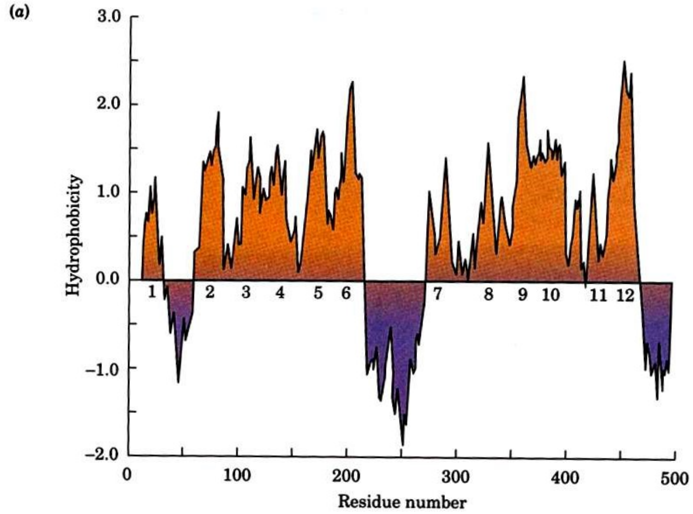
# A Closer Look at the Glucose Transporter




➢ integral membrane proteins have a directionality and do not flip-flop

⇒ they cannot work as an ionophore (mobile carrier)!

➢ the erythrocyte glucose transporter:

♣ 55 kD glycoprotein; 492 aa

♣ four major domains:

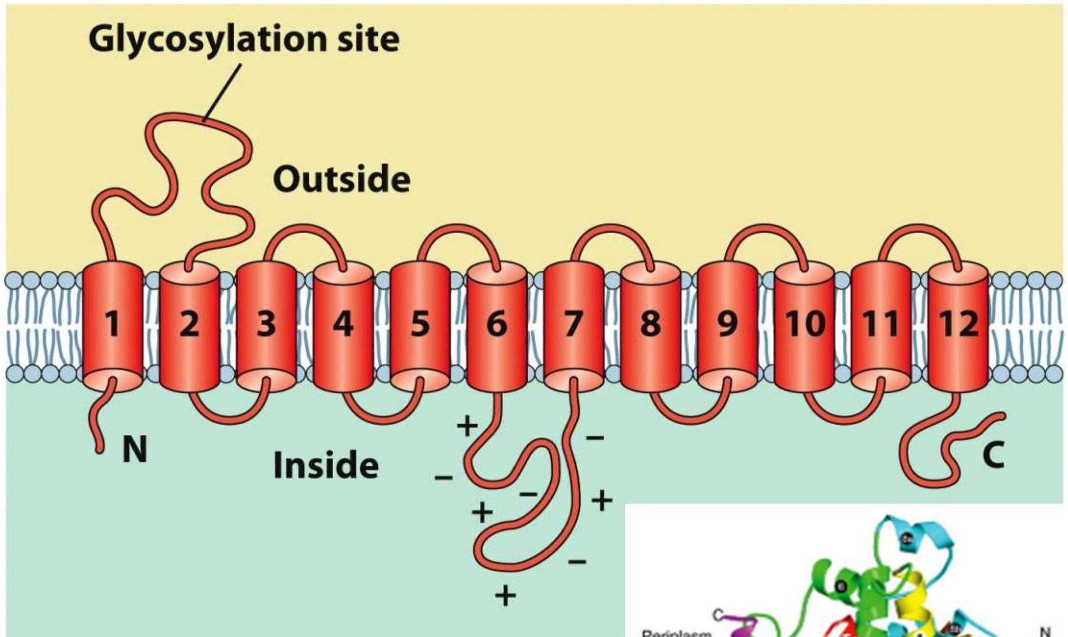
(1) 12 membrane-spanning α-helices;

(2) large highly charged cytoplasmatic domain (between helices 6 & 7)

(3) smaller, carbohydrate bearing external domain (between helices 1 & 2)

(4) cytoplasmatic C-terminal domain

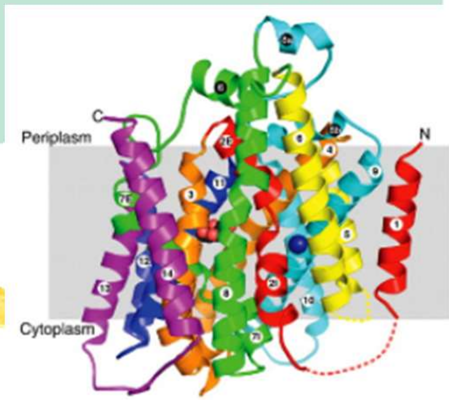
♣ accounts for 2% of erythrocyte membrane proteins



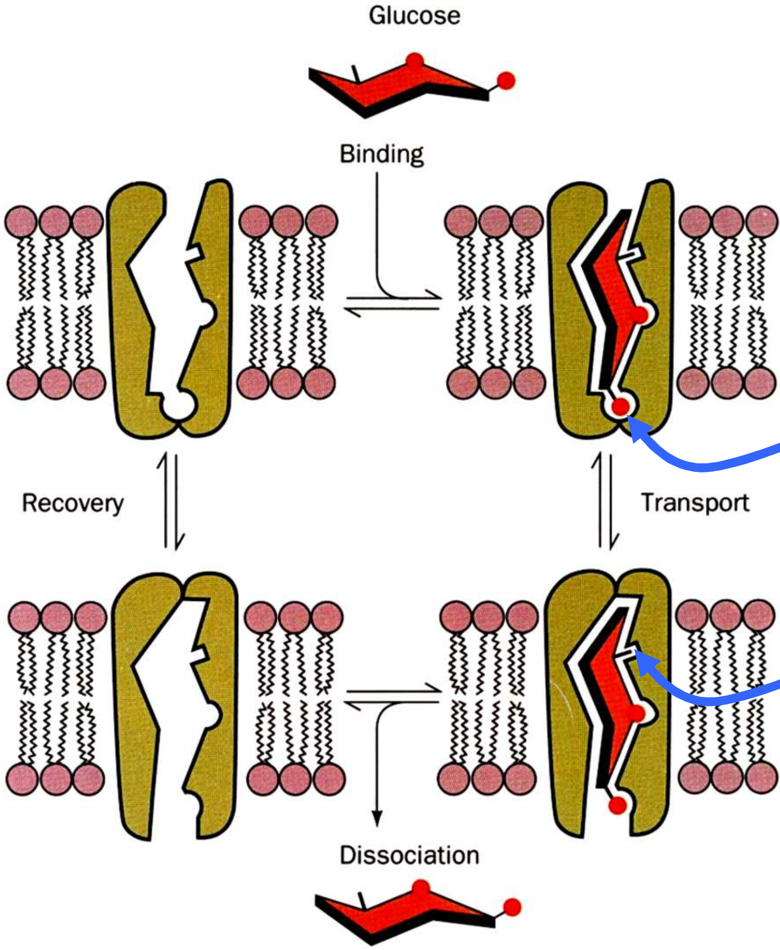

➢ must be asymmetric:

♣ galactose oxidase oxidizes oligosaccharide chain only on the outside;

♣ trypsin disrupts transport only from the inside of an erythrocyte ghost



# Glucose Transporter:  A Passive Gated Pore




O1 must not be methylated

O6 must not be methylated

- transport is passive:
  (1) glucose is bound on the outside,
  (2) a conformational change occurs,
  (3) glucose is released on the inside

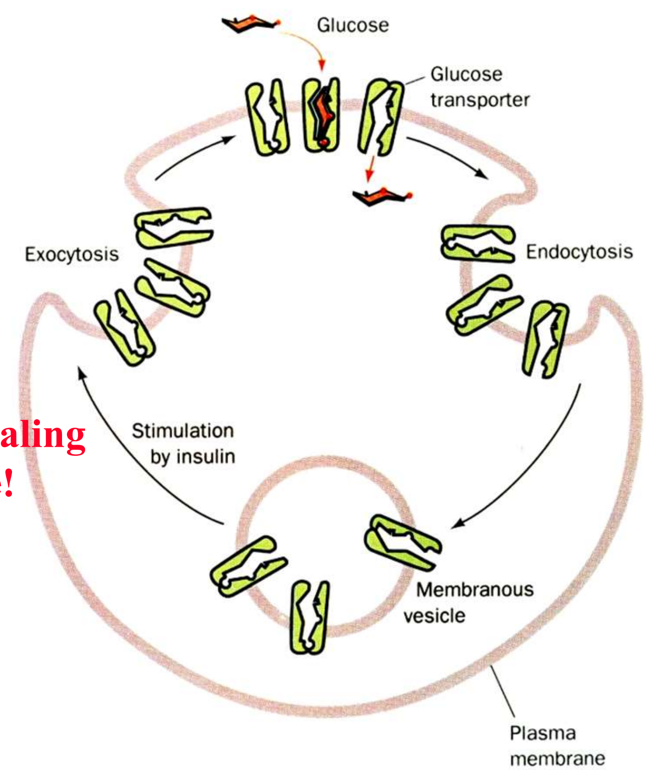
- transporter "only" equilibrates glucose concentration, but inside the cell glucose is rapidly consumed!

- But 15 min after insulin administration, $J_{max}$(glucose) increases by 6- to 12-fold, while $K_M$ stays constant

- 20 min to 2 h after insulin withdrawal, glucose uptake returns to normal

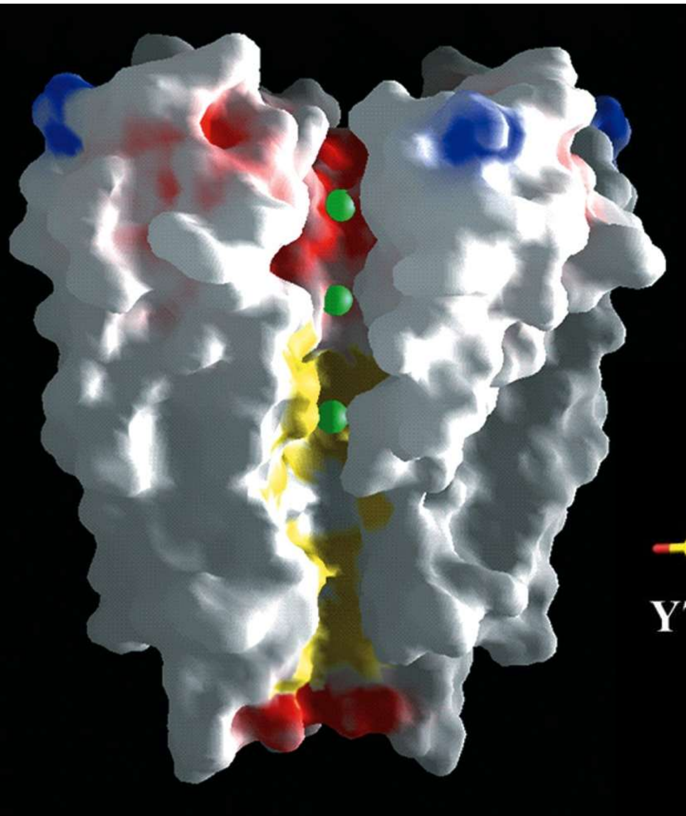
How?

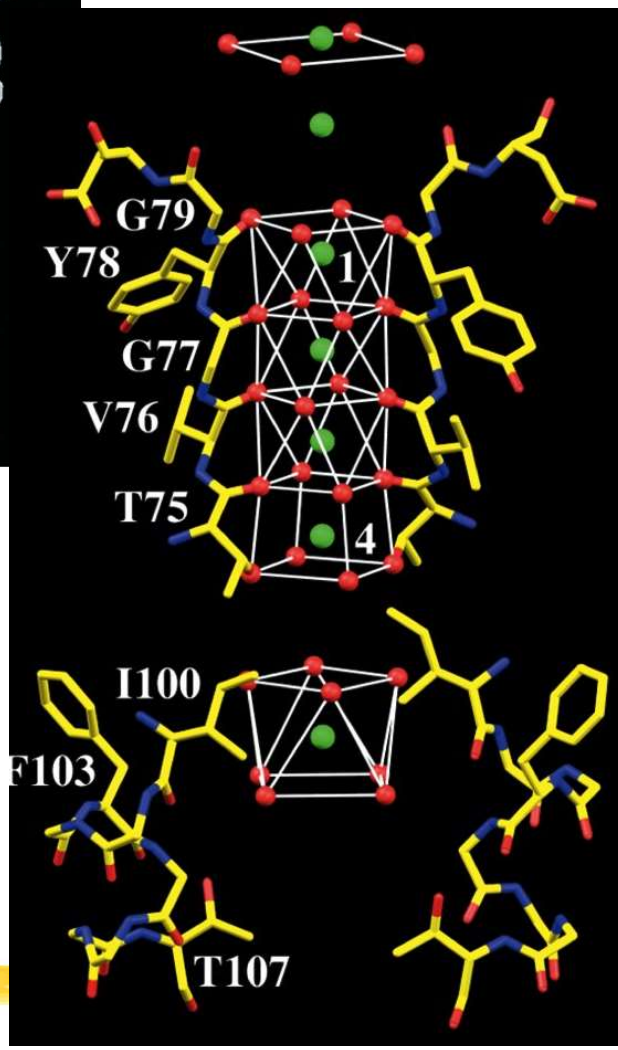
Kinase signaling cascade!




Nils

# Selectivity of $K^+$ Channels and Aquaporines

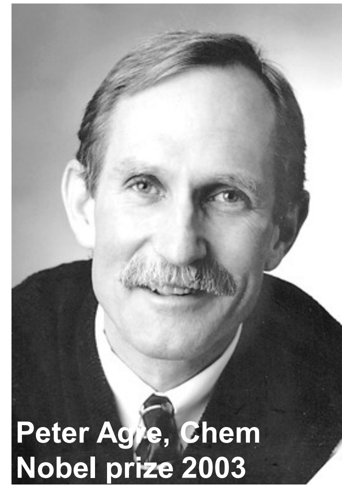


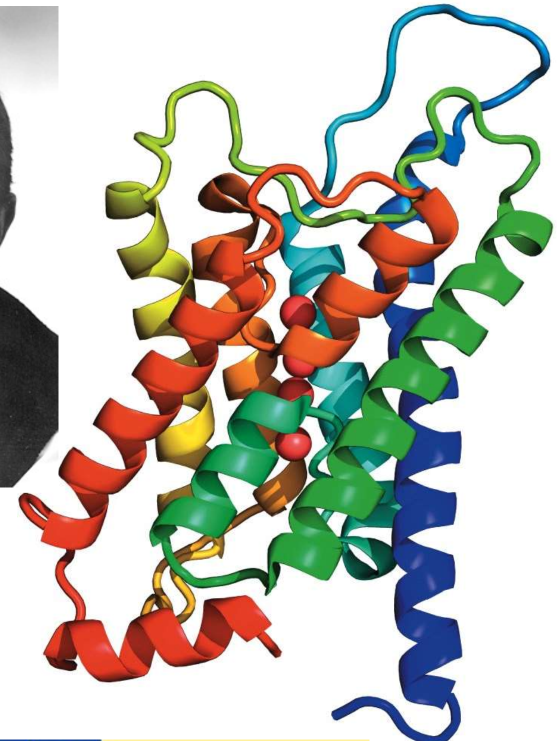


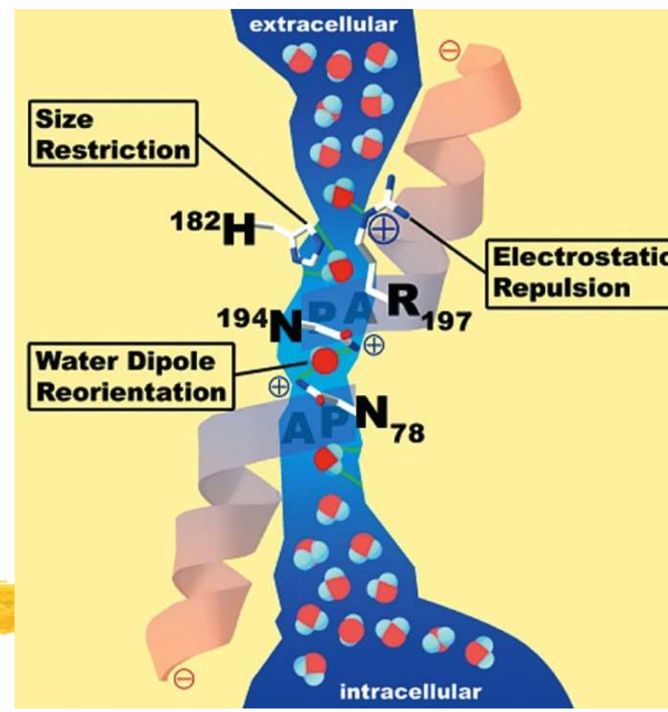


Roderick MacKinnon, Chem Nobel prize 2003

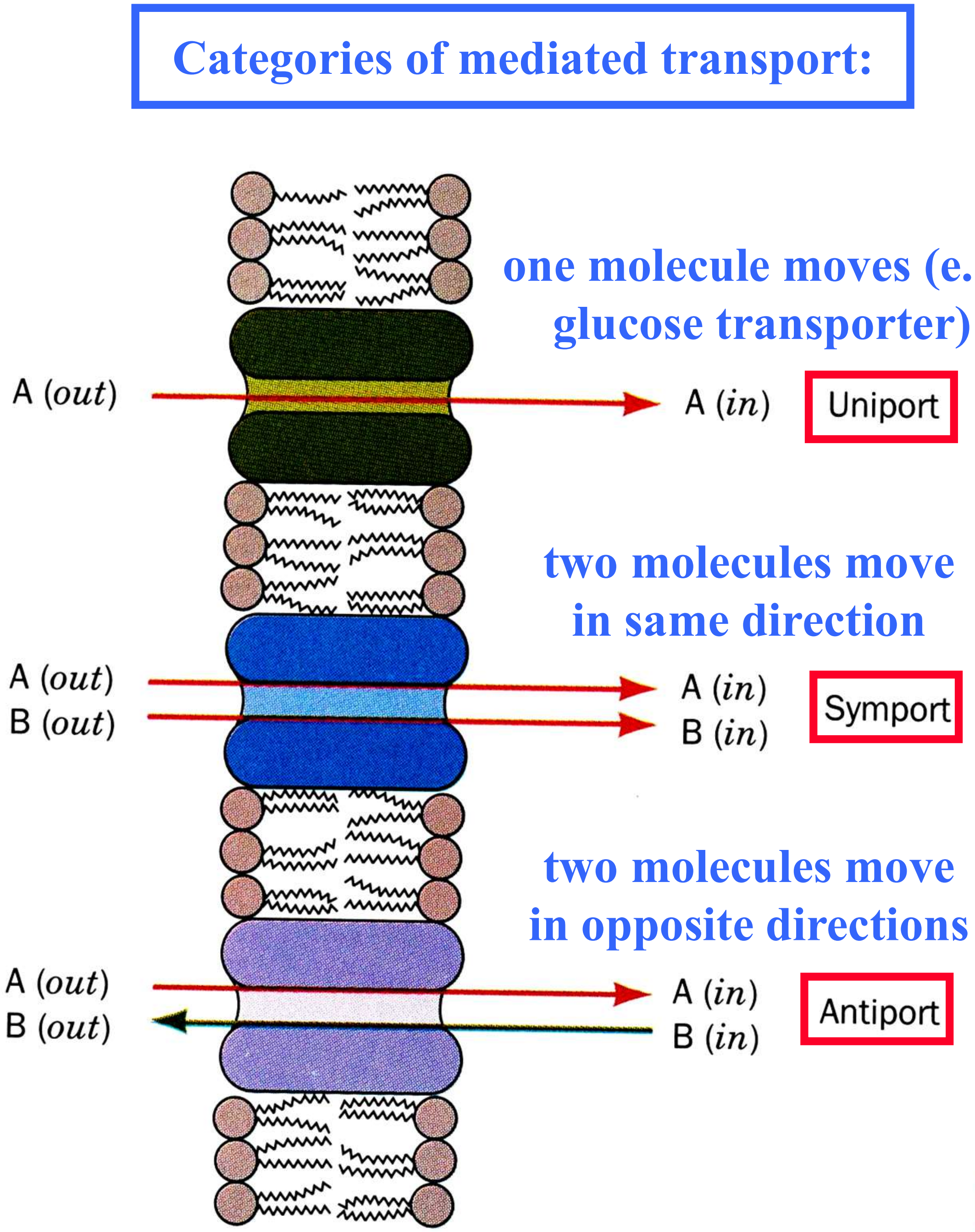
https://www.youtube.com/watch?v=VFqufDp4L5g


Peter Agre, Chem Nobel prize 2003





# ATP-Driven Active Transport




**Electroneutral:** Simultaneous charge neutralization (symport of opposite charges or antiport of like charges)

**Electrogenic:** Transport results in charge separation across membrane

**Active transport against a gradient is endergonic ⇒ often coupled to ATP hydrolysis**

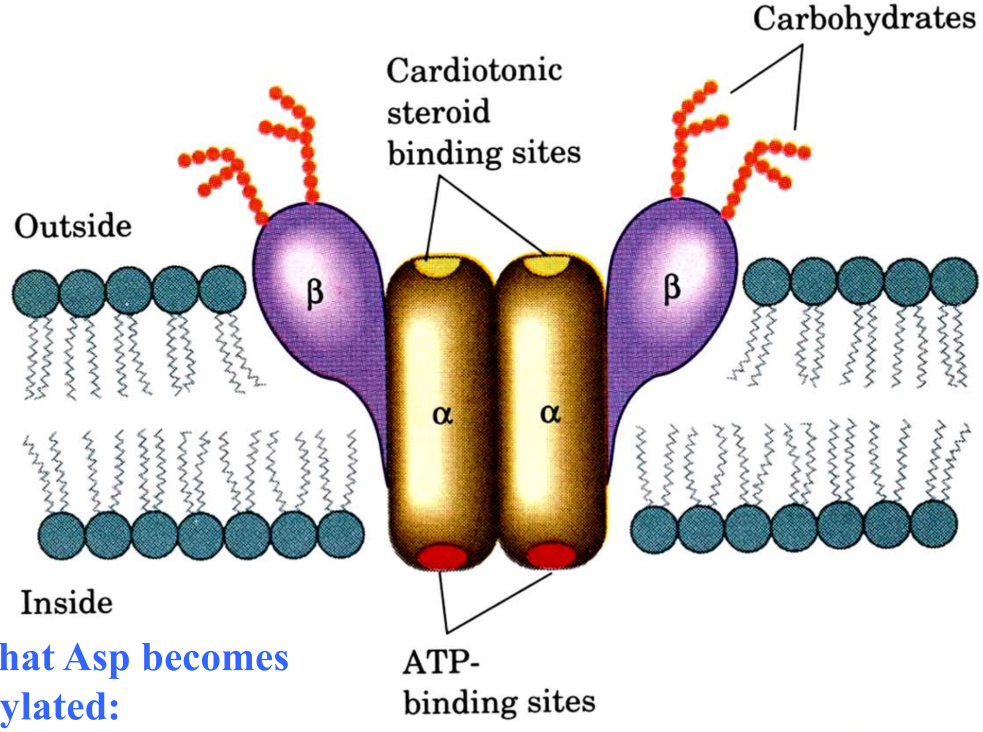
➢ **Examples:**

♣ **P-type ATPases**; in plasma membrane, directly phosphorylated by ATP; inhibited by vanadate ($VO_4^{3-}$) as $P_i$ analog

♣ **F-type ATPases**; in mitochondrial membrane; important for oxidative phosphorylation

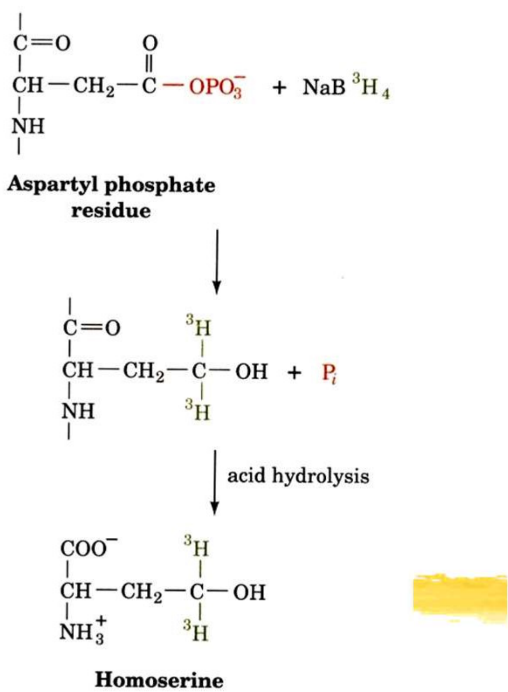
♣ **V-type ATPases**; in plant vacuolar membranes; analogous to F-type ATPases

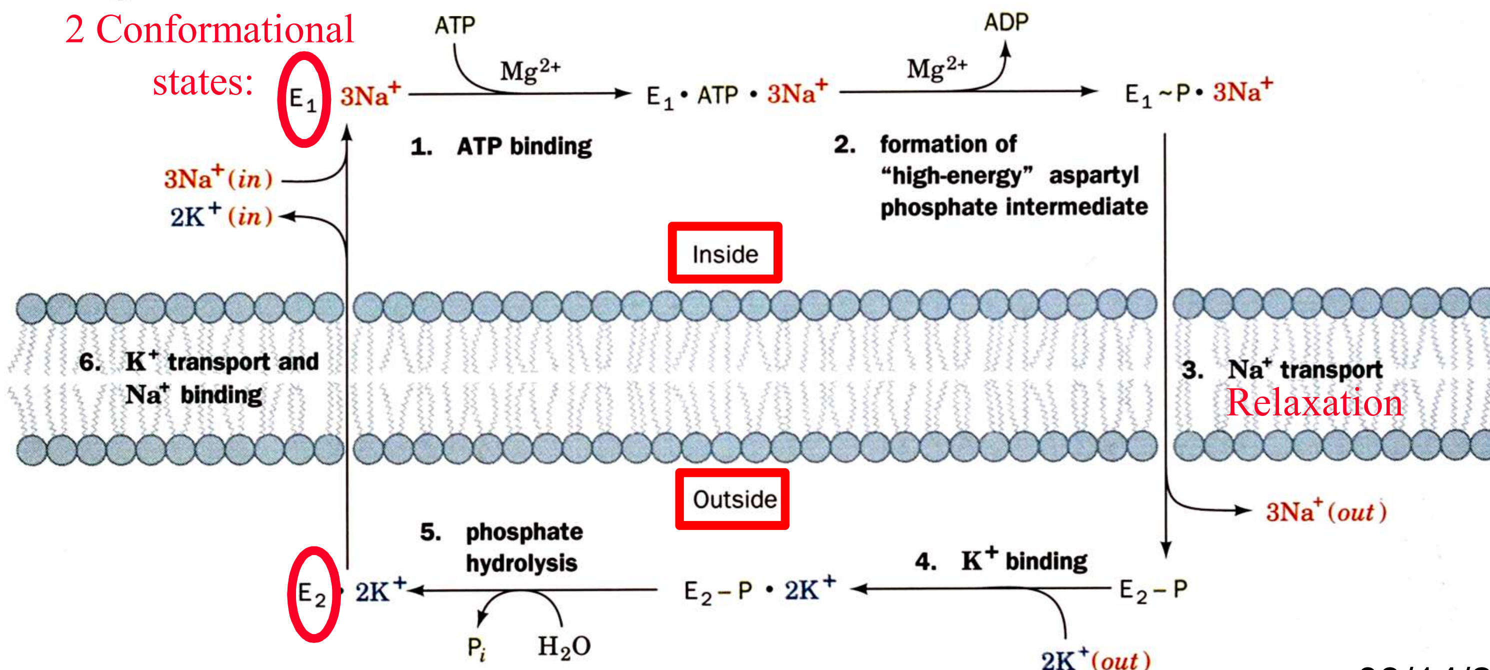
# The ($Na^+$-$K^+$)-ATPase of Plasma Membranes




- **The facts:**
  - ♣ $(\alpha\beta)_2$ subunit composition
  - ♣ α subunit: 110 kD, non-glycosylated; contains ATPase activity and ion-binding sites; 8 transmembrane α-helices
  - ♣ β subunit: 55 kD, glycosylated; 1 transmembrane α-helix
  - ♣ electrogenic antiport
  - ♣ also called ($Na^+$-$K^+$) "pump"
  - ♣ sequential kinetic mechanism accounts for coupling of active transport with ATP hydrolysis

- **Proof that Asp becomes phosphorylated:**



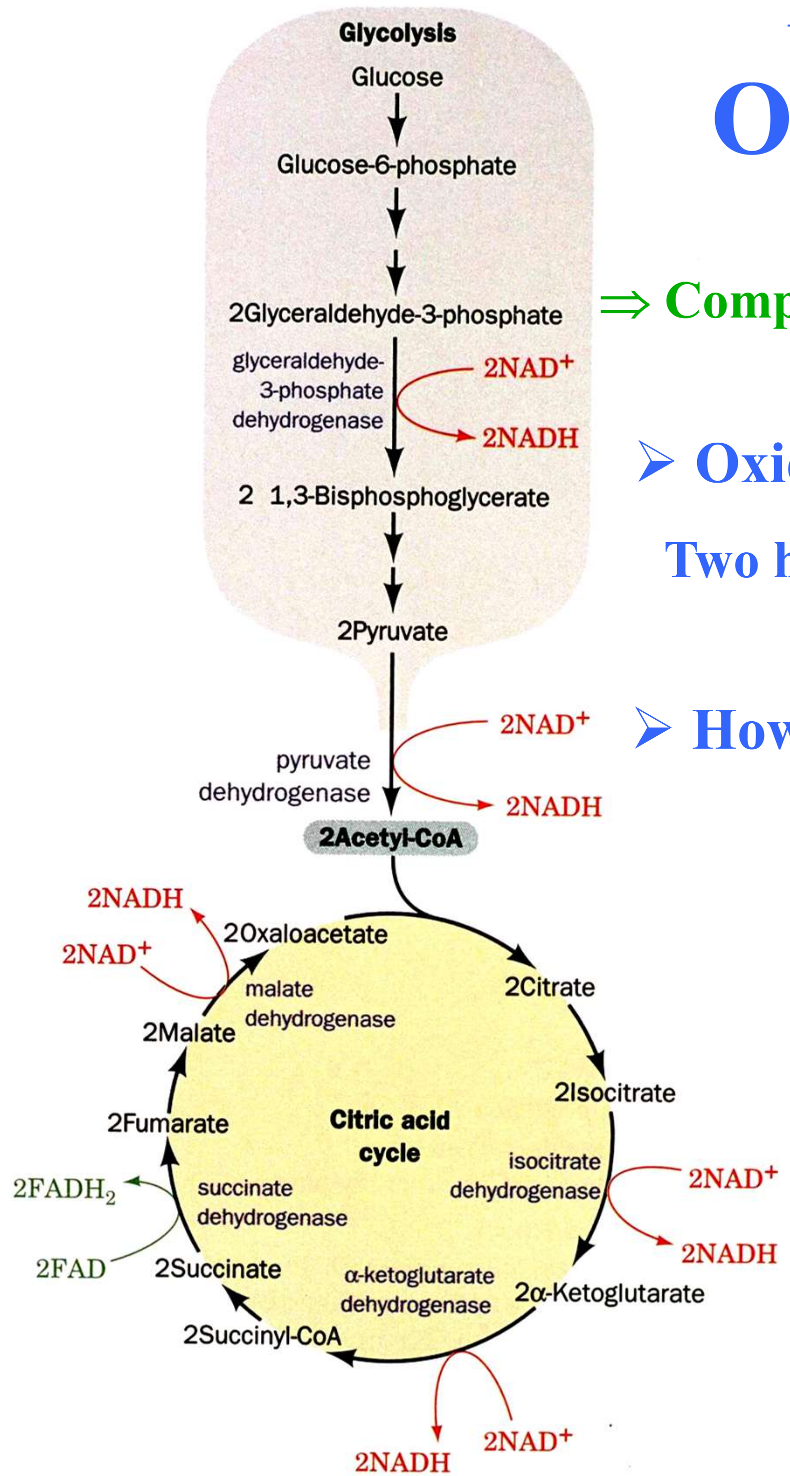
# Chapter 20: What have we learned about transport?

- Thermodynamics, kinetics, nomenclature (symport, antiport…)
- Carrier and Channel-Forming Ionophores as models

| | Non-mediated | Mediated | |
|---|---|---|---|
| | | Passive | Active |
| Carrier | No | Yes | Yes |
| Transport direction | [High]→[Low] | [High]→[Low] | [Low]→[High] |
| Energy used? | No | No | Yes |
| Examples | $O_2$, $H_2O$ | Glucose | ($Na^+$-$K^+$)-ATPase, $Ca^{2+}$-ATPase, Translocation systems |

# Electron Transport and Oxidative Phosphorylation

## Voet & Voet, Chapter 22




⇒ Complete glucose oxidation: $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$; $\Delta G^{0'} = -2{,}823$ kJ/mol

- Oxidation = loss of electrons:

Two half-reactions: $C_6H_{12}O_6 + 6H_2O \rightarrow 6CO_2 + 24H^+ + 24e^-$

$$6O_2 + 24H^+ + 24e^- \rightarrow 12H_2O$$

- How can the energy of these electrons be transferred to ATP?

24 $e^-$ are carried in 10 NADH and 2 $FADH_2$

↓

Pass into electron-transport chain (participate in reduction-oxidation of >10 redox centers)

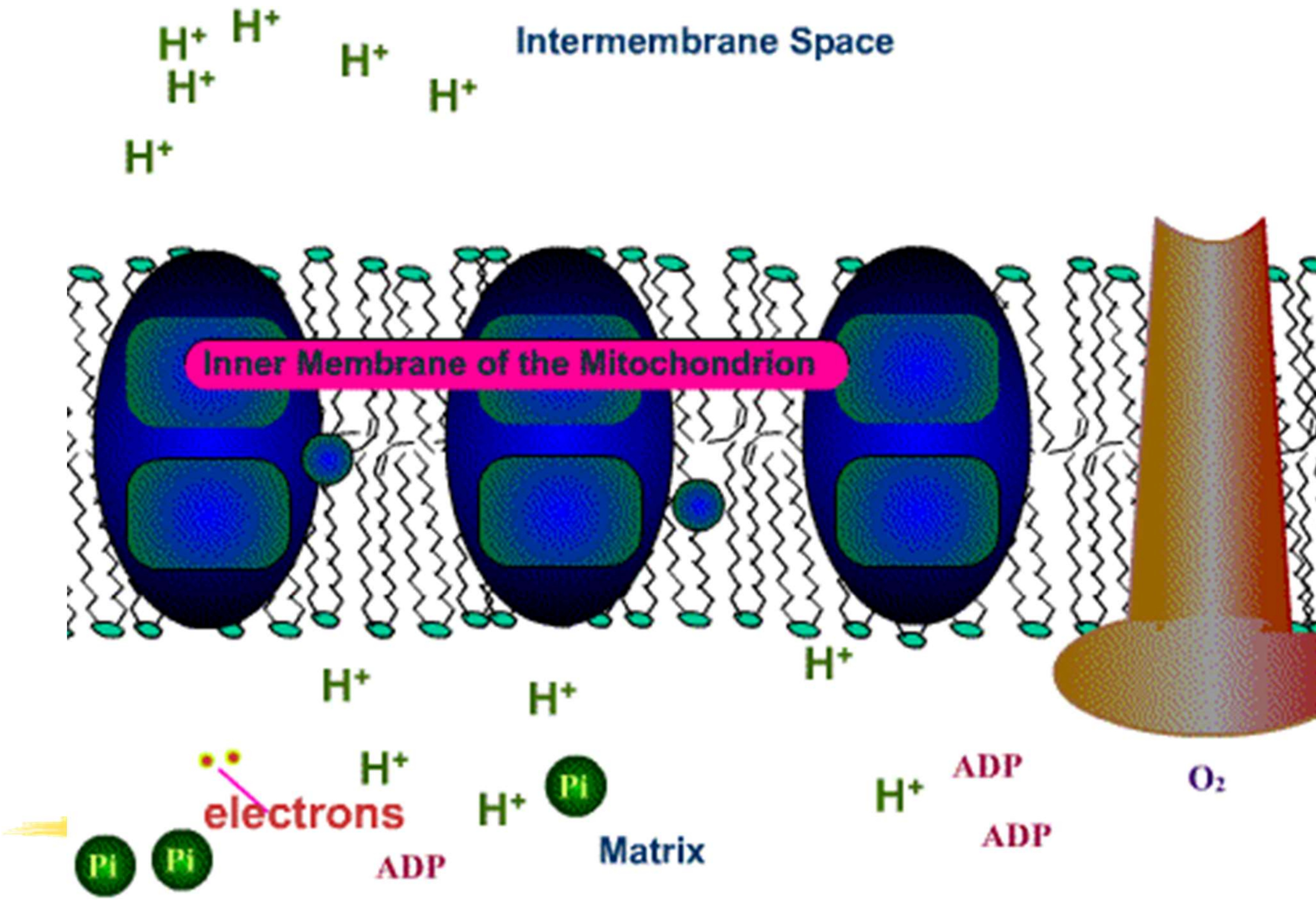
↓

Reduce $O_2$ to $H_2O$, expel $H^+$ from mitochondrion

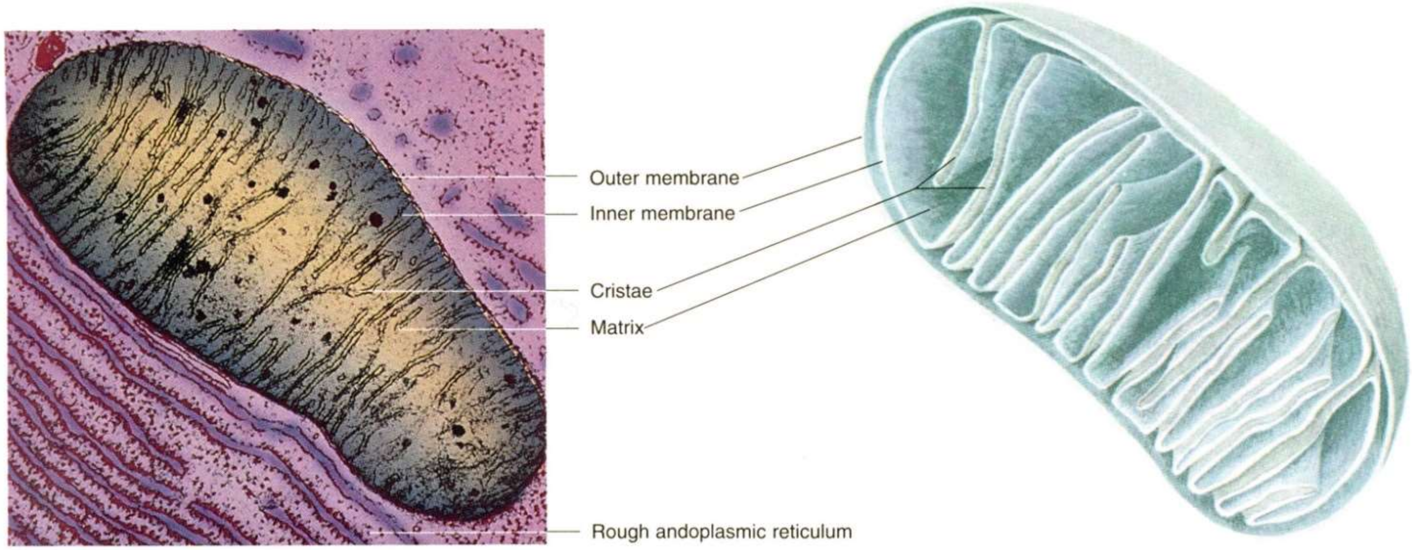
↓

$H^+$ gradient drives ATP production

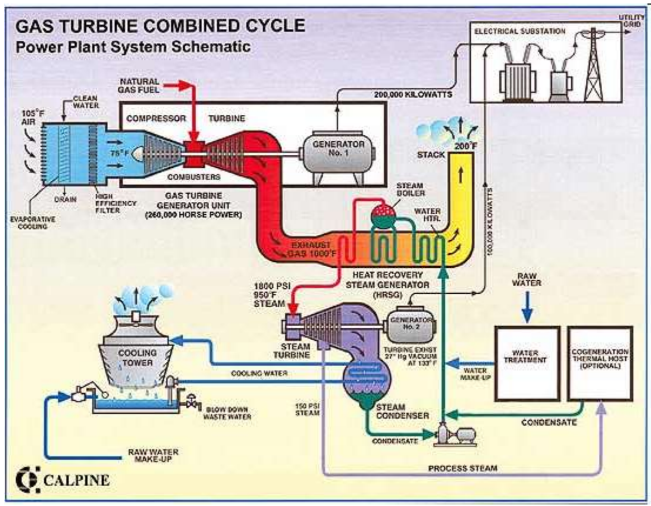
# The Movie of Electron Transport and Oxidative Phosphorylation

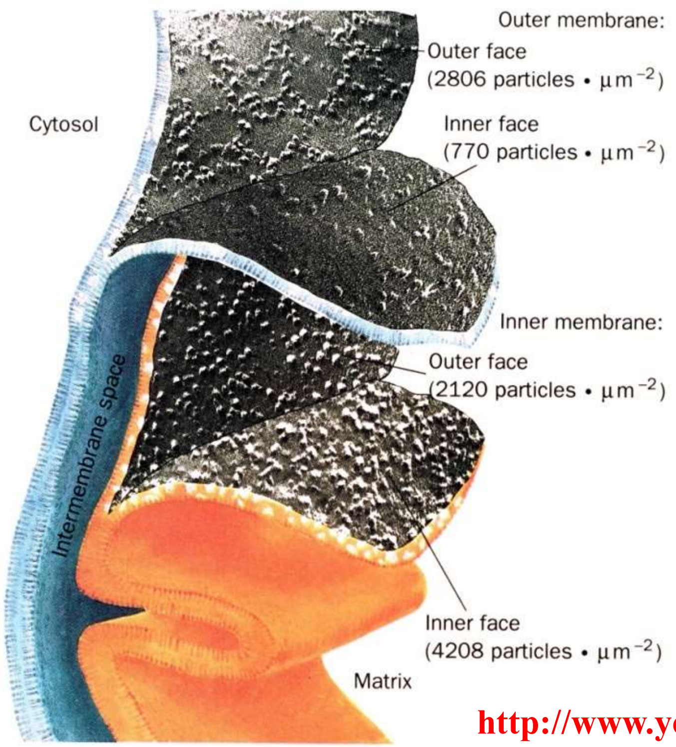


# Where it All Happens: The Mitochondrion




(*a*) (*b*)




**The mitochondrion contains:**

- Pyruvate dehydrogenase
- Citric acid cycle enzymes
- Enzymes that catalyze fatty acid oxidation
- Enzymes and redox proteins for electron transport and oxidative phosphorylation

⇒ The cellular "power plant"

http://www.youtube.com/watch?v=RrS2uROUjK4&list=UUAUL7Wl_lydKXI8q0oi4CUw