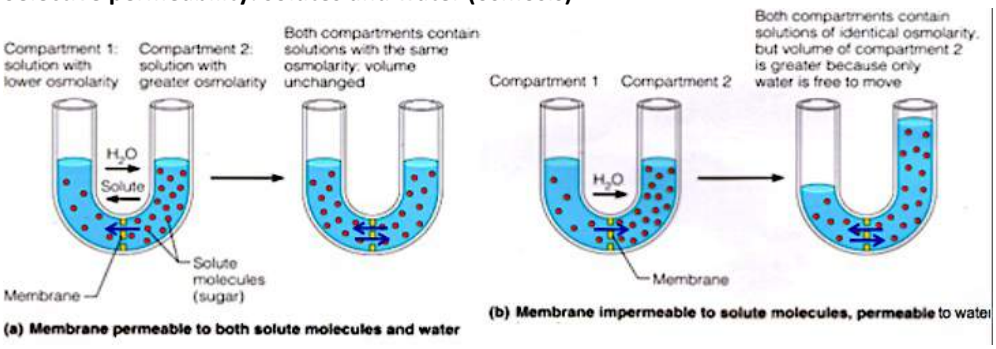
As more of molecules goes inside of the cell, you are pulling the reaction to the left, so more and more molecules go inside cell
It can also be metabolised or coupled to its receptor – pulls reaction to left even more

- Polar and large molecules don't penetrate lipid bilayer
- **The fluid mosaic membrane: selective penetration mechanisms**
    - How do these *other* molecules cross biological membranes?
        - Chemical concentration gradients + diffusion: uncharged solutes
        - Electrochemical gradients + diffusion: ions
        - Osmosis + diffusion: concentration gradient of water
        - Selective transporters
        - Energy (usually ATP; movement against gradients)

Concentration gradients and diffusion

- Move from areas of high concentration to low concentration until its evenly spread

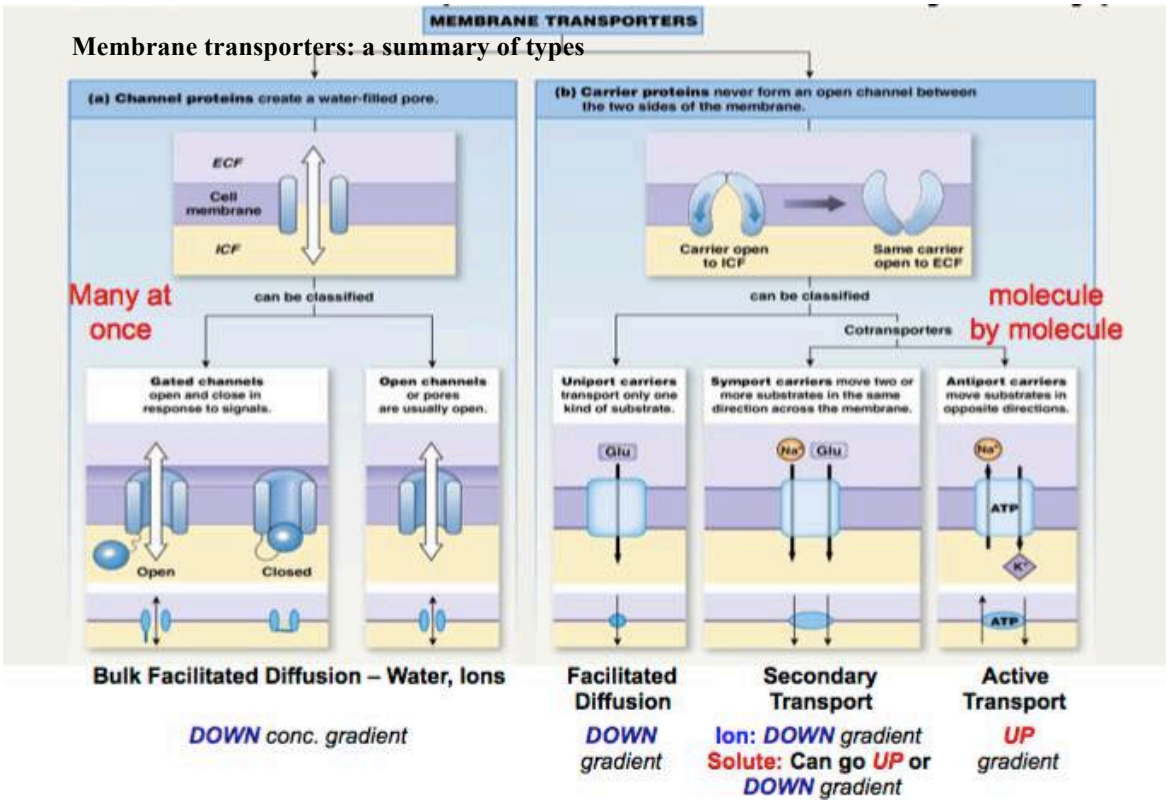
Selective permeability: solutes and water (osmosis)



- Osmolality is concentration of all dissolved particles in solution
- ***1 M sucrose = 1 Osmole/L = 1 Osm/L***
- ***1 M KCl = 1 M K^+ + 1 M Cl^- = 2 Osm/L***
- In the presence of an artificial barrier
- Tube separated into 2 areas with barrier in between, permeable to solute and water → solute shifts
- When not permeable to solute, water moves to make concentration of solute the same (osmosis)

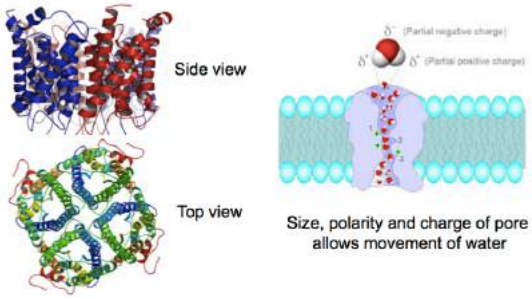
- Just because concentrations equal, doesn't mean water and solute cease to flow → just do it at same rate
- Will have to apply pressure on water to reverse situation → pressure needed is the ***osmotic pressure***

Membrane transporters: a summary of types



- Channel proteins allow movement of many molecules at the same time e.g. water and ions
  - Net flow is down the concentration gradient
- Intracellular proteins are never open to ICF and ECF at the same time
  - Generally, transport one molecule at a time
  - **Facilitated diffusion** → allow molecules to flow down concentration gradient but molecule by molecule pretty much
  - **Active transport** → flow occurs if you supply energy (often in the form of ATP)
    - Drive molecules and ions against concentration gradient
    - Antiport → drive molecules in different directions against their concentration gradients
  - **Secondary transport** → relies on active transport to set up conditions to allow it to work
    - E.g. active transport allowed Na to be pushed out of cell at high concentration
    - This high concentration is used as vehicle to drive transport of another
    - No direct use of ATP here

Aquaporin: the water channel/pore

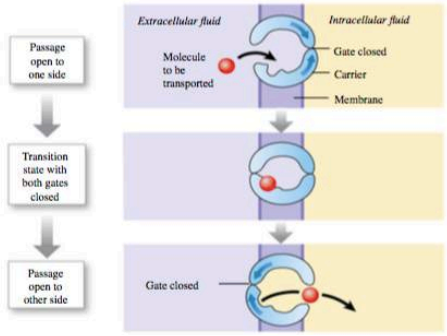


- Just an example but all principles can be generalised to other channel proteins
- Allow bulk movement of water very rapidly through membrane

Red cells in isosmotic, hyperosmotic and hypoosmotic solutions

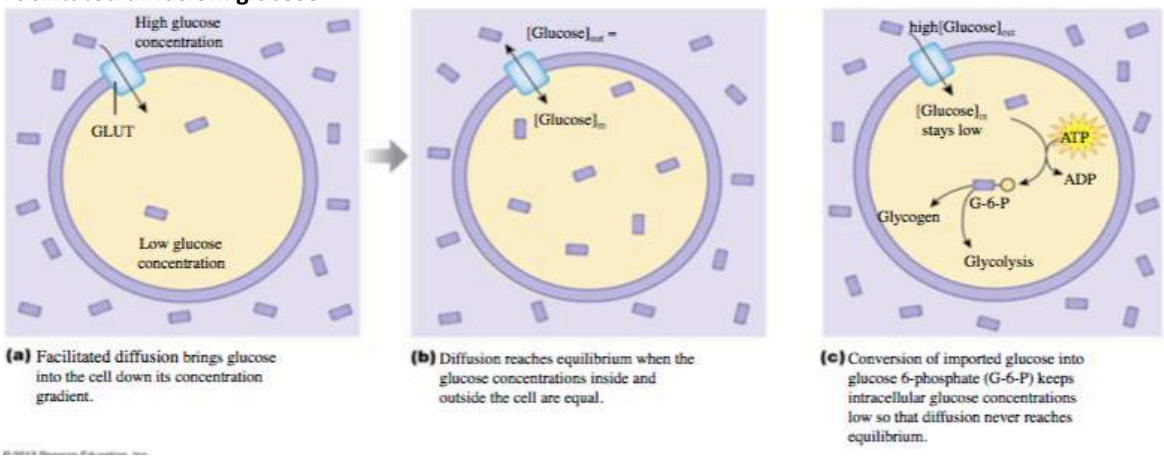
- **Isosmotic** → concentration same in and out of red blood cells
- **Hyperosmotic** → Low solute concentration *inside* so water flows out of cell. This causes red blood cells to shrink
- **Hypoosmotic** → low solute concentration *outside* the cell so water runs in. This causes the red blood cell to burst (cytoskeleton can no longer hold cell in tact) e.g. distilled water
- This happens quickly due to presence of aquaporins in membrane

Facilitated diffusion is molecule by molecule



- Largely solute by solute and channel is never open to both sides at same time

Facilitated diffusion: glucose



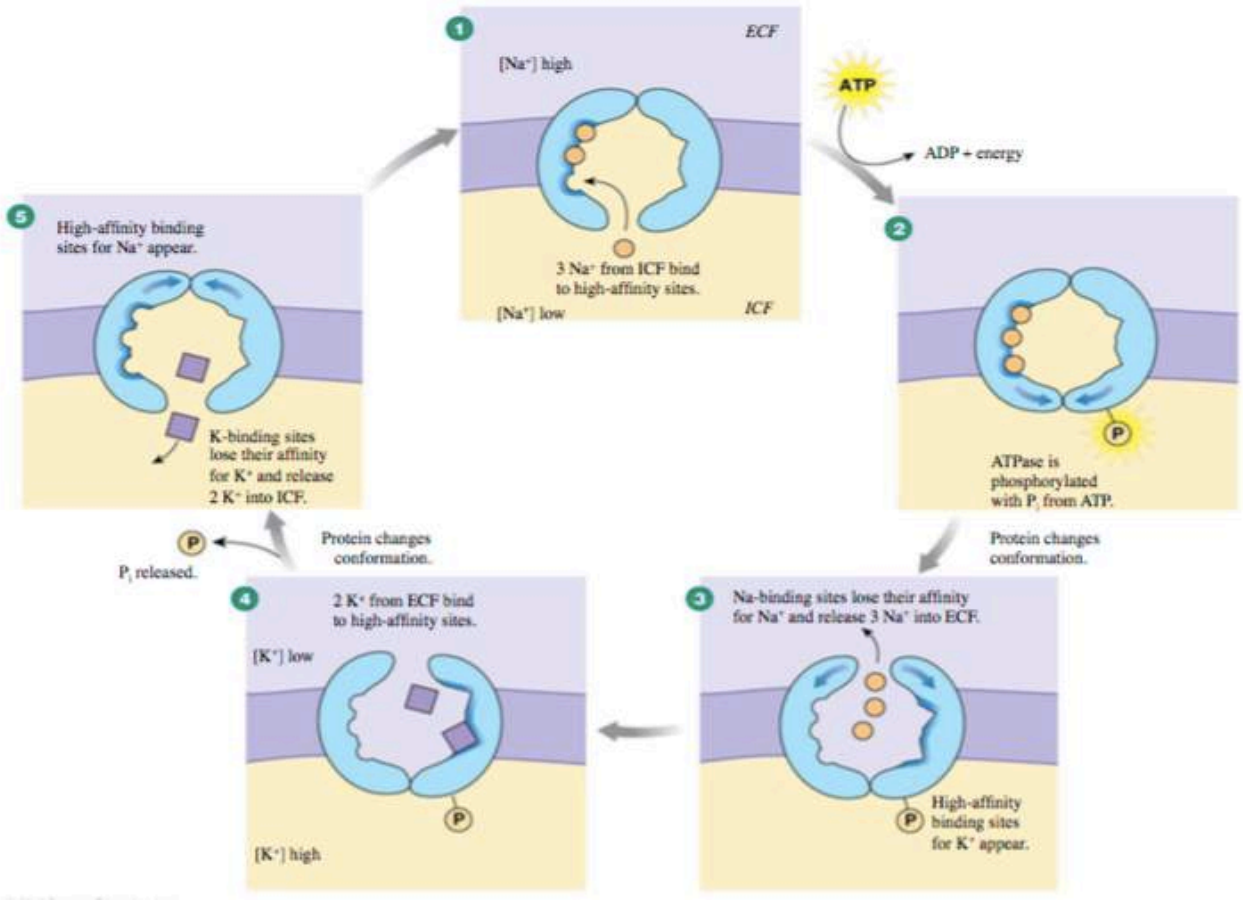
(a) Facilitated diffusion brings glucose into the cell down its concentration gradient.

(b) Diffusion reaches equilibrium when the glucose concentrations inside and outside the cell are equal.

(c) Conversion of imported glucose into glucose 6-phosphate (G-6-P) keeps intracellular glucose concentrations low so that diffusion never reaches equilibrium.

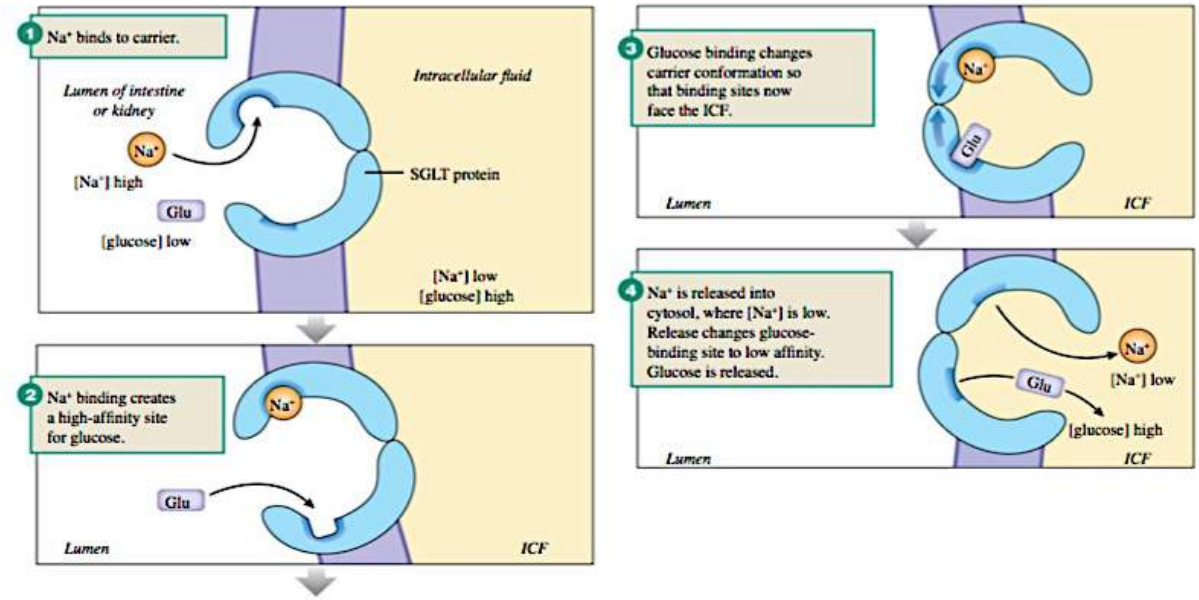
- Cells exploit basic chemistry to keep glucose coming in when they need it e.g. take glucose and modify it e.g. by putting a P on it, concentration of glucose in cell has gone down, glucose may also be changed to glycogen to store it or be used in glycolysis to make ATP

Active transport: the sodium-potassium pump Na^+-K^+-ATPase



- ATP used as energy source to change confirmation of transporter → sodium trapped in it

Secondary transport: mechanism of the SGLT transporter



1. High concentration of Na outside cell, sodium goes in and binds to site
2. When it does this, creates binding site for glucose (need to go into cell where [glucose] is likely high)
3. Closes to outside and opens to inside
4. Both released