Key knowledge base

- Know the general structure of glycogen. Be able to write the chemical structure of a segment of glycogen showing the two types of glycosidic bonds. Understand why 2 kinds of glycosidic bonds give a branched polymer. Be able to identify the 'reducing' vs 'non-reducing' ends.
- Understand that glycogen breakdown requires two enzymes. A phosphorylase cleaves the (α-1,4) bonds at the non-reducing ends, adding the elements of orthophosphate (PO_3^{2-} or P_i) to give glucose-1-phosphate. A 'debranching' enzyme cleaves the (α-1,6) glycosidic bonds. Be able to write down these reactions.
- Understand that free glucose is obtained by the enzymatic conversions: glucose-1-phosphate →glucose-6-phosphate →glucose. Know the structure of glucose-1-phosphate.
- Be able to recognize the structure of UDP-glucose. Understand that glycogen synthesis is initiated by glycogen synthase which adds UDP-glucose to the nonreducing end of a growing chain.
- Be able to reproduce the key converstions in the phosphatase/kinase cascade that regulates the degradation of glycogen and the synthesis of glycogen.
- Regarding cyclic AMP, know (i) its structure, (ii) its synthesis and the enzyme involves, and (iii) how its cellular levels are regulated.

Structure and function of glycogen

Main stores of glycogen are skeletal muscle and liver
Formation and breakdown of glycogen occurs in the cytosol

Muscle glycogen - fuel reserve for ATP synthesis during muscle contraction

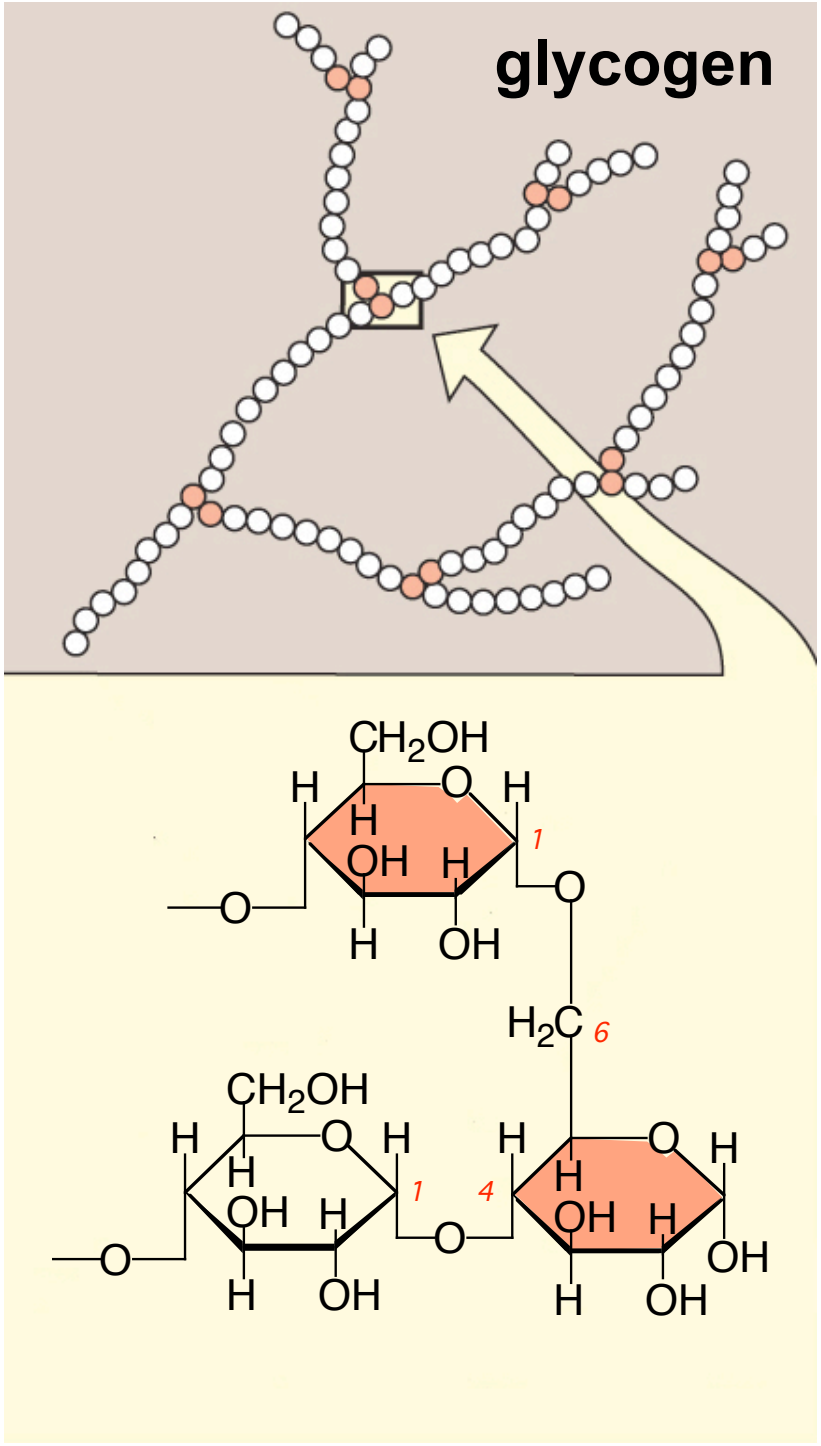
400 g glycogen ~ 1-2% fresh weight of resting muscle

Glycogen stores not affected by short periods of fasting and only decreased in prolonged fasting

Liver glycogen - maintain blood glucose concentration

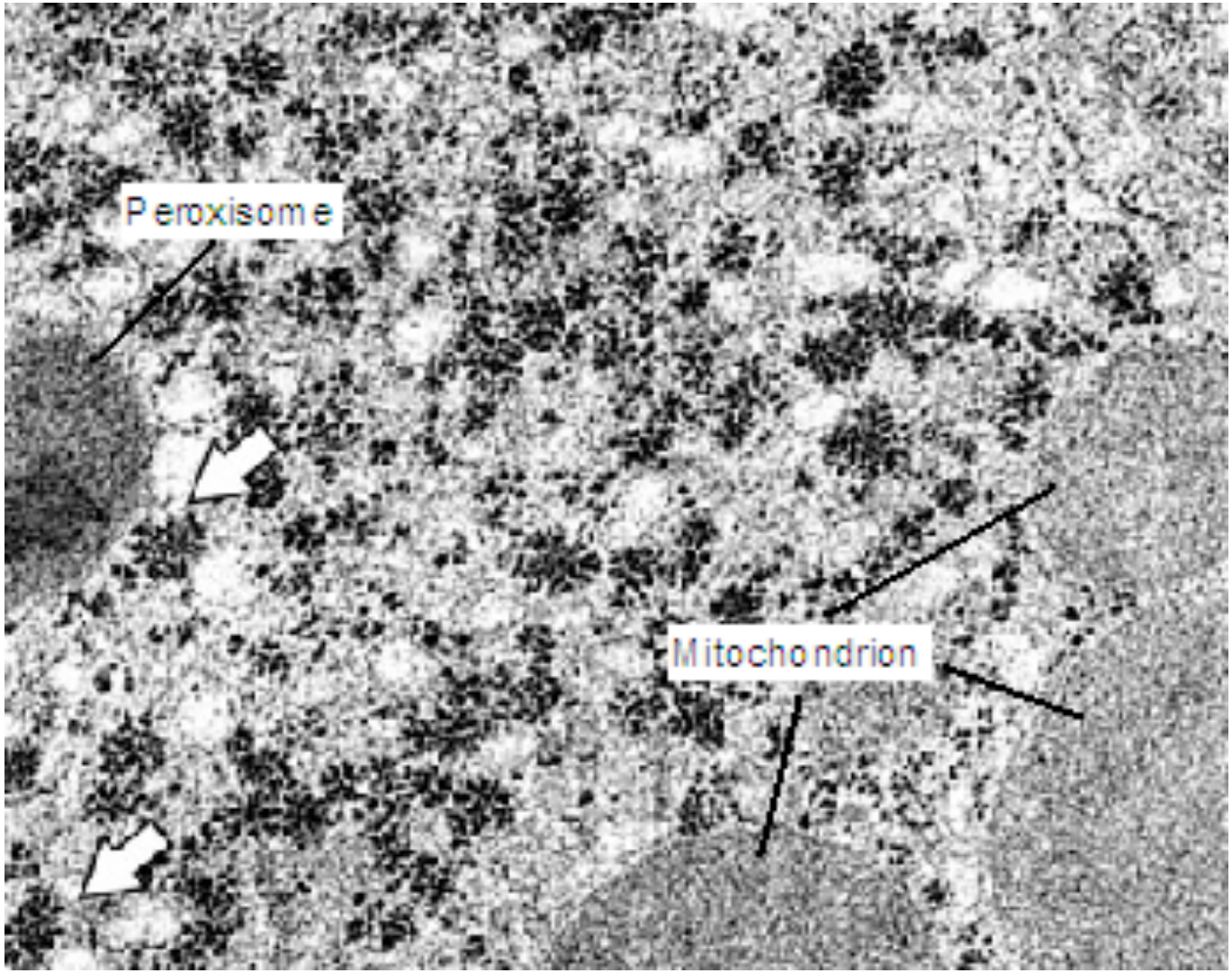
100 g glycogen ~ 10% adult liver

Glycogen stores increase during the well-fed state and are depleted during a fast



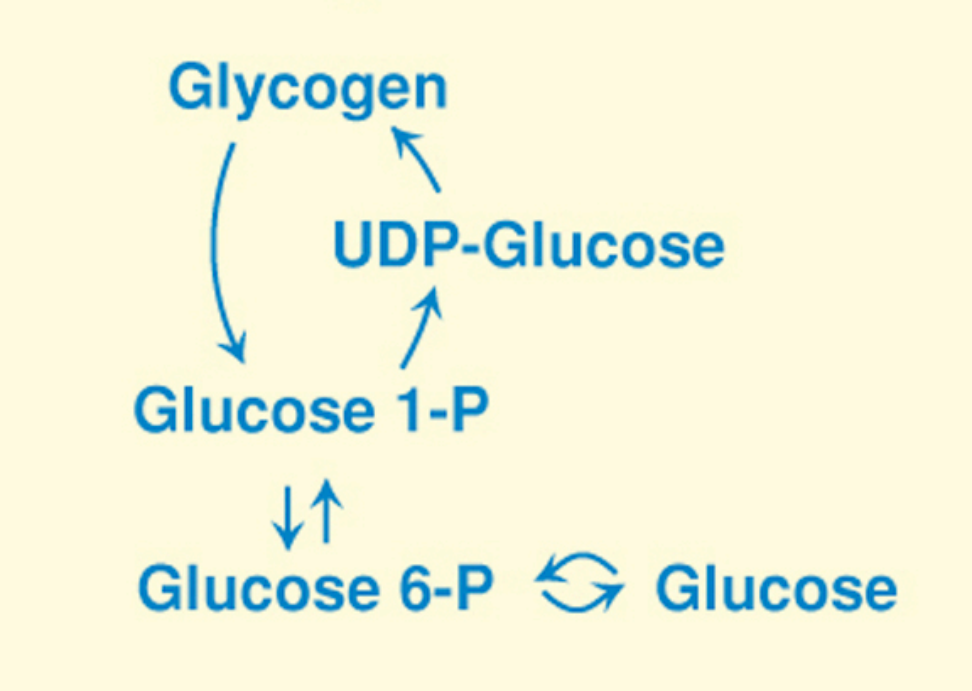
Polysaccharides: glycogen

Chemical bonds at the branch points are different from those in the linear polysaccharide.



Electron micrograph of a section of a liver cell showing glycogen deposits as accumulations of electron dense particles (arrows).

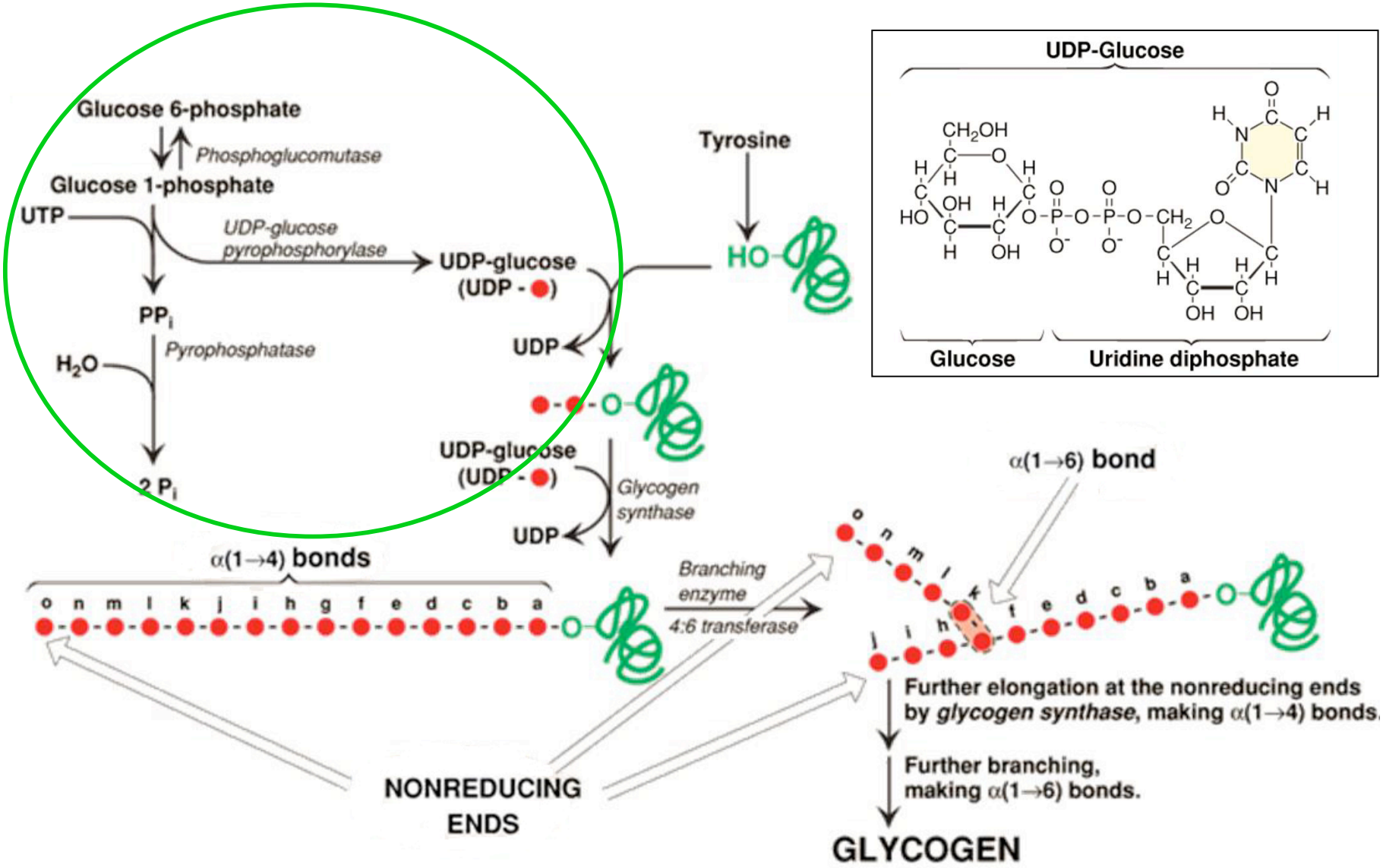
Metabolic pathways involving glycogen



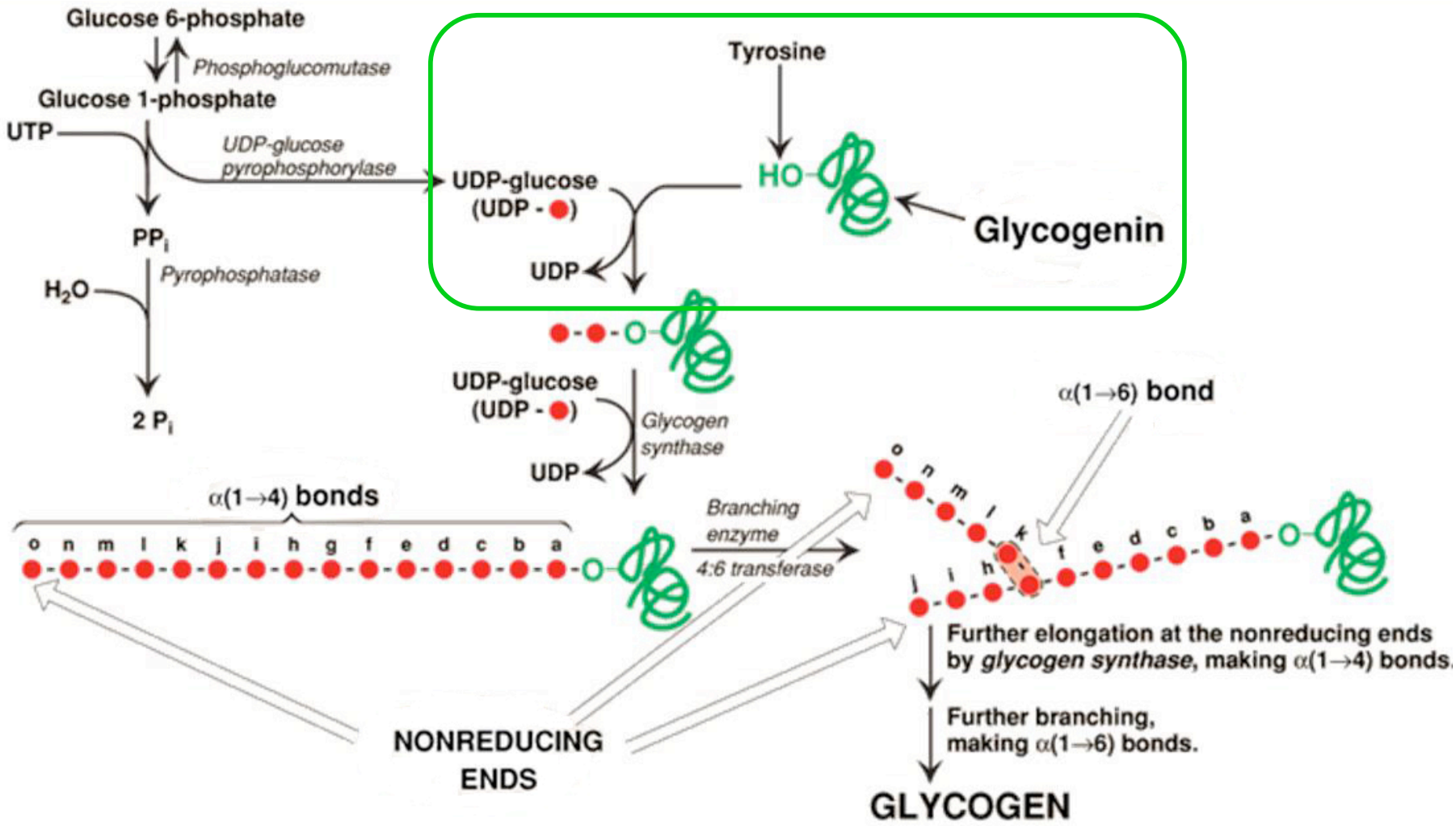
Glycogen formation = ***glycogenesis***

Glycogen breakdown = ***glycogenolysis***

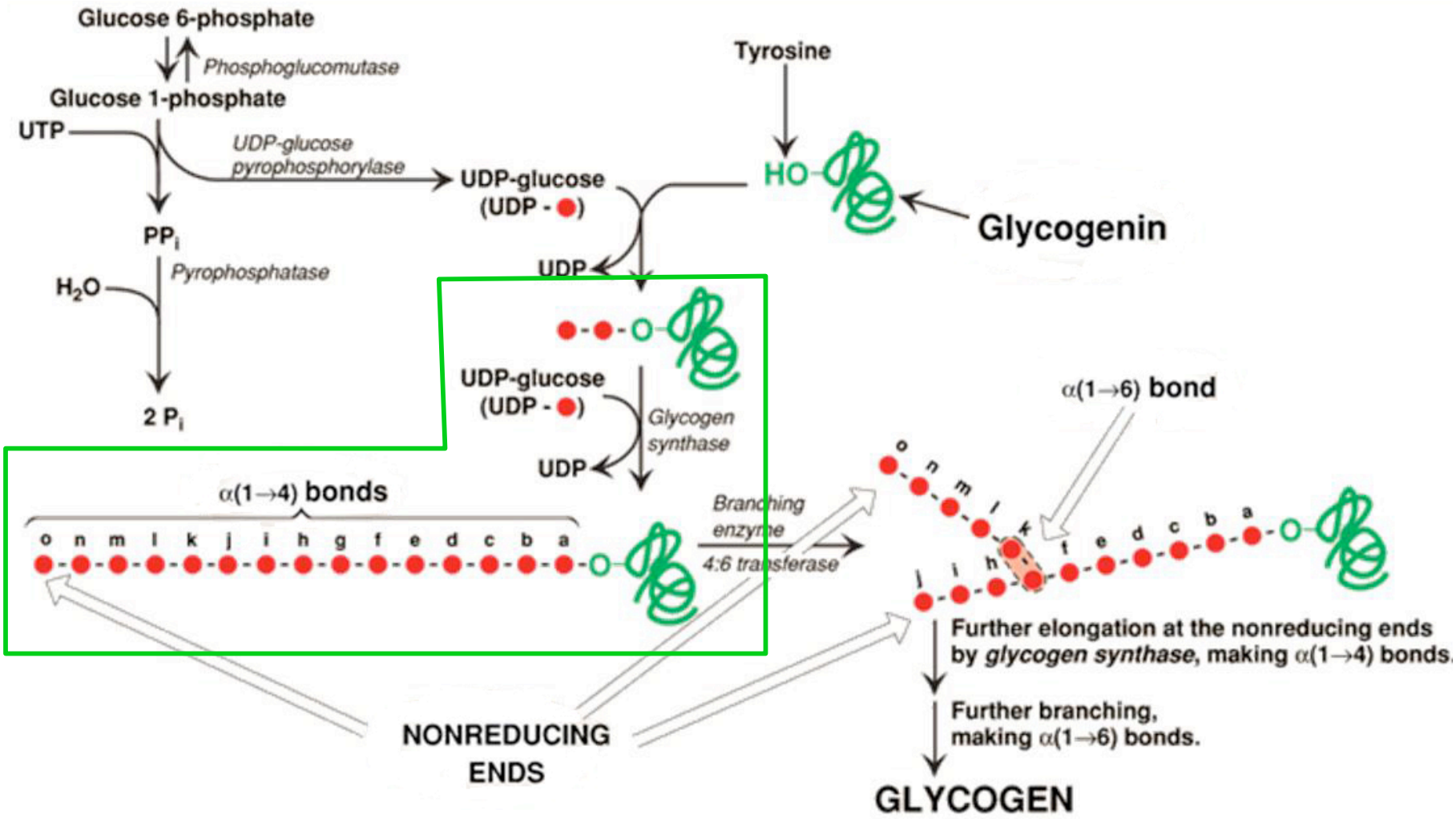
Glycogenesis: synthesis of UDP-glucose



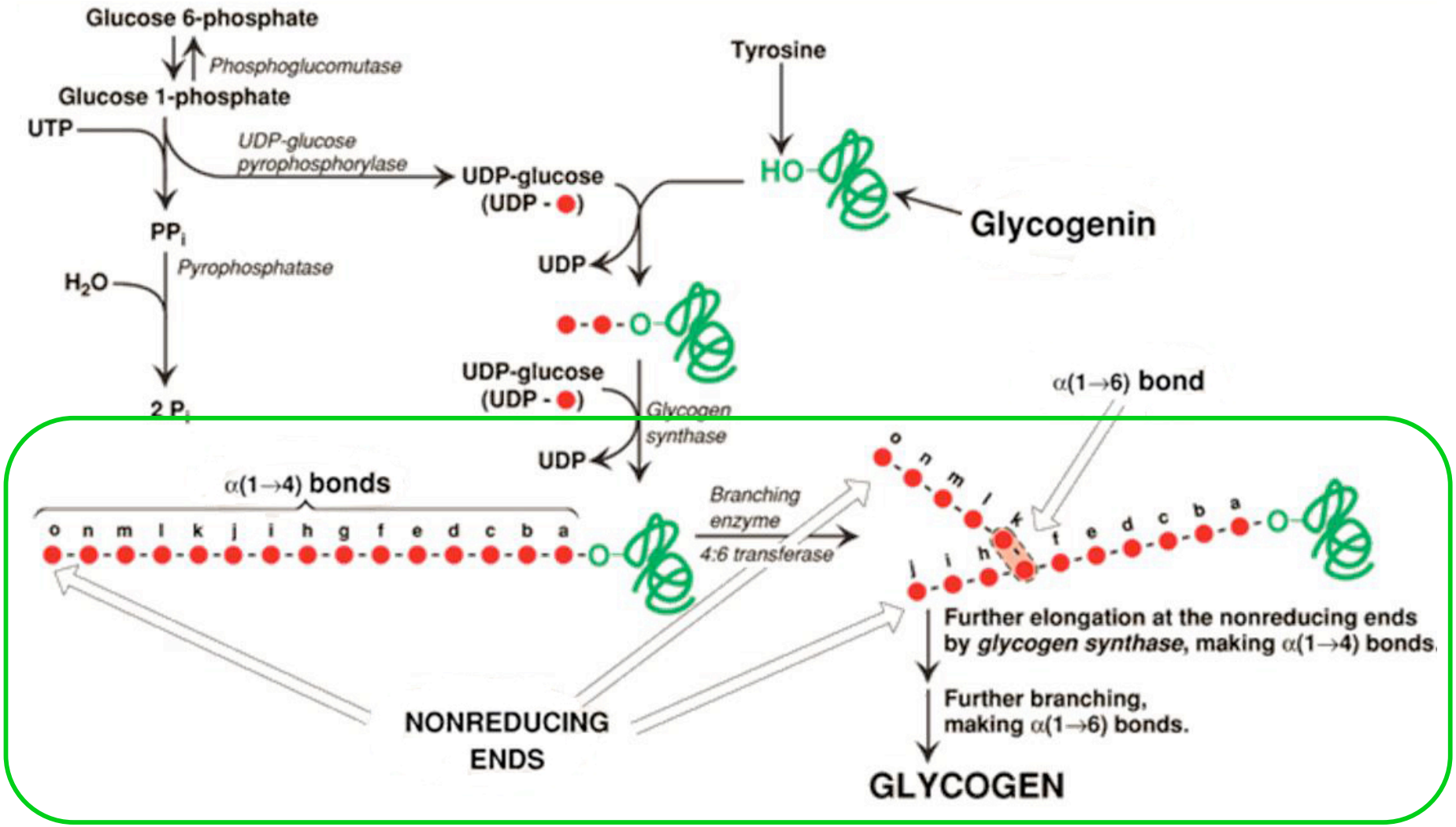
Glycogenesis: synthesis of primer



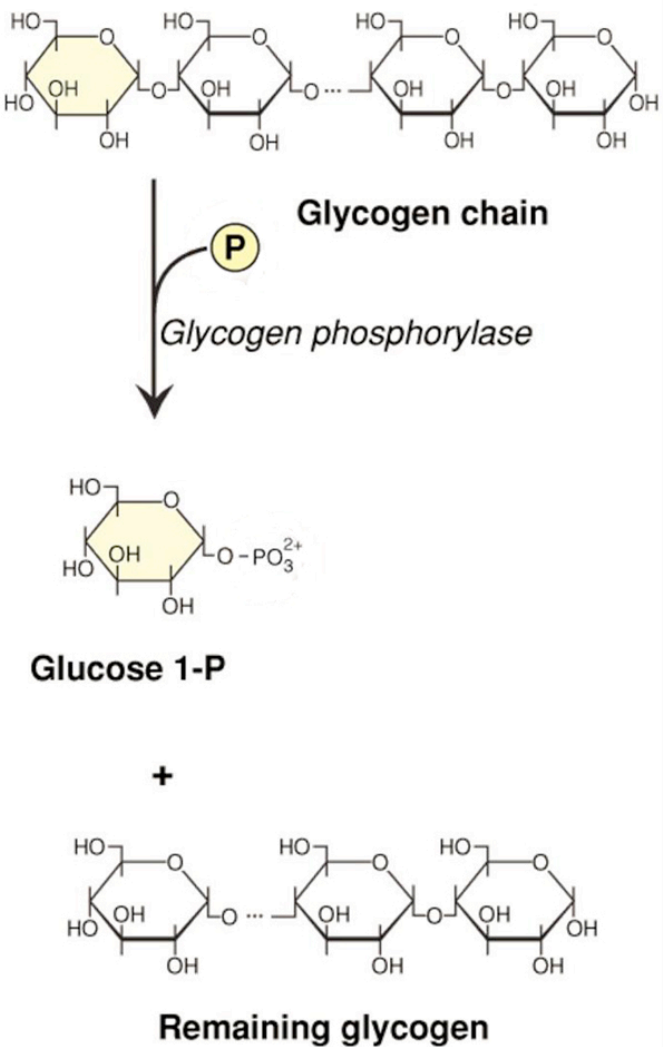
Glycogenesis: elongation

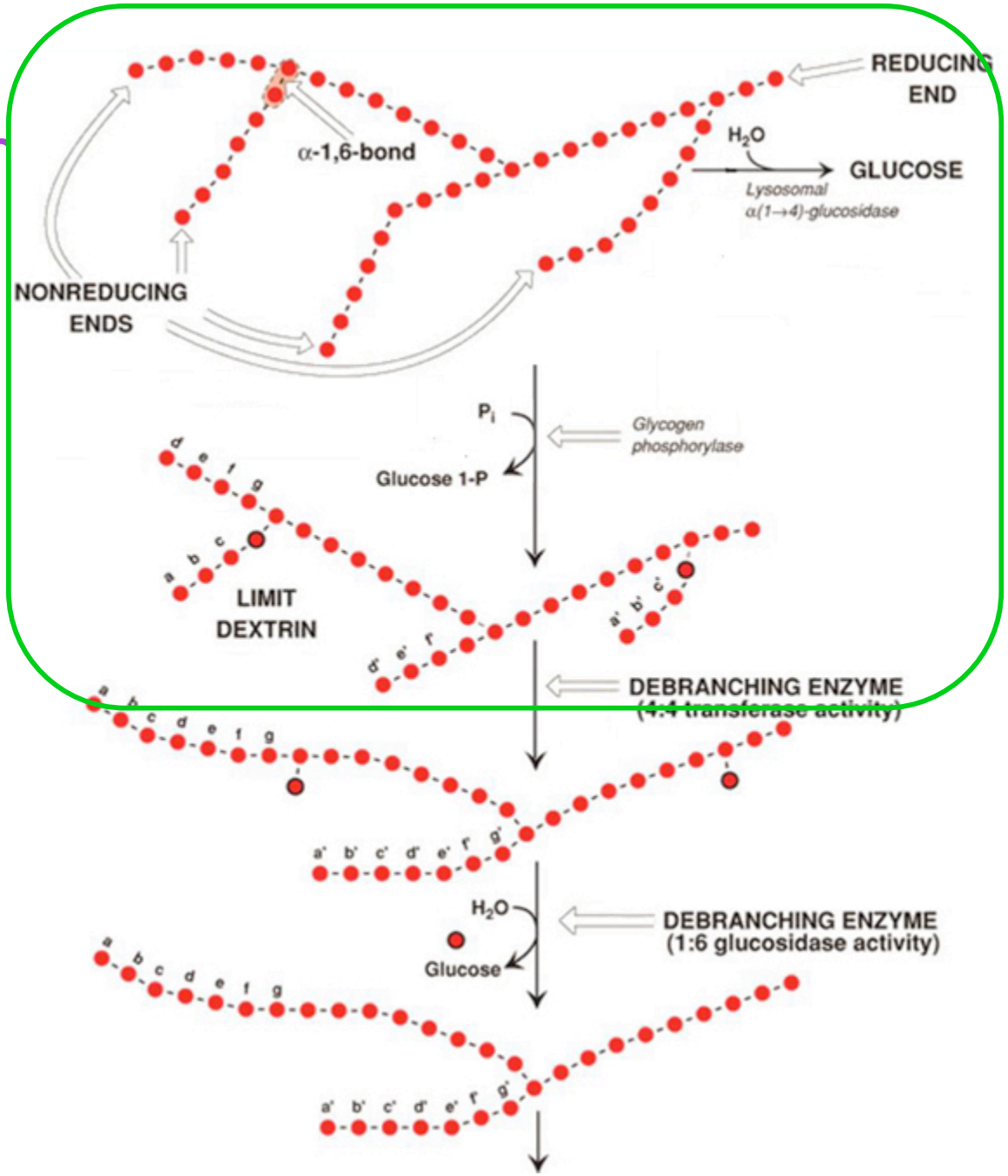


Glycogenesis: branch formation

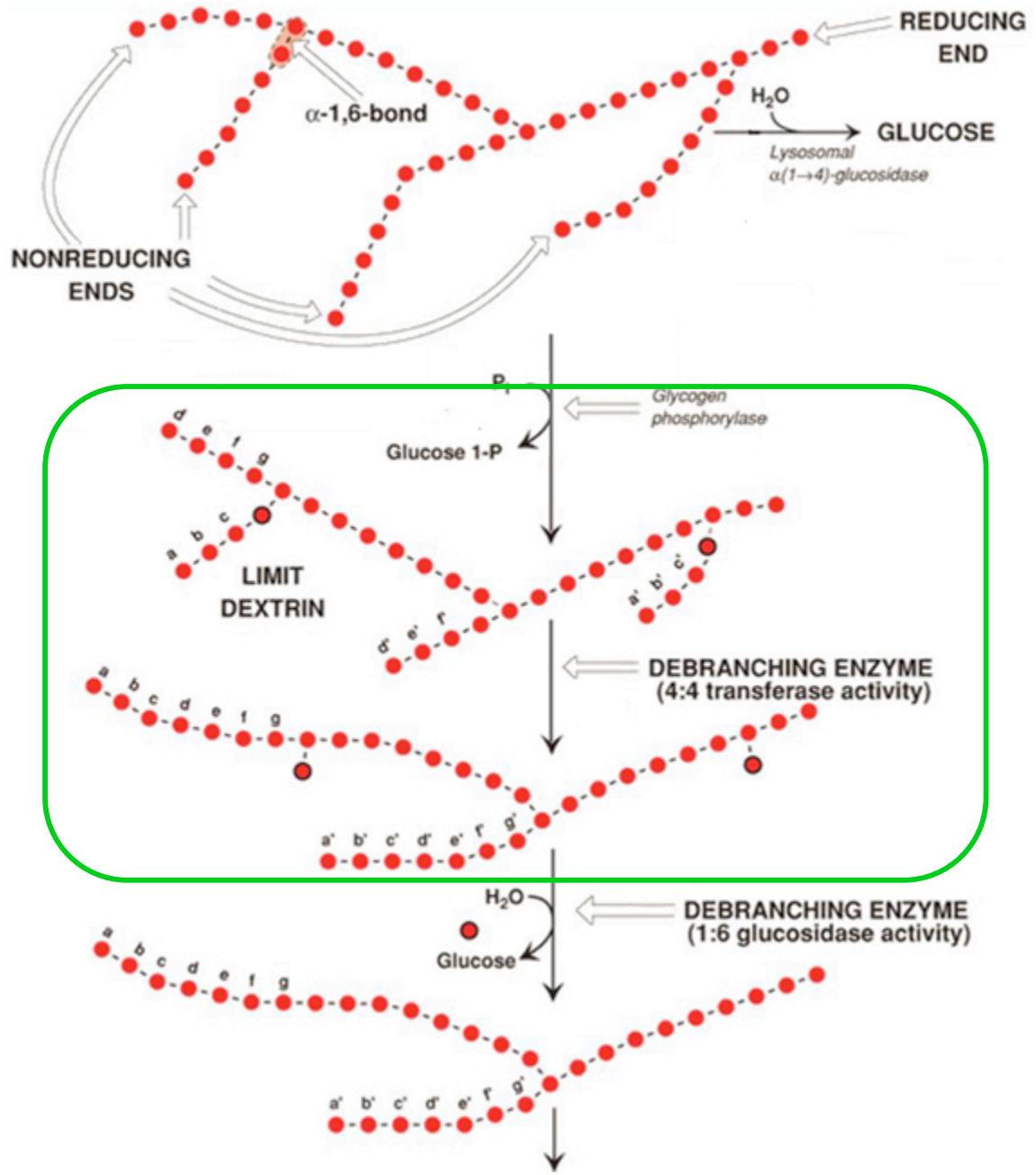


Glycogenolysis: shortening of chain

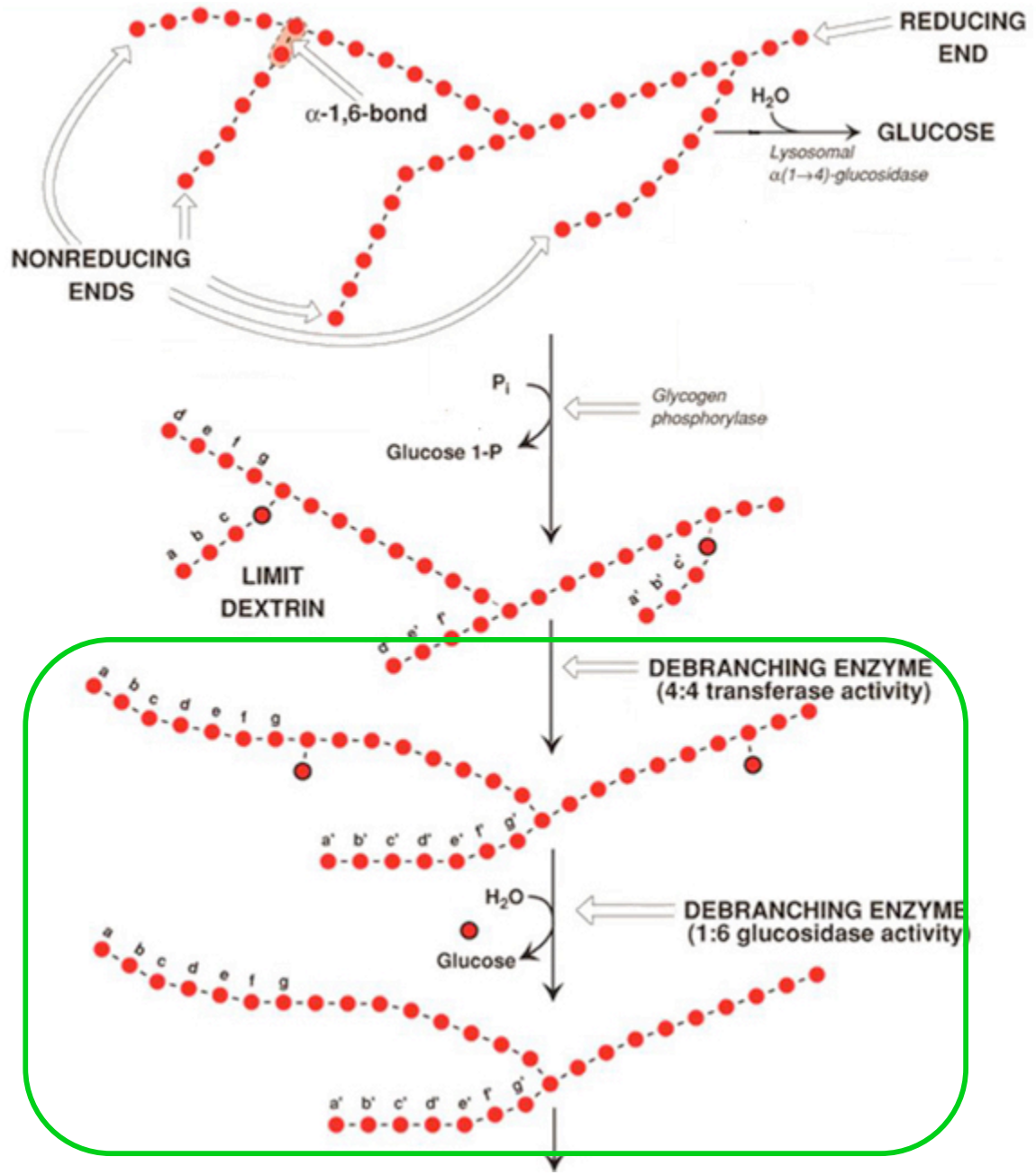




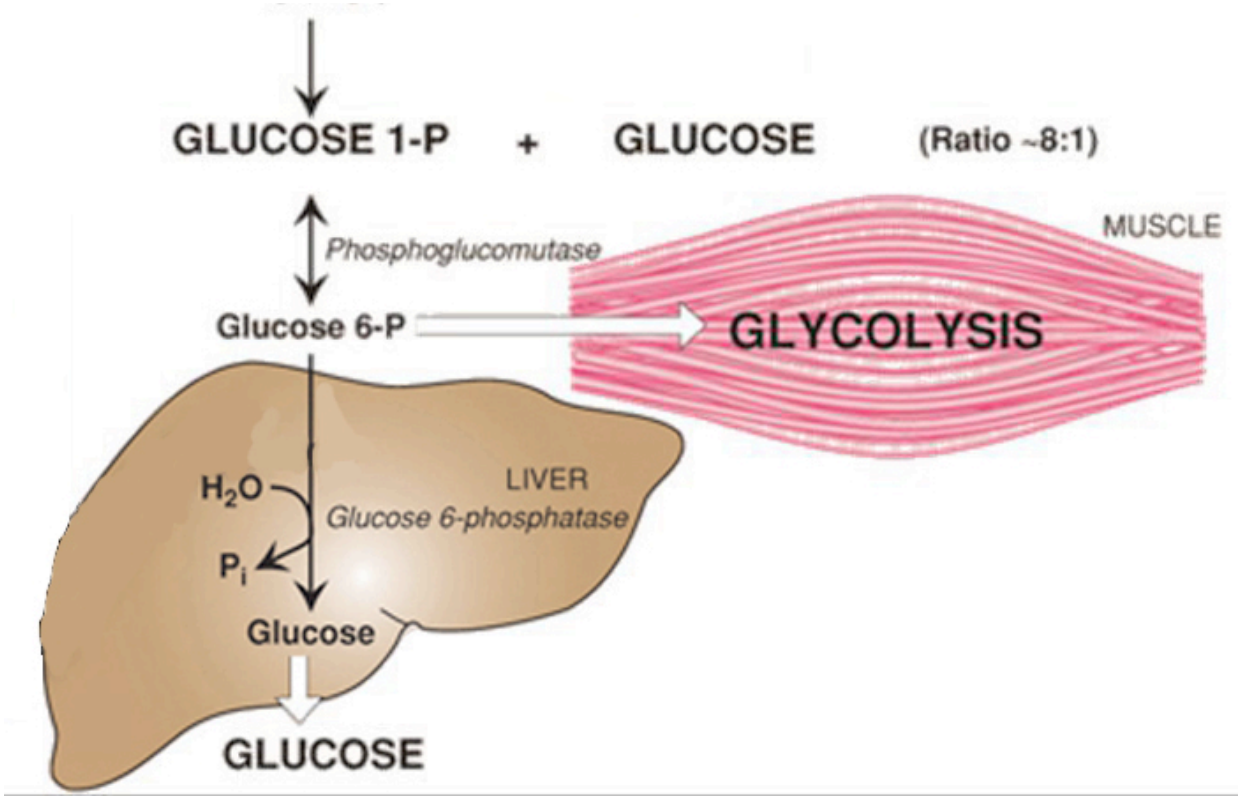
Glycogenolysis: branch removal

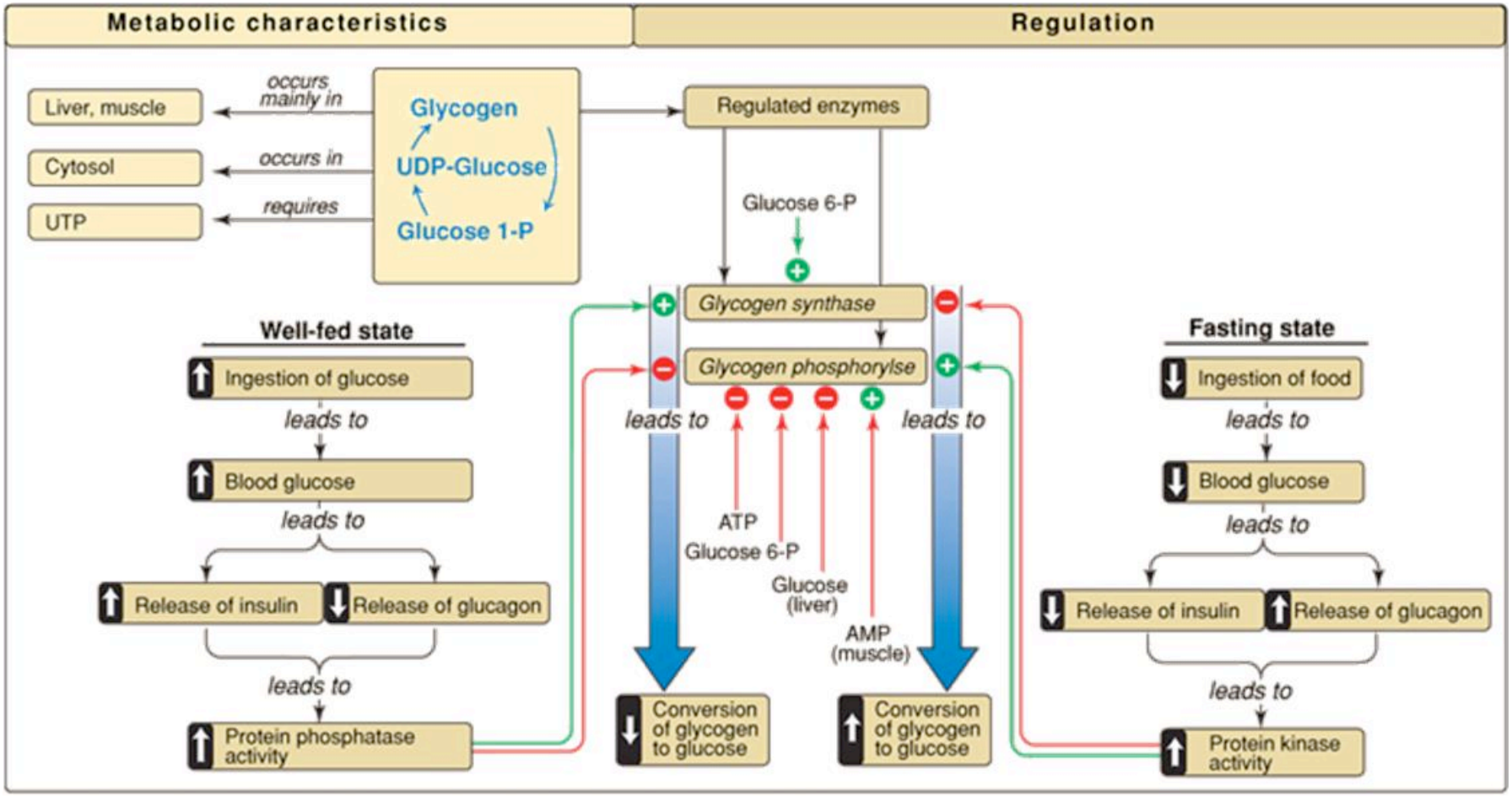


Glycogenolysis: branch removal

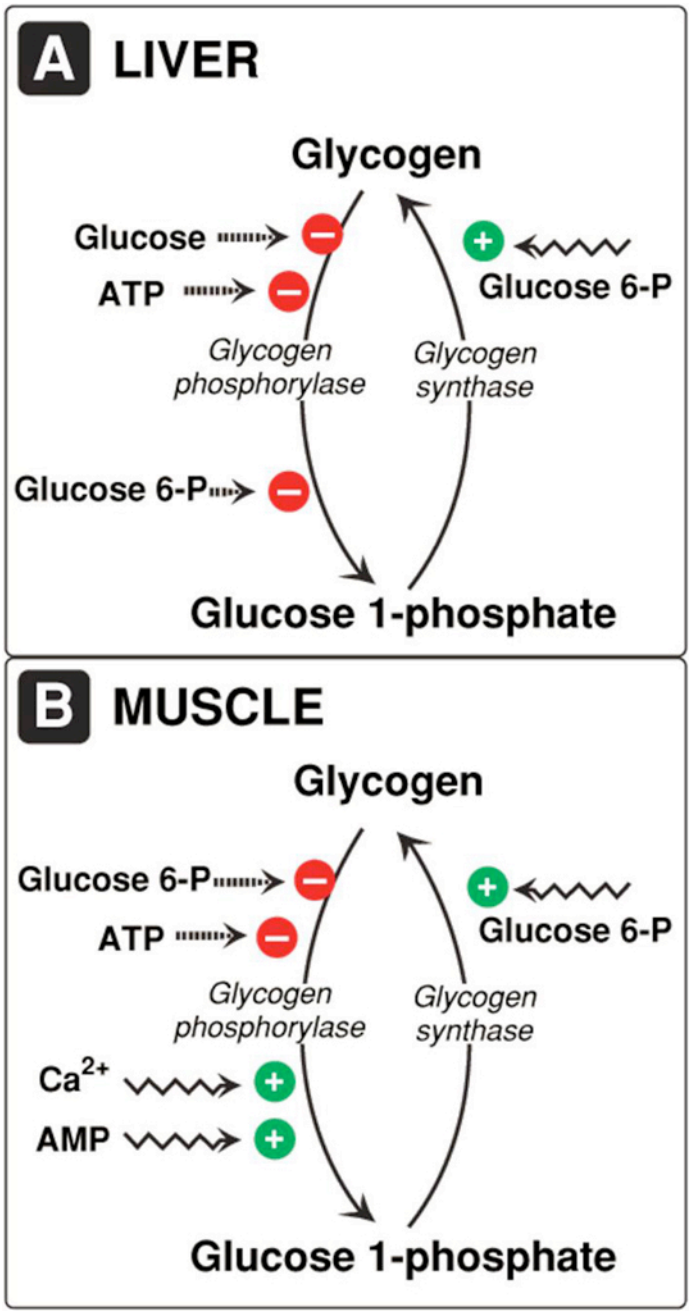


Glycogenolysis: conversion of glucose 1-phosphate to glucose 6-phosphate

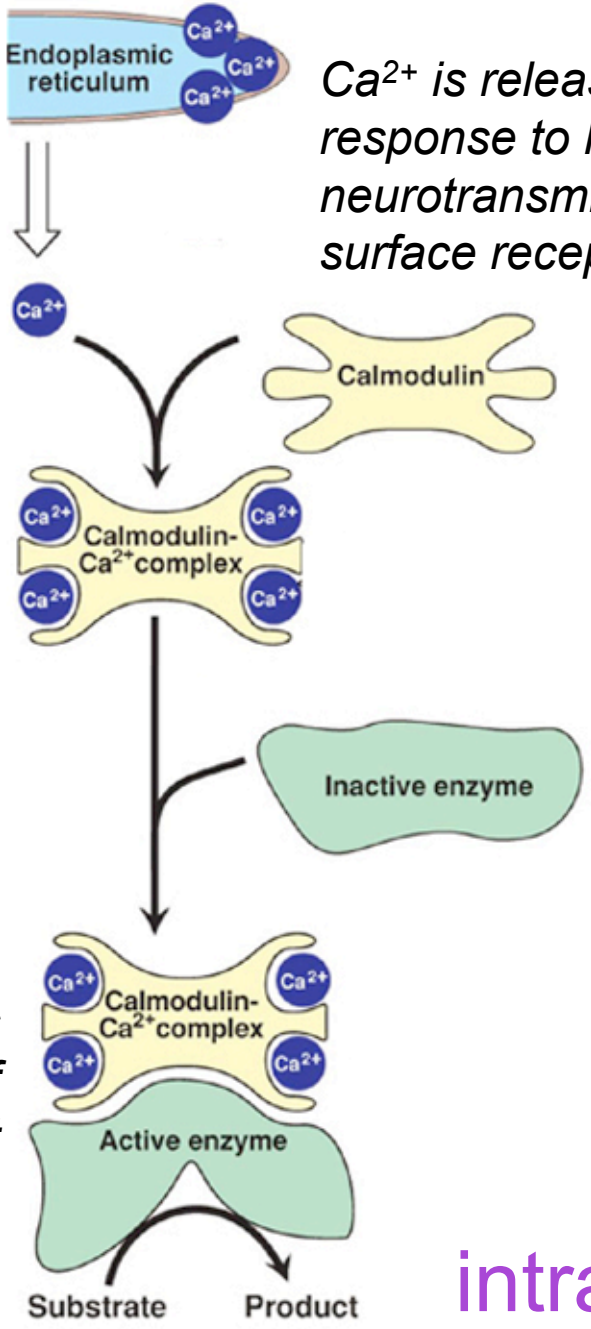



Metabolic characteristics
Regulation
Liver, muscle
occurs mainly in
Cytosol
occurs in
UTP
requires
Glycogen
UDP-Glucose
Glucose 1-P
Regulated enzymes
Glucose 6-P
Glycogen synthase
Glycogen phosphorylse
leads to
leads to
Well-fed state
Ingestion of glucose
leads to
Blood glucose
leads to
Release of insulin
Release of glucagon
leads to
Protein phosphatase activity
ATP
Glucose 6-P
Glucose (liver)
AMP (muscle)
Conversion of glycogen to glucose
Conversion of glycogen to glucose
Fasting state
Ingestion of food
leads to
Blood glucose
leads to
Release of insulin
Release of glucagon
leads to
Protein kinase activity

Allosteric regulation of glycogen synthesis and degradation



Calmodulin mediation of intracellular calcium

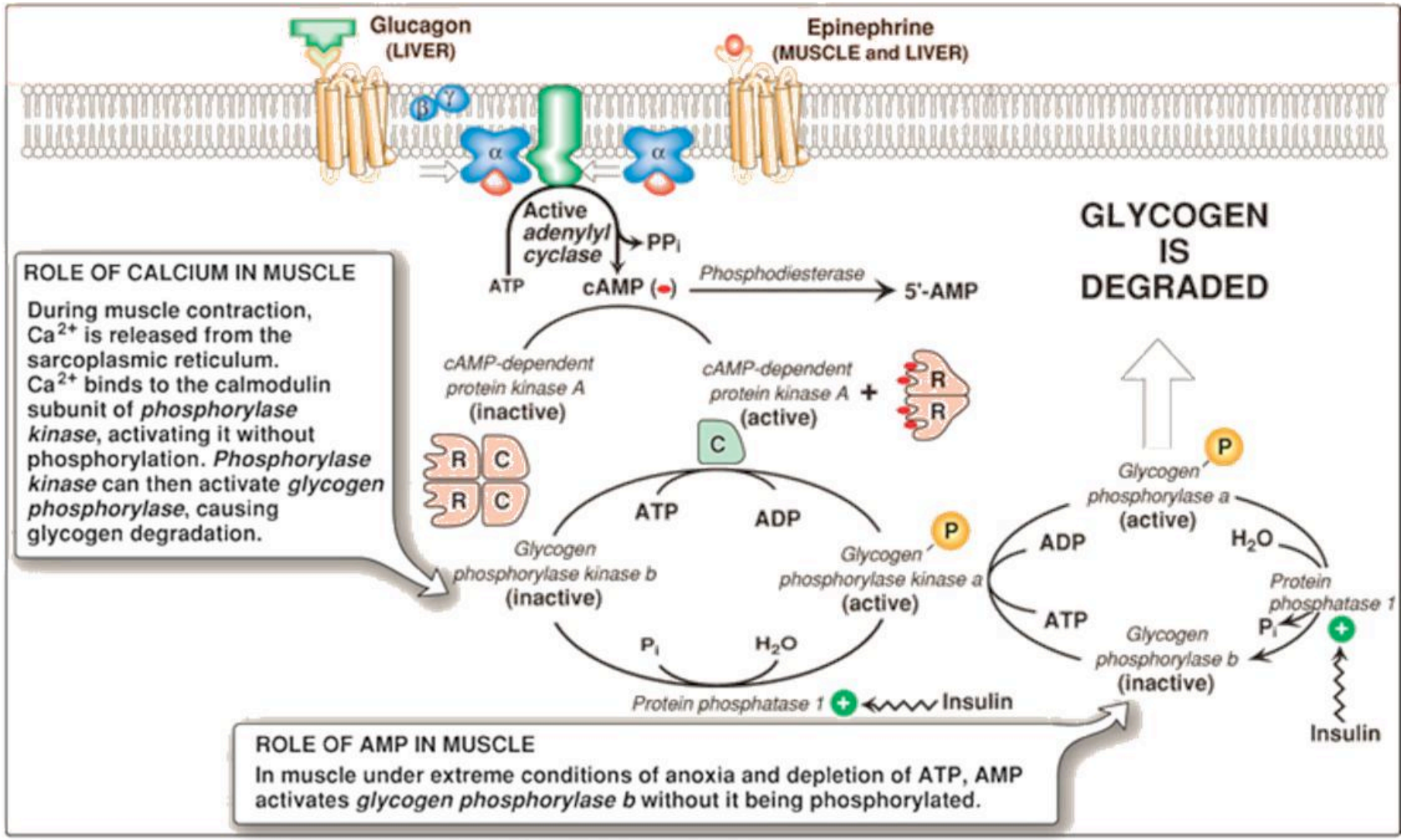


Ca^{2+} is released from the ER in response to hormones or neurotransmitters binding to cell surface receptors

Transient increase in the intracellular [Ca^{2+}] favors formation of the calmodulin-Ca^{2+} complex

Calmodulin-Ca^{2+} complex is an essential component of many Ca^{2+}-dependent enzymes.

Stimulation & inhibition of glycogenolysis



Hormonal regulation of glycogen synthesis