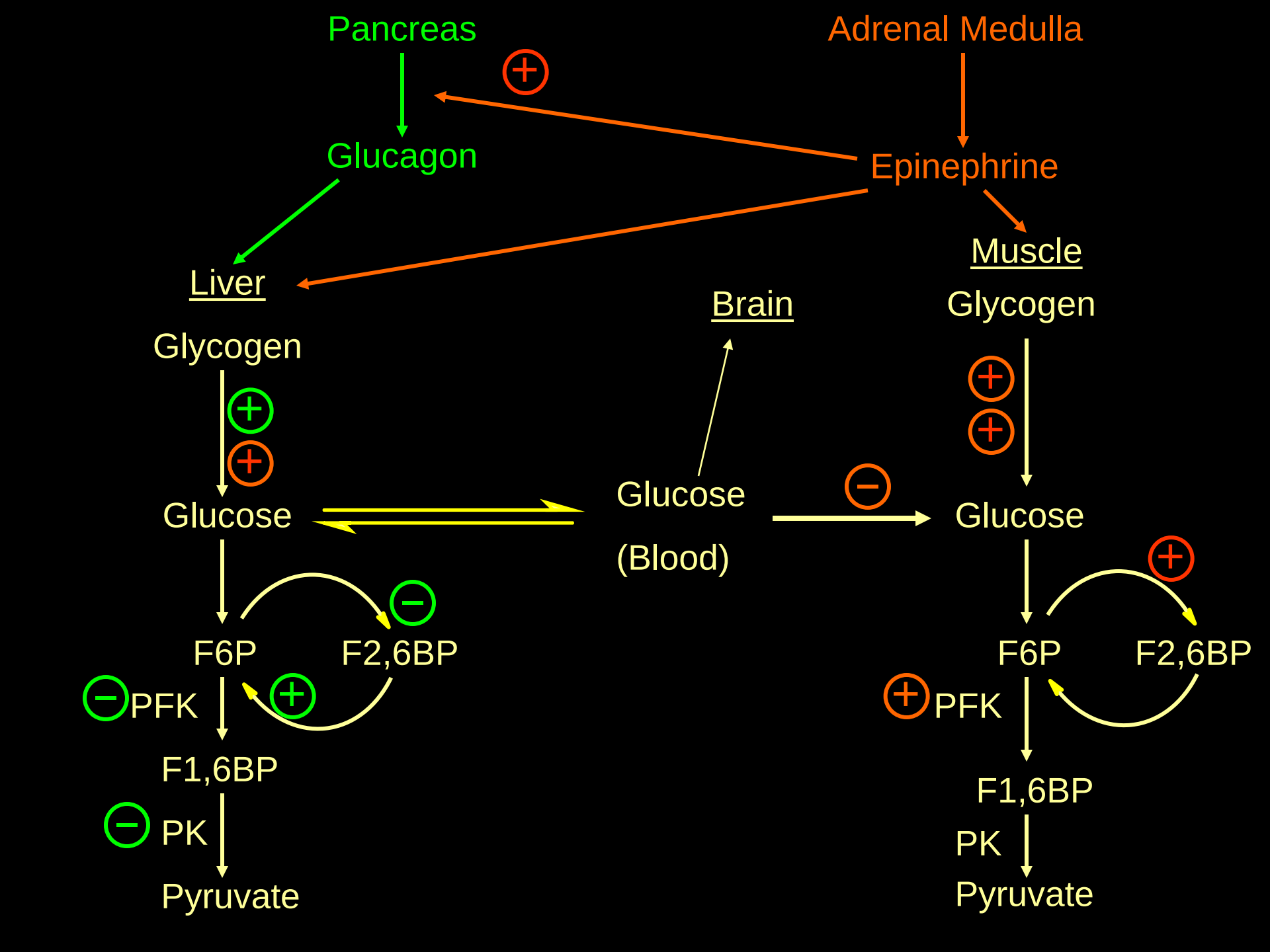
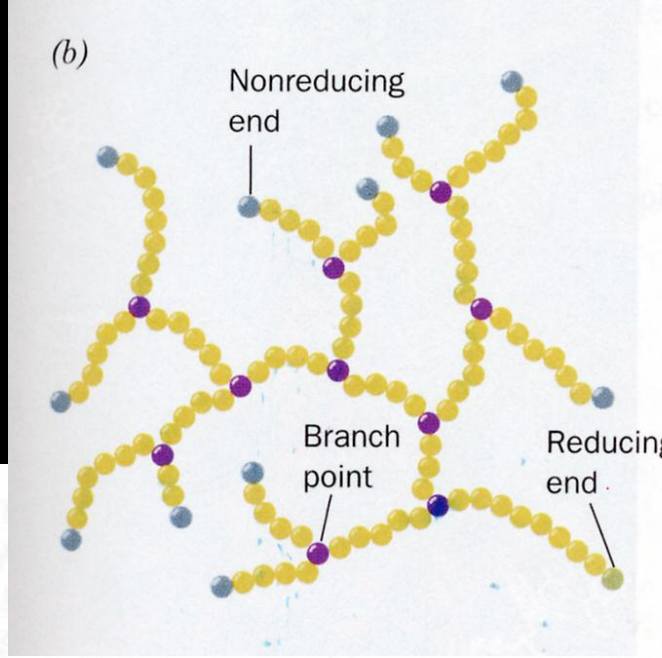
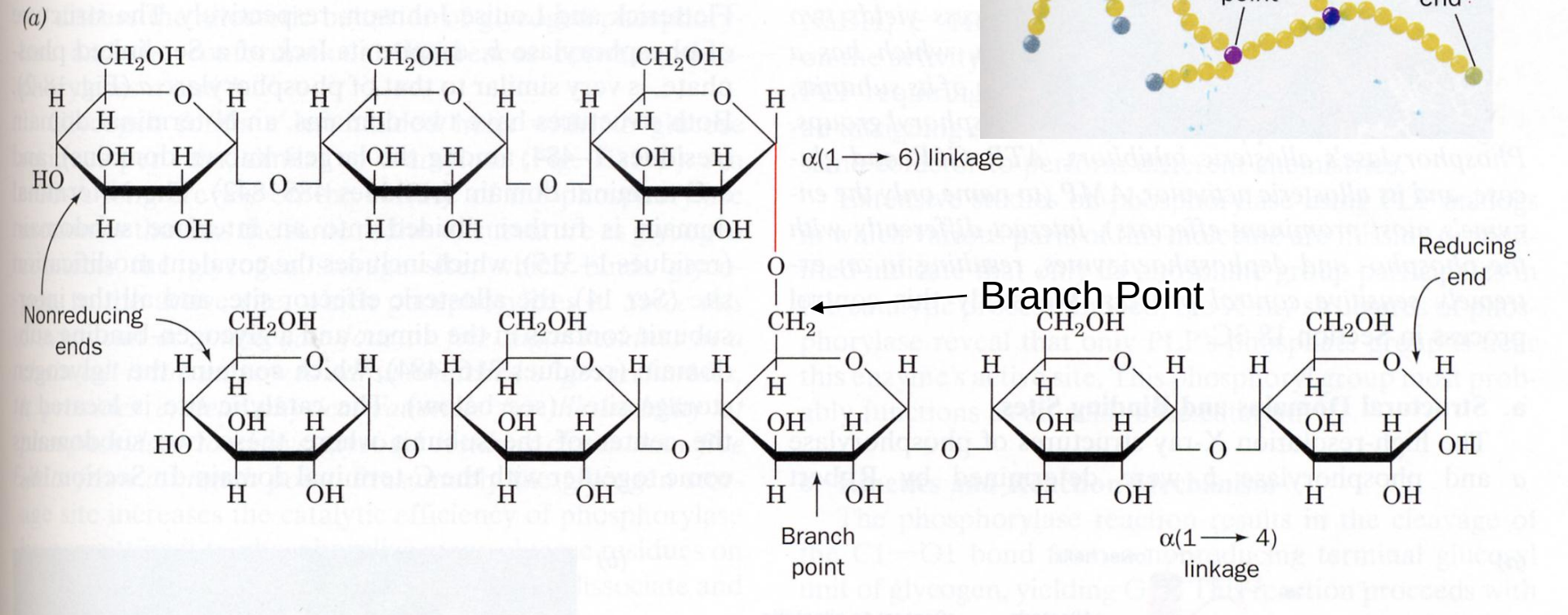

Pancreas
Adrenal Medulla
Glucagon
Epinephrine
Liver
Muscle
Brain
Glycogen
Glycogen
Glucose
Glucose
(Blood)
Glucose
F6P
F2,6BP
PFK
F1,6BP
PK
Pyruvate
F6P
F2,6BP
PFK
F1,6BP
PK
Pyruvate

Glycogen

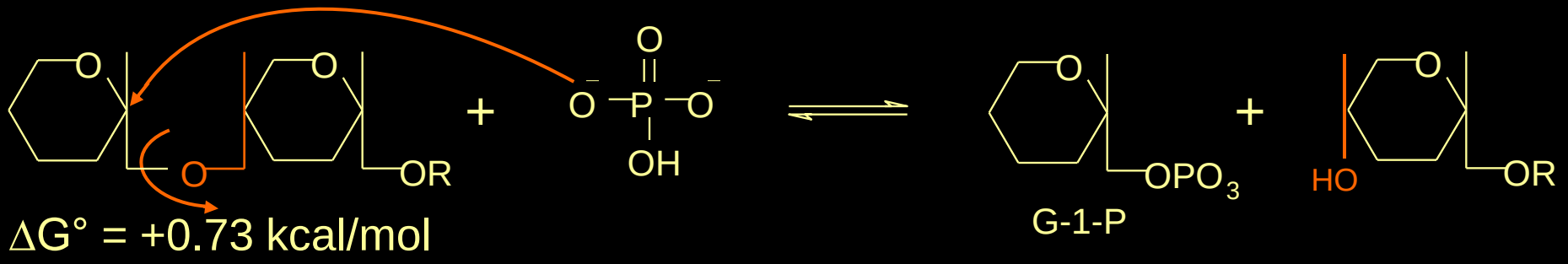




Branch points occur at ~ 1:10 glycosyl residues

Glycogen Breakdown

- α1-4 linkages are broken by phosphorylase, starting from the non- reducing ends. Breakdown is phosphorylytic.
- Product is G-1-P and glycogen$_{n-1}$

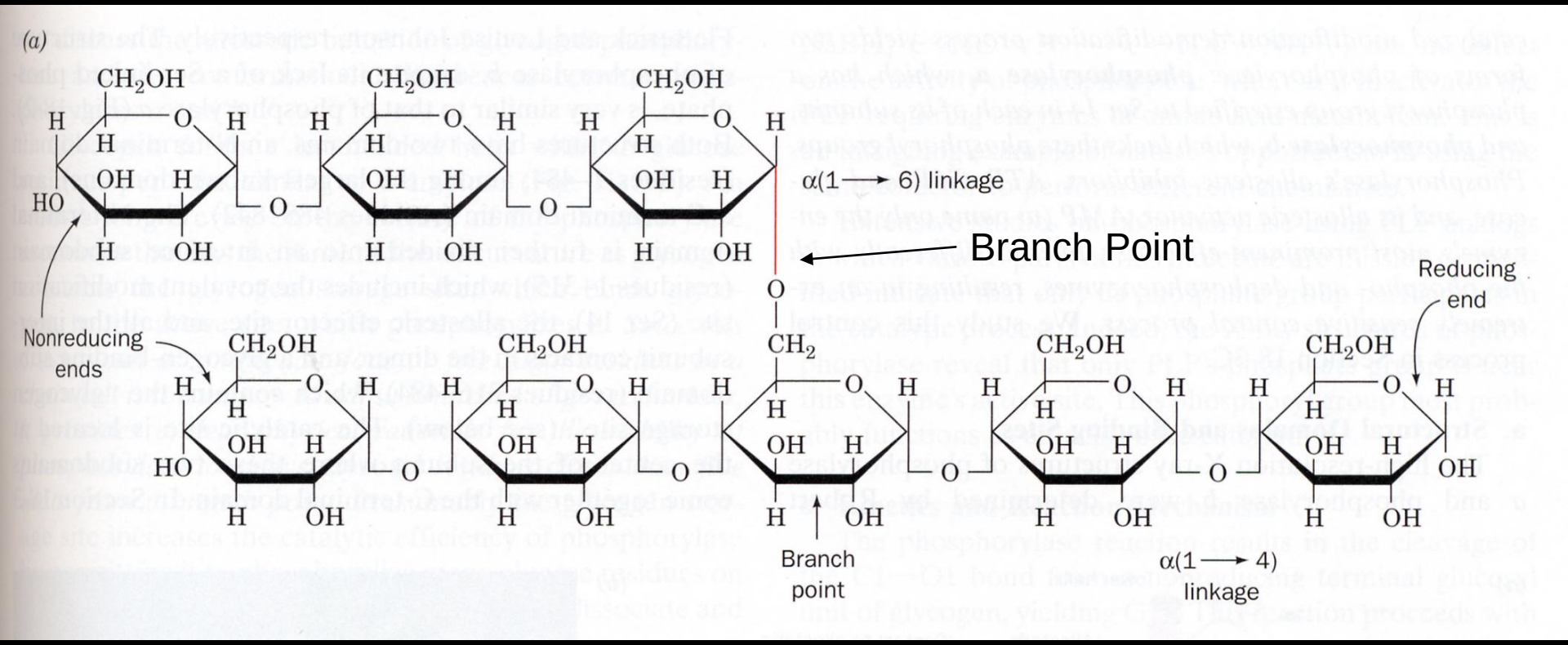


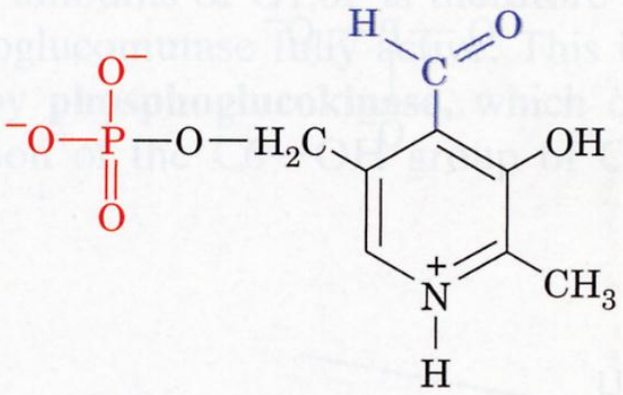
ΔG° = +0.73 kcal/mol

- α1-6 debranching is HYDROLYTIC, as opposed to phosphorylytic.
- Carried out by an α1-6 glucosidase

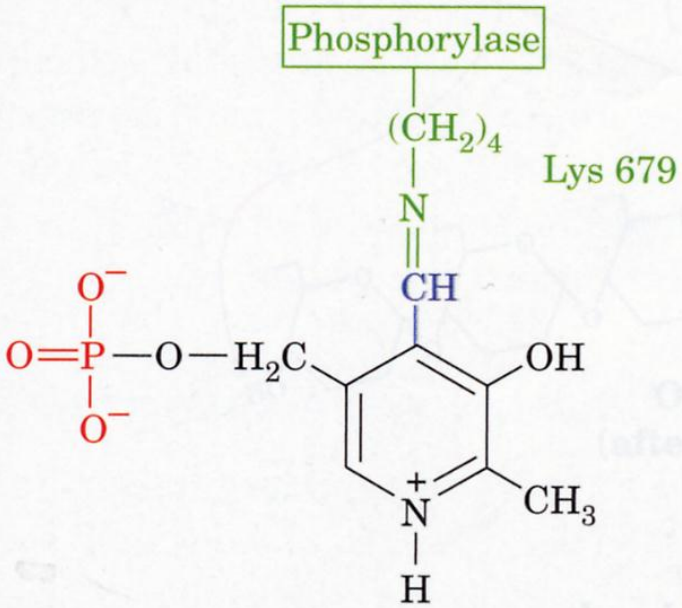
α1-4: phosphorylysis gives G1P → G6P

α1-6: hydrolysis gives glucose $\xrightarrow{ATP}$ G6P





Pyridoxal phosphate (PLP)



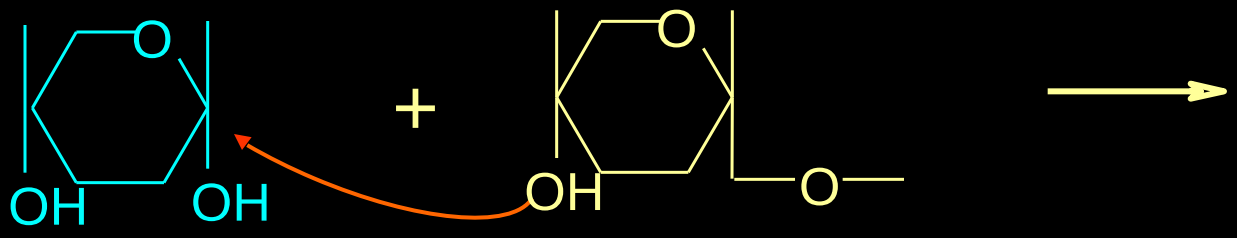
PLP covalently bound to phosphorylase via a Schiff base to Lys 679

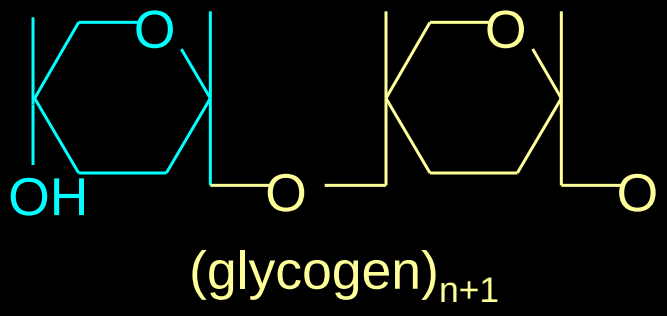
Glycogen Phosphorylase requires pyridoxal phosphate (vit. B6) as an active site cofactor.

The phosphate group probably acts as an acid-base catalyst.

This is not the same phosphate molecule that is incorporated into glucose

Glycogen Synthesis

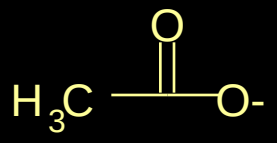


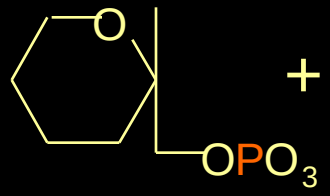


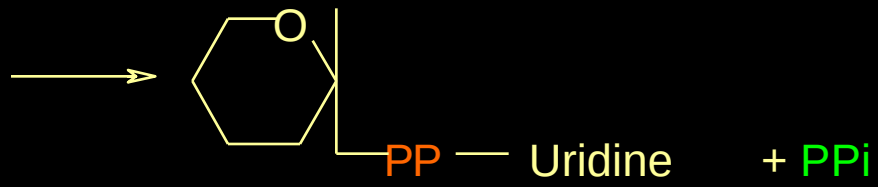
Activation of Glucose-1-P

Examples of “activated molecules” :

1. PO_4 + ADP + energy → ATP (activated PO_4)

2.  + HS—CoA + Energy → Acetyl-CoA (Activated Acetyl)

3.  + PPP—Uridine + Energy



UDP-glucose

(Activated Glucose)

UDP-glucose
pyrophosphorylase

G1P + UTP ⇌ UDP-Glucose + PP_i

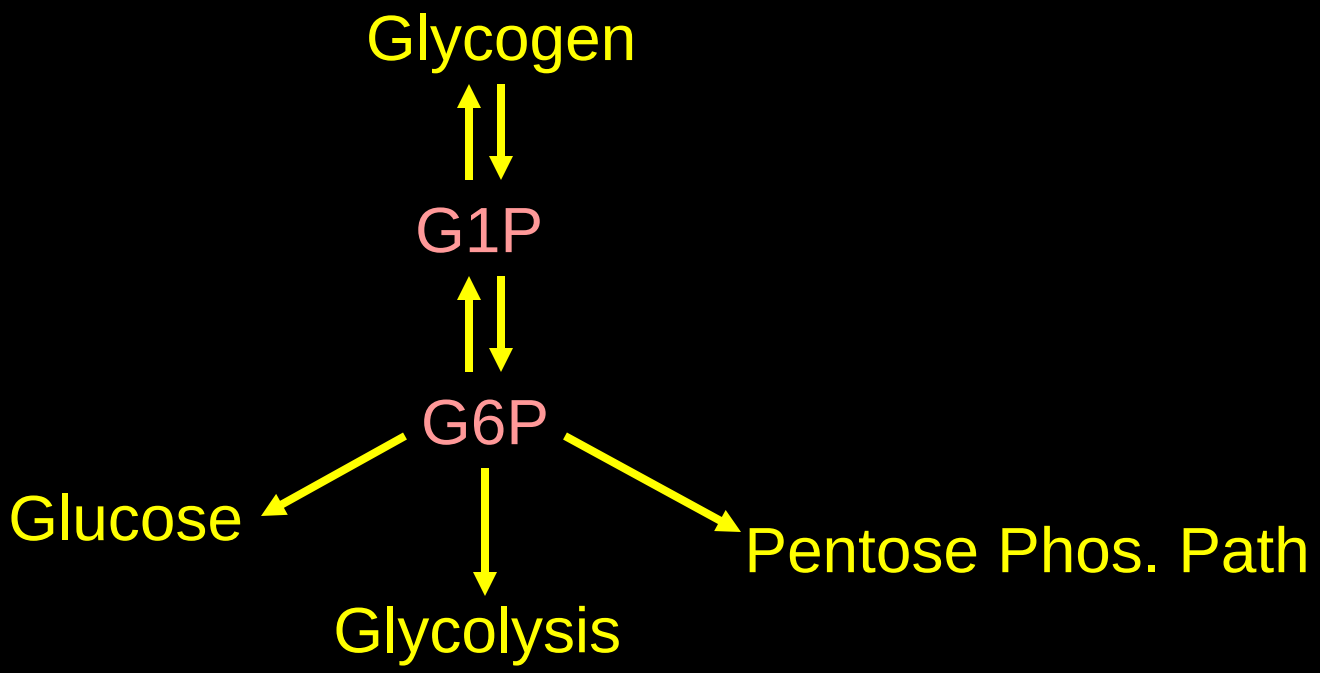
$\Delta G° = -8$ kcal/mol

↓

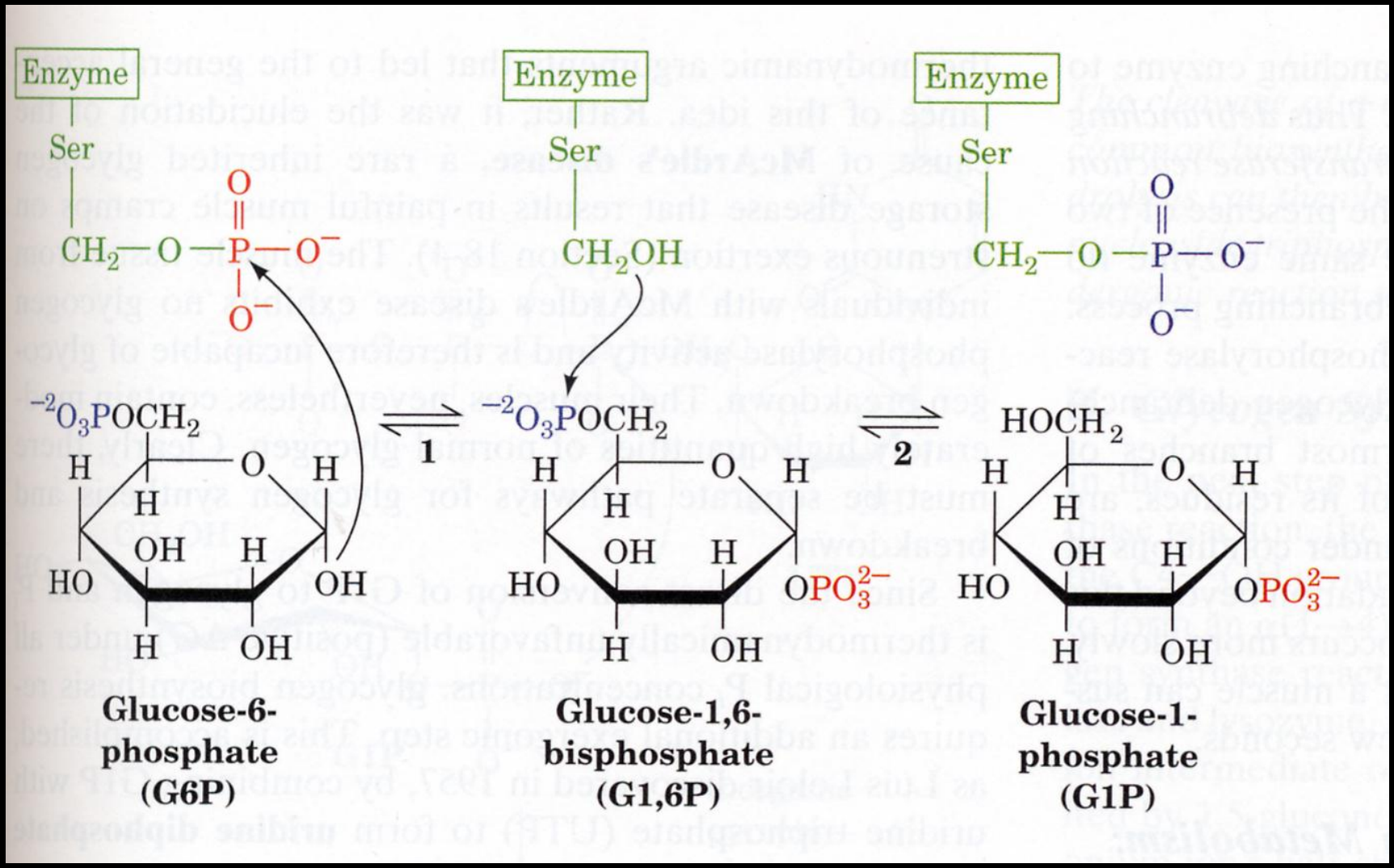
$P_i + P_i$

Glycogen Synthase

Where does G1P come from?



Isomerization of G6P to G1P



Details on Glycogen Breakdown/Synthesis

1. Glucose-1-P + $Glyc_n$ → $Glyc_{n+1}$
   - requires 1 ATP (UDP + ATP → UTP + ADP)

2. $Glyc_n$ → $Glyc_{n-1}$ + Glucose-1-P
   - 90% no energy cost
   - 10% 1 ATP per Glucose

Efficiency of storing G6P as glycogen

G6P → UDP-glucose → glycogen 1 ATP

glycogen → G6P 0.1 ATP

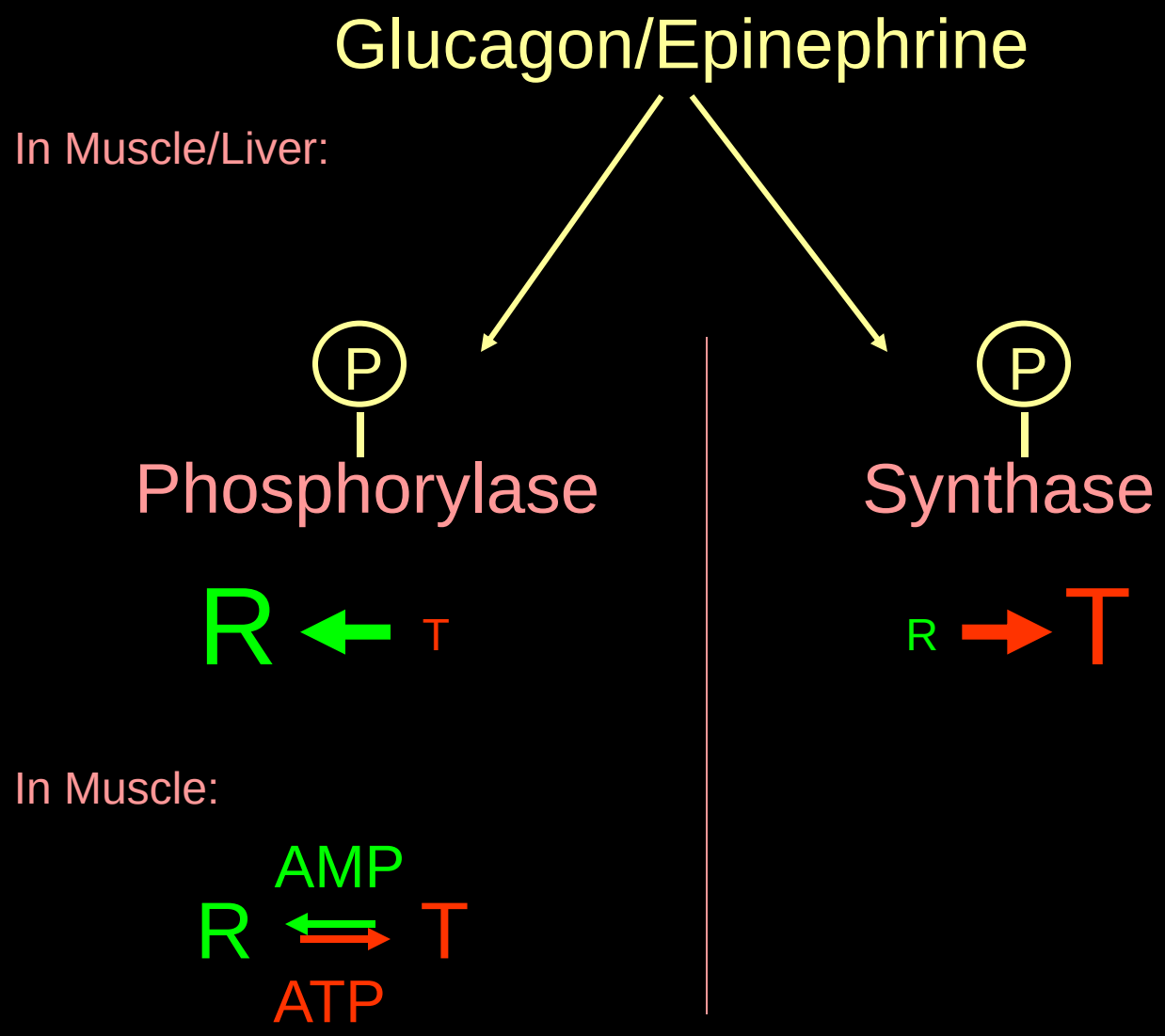
1.1 ATP

G6P → $CO_2 + H_2O$ 31 ATP

96%

Enzyme Regulation – Levels of Complexity

- Michaelis-Menten
- Cooperative (T vs R)
    - regulated by substrate conc’n
    - regulated by allosteric ligands
    - regulated by phosphorylation


Glucagon/Epinephrine
In Muscle/Liver:
P
Phosphorylase
P
Synthase
R
T
R
T
In Muscle:
AMP
R
T
ATP

Control by Phosphorylation

- Brought about by glucagon (liver) or epinephrine (liver & muscle).
- extracellular “sensor” of environmental conditions
    - In muscle : GP is activated for “fight or flight”
    - In liver: GP is activated in response to fasting

Allosteric Control

- In muscle: “intracellular sensor” of energy charge.