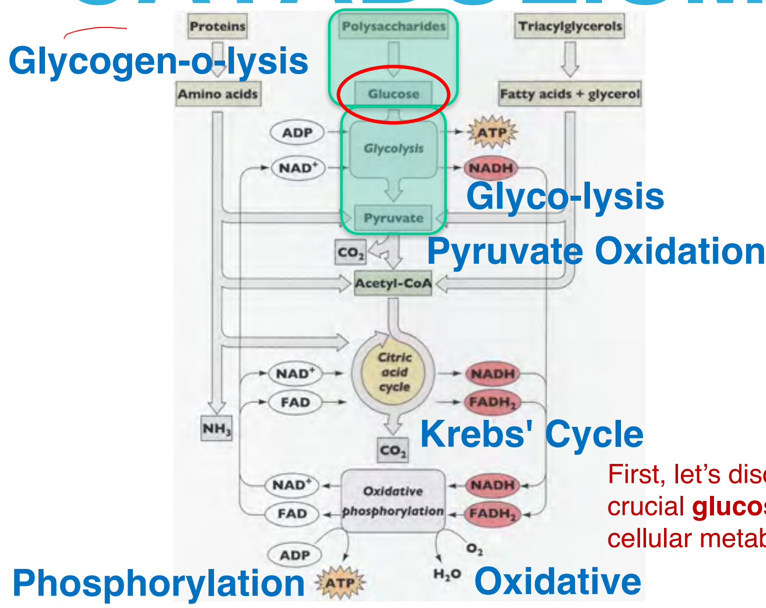
CATABOLISM



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

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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!!

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Glucose Utilization:

- Storage
  - can be stored in the polymeric form (starch, glycogen)
  - used for later 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

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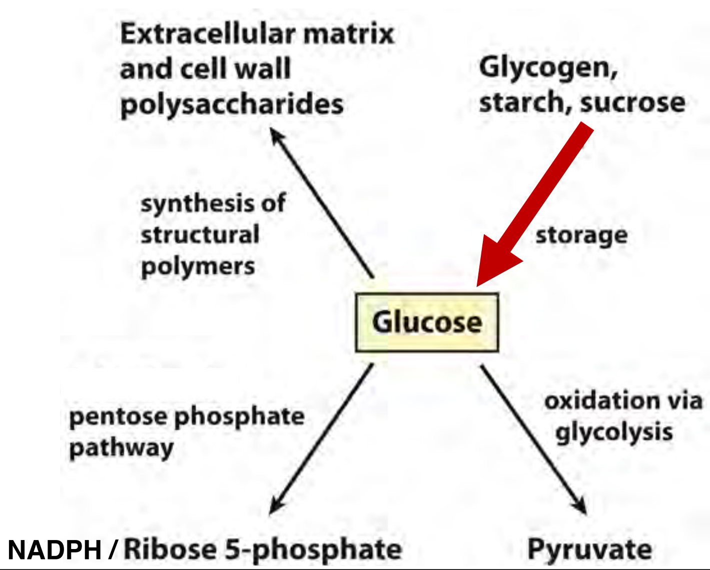
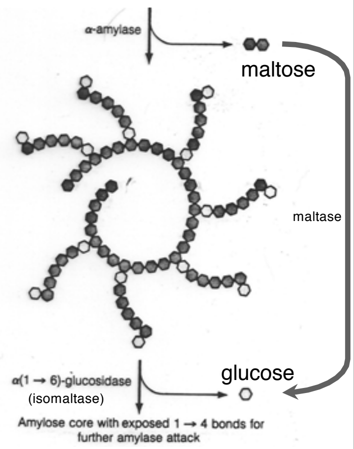
Glucose Utilization: Four Major Fates of Glucose



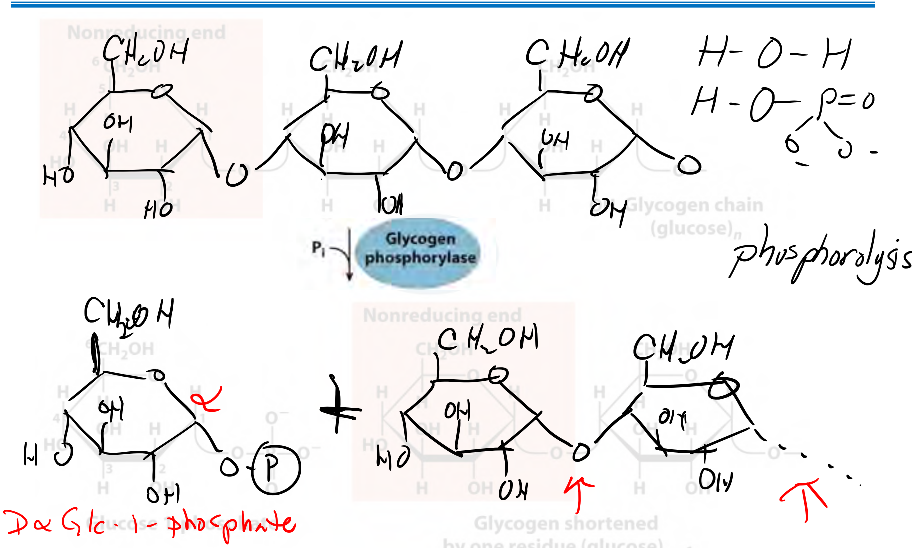
Glucose is Stored for Later Use as Glycogen (animals) or Starch (plants)

- 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



Digestion *versus* intra-cellular utilization

Glycogenolysis is performed mainly by Glycogen Phosphorylase



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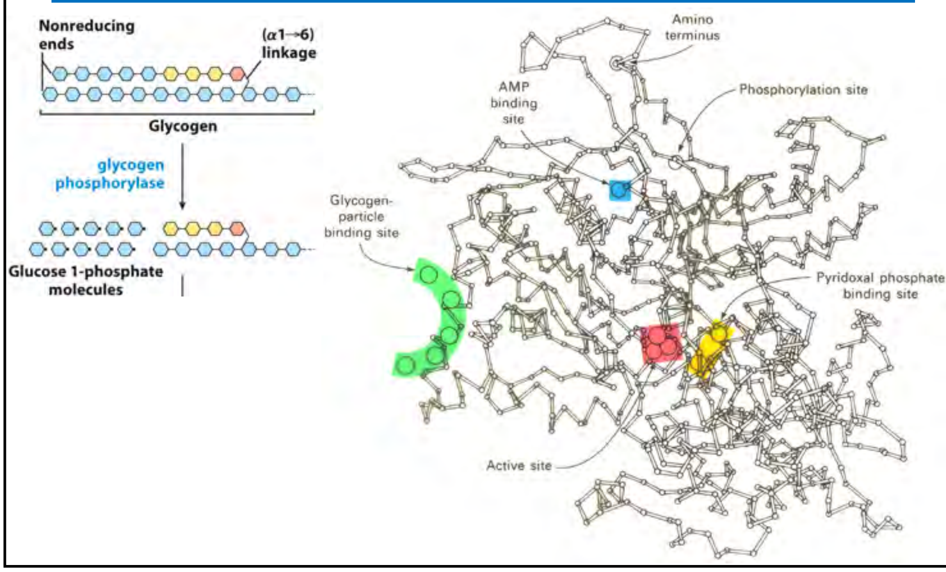

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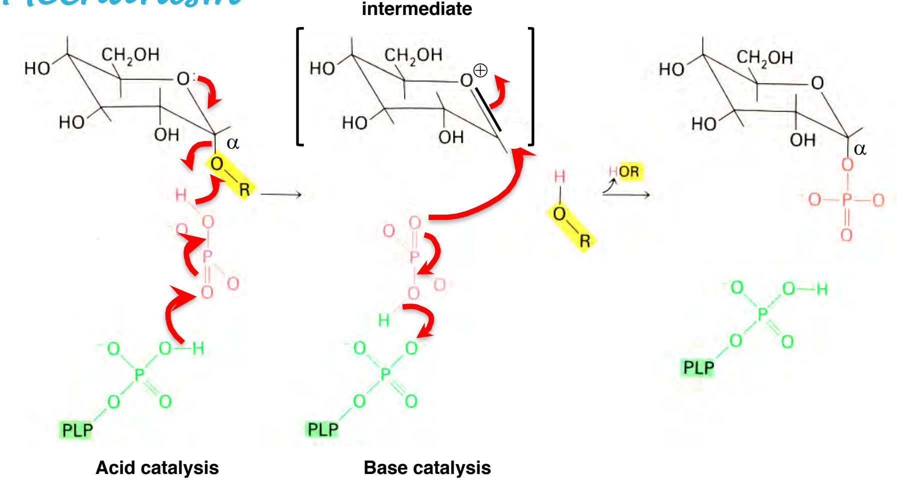
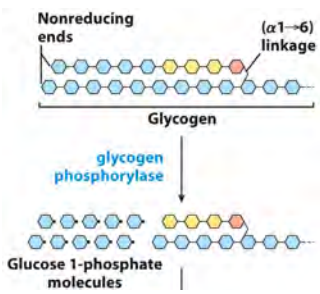
Mechanism



Glycogenolysis must deal with Branch Points in Glycogen



- Glycogen phosphorylase works on nonreducing ends until it reaches four residues from an (α1→ 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 (α1→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 a glycolytic intermediate first.
- How?

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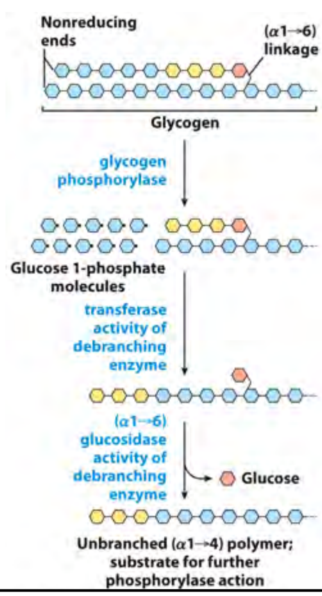

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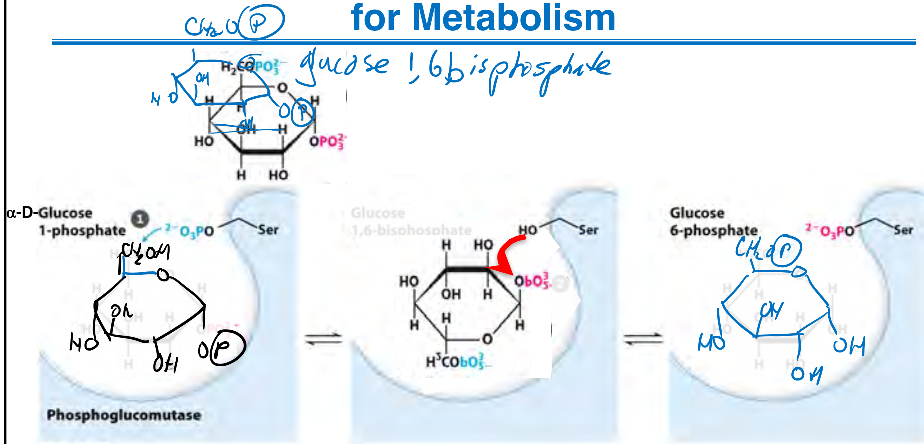
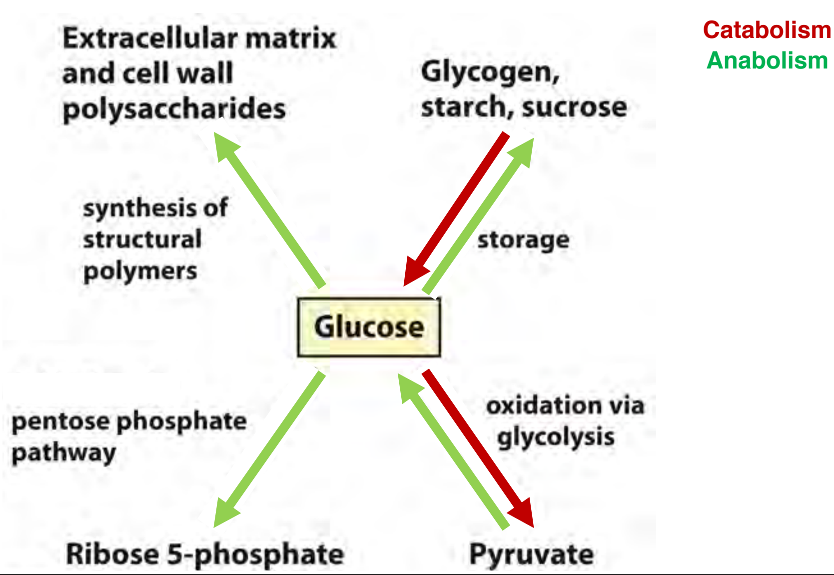
Glycogenolysis produces Glucose 1-Phosphate, which must be converted to Glucose 6-Phosphate for Metabolism



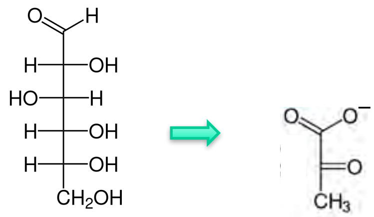
- Phosphoglucomutase must be phosphorylated at an active-site Ser.
- This is performed by a Glc 1,6-P_2 to initiate the active form.
- During turnover, the bisphosphate flips within a "vestibule"

Glucose Utilization

Four Major Fates of Glucose



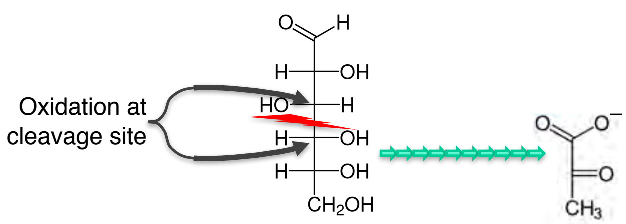
Glycolysis



Learning outcomes for each pathway in course:
1. Understand the logic for getting from starting compound to end product
2. Know the names, structures, enzymes of each step
3. Energetics
4. Control mechanisms

- Sequence of enzyme-catalyzed reactions by which glucose is converted into pyruvate
  - Pyruvate can be further aerobically oxidized.
  - Pyruvate can be used as a precursor in biosynthesis.
- In the evolution of life, glycolysis probably was one of the earliest energy-yielding pathways.
- Research of glycolysis played a large role in the development of modern biochemistry.
  - understanding the role of coenzymes
  - discovery of the pivotal role of ATP
  - development of methods for enzyme purification
  - inspiration for the next generations of biochemists

Glycolysis



- Enols are not stable and they isomerize to the corresponding aldehyde or ketone in a process known as keto-enol tautomerism.

- It developed before photosynthesis, when the atmosphere was still anaerobic.
- Thus, the task upon early organisms was how to extract free energy from glucose anaerobically.
- Some of the free energy is captured in the synthesis of ATP and NADH.
- The solution:
  - First: All intermediates are phosphorylated: keeps them in the cell and "Activates" them for chemical degradation.
  - Second: Need to split in middle to make pathway convergent
  - Third: Overall oxidation (loss of only 4 e^-)
  - Fourth: Keto-enol tautomerization is key
  - Fifth: Collect energy from the high-energy metabolites.

substrate-level phosphorylation