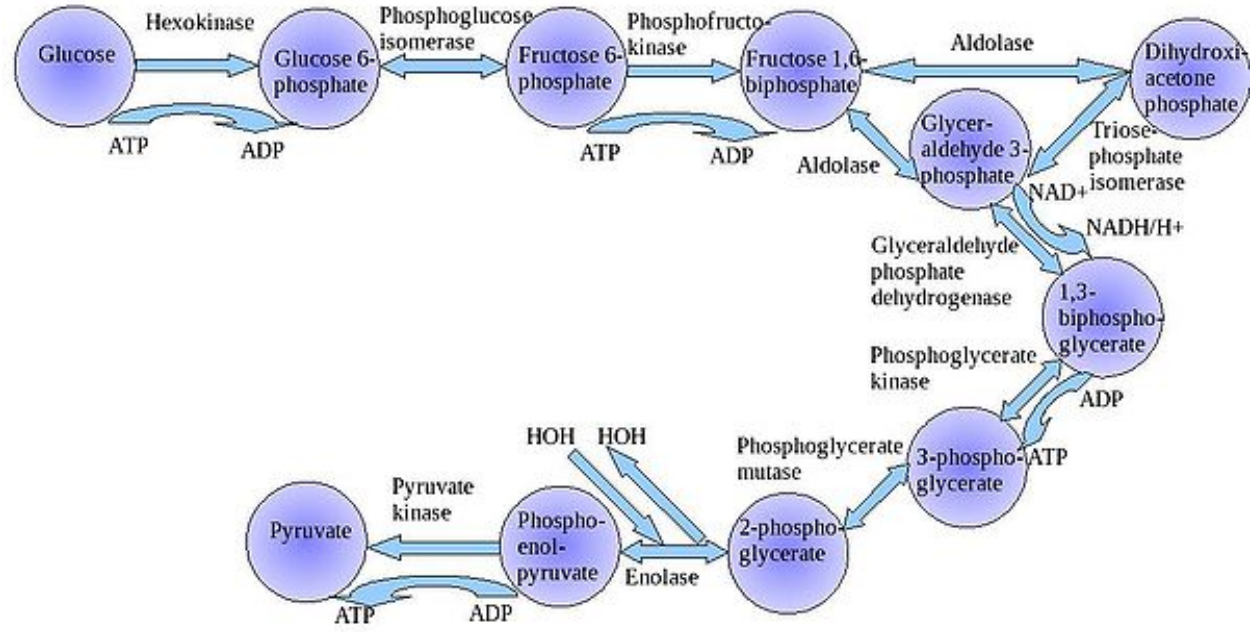
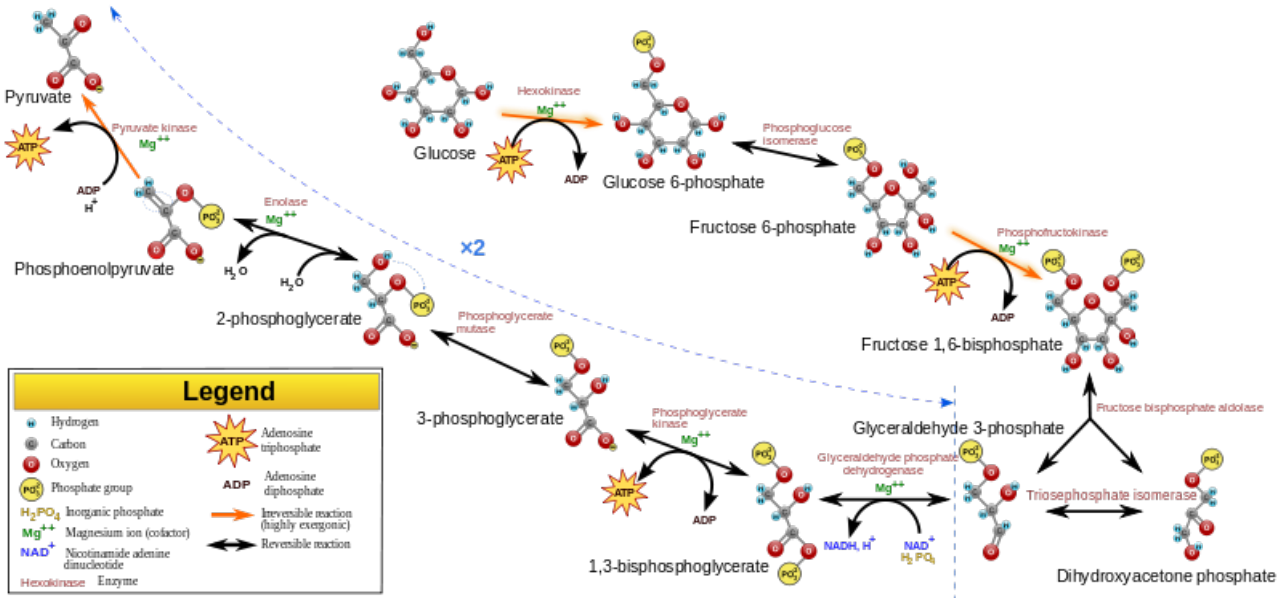
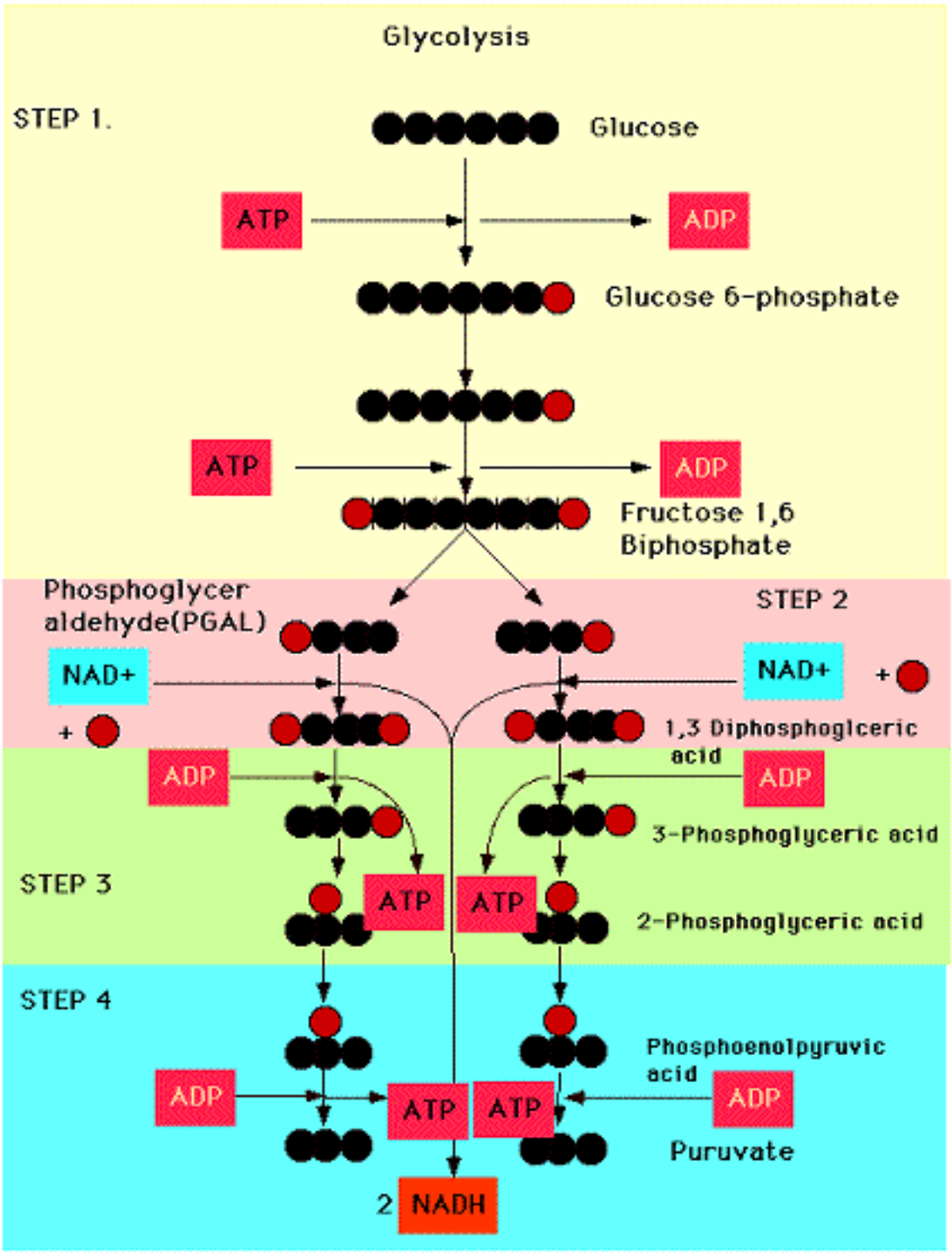
ANSC/FSTC 607
Physiology and Biochemistry of Muscle as a Food
GLYCOLYSIS AND THE KREBS CYCLE

I. Glycolysis

A. Pathways







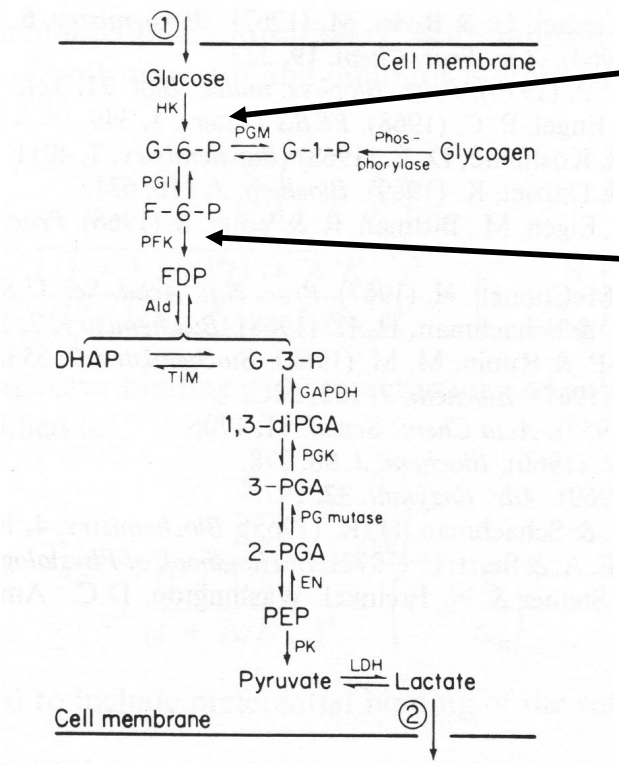
B. Reactants and products

A. Reactants = 1 glucose, 2 NAD+ and 2 ATP, and 4 ADP

B. Products = 2 pyruvates (or 2 lactates), 2 NADH, and 2 ATP (net)

II. Control reactions in glycolysis

A. Control points



Hexokinase:

Activated by glucose.

Inhibited by G6P.

6-Phosphofructokinase:

Inhibited by ATP, especially in the presence of citrate.

Activated by AMP, fructose-2,6-*bis*-phosphate.

B. Why are these good control points?

1. Inhibition at hexokinase: Prevents glucose from being sequestered in the muscle fiber if energy is plentiful.

   a. Phosphorylation of glucose to G-6-P traps glucose carbon in the muscle fiber.

   b. Accumulation of G-6-P inhibits hexokinase, allows glucose to be used elsewhere.

2. Inhibition at 6-phosphofructokinase: Spares glucose carbon for the synthesis of glycogen or nucleotide bases (via the pentose phosphate pathway).

   a. Phosphorylation of F-6-P to F-1,6-P_2 (or FDP) commits the carbon to glycolysis.

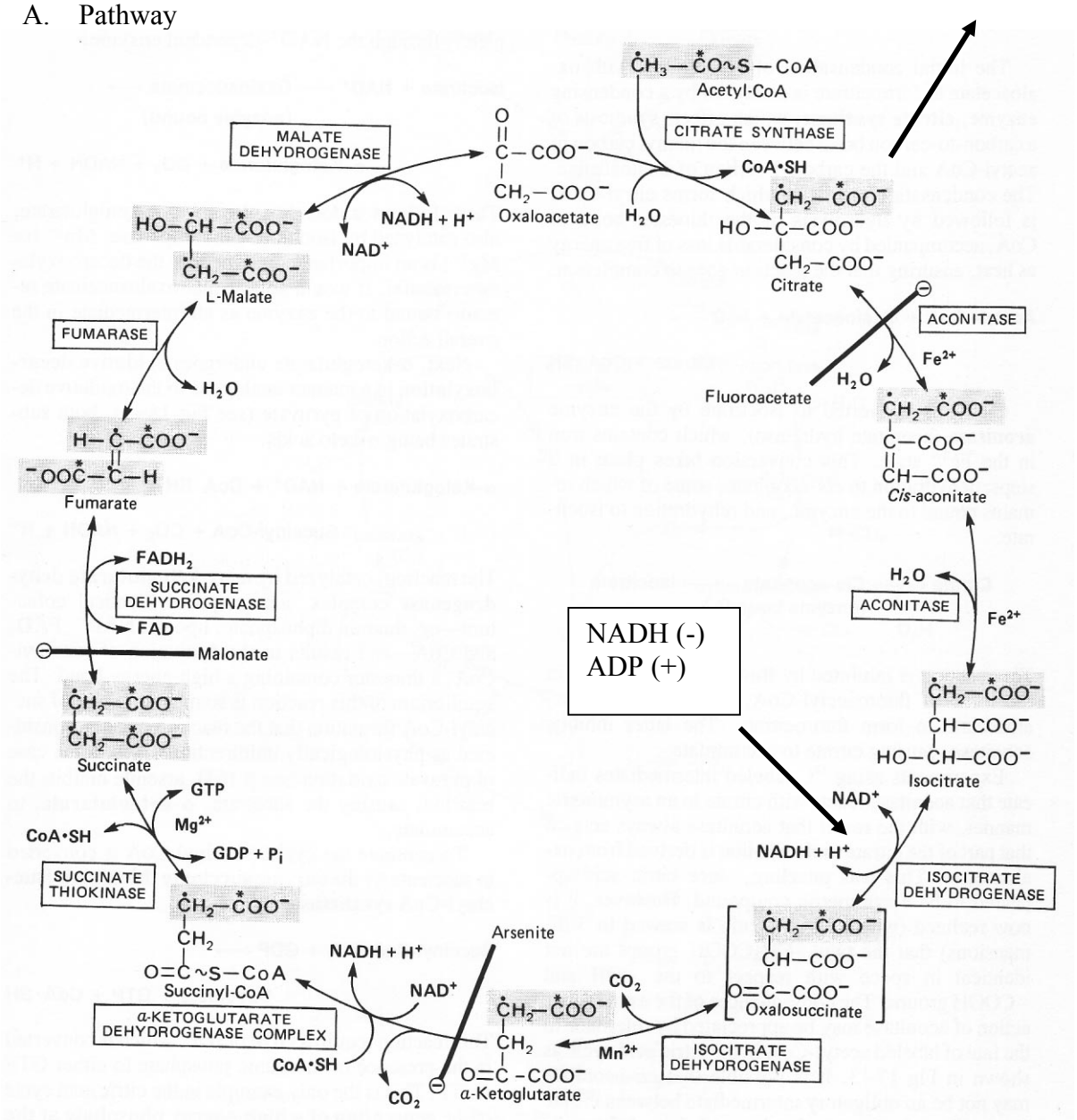
   b. If 6-PFK is inhibited, G-6-P accumulates and inhibits hexokinase.

   c. Accumulation of G-6-P also provides substrate for other pathways.

III. Krebs (tricarboxylic acid or citric acid) cycle

to sarcoplasm

A. Pathway



B. Regulation

1. NADH accumulates if more is made than can be oxidized by the electron transport system.
2. NADH inhibits isocitrate dehydrogenase, which causes citrate to accumulate.
3. Citrate is transported out of the mitochondria by a specific transporter.

IV. Energy production by the electron transport system

A. NADH is oxidized by the electron transport system beginning with the first reductase.

1. Protons are pumped out of the mitochondrial matrix at three sequential reductases.

2. 3 ATP are synthesized by ATP synthase as protons (H^+) flow along their concentration gradient back into the mitochondrial matrix.

B. $FADH_2$ enters the electron transport system at the second reductase.

1. Protons are pumped out of the mitochondrial matrix at two of the reductases.

a. The first reductase includes succinate dehydrogenase.

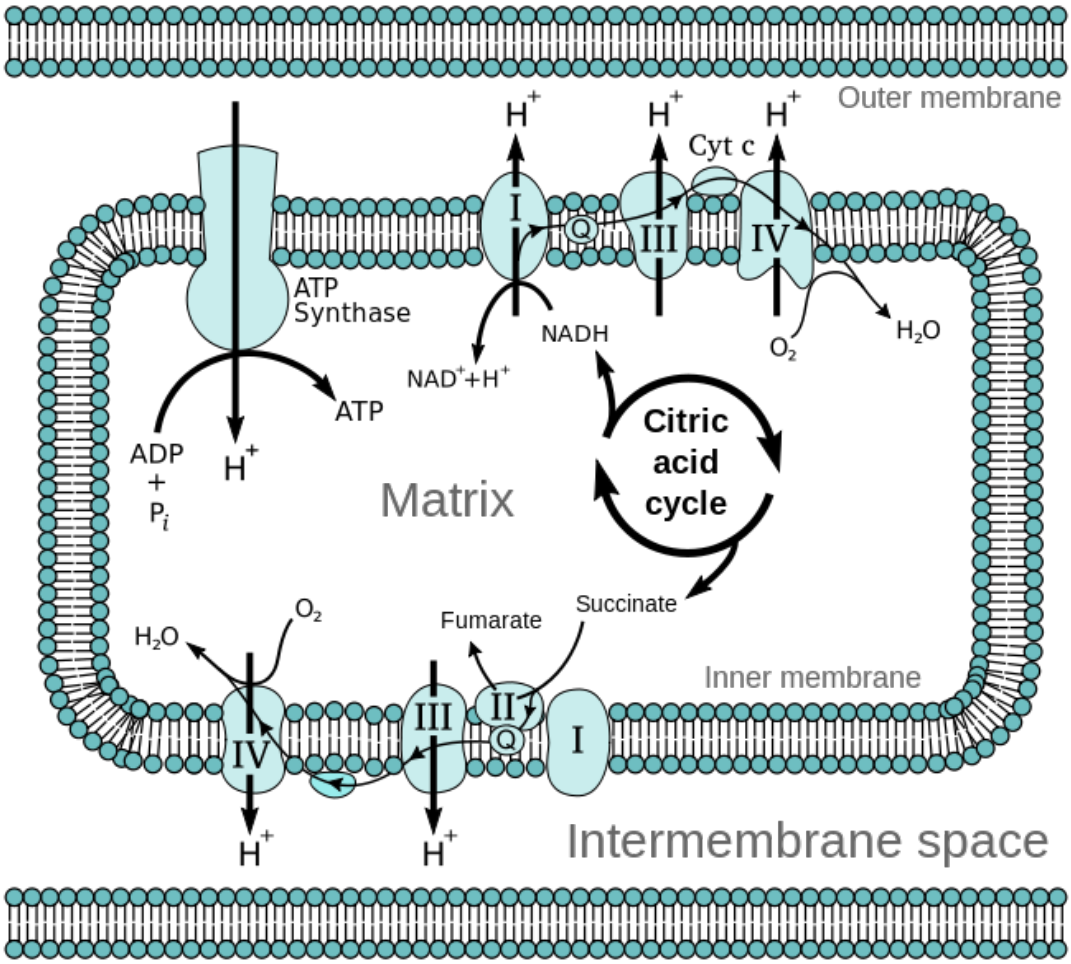
b. This reductase uses FAD to transport electrons and protons.

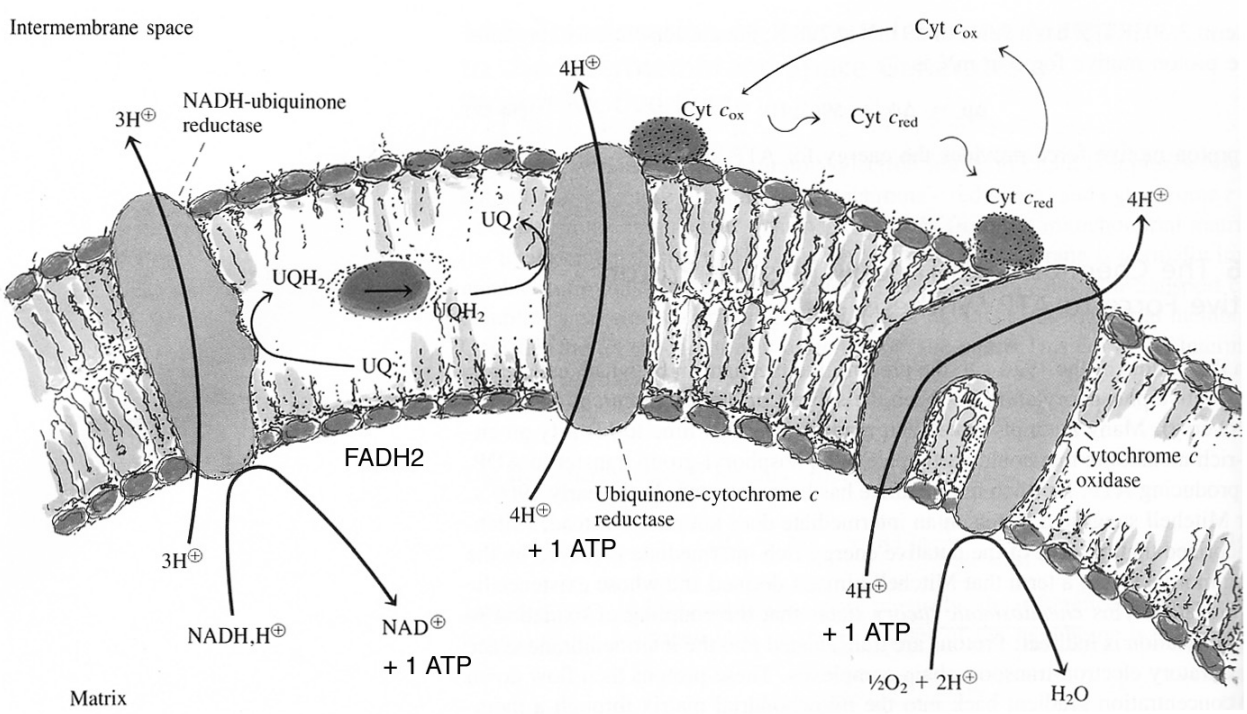
2. 2 ATP are synthesized by ATP synthase.

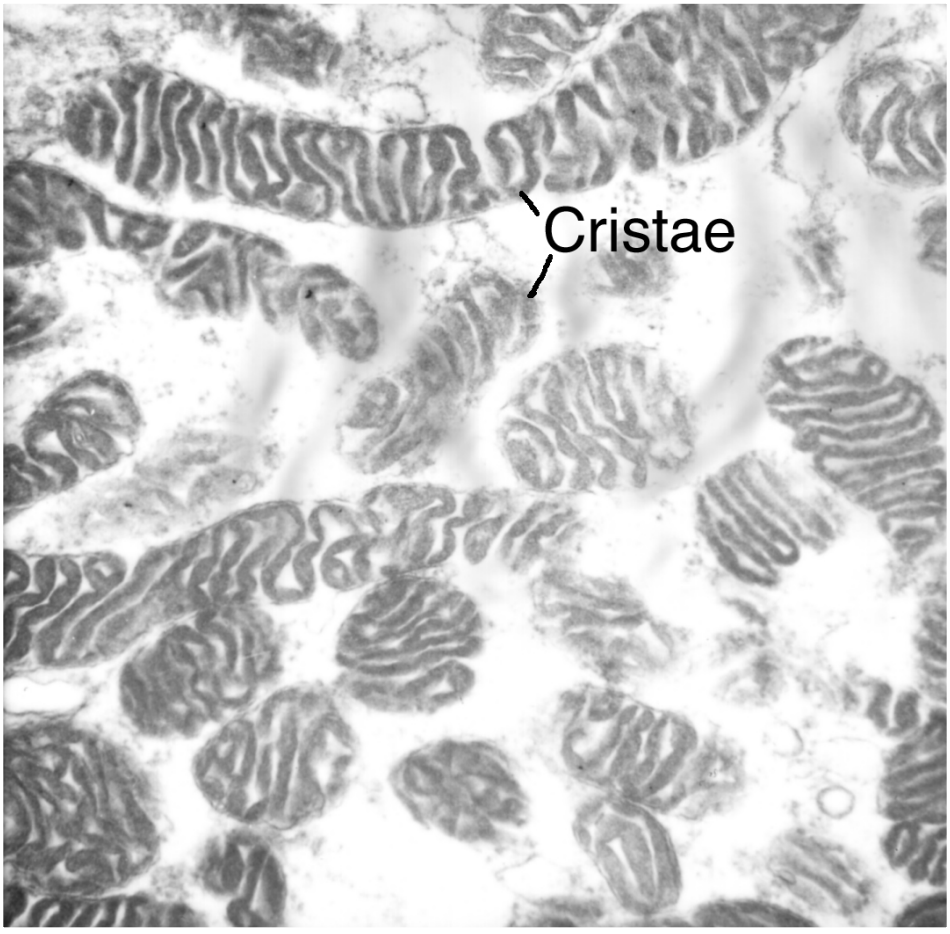
C. Oxygen is the terminal electron acceptor.

1. Electrons and protons are transferred to ½ O_2.

2. Metabolic water is produced.




Intermembrane space
3H⊕
NADH-ubiquinone reductase
4H⊕
Cyt c_{ox}
Cyt c_{red}
Cyt c_{ox}
Cyt c_{red}
4H⊕
UQ
UQH2
UQH2
UQ
FADH2
Cytochrome c oxidase
4H⊕
Ubiquinone-cytochrome c reductase
+ 1 ATP
3H⊕
NADH,H⊕
NAD⊕
+ 1 ATP
4H⊕
+ 1 ATP
½O2 + 2H⊕
H2O
Matrix


Cristae

V. Citrate and the regulation of glycolysis

A. Citrate exits mitochondria

B. Citrate inhibits 6-PFK.

C. Inhibition of 6-PFK causes accumulation of G-6-P.

D. G-6-P inhibits hexokinase, which causes muscle to stop taking up glucose.

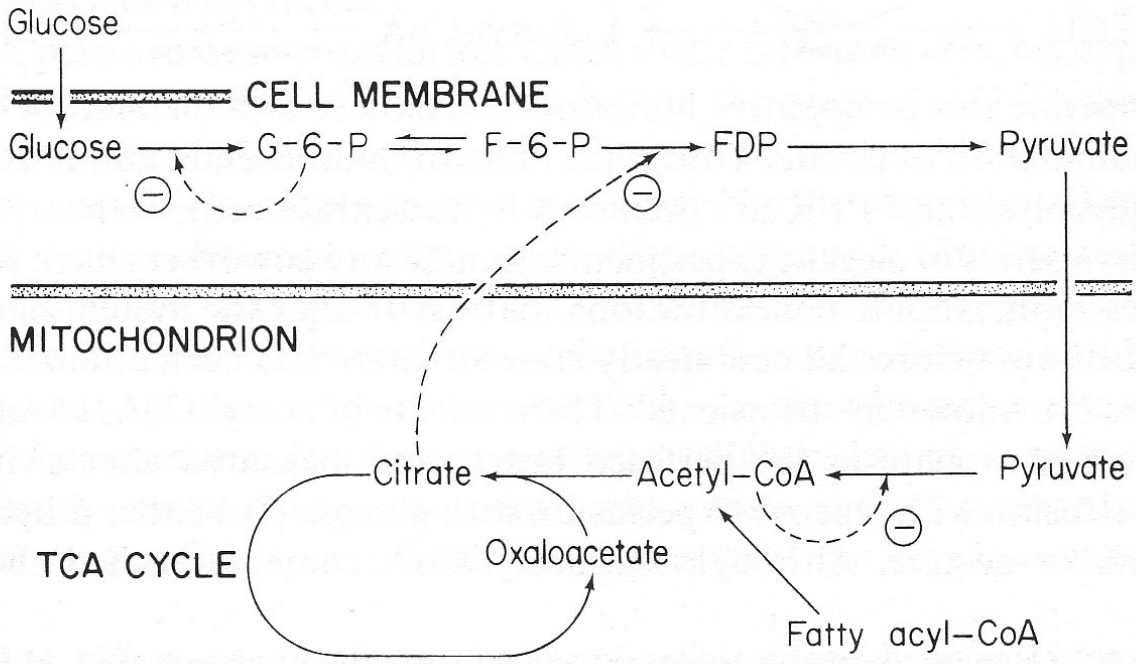


Figure 3.15. Control of glycolysis and pyruvate oxidation in muscle by citrate and acetyl-CoA