

## Transport across cell membranes

### Carriers



## Three types of membrane transport protein

- Pumps
- Carriers
- Channels



## Carriers

- Secondary transporters
  - Do not use “fresh” energy
  - Their source of energy are gradients created by pumps (primary transporters)
- Integral membrane proteins
  - Provide transmembrane “passages”
  - Molecules move down the gradient (from high to low concentration)



## Carriers

- Some carriers do a “double job”. They use the energy of an existing gradient to transport one type of ions down the gradient and other up the gradient



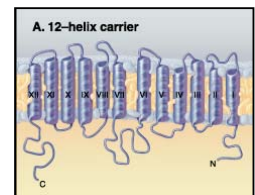
## Carriers

- Ubiquitous
- Selective for the transported molecule
  - D-glucose is transported but no L-glucose
- Medium velocity 1000 molecules/sec
- Reversible



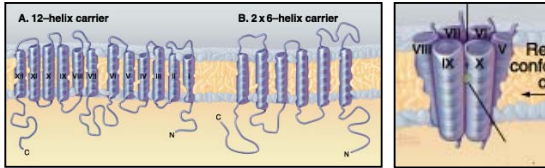
## Molecular structure of carrier proteins

- Usually single polypeptide
- Usually 12 transmembrane  $\alpha$  helices
- Active as monomers



## Molecular structure of carrier proteins

- Helices line the passageway
- Likely arose from common ancestral gene



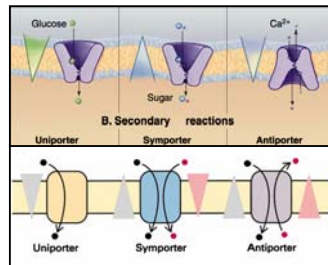
## Transport by carrier proteins

- Work like enzymes
  - Bind substrate on one side of the membrane
  - Reorient binding site
  - Release substrate on the other side
- Significant conformational change
- Carrier protein can be open only to one side of the membrane



## Three types of transporters

- Uniporter
- Cotransporters
  - Symporter
  - Antiporter

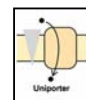
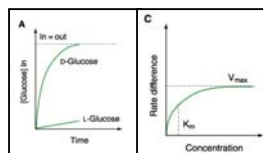


## Uniporter

- Transports single substrate
- Facilitated "low resistance" diffusion
  - Down the concentration gradient
  - Accelerates a reaction that is already thermodynamically favored
- Reversible

## Features of uniporter-catalyzed transport

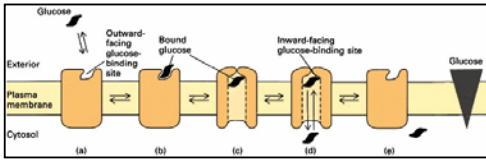
- The rate of movement is much higher than passive diffusion because the molecule never comes in contact with hydrophobic core of the membrane
- Transport is specific
- Transport occurs via limited number of uniporters (saturable)



## Uniporter - examples

- GLUT1 – widely distributed glucose transporter
- GLUT4 - primary insulin regulated glucose transporter in muscle and adipose tissue
- UCP – uncoupler of proton gradient in mitochondria (termogenin)

## Glucose uniporter - GLUT1



- Glucose uniporter shuttles between two conformational states
- Net flow is reversed when the concentration of glucose changes



## UCP uniporter and thermogenesis

- Normally proton gradient produced during oxidative phosphorylation in mitochondria is coupled to ATP synthesis (F type pump)

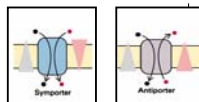
## What happens when we are cold?

- Brown fat - special heat generating tissue
- Brown-fat mitochondria contain the UCP uniporter also called thermogenin
- UCP can uncouple H<sup>+</sup> flow from ATP synthesis by dissipating proton gradient
  - Instead of flowing through ATP synthase protons escape through UCP uniporter and produce heat (do not produce ATP)

## Cold adaptation

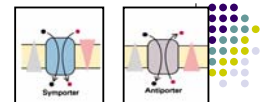
- Brown fat in human newborns is used to warm up the body during adjustment to outside living
- UCP is upregulated during cold adaptation
  - In cold condition the synthesis of UCP increases

## Cotransporters

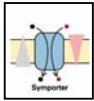


- Couple movement of one substrate down the gradient to the movement of another substrate against the gradient
  - Symporter - both go in the same direction
  - Antiporter - molecules go in opposite directions
- Cotransporters require the existence of a gradient of one molecule (created by pumps)

## Cotransporters



- Energy of the transport down the gradient allows for the transport of second substrate against the gradient
  - A hitchhiker's ride for the molecule transported against the gradient
- Can transport different number of molecules in different directions



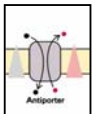
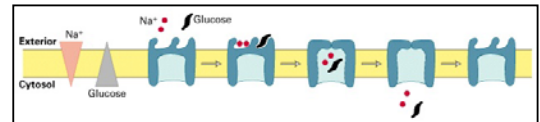
## Symporter

- Both molecules go in the same direction
- Examples
  - SGLT1 -  $\text{Na}^+$  /glucose symporter in gut epithelia
  - Important for transport of nutrients through intestinal epithelium
  - Amino acids are transported in similar manner



## SGLT1 symporter

- Two sodium/one glucose symporter
  - 2 sodium go in
  - 1 glucose goes in, too
- Glucose is dragged by sodium ions that naturally go in (transmembrane gradient)



## Antiporter

- Molecules go in opposite direction
- Examples
  - NHE-1 -  $\text{Na}^+/\text{H}^+$  antiporter in kidney and gut epithelia
  - NCE -  $3\text{Na}^+/\text{Ca}^{2+}$  antiporter in the heart
  - Band 3 protein -  $\text{HCO}_3^-/\text{Cl}^-$  in erythrocytes



## NHE-1 or $\text{Na}^+/\text{H}^+$ antiporter

- Regulation of cytosolic pH
- Exchange of 1  $\text{Na}^+$  for 1  $\text{H}^+$
- $\text{Na}^+$  goes in naturally
- $\text{H}^+$  goes out



## NCE or $3\text{Na}^+/\text{Ca}^{2+}$ antiporter

- Important in cardiac muscle
- Regulates heart contractility
- Exchange of 3  $\text{Na}^+$  for 1  $\text{Ca}^{2+}$
- $\text{Na}^+$  goes in due to the gradient
- $\text{Ca}^{2+}$  is driven out

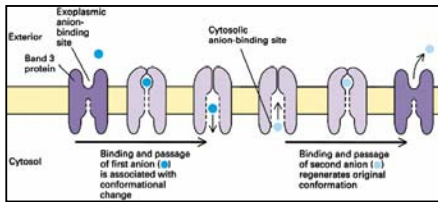


## Band 3 protein or $\text{HCO}_3^-/\text{Cl}^-$ antiporter

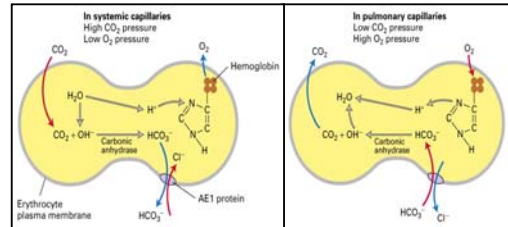
- One for one exchange of anions
- The anion binding site is either on the outside or inside of the membrane, but never on the same side
- Passage of the anion against the gradient regenerates the preferred conformational state



## Band 3 protein or HCO<sub>3</sub><sup>-</sup> / Cl<sup>-</sup> antiporter



## CO<sub>2</sub> transport by erythrocytes



## CO<sub>2</sub> transport by erythrocytes

- In systemic circulation CO<sub>2</sub> diffuses to red blood cells
- Carbonic anhydrase changes it to bicarbonate ion
- Bicarbonate ion exits through band 3 protein to blood to be carried to lungs
- In lungs the direction is reversed

## Chemiosmotic cycle

- Couples ion fluxes through pumps and carriers to maintain homeostasis
  - Cation transporting pump and transport of a substrate by a carrier

