## Membrane Transport

Examples:

- Facilitative Diffusion
  - Ionophore
  - Maltoporins
  - GLUT1 transprter
  - Aquaporin
  - Selective ion channel for potassium (K-channels)
- Active Transport
  - Primary (1°)
    - $Na^+/K^+$
    - ABC
  - Secondary (2°)
    - $Na^+$/Glc
    - Bicarb/$Cl^-$
    - Lactose/$H^+$
  - Group Translocation
    - Bacterial phosphotransferase system (PTS)

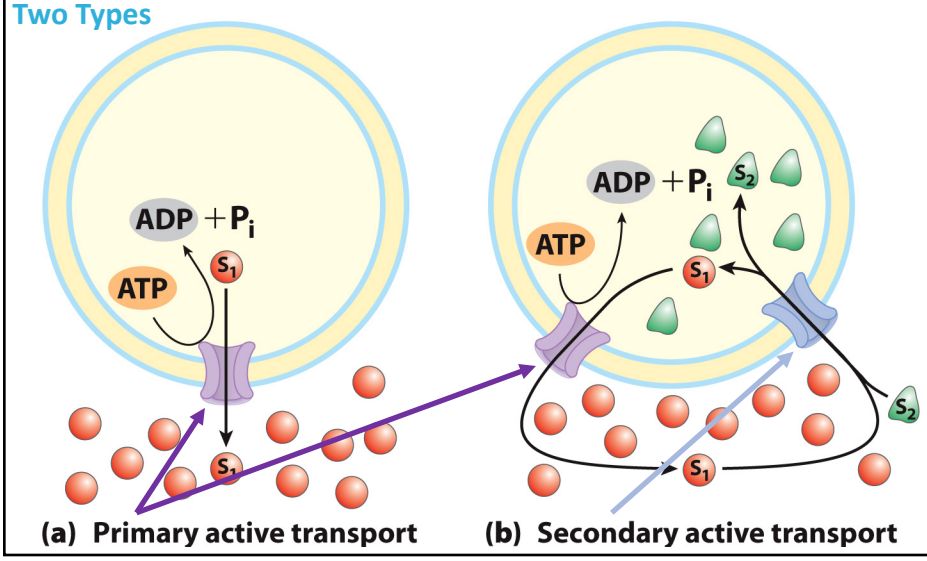
## Membrane Transport

# Active Transport

# Membrane Transport

## Examples of Active Transport

Two Types



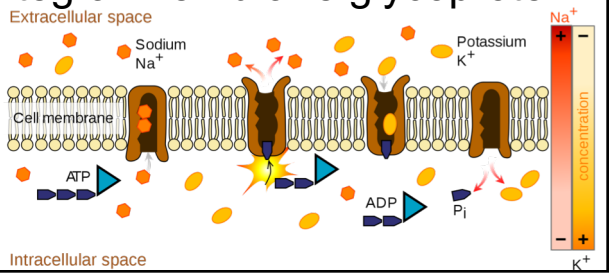

# Membrane Transport

## One of the best and most important examples of Active Transport (primary):

The **sodium–potassium ($Na^+$–$K^+$) pump** is primary active transport.

Found in all animal cells.

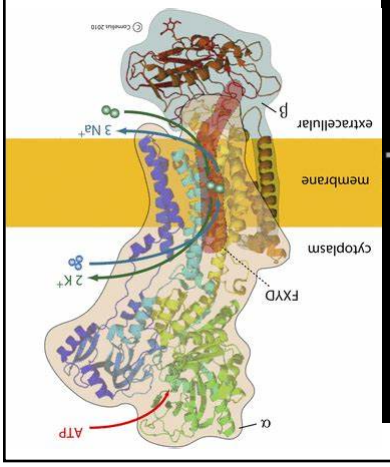
The pump is an integral membrane glycoprotein (an antiporter).

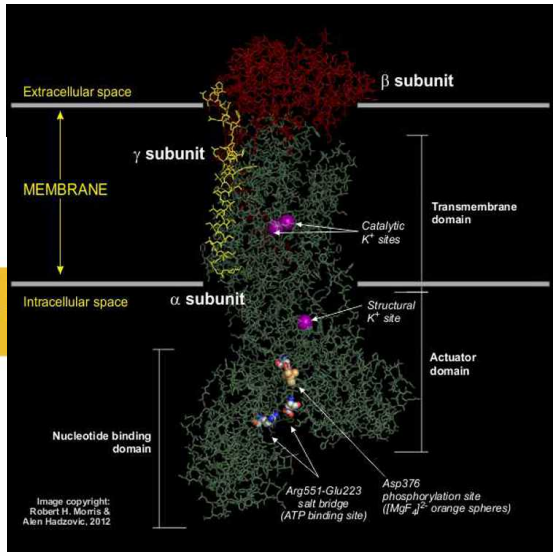


# Membrane Transport

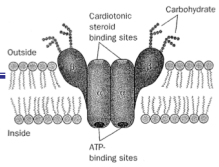
## Sodium–potassium ($Na^+$–$K^+$) pump

$\alpha_2\beta_2\gamma$ pentamer

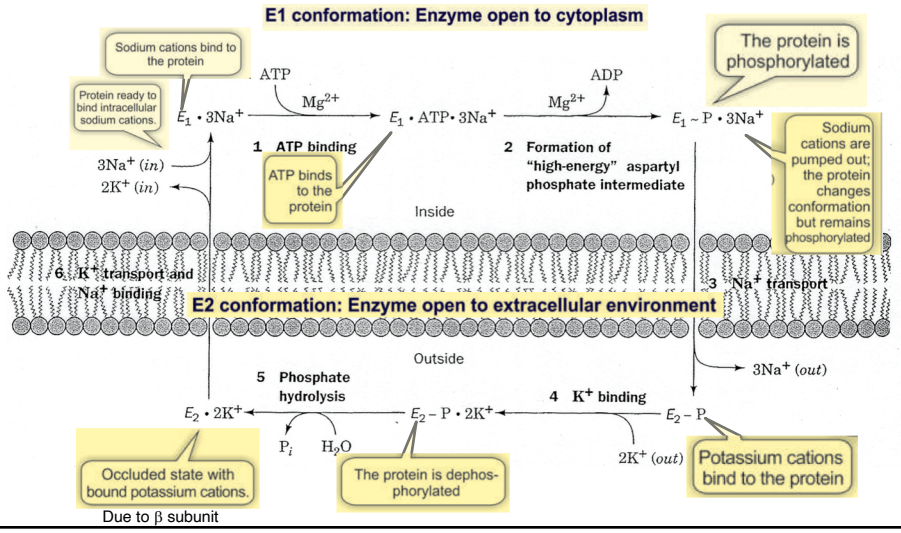



# Membrane Transport

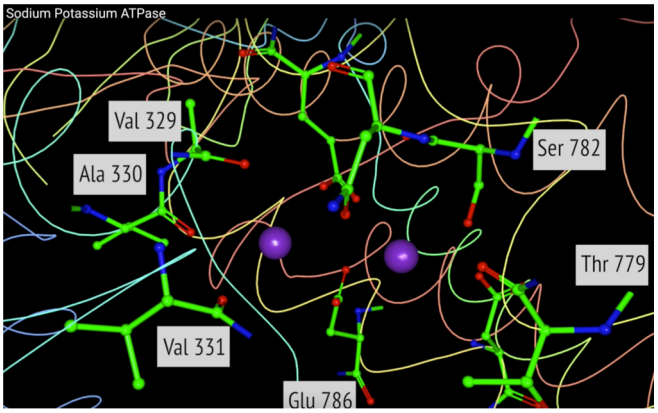



Sodium–potassium ($Na^+$–$K^+$) pump



## Membrane Transport

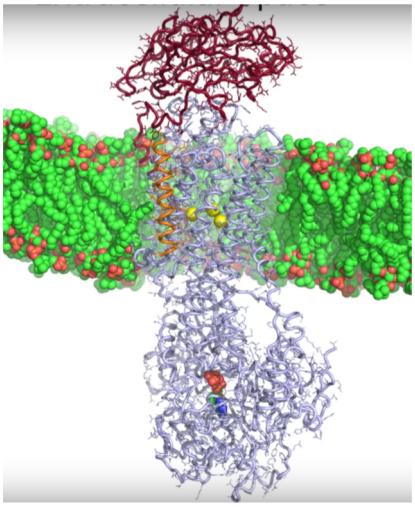
### Sodium–potassium ($Na^+$–$K^+$) pump




Calls secondary active transport “facilitative diffusion”

## Membrane Transport

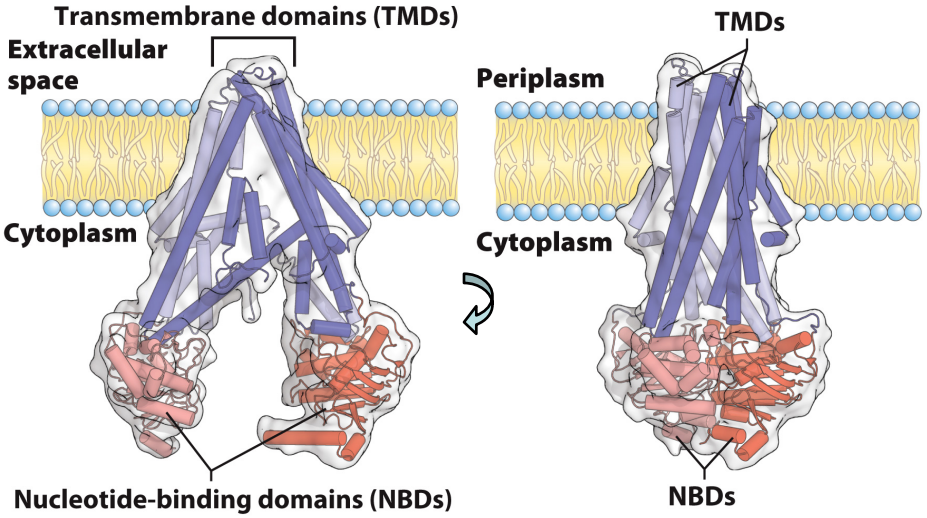
### Sodium–potassium ($Na^+$–$K^+$) pump



Molecular Dynamics video

https://youtu.be/1zvnsrKQ2Jg

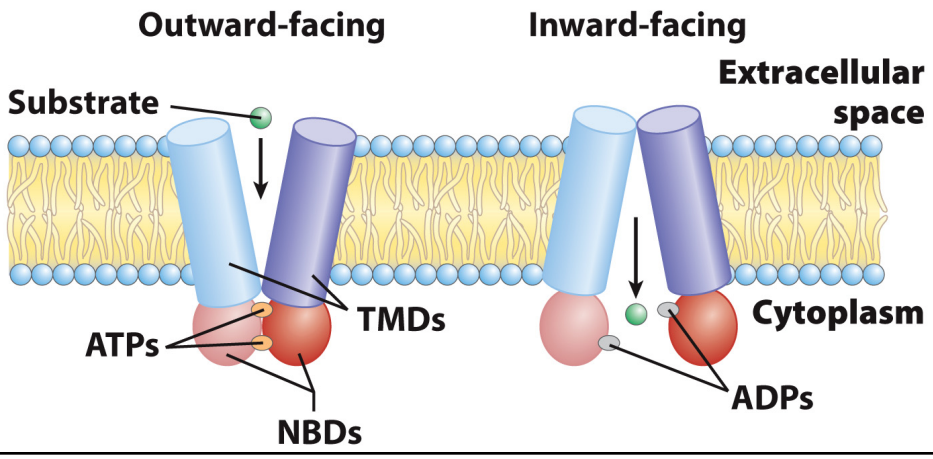
# Membrane Transport




ABC Transporters Use ATP Hydrolysis to Drive Transport of Substrates OUT

# Membrane Transport

ABC Transporters Use ATP Hydrolysis to Drive Transport of Substrates IN



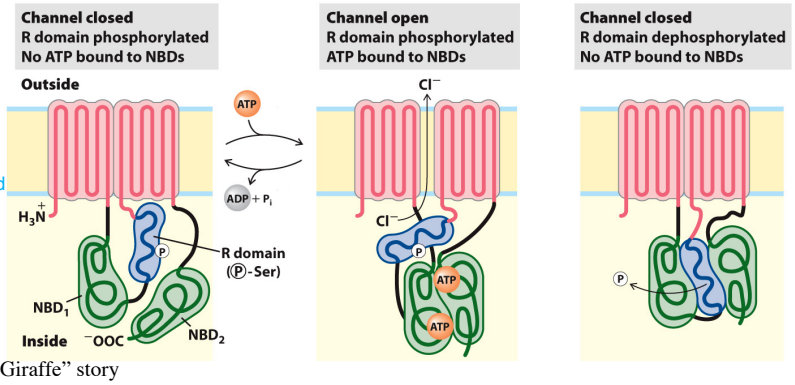
# Membrane Transport

## Failure of ABC-Transporters Can Lead to Human Disease

- Mutations in the human CFTR transporter (an ABC-type transporter-like **channel** for chloride ions)(cystic fibrosis transmembrane-conductance regulator) result in the human disease cystic fibrosis.
- Single-amino-acid mutations can render the protein misfolded and/or unable to transport chloride ions, resulting in an imbalance of water across the membrane.

Regulated Facilitative Diffusion

- Phosphorylated by PKA
- Puts it in ATP cycle



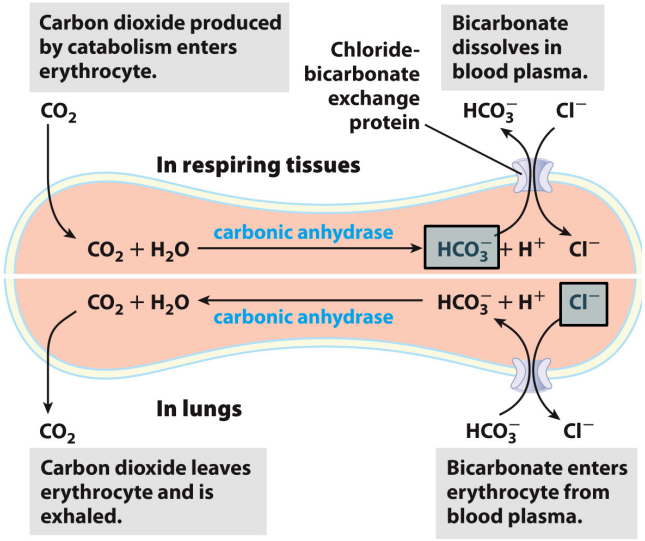

Dr. Kornberg's "Giraffe" story

# Membrane Transport

## Examples of Secondary Active Transport

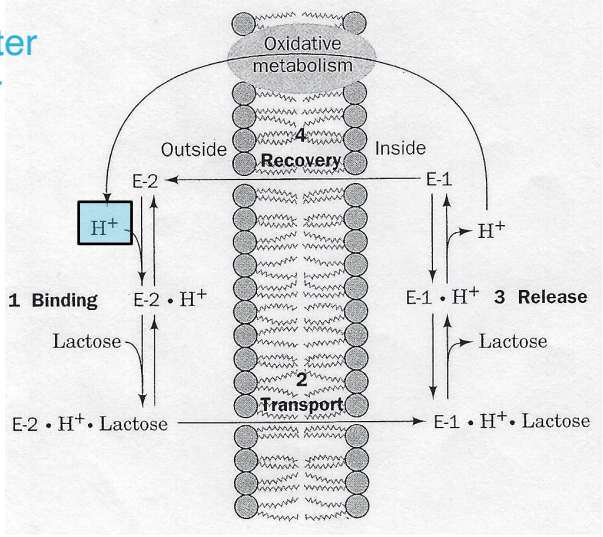
Bicarbonate Transporter is an Antiporter

Maintains the electrochemical potential across the membrane



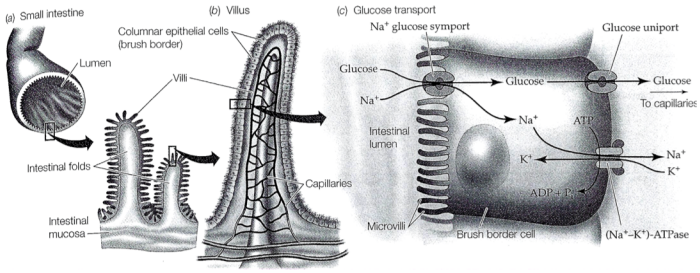
# Membrane Transport

The bacterial Lactose Transporter is an Symporter

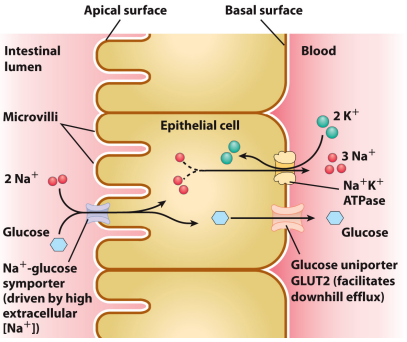



Uses the power of a proton gradient across the plasma membrane

# Membrane Transport




Efficient Import of Glucose uses Multiple Glucose Transporters




- A $Na^+$-glucose symporter and a glucose uniporter operate on opposite sides of epithelial cells to facilitate movement of glucose from the intestine to the blood.
- Uses the Na/K gradient set up by "the pump."

# Membrane Transport

**TABLE 11-7a Transport Systems Described Elsewhere in This Text**

| Transport system and location | Figure | Role |
|---|---|---|
| $IP_3$-gated $Ca^{2+}$ channel of ER | 12-11 | Allows signaling via changes in cytosolic $[Ca^{2+}]$ |
| ✓ Glucose transporter of animal cell plasma membrane; regulated by insulin | 12-20 | Increases capacity of muscle and adipose tissue to take up excess glucose from blood |
| ✓ Voltage-gated $Na^+$ channel of neuron | 12-29 | Creates action potentials in neuronal signal transmission |
| ✓ Fatty acid transporter of myocyte plasma membrane | 17-3 | Imports fatty acids for fuel |
| ✓ Acyl-carnitine/carnitine transporter of mitochondrial inner membrane | 17-6 | Imports fatty acids into matrix for β oxidation |
| ✓ Complex I, III, and IV proton transporters of mitochondrial inner membrane | 19-16 | Act as energy-conserving mechanism in oxidative phosphorylation, converting electron flow into proton gradient |
| ✓ $F_0F_1$ ATPase/ATP synthase of mitochondrial inner membrane, chloroplast thylakoid, and bacterial plasma membrane | 19-25, 20-20a, 20-24 | Interconverts energy of proton gradient and ATP during oxidative phosphorylation and photophosphorylation |
| ✓ Adenine nucleotide antiporter of mitochondrial inner membrane | 19-30 | Imports substrate ADP for oxidative phosphorylation and exports product ATP |
| ✓ $P_i$-$H^+$ symporter of mitochondrial inner membrane | 19-30 | Supplies $P_i$ for oxidative phosphorylation |
| ✓ Malate-α-ketoglutarate transporter of mitochondrial inner membrane | 19-31 | Shuttles reducing equivalents (as malate) from matrix to cytosol |
| ✓ Glutamate-aspartate transporter of mitochondrial inner membrane | 19-31 | Completes shuttling begun by malate-α- ketoglutarate shuttle |

# Membrane Transport

**TABLE 11-7b Transport Systems Described Elsewhere in This Text**

| Transport system and location | Figure | Role |
|---|---|---|
| ✓ Uncoupling protein UCP1, a proton pore of mitochondrial inner membrane | 19-36, 23-35 | Allows dissipation of proton gradient in mitochondria as means of thermogenesis and/or disposal of excess fuel |
| ✓ Cytochrome *bf* complex, a proton transporter of chloroplast thylakoid | 20-19 | Acts as proton pump, driven by electron flow through the Z scheme; source of proton gradient for photosynthetic ATP synthesis |
| ✓ Bacterorhodopsin, a light-driven proton pump | 20-27 | Is light-driven source of proton gradient for ATP synthesis in halophilic bacterium |
| $P_i$-triose phosphate antiporter of chloroplast inner membrane | 20-42, 20-43 | Exports photosynthetic product from stroma; imports $P_i$ for ATP synthesis |
| ✓ Citrate transporter of mitochondrial inner membrane | 21-10 | Provides cytosolic citrate as source of acetyl-CoA for lipid synthesis |
| ✓ Pyruvate transporter of mitochondrial inner membrane | 21-10 | Is part of mechanism for shuttling citrate from matrix to cytosol |
| ✓ LDL receptor in animal cell plasma membrane | 21-41 | Imports, by receptor-mediated endocytosis, lipid-carrying particles |
| Protein translocase of ER | 27-40 | Transports into ER proteins destined for plasma membrane, secretion, or organelles |
| Nuclear pore protein translocase | 27-44a | Shuttles proteins between nucleus and cytoplasm |
| Bacterial protein transporter | 27-46 | Exports secreted proteins through plasma membrane |

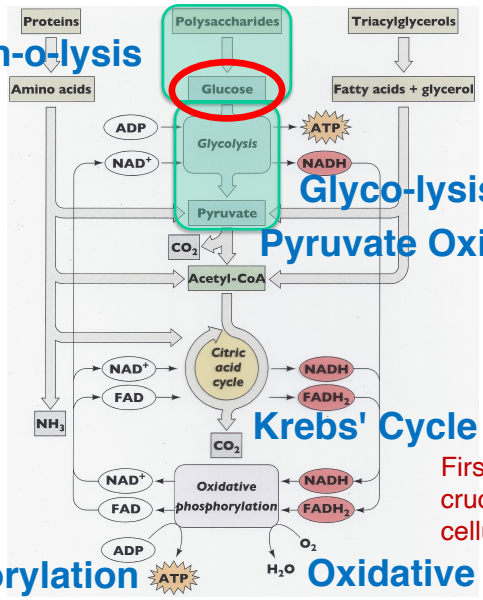
# Membrane Transport

## Summary

We learned that:

- Membrane proteins play an important functional role in the transport of solutes across the membrane
- Transport is mediated or non-mediated.
- In mediated transport, there is a facilitative diffusion mechanism or an active transport mechanism
- Active transport is either primary or secondary
- Primary active transport of solutes across membranes requires ATP
- The most important, and one of the best examples of primary active transport, is the Na/K ATPase.
- Secondary active transport but can be accomplished in many ways, but uses the potential energy established by primary active transport or pre-established concentration gradients

# CATABOLISM




Glycogen-o-lysis

Glyco-lysis

Pyruvate Oxidation

Krebs' Cycle

Phosphorylation

Oxidative

First, let's discuss how crucial **glucose** is for cellular metabolism

# CATABOLISM

## Glucose Importance:

- Glucose is an excellent fuel.
  - yields good amount of energy upon oxidation
    - –2840 kJ/mol glucose (–678 kcal/mol)
  - can be efficiently stored in the polymeric form
  - Many organisms and tissues can meet their energy needs on glucose only.

- Glucose is a versatile biochemical precursor.
  - Many organisms can use glucose to generate:
    - all the amino acids
    - membrane lipids
    - nucleotides in DNA and RNA
    - cofactors needed for the metabolism of EVERYTHING
    - IOW, EVERYTHING!!

# CATABOLISM

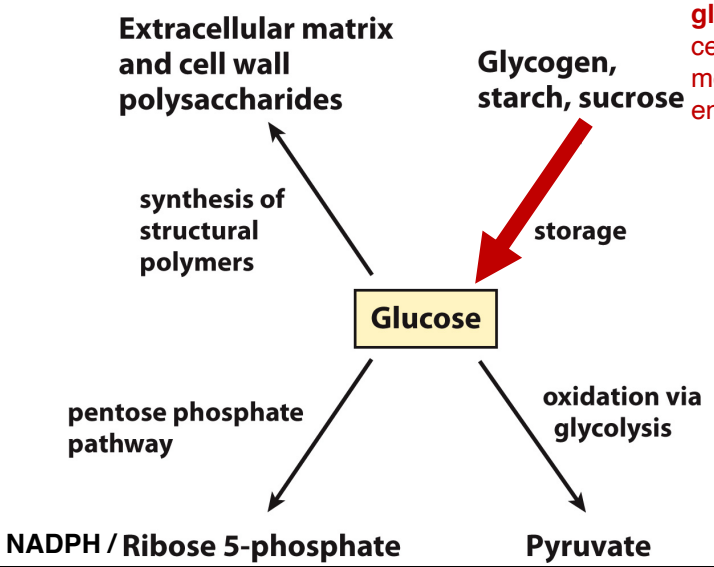
## Glucose Utilization:

- Storage
  - can be stored in the polymeric form (starch, glycogen)
  - used for long-term energy needs
- Energy production
  - generates energy via oxidation of glucose
  - short-term energy needs
- Production of NADPH and pentoses
  - generates NADPH for use in relieving oxidative stress and synthesizing fatty acids, amino acids, etc. (anabolism)
  - generates pentose phosphates for use in DNA/RNA biosynthesis
- Structural carbohydrate production
  - used for generation of alternate carbohydrates used in cell walls of bacteria, fungi, and plants

# CATABOLISM

## Glucose Utilization: Four Major Fates of Glucose

What if you need **glucose** for cellular metabolism and energy?



# Glucose is Stored for Later Use as Glycogen (animals) or Starch (plants)

- Glycogen/starch are branched polymers of $\alpha(1\rightarrow4)$-linked glucose with $\alpha(1\rightarrow6)$ linkages (glycogen every 8-12 glucose units; starch every 24-30 glucose units).
- Glycogen storage occurs mainly in the liver and muscle.
- Starch storage occurs mainly in the leaves

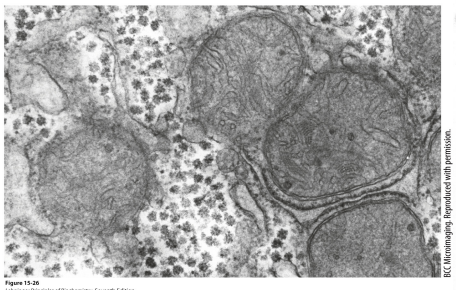


Figure 15-26
Lehninger Principles of Biochemistry, Seventh Edition
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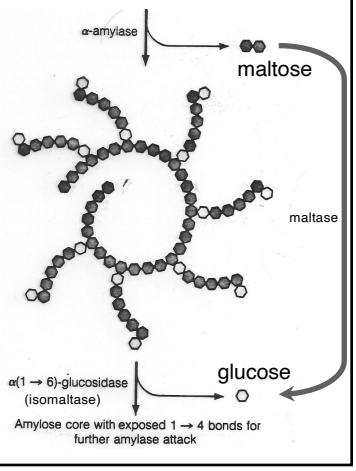
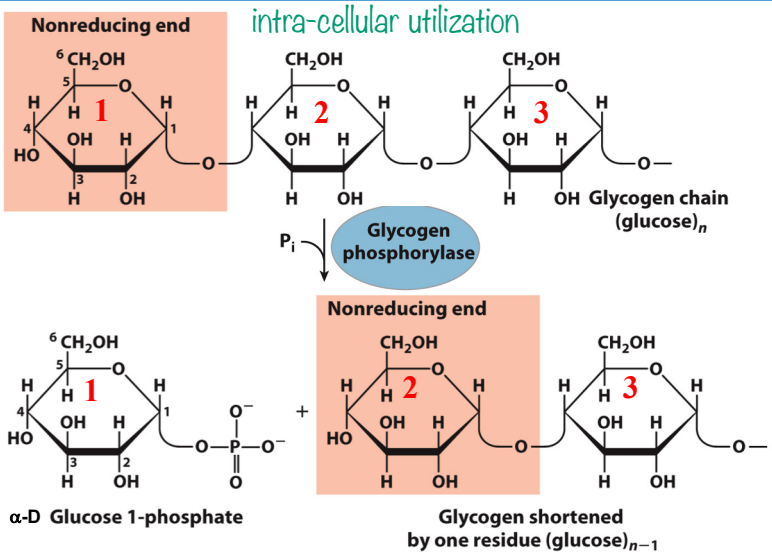
Digestion *versus* intra-cellular utilization

Digestion




# Glycogenolysis is performed mainly by Glycogen Phosphorylase

intra-cellular utilization



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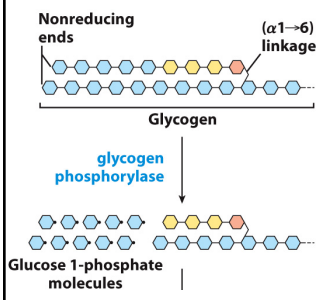
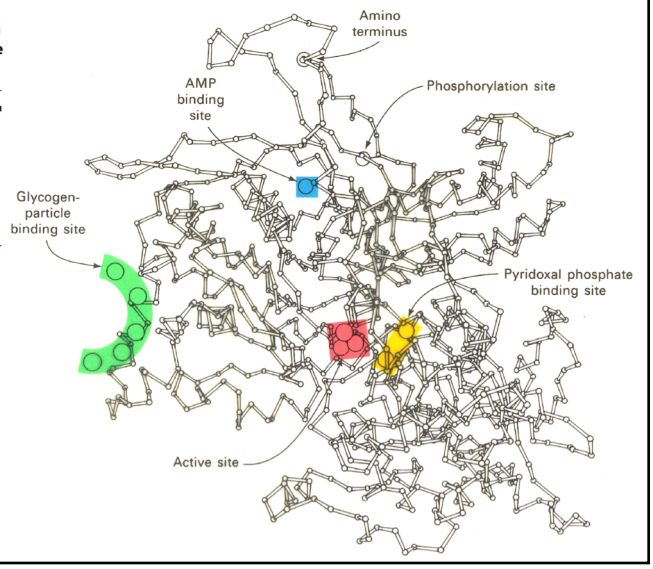
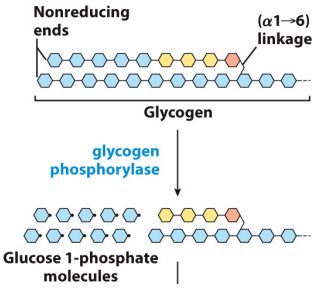


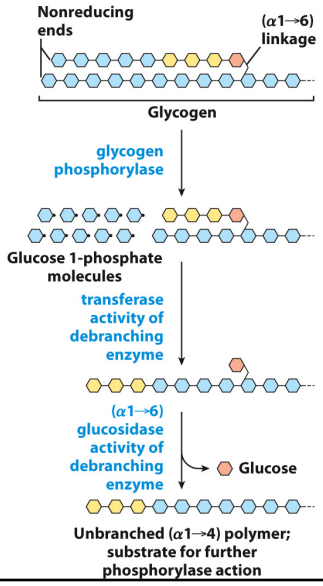




# Glycogenolysis must deal with Branch Points in Glycogen




- Glycogen phosphorylase works on nonreducing ends until it reaches four residues from an ($\alpha 1 \rightarrow 6$) branch point.
- Debranching enzyme has two activities; a glycosyltransferase and a glycosidase
  - Debranching enzyme transfers a block of three residues to the nonreducing end of the chain.
  - Debranching enzyme hydrolyzes the single remaining ($\alpha 1 \rightarrow 6$)-linked glucose, which becomes a free glucose unit (i.e., NOT glucose 1-phosphate).
- The Glc enters glycolysis, but the Glc 1-P must be converted to the glycolytic intermediate Glc 6-P first.
- How?

# Glycogenolysis must deal with Branch Points in Glycogen

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