

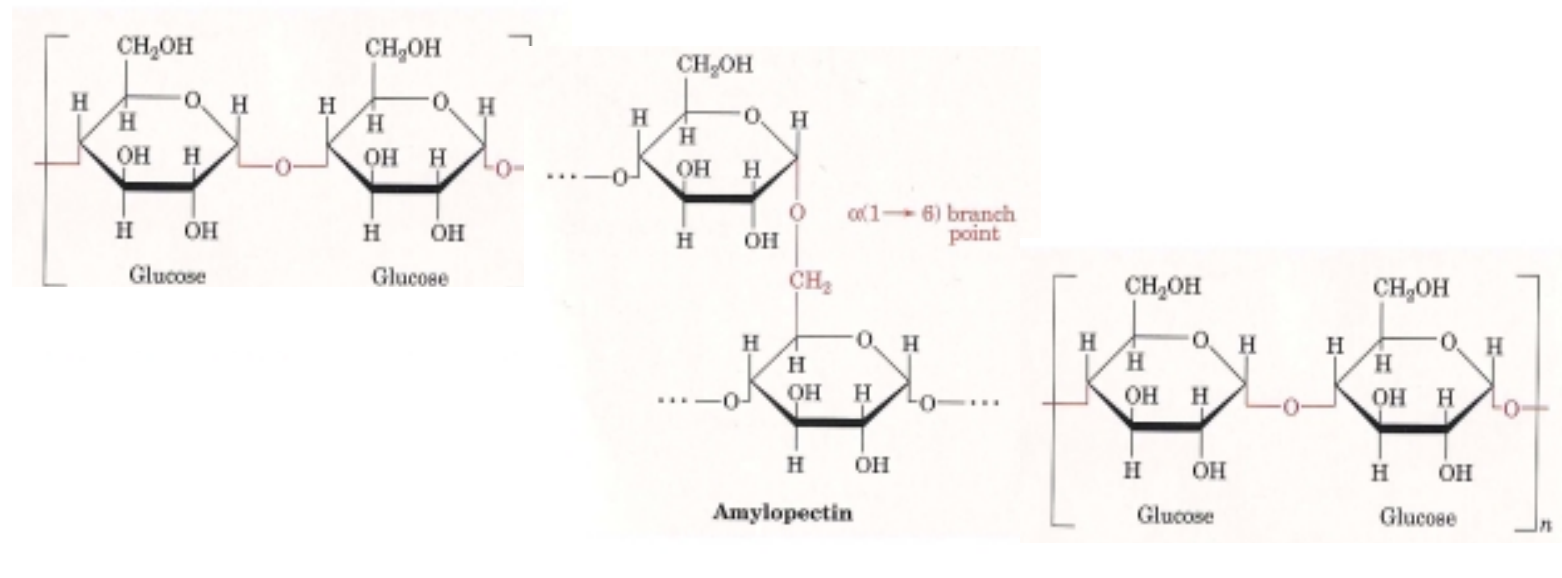
Lecture 2 Announcements (24 January 2001):

There is a REVISED syllabus posted on the course web site. Note that we will have a guest lecturer on 6 Feb, DR. RICHARD LOSICK (Harvard University), who will speak on “A four-dimensional view of the bacterial cell”. In preparation for this lecture, you should peruse Dr. Losick’s web site to get an idea of the research in his lab. The link to his site is on the course site. Dr. Losick will also give two public lectures at SUNYA, one on 5 Feb and the other on 6 Feb. You should try to attend one or both. He is here as a Phi Beta Kappa speaker, and will also meet with interested students. If interested, you should contact the Biology Office staff. More later.....

Lecture 2: Glycogen metabolism (Chapter 15)

Review: Animals use glycogen for ENERGY storage.

Glycogen is a highly-branched polymer of glucose units

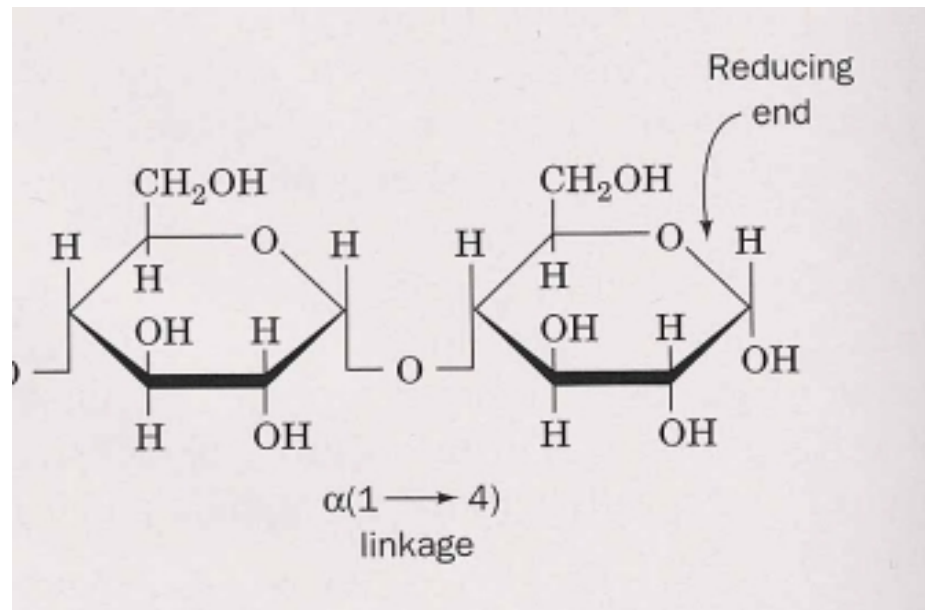


Basic structure is similar to that of amylopectin, but with only about 8 to 12 glucose units between branch points.

GLYCOGEN BREAKDOWN INSIDE CELLS:

Glycogen's glucose units are mobilized by their sequential removal from the glucan chain's **nonreducing** ends---that is, the ends that lack a C₁-OH group. This is the **reducing** end of glucose:

Fig. 15-2a



The ends of some sugars have a free anomeric carbon, which can act as a mild reducing agent. In glycogen, the reducing end is actually bound by a protein named **GLYCOGENIN**.

The branched structure of glycogen permits the rapid release of glucose simultaneously from every **non-reducing** end of every branch (emphasized here by the black arrows):

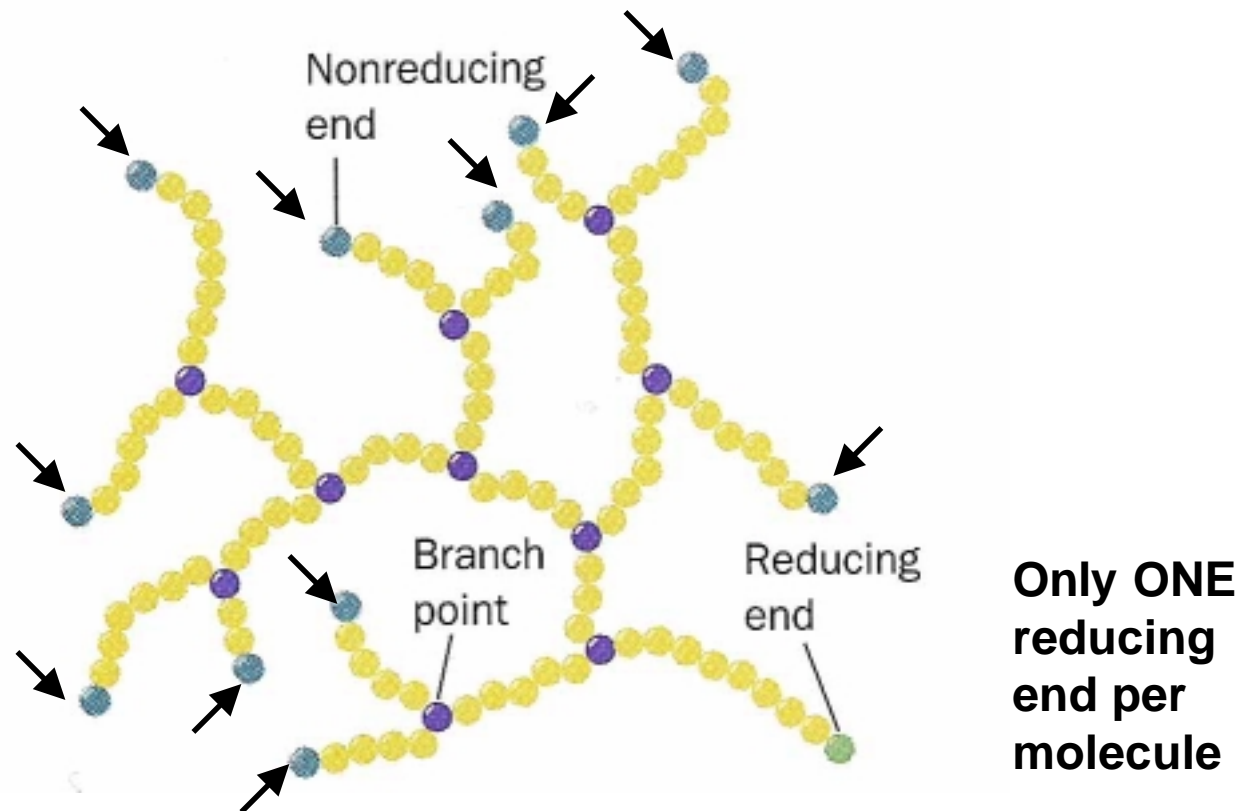


Fig. 15-2b

(Note that the number of glucose units between branch points in this figure is not accurate. Don't let this confuse you!)

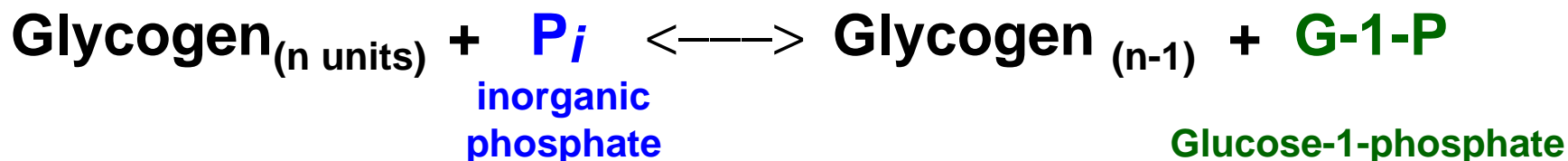
Why use **glycogen** to store energy rather than just using **fat**? - (which is more abundant than glycogen in the body and also stores energy)

- 1. Muscles "mobilize" (convert to energy) glycogen faster than fat.**
- 2. Fatty acid residues cannot be metabolized anaerobically.** (If you want to burn fat while you are exercising, you must be able to breathe fairly easily.)
- 3. Animals cannot convert fat to glucose,** so fat metabolism cannot maintain blood glucose levels. Glucose is "Brain food"—it is the major energy form that crosses the blood-brain barrier.

Glycogenolysis (or glycogen breakdown) requires 3 major enzymes:

1) GLYCOGEN PHOSPHORYLASE (Fig. 15-4; more later)

(bond cleavage by phosphorolysis)



2) GLYCOGEN DEBRANCHING ENZYME (Fig. 15-6)

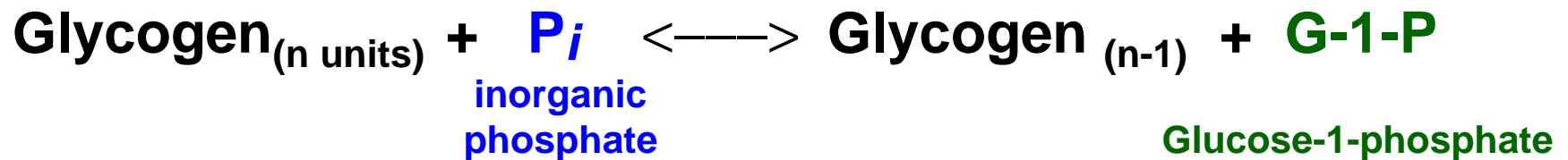
3) PHOSPHOGLUCOMUTASE (Fig. 15-7):



G-6-P has several fates (see Fig 15-1).
In LIVER, it is hydrolyzed to glucose + **P_i**
by **GLUCOSE-6-PHOSPHATASE**.

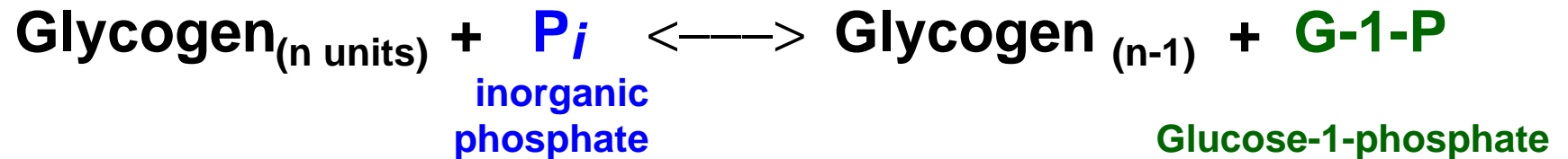
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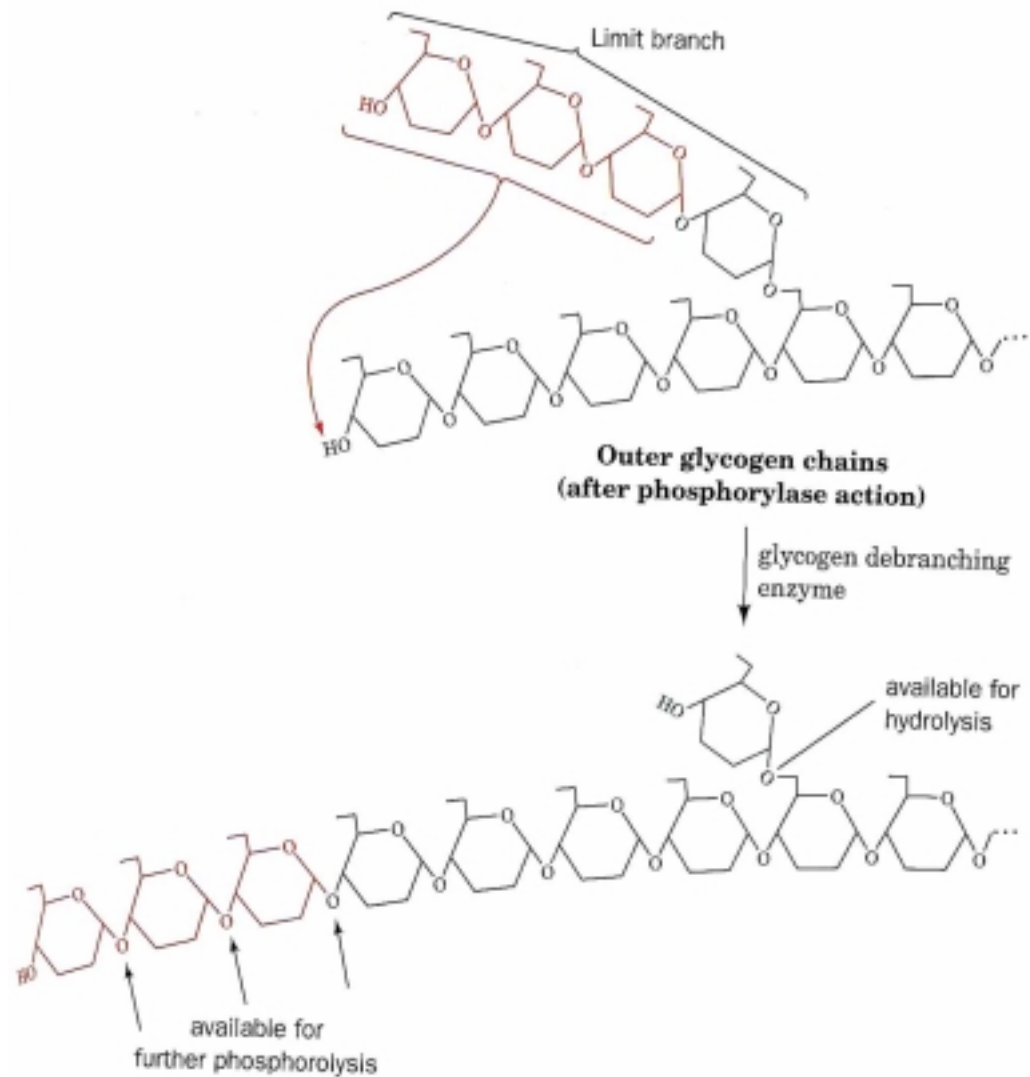
Glycogenolysis (or glycogen breakdown) requires 3 major enzymes:

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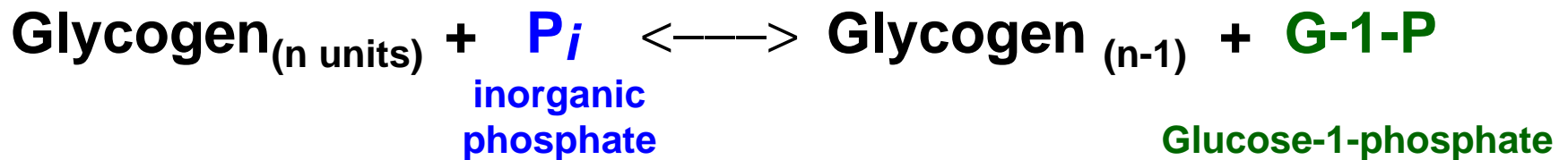
Fig. 15-6: Two activities of GLYCOGEN DEBRANCHING ENZYME



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1) GLYCOGEN PHOSPHORYLASE (Fig. 15-4; more later):

(bond cleavage by phosphorolysis)



2) GLYCOGEN DEBRANCHING ENZYME (Fig. 15-6)

→3) PHOSPHOGLUCOMUTASE (Fig. 15-7):



G-6-P has several fates (see Fig 15-1).
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Fig. 15-7: Phosphoglucomutase mechanism

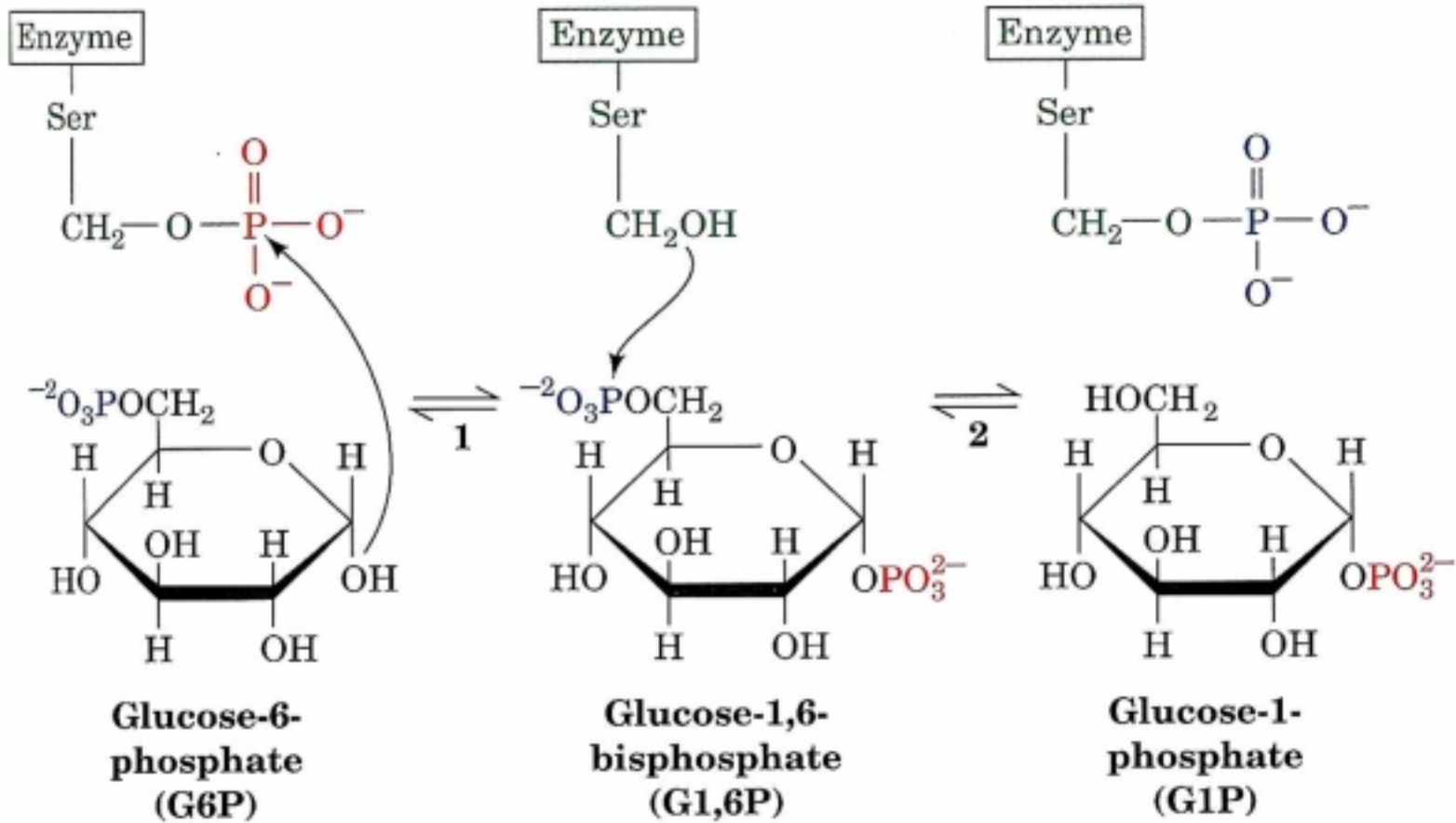
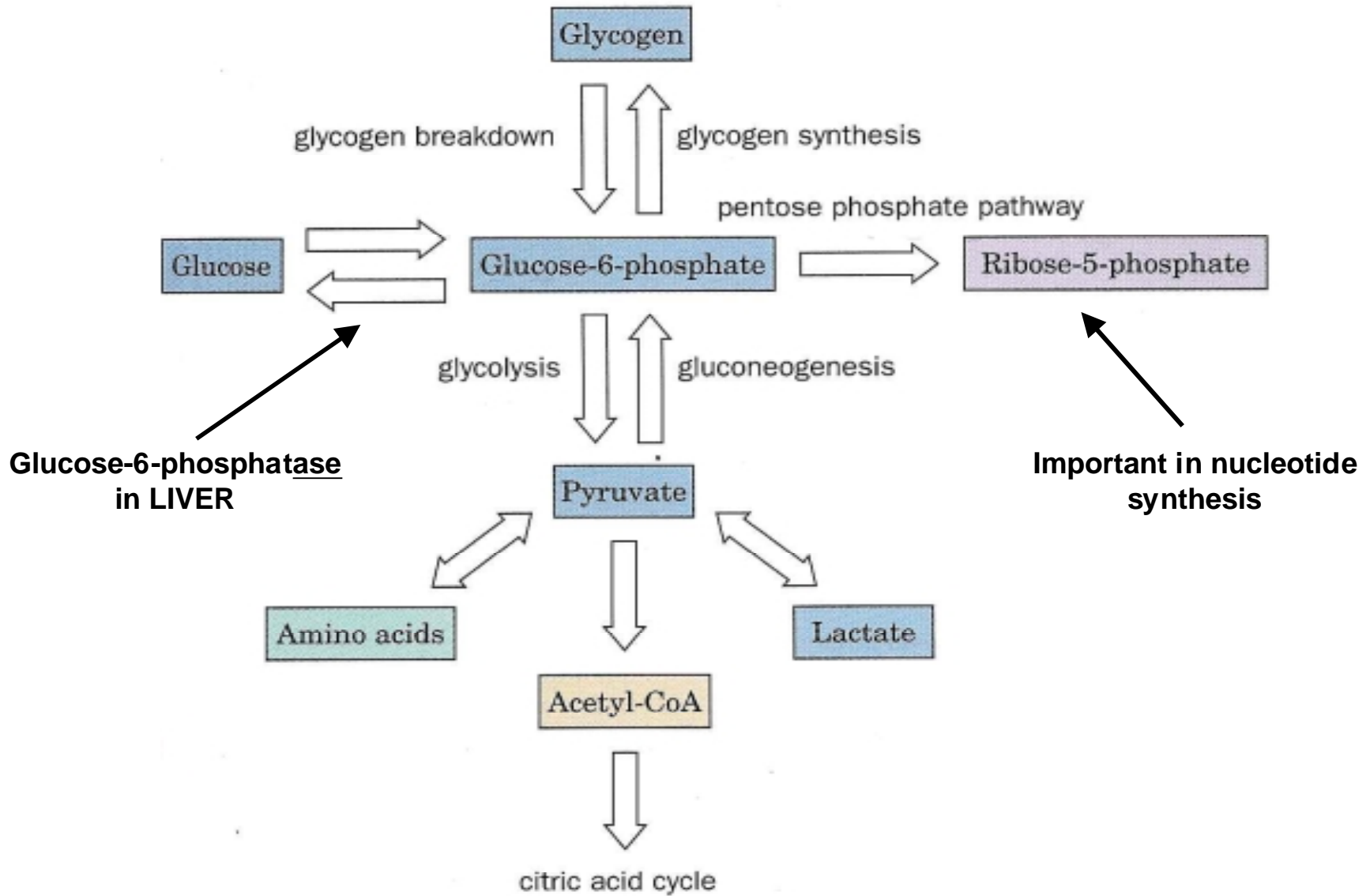
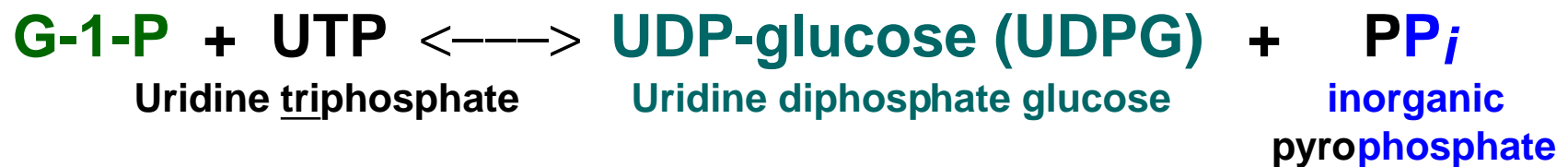


Fig. 15-1: G6P is a major intermediate in glucose metabolism



Glycogen SYNTHESIS requires 3 major enzymes, and occurs by a **SEPARATE PATHWAY** from glycogenolysis:

1) UDP-GLUCOSE PYROPHOSPHORYLASE (Fig. 15-9):



2) GLYCOGEN SYNTHASE (Fig. 15-10):



This reaction must be “primed” by GLYCOGENIN

3) GLYCOGEN BRANCHING ENZYME (Fig. 15-11) or
AMYLO (1,4→1,6) TRANSGLYCOSYLASE.

(Will be covered next lecture.)

GENERAL RULES FROM ABOVE:

BIOSYNTHETIC AND DEGRADATIVE PATHWAYS OF METABOLISM ARE (ALMOST) ALWAYS COMPLETELY DIFFERENT. THAT IS, THEY USED DIFFERENT ENZYMES.

POLYMERIZATION OF MONOMERIC UNITS INTO MACROMOLECULES USUALLY REQUIRES A 'PRIMER' TO INITIATE THE REACTION. THAT IS, THE FIRST TWO UNITS CANNOT BE LINKED BY THE ENZYME THAT DOES THE POLYMERIZATION.

1. GLYCOGEN PHOSPHORYLASE (or simply PHOSPHORYLASE)

- **Removes GLUCOSE UNITS from the NONREDUCING ends of GLYCOGEN.**
- **Is a FAST enzyme: the outermost branches of glycogen are degraded in seconds in muscle tissue.**
- **Is a dimer of identical 842-residue subunits (Fig. 15-3).**
- **Catalyzes the CONTROLLING STEP in glycogen breakdown.**
- **The standard-state free-energy change (ΔG°) for phosphorylase reactions is + 3.1 kJ/mol, but the intracellular $[Pi] / [G1P]$ ratio is about 100, so ΔG *in vivo* is actually about - 6 kJ/mol.**

1. GLYCOGEN PHOSPHORYLASE (continued)

- It is a highly and complexly regulated enzyme, both by:
 - **ALLOSTERIC INTERACTIONS** (Fig. 15-13)—ATP, G6P & glucose inhibit it; AMP activates it—and by
 - **COVALENT MODIFICATION** by phosphorylation and dephosphorylation (Fig. 15-5).
 - Yields 2 major forms of phosphorylase
 - Phosphorylase *A*: Has a phosphoryl group esterified to Ser-14 in each subunit
 - Phosphorylase *B*: Is not phosphorylated.
- Only releases units that are 5 or more from the branch.
- **WHY?** Robert Fletterick (UCSF) solved the 3D structure of Phosphorylase *A*: Its crevice can admit 4 or 5 sugar residues, but it too narrow to admit a branch.