BCMB 8020
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Glycogen

Most common storage form of glucose in animals, bacteria (yeast)

Branched polymer of α1,4- & α1,8-linked glucose

Similar to amylopectin; but with smaller and more frequent branching: branching every 8-12 residues

In animals glycogen is stored largely in the liver and muscle

In mammals glycogen can make up ~10% liver mass & 2% of muscle mass

Glycogen use in animals

Insulin — glucagon or adrenaline
(fasting) (flight or fight)

Excess Glucose →→ GLYCOGEN →→replenished glucose
(i.e. after feeding)

glycogen synthesis — glycogenolysis

In vertebrates ~ 2/3 of dietary glucose is converted to glycogen

transported in blood
Food → Glucose → Intestine → cells→ converted to Glc-6-P
absorbed *hexokinase*

liver (GLUT1)
muscle (*GLUT4, GLUT 1)
*=insulin stimulated

The stimulation of glycogen synthesis is one of the major physiological responses modulated by insulin

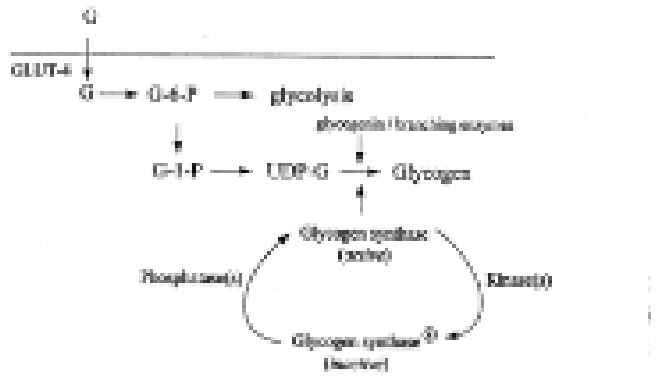
The exact mechanism by which insulin stimulates glycogen synthesis is not known

Insulin:

* Controls uptake and transport of glucose (GLUT4)

* Regulates phosphorylation and activation state of glycogen biosynthetic and catabolic enzymes (glycogen synthase; glycogen phosphorylase)

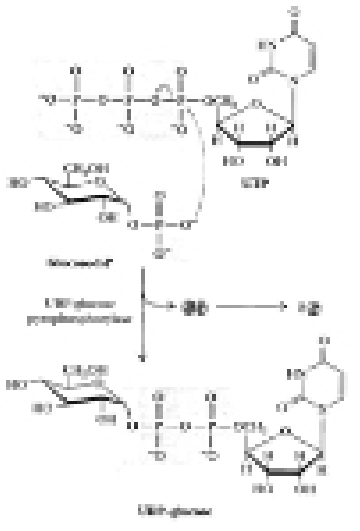
Steps in Glycogen Synthesis



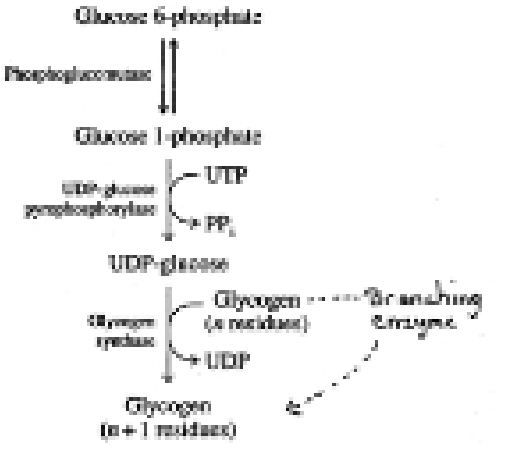
Synthesis of the chemically activated substrate for glycogen synthesis, UDP-Glc, by UDP-Glc pyrophosphorylase

(Luis Leloir, discovered NDP-sugars)

The synthesis of UDP-Glc is driven by the subsequent hydrolysis of pyrophosphate



Simplified reactions for the bulk of glycogen synthesis



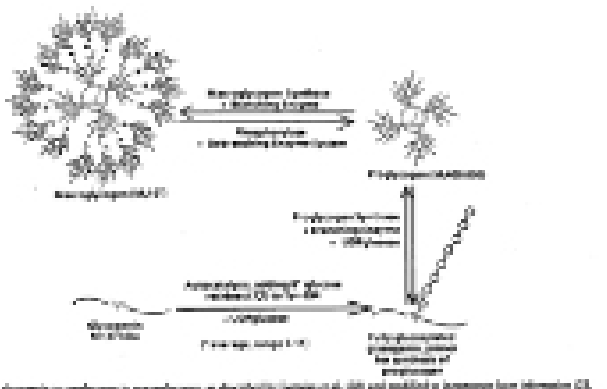
The question of how glycogen synthesis was initiated remained open for many years. It is now known that glycogen synthesis begins by the Mn++-dependent self glucosylation of glycogenin on Tyr194 to form a glycogenin with an average glucan chain of DP 8 (maltooctaose).

Steps in glycogen synthesis

Self-glucosylation of glycogenin (~37 kD) on Tyr-194 in a glycosidic linkage

UDP-Glc + Proglycogen Synthase + Branching Enzyme →
Proglycogen (~ 400,000 daltons; ~DP 2470)

Proglycogen + UDP-Glc + Macroglycogen Synthase + Branching Enzyme → Macroglycogen (~ 10^7 daltons; ~DP 61,728)



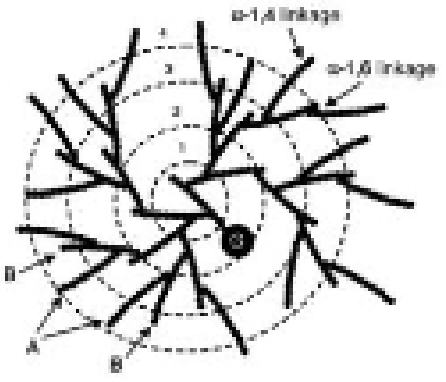
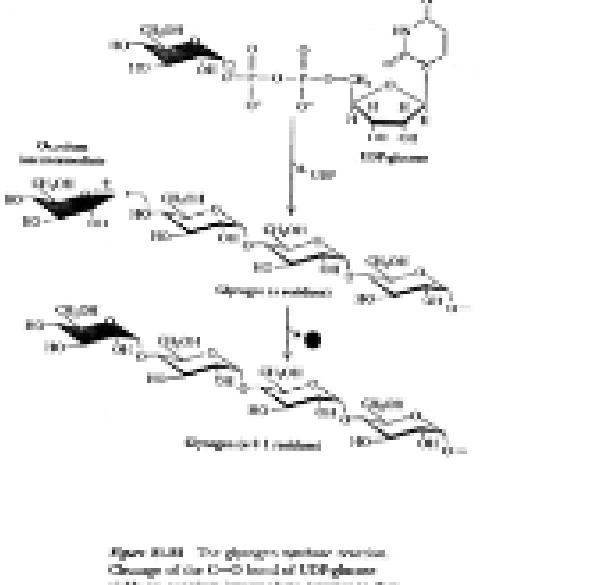
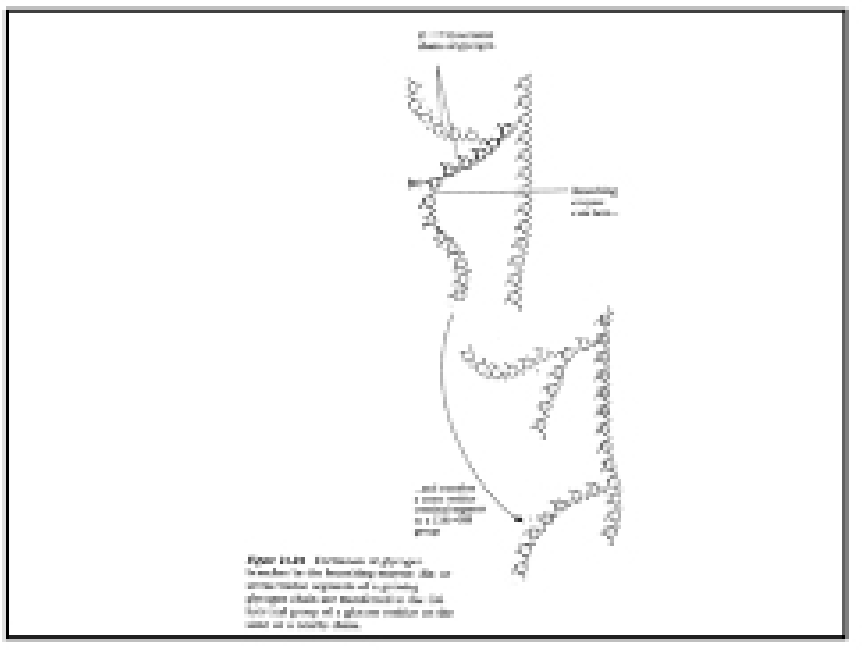
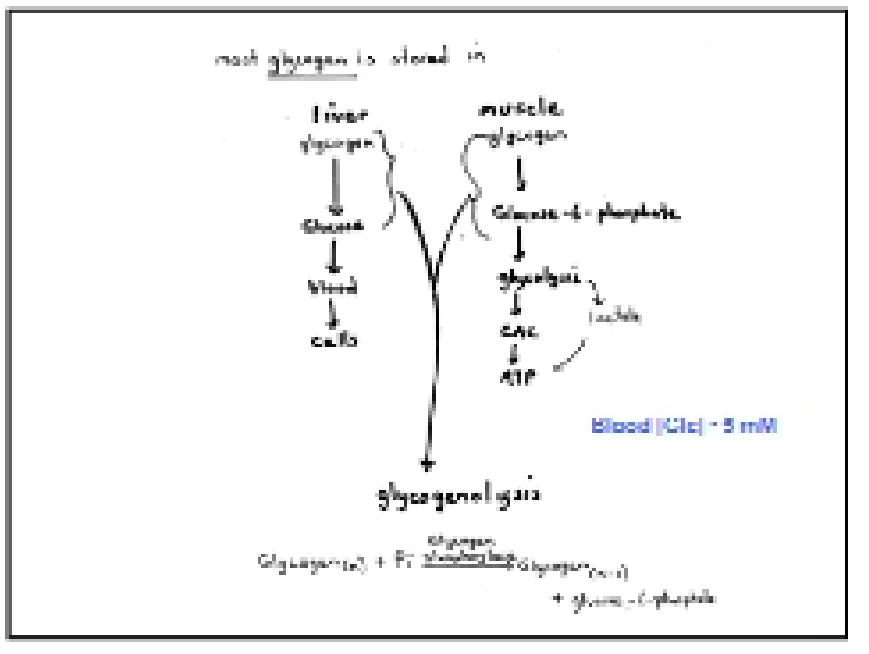


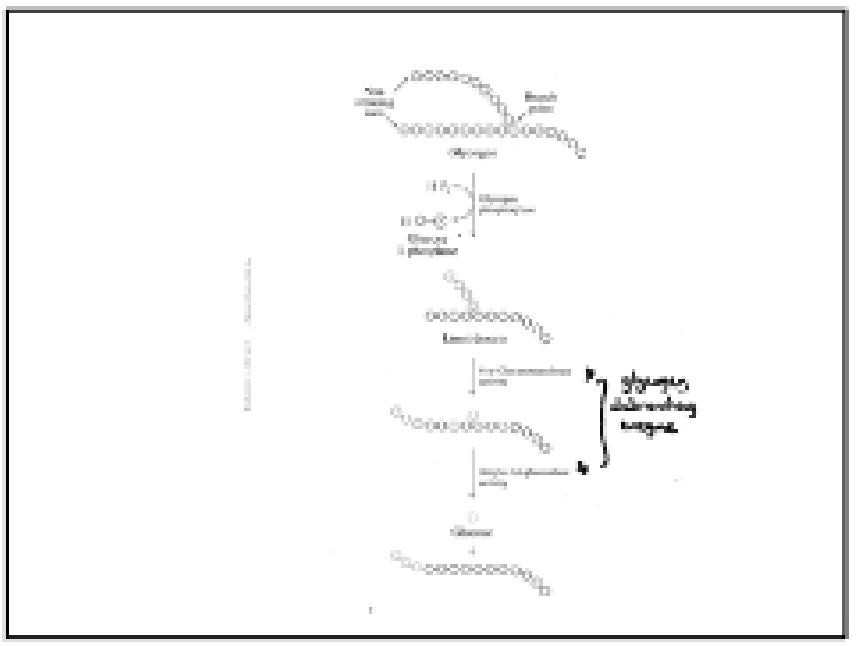
Figure 1. Diagram illustrating the first four tiers of the glycogen granule. Each B chain is linked by α-1→6 glycosidic bonds, whereas each A chain is unbranched and is linked by α-1→4 glycosidic bonds. G, glycogenin, the self-glycosylating protein primer of glycogen.

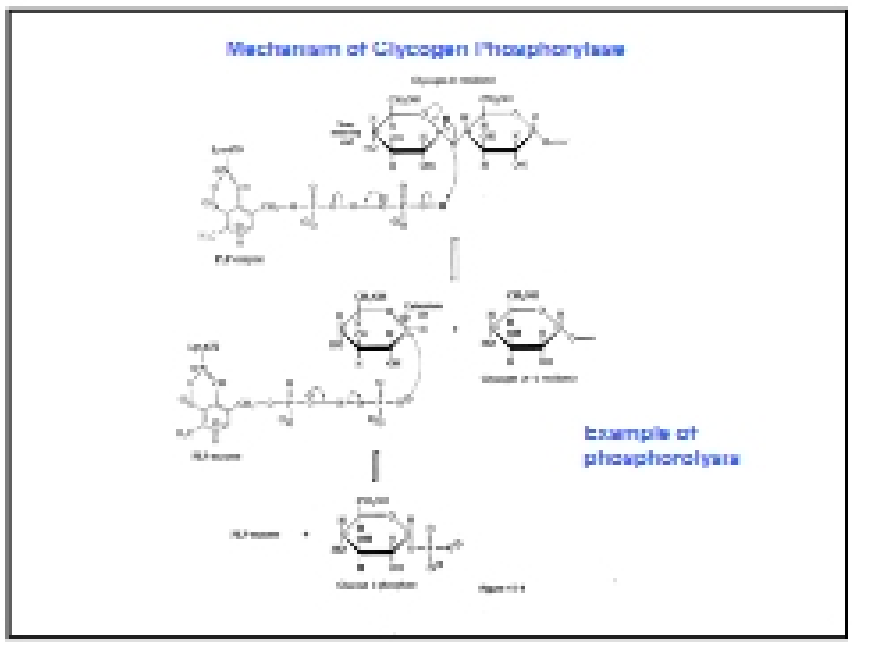
from Shearer, Exerc Sport Sci Rev, Volume 32(3) July 2004 120-126

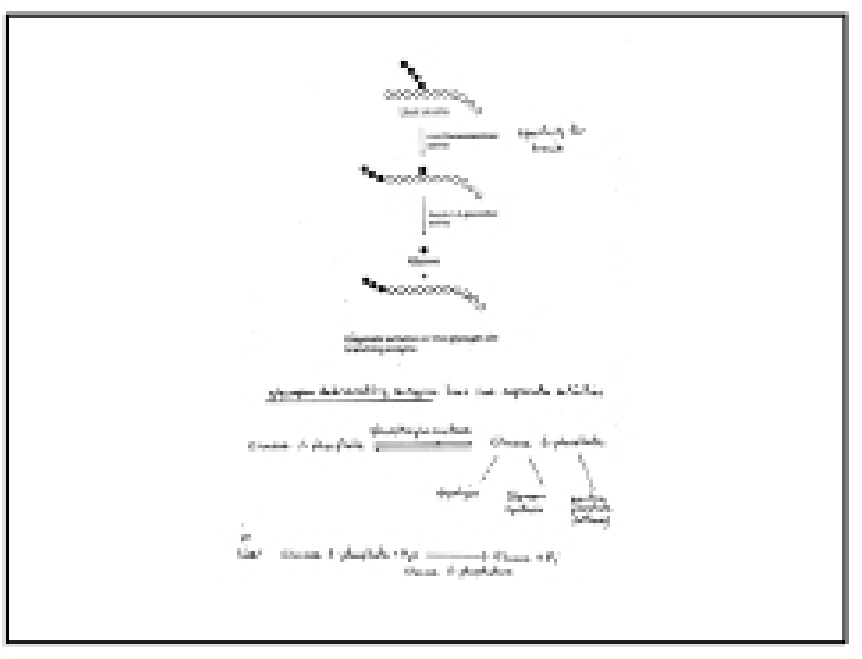












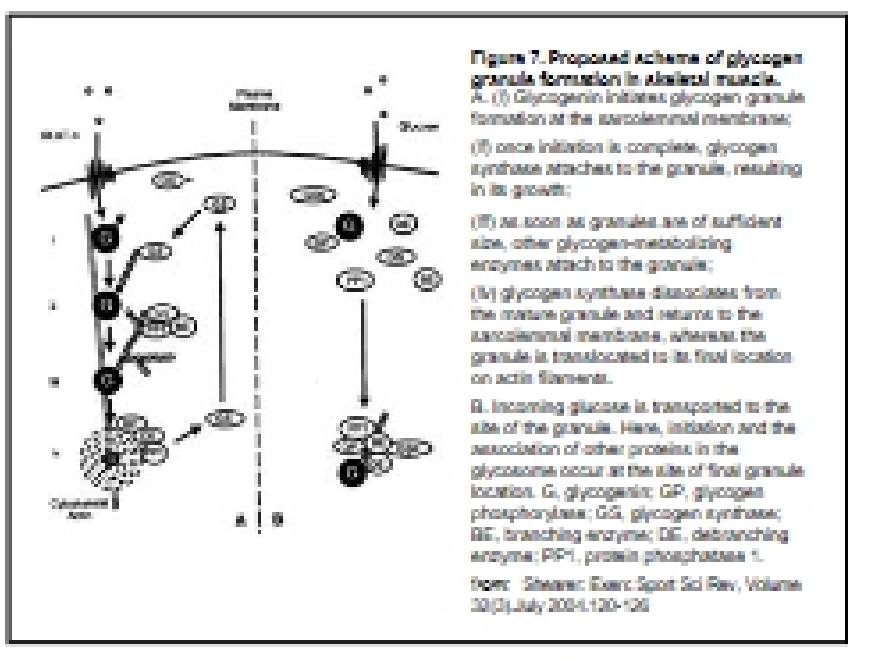


Figure 7. Proposed scheme of glycogen granule formation in skeletal muscle.
A, (I) Glycogenin initiates glycogen granule formation at the sarcolemmal membrane;

(II) once initiation is complete, glycogen synthase attaches to the granule, resulting in its growth;

(III) as soon as granules are of sufficient size, other glycogen-metabolizing enzymes attach to the granule;

(IV) glycogen synthase dissociates from the mature granule and returns to the sarcolemmal membrane, whereas the granule is translocated to its final location on actin filaments.

B, Incoming glucose is transported to the site of the granule. Here, initiation and the association of other proteins in the glycosome occur at the site of final granule location. G, glycogenin; GP, glycogen phosphorylase; GS, glycogen synthase; BE, branching enzyme; DE, debranching enzyme; PP1, protein phosphatase 1.

from: Shearer: Exerc Sport Sci Rev, Volume 33(3),July 2005,120-126