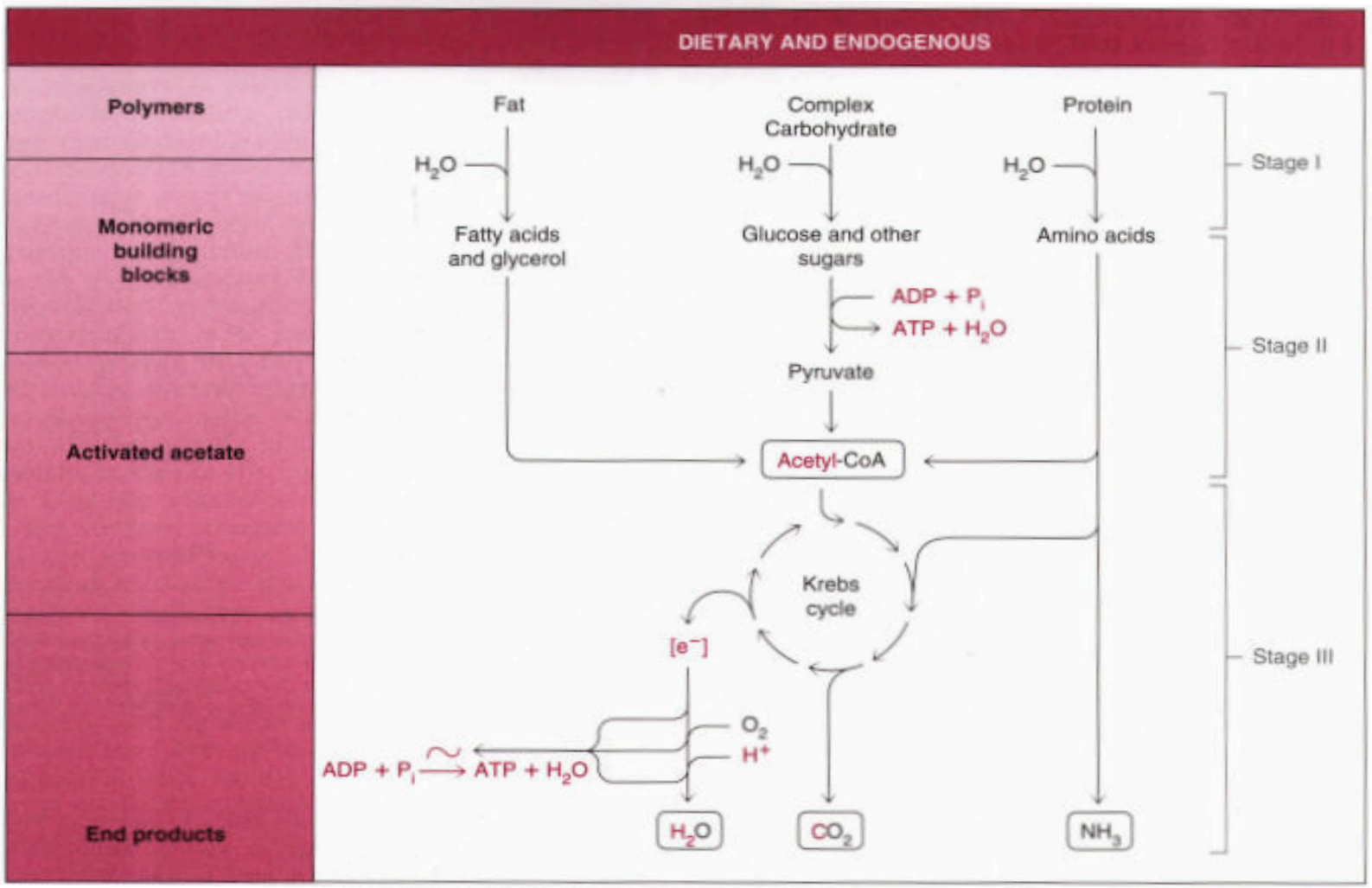
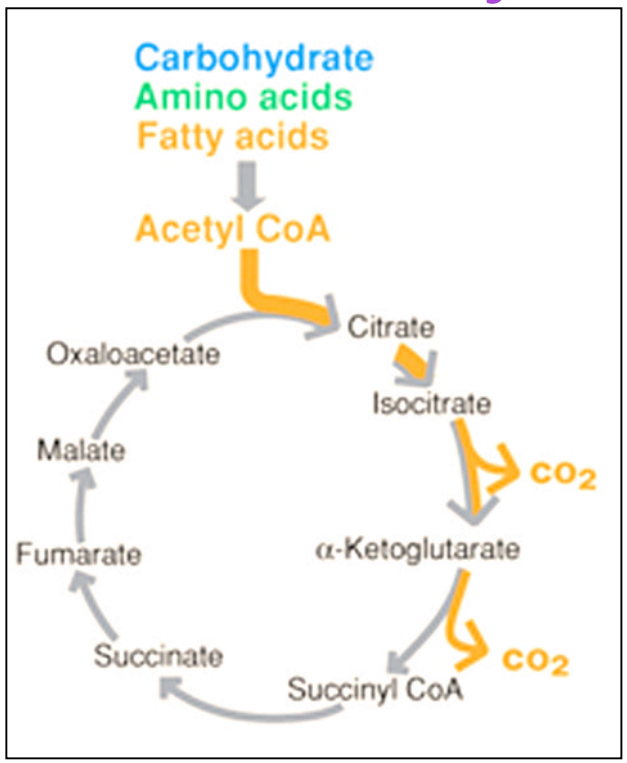
Key knowledge base

- To discuss the function of the citric acid cycle in intermediary metabolism, where it occurs in the cell, and how pyruvate is converted into acetyl coA and enters the cycle.
- Be able to write down the structures and names of the CAC intermediates and the name of the enzyme catalyzing each step.
- Understand and be able to write down the net reaction of the citric acid cycle.
- Be able to name all the steps in the citric acid cycle in which reduced NAD or reduced FAD is formed.
- Be able to name all the decarboxylation steps in the citric acid cycle.
- To describe and discuss the regulation of the citric acid cycle.
- To describe and discuss how the citric acid cycle functions as the final common pathway for the oxidation of polysaccharides, proteins, and lipids.

The Three Stages of Metabolism



Citric Acid Cycle



Glycogen

R5P

Glucose

Disaccharides

$NADH + H^+$ and ATP

Pyruvate

aerobic conditions

Acetyl CoA

citric acid cycle

$NADH + H^+$ and $FADH_2$ and CO_2

O_2 → H_2O

Electron transport
Oxidative phosphorylation

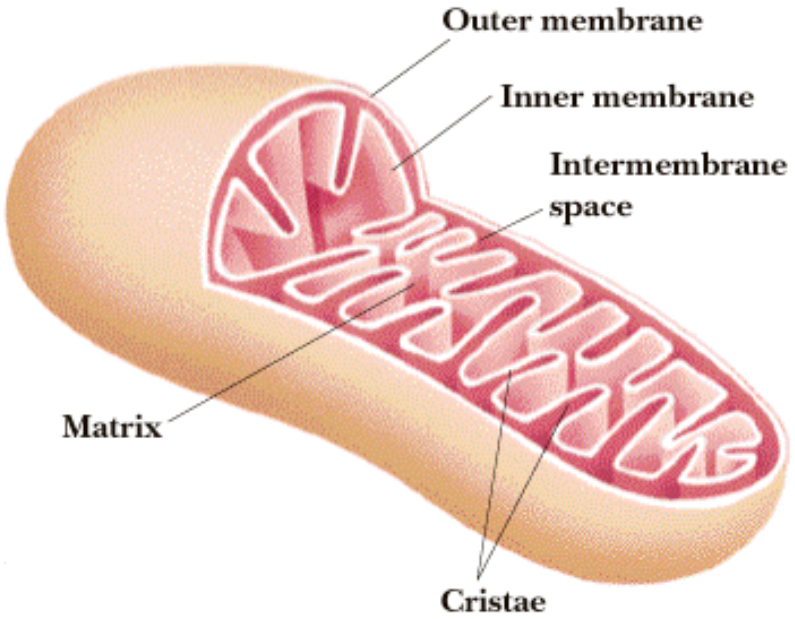
$ADP + P_i$ → ATP

The Krebs Cycle

Citric Acid Cycle; The TCA Cycle

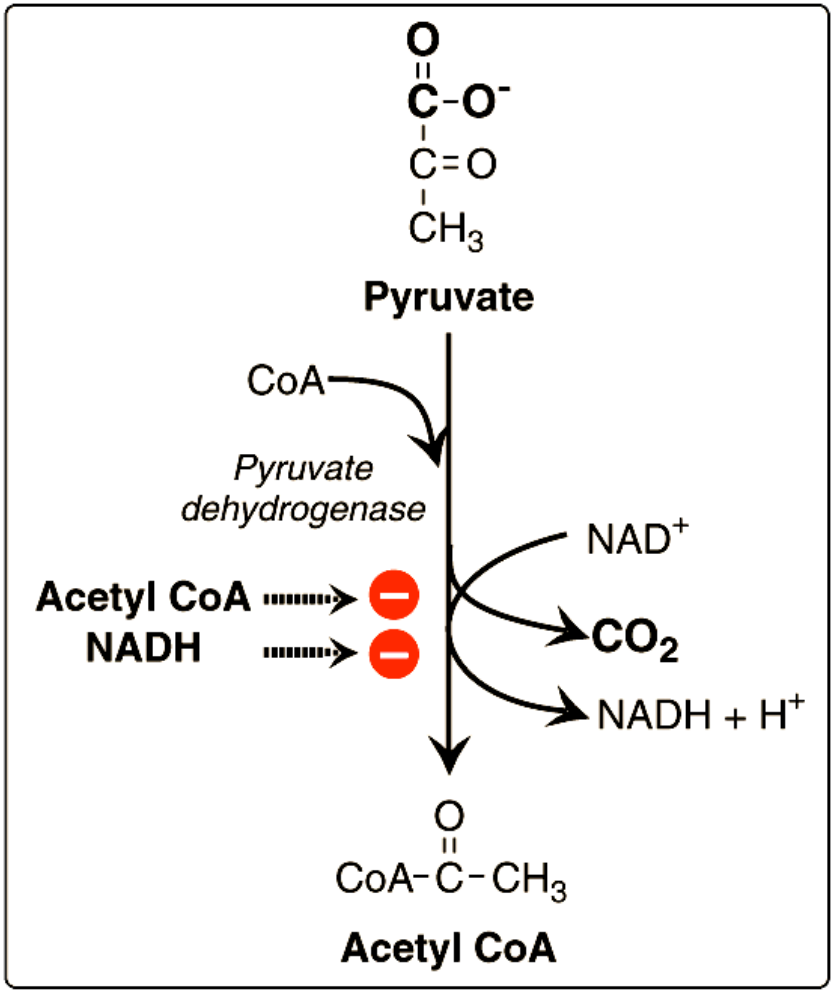
- Function of citric acid cycle is to oxidize organic molecules under aerobic conditions.
- 8 reactions in the Krebs cycle
- Pyruvate is degraded to CO_2.
- 1 GTP (ATP in bacteria) and 1 $FADH_2$ are produced during one turn of the cycle.
- 3 NADH are produced during one turn of the cycle.
- NADH and $FADH_2$ energize electron transport and oxidative phosphorylation.

Mitochondrion



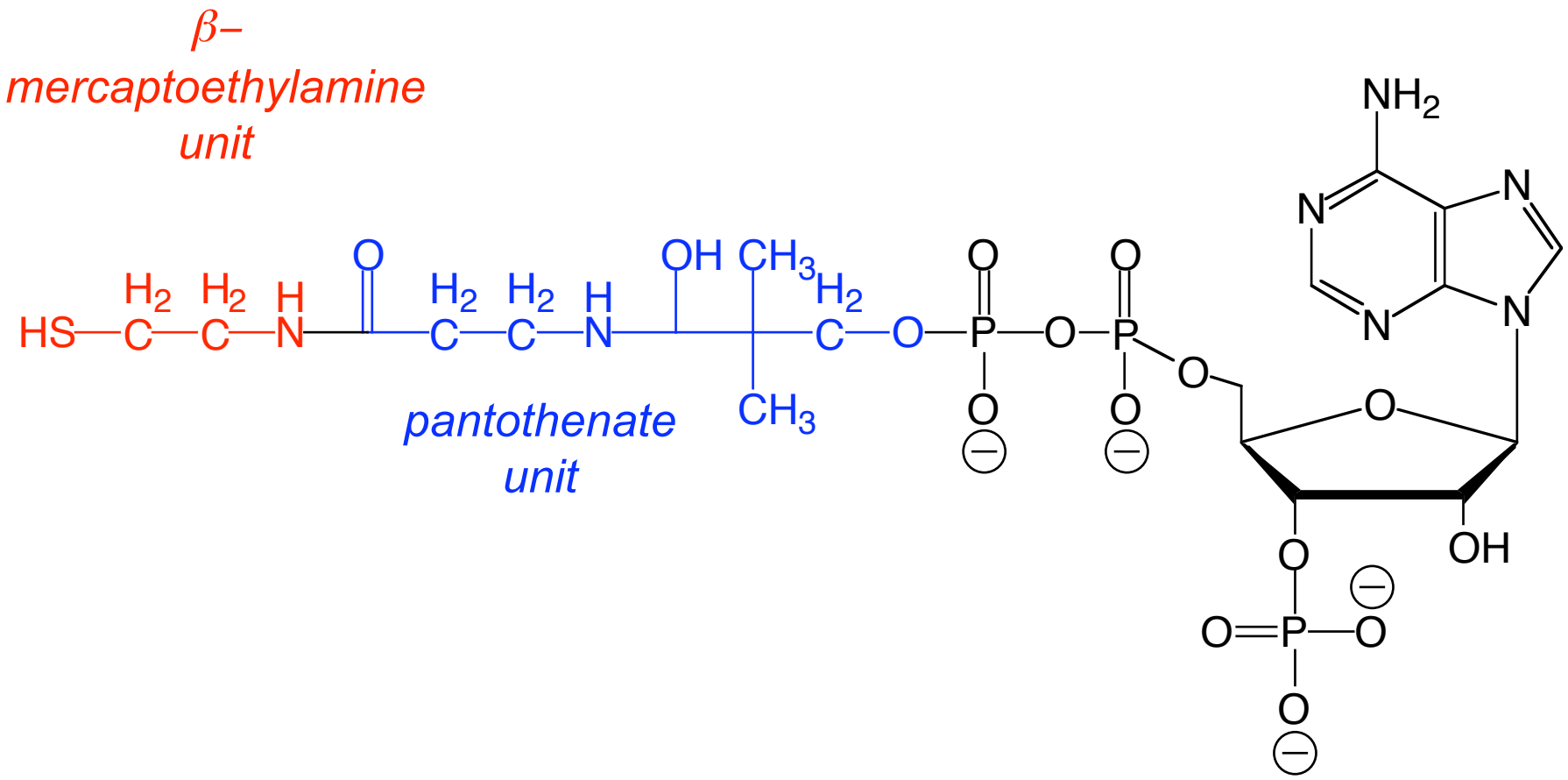
- Which membrane is impermeable to protons and other ions?
- Which membrane will allow for the transport of molecules up to a molecular weight of about 1000?

Pyruvate Dehydrogenase Complex



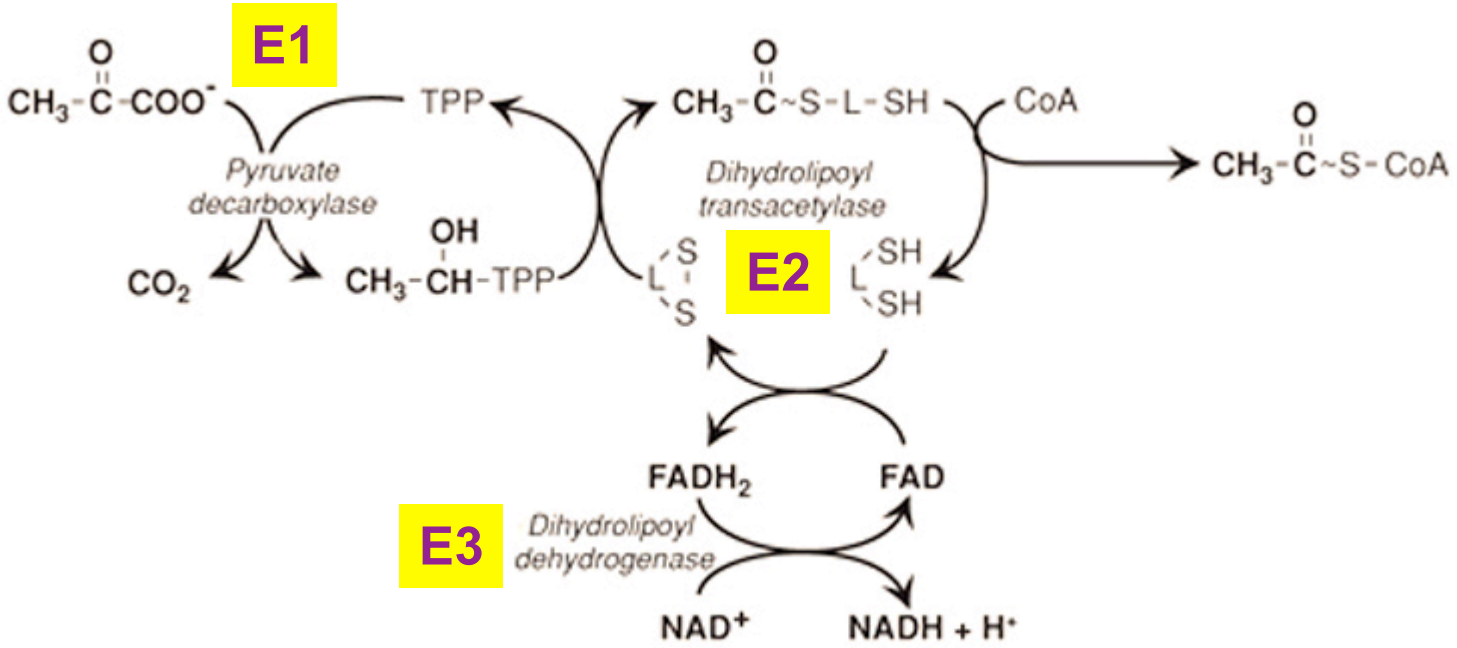
A dehydrogenase is a class of enzymes that catalyze metabolic oxidations involving loss of hydrogen from the electron donor.

Chemical structure of Coenzyme A



Pyruvate Dehydrogenase Complex

Pyruvate dehydrogenase *complex is an enzyme assembly of three types of subunits (E1, E2, and E3) and 5 coenzymes that catalyze 5 reactions.*



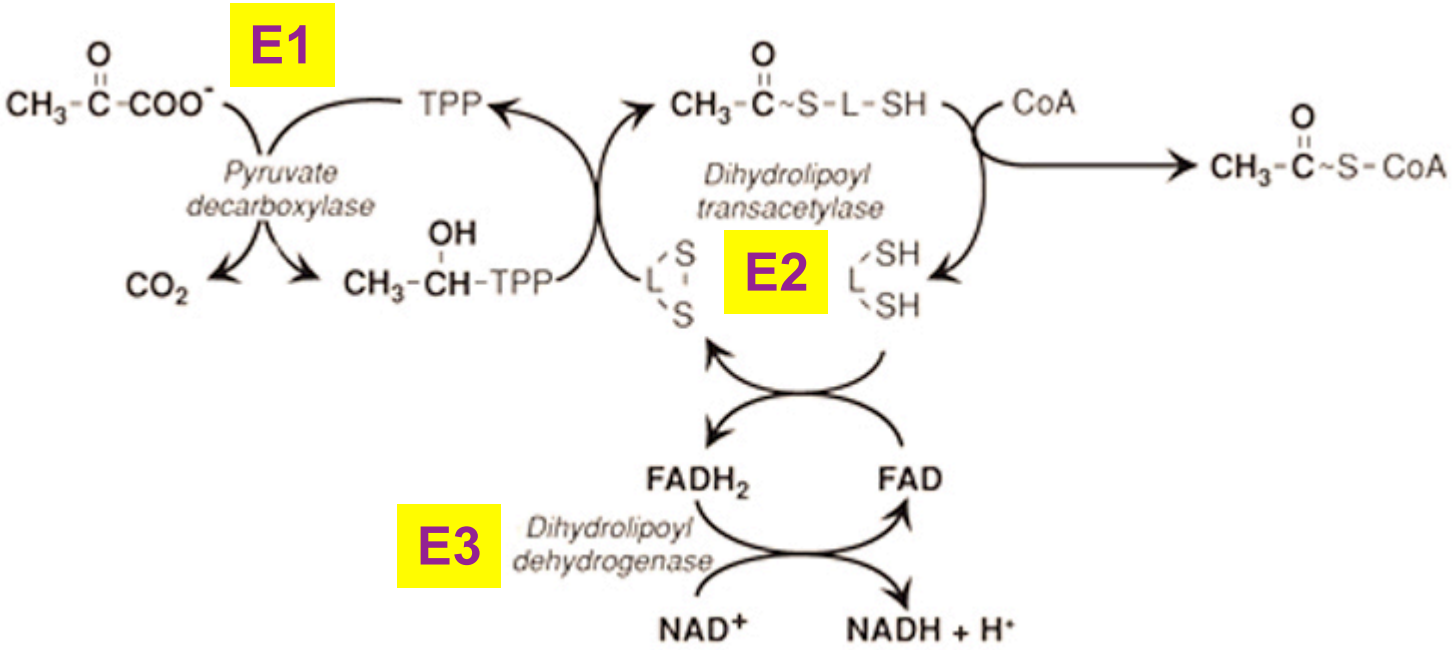
Pyruvate Dehydrogenase Complex

Pyruvate decarboxylated by E1 (pyruvate decarboxylase)

Hydroxyethyl intermediate oxidized by transfer to E2

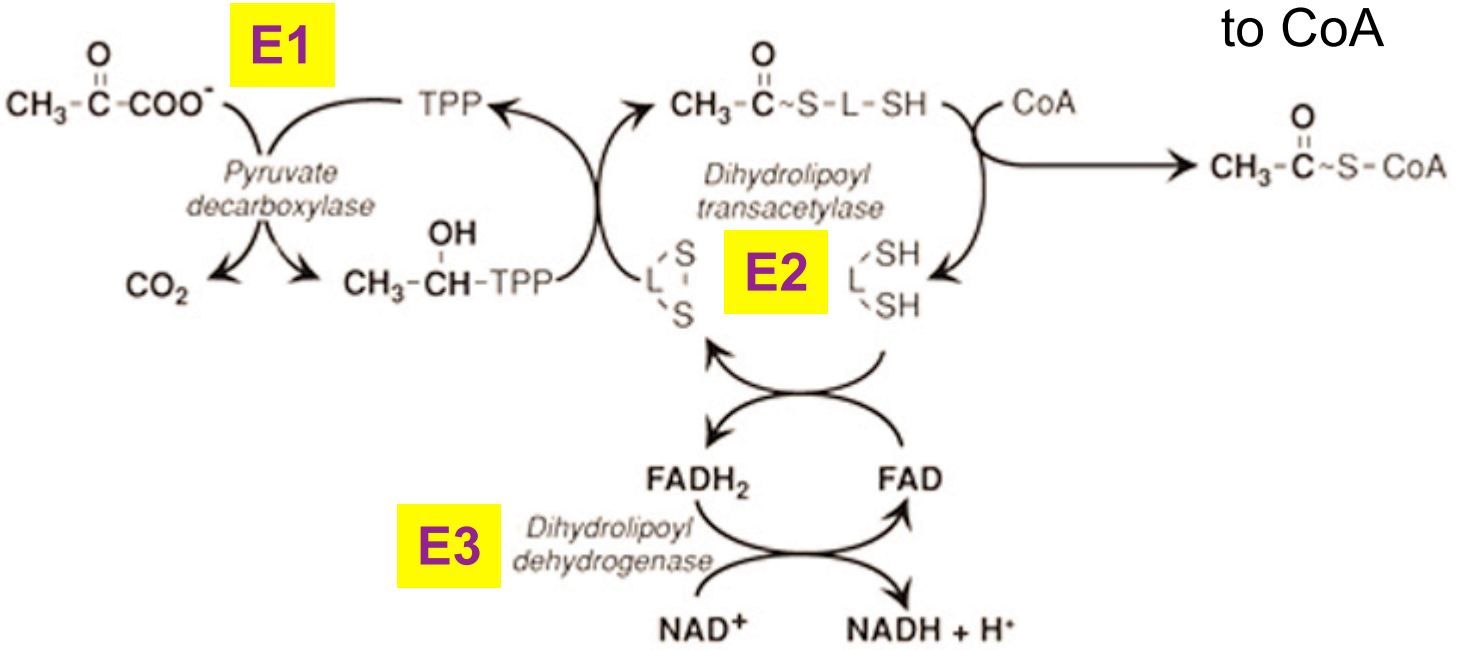
TPP required

Lipoic acid required

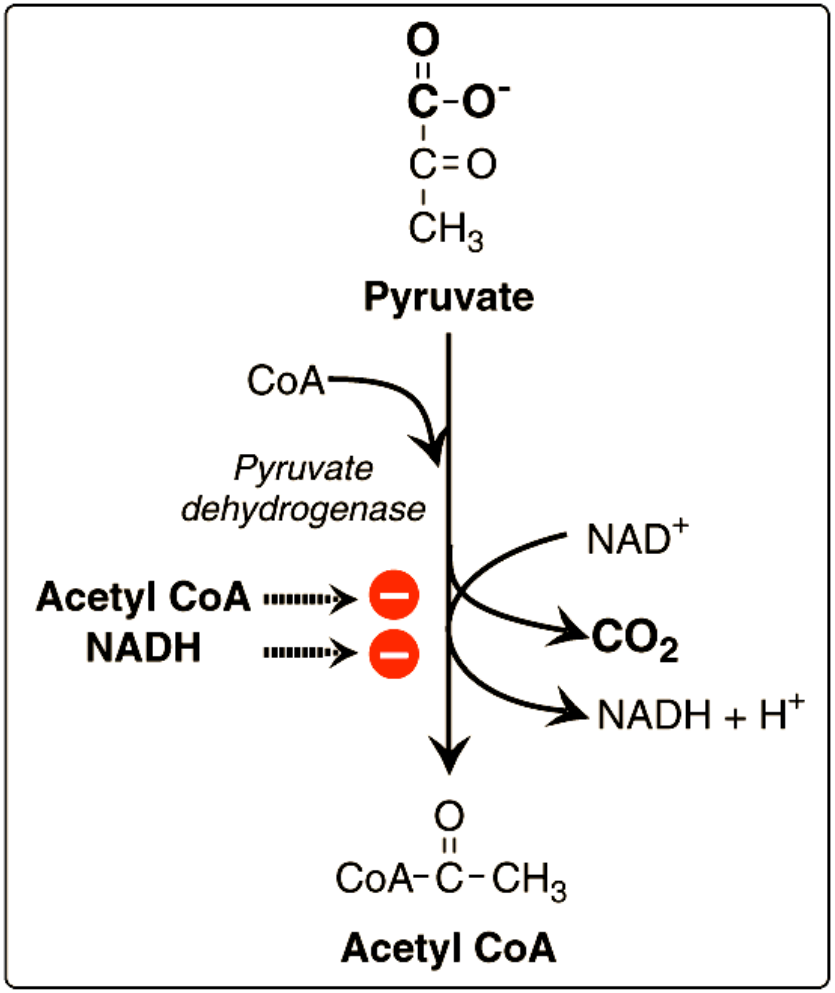


Pyruvate Dehydrogenase Complex

Acetyl group bound to lipoic acid is transferred to CoA

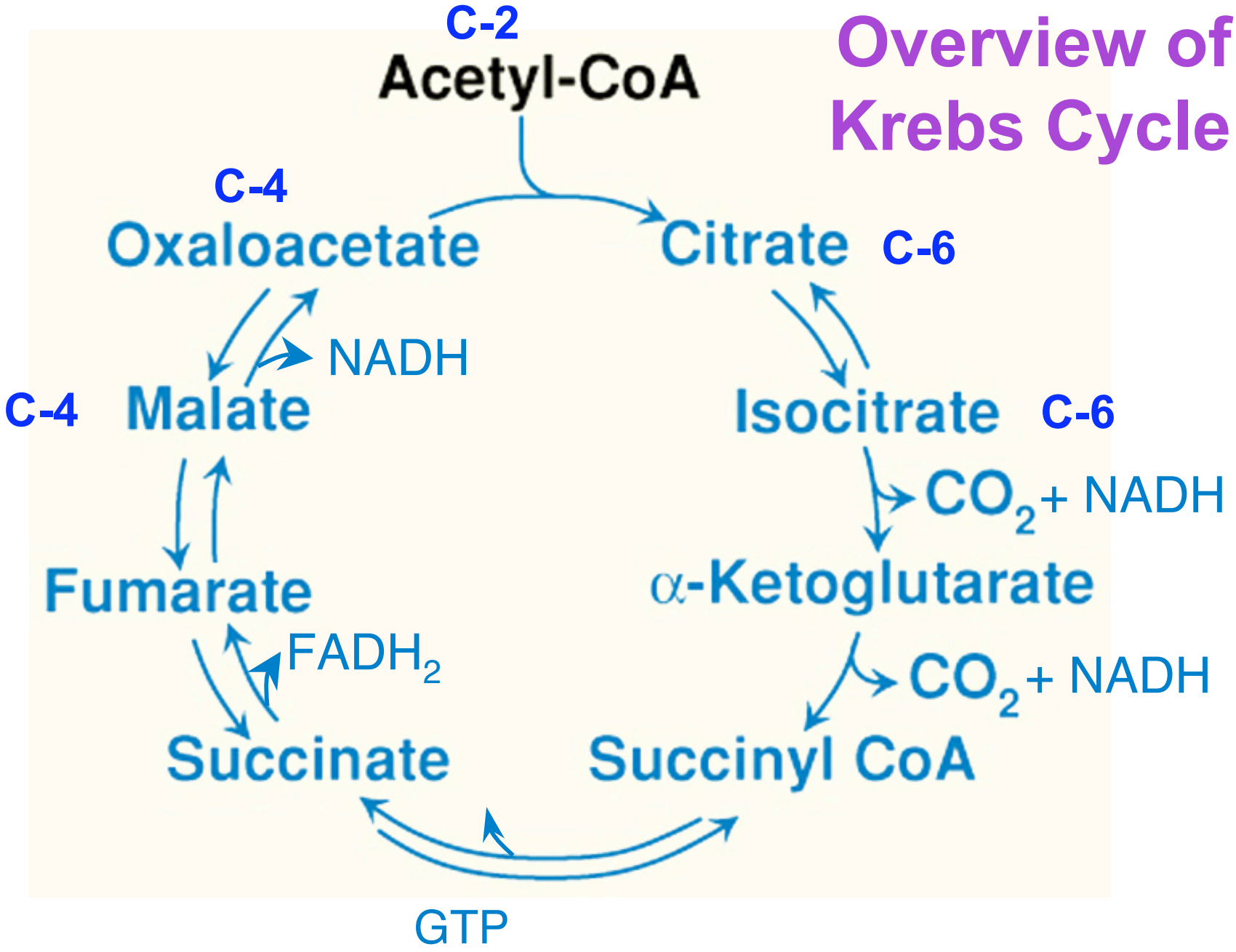


Pyruvate Dehydrogenase Complex

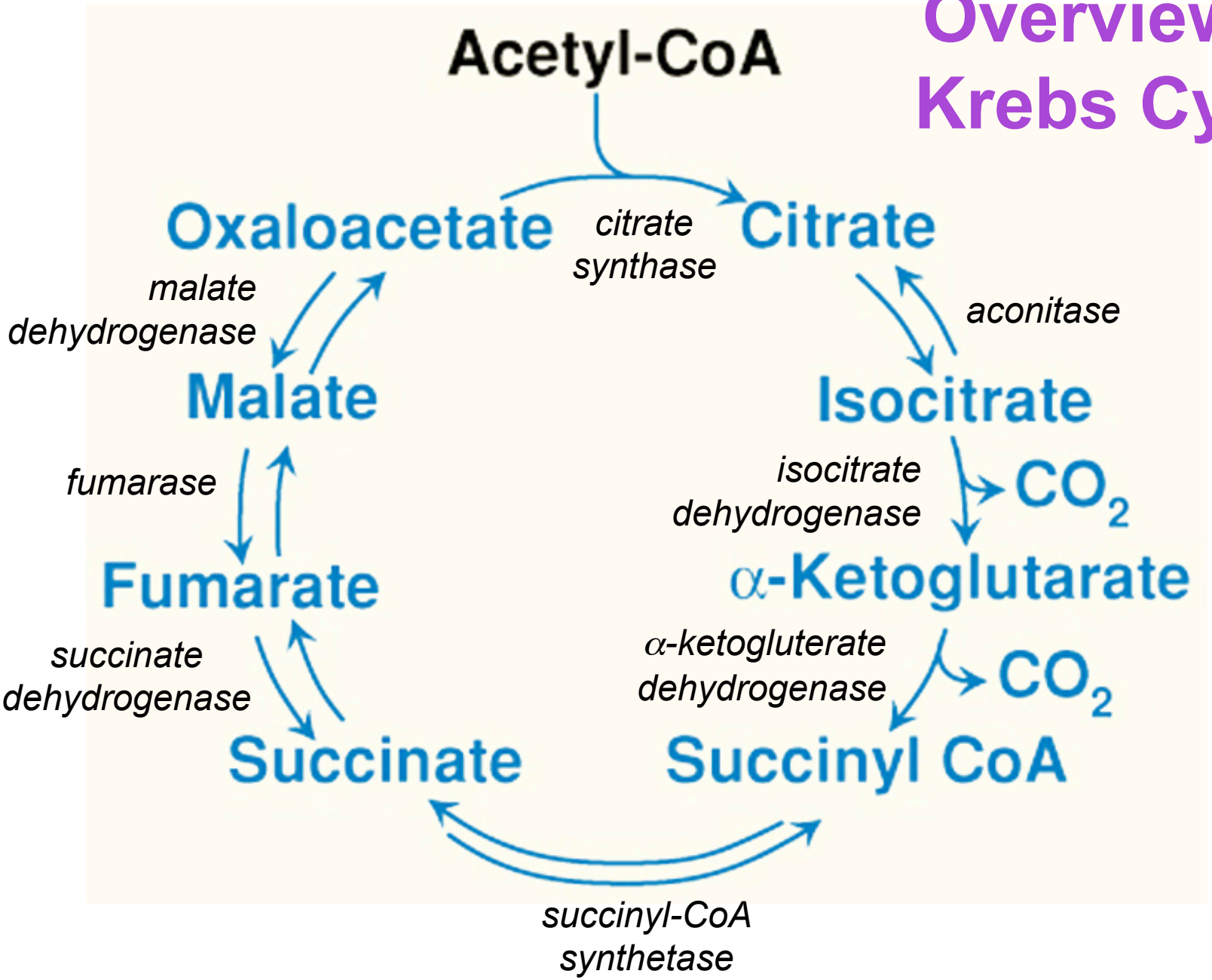


Pyruvate dehydrogenase *complex is highly regulated.*

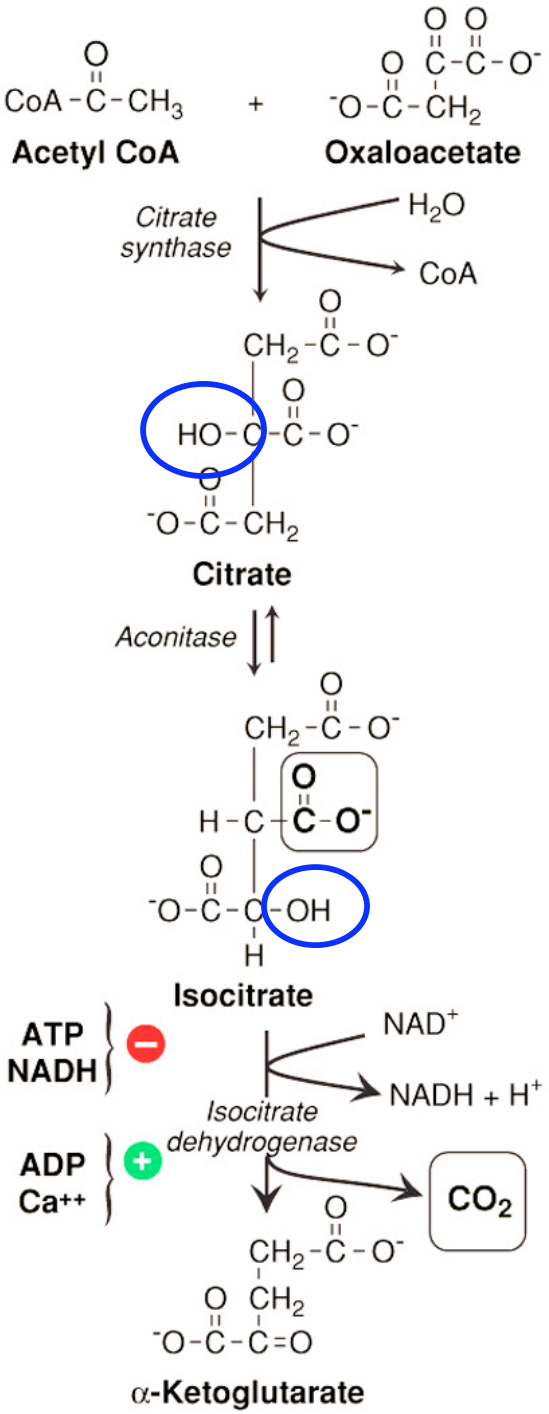
Overview of Krebs Cycle



Overview of Krebs Cycle



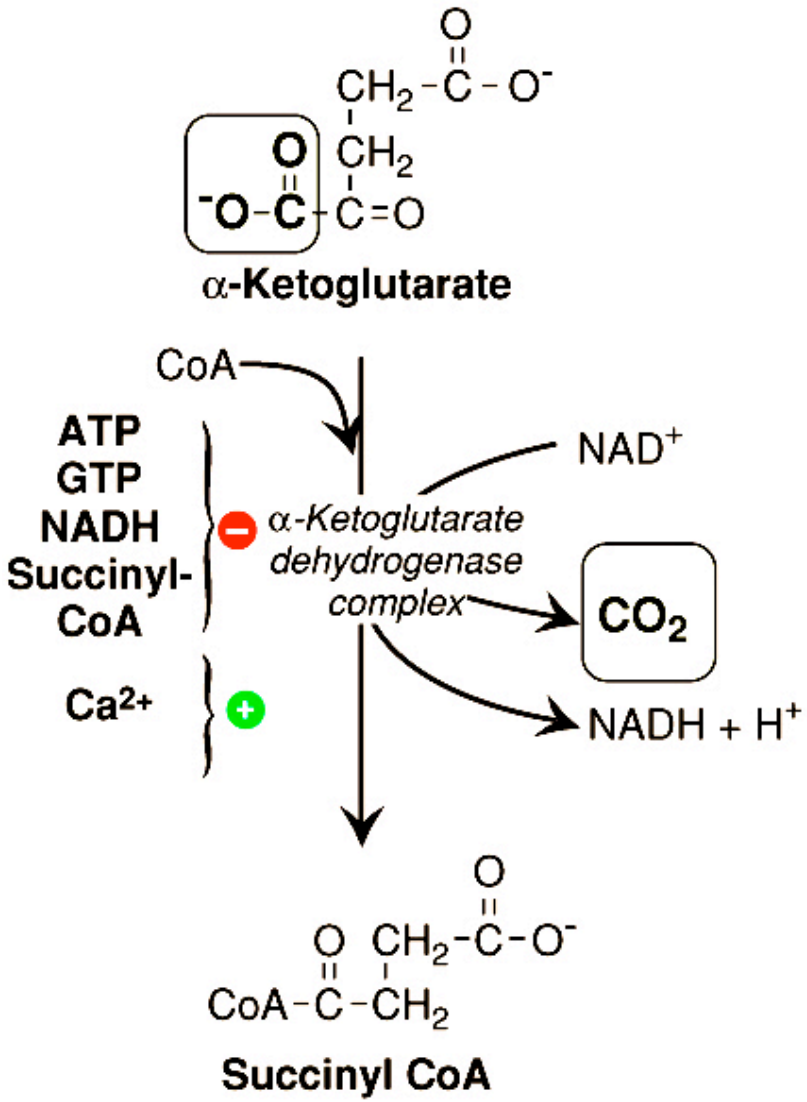
Entrance of acetyl CoA does not ↑ or ↓ intermediates in CAC



aldol condensation

isomerization

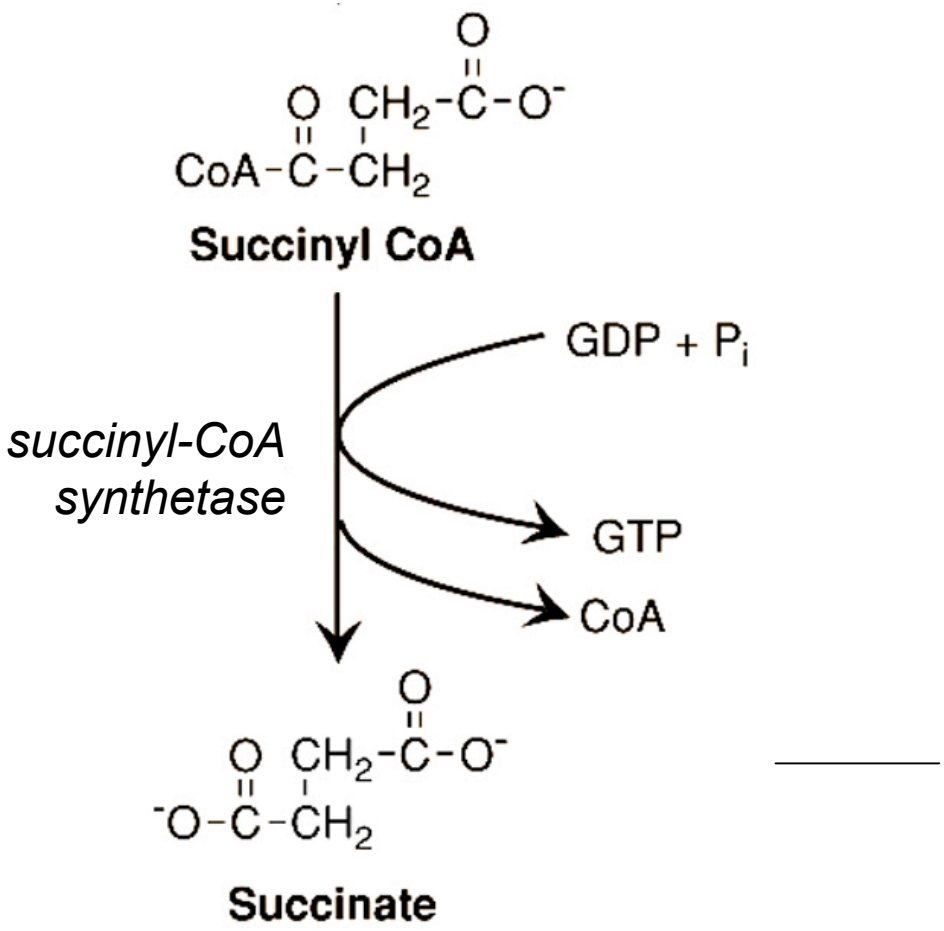
oxidative decarboxylation



oxidative decarboxylation

Irreversible

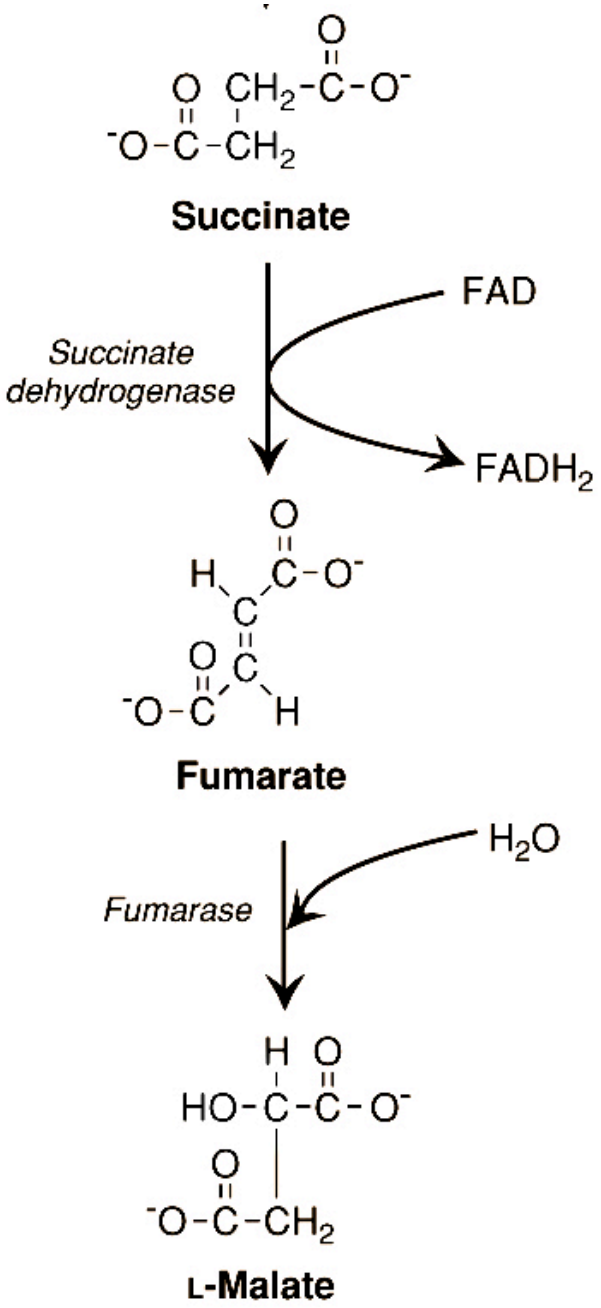
Coupled reaction: substrate level phosphorylation



succinyl-CoA → succinate + CoA ΔG^o **= -34 kJ/mol**

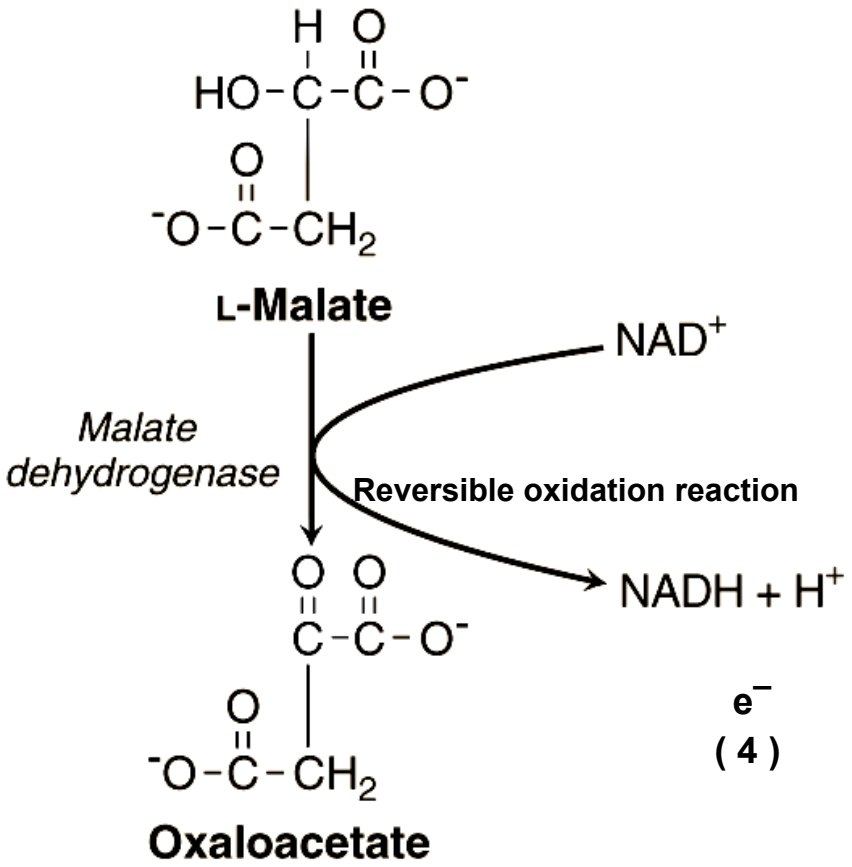
GDP + P_i → GTP ΔG^o **= +31 kJ/mol**

Net reaction ΔG^o **= -3 kJ/mol**

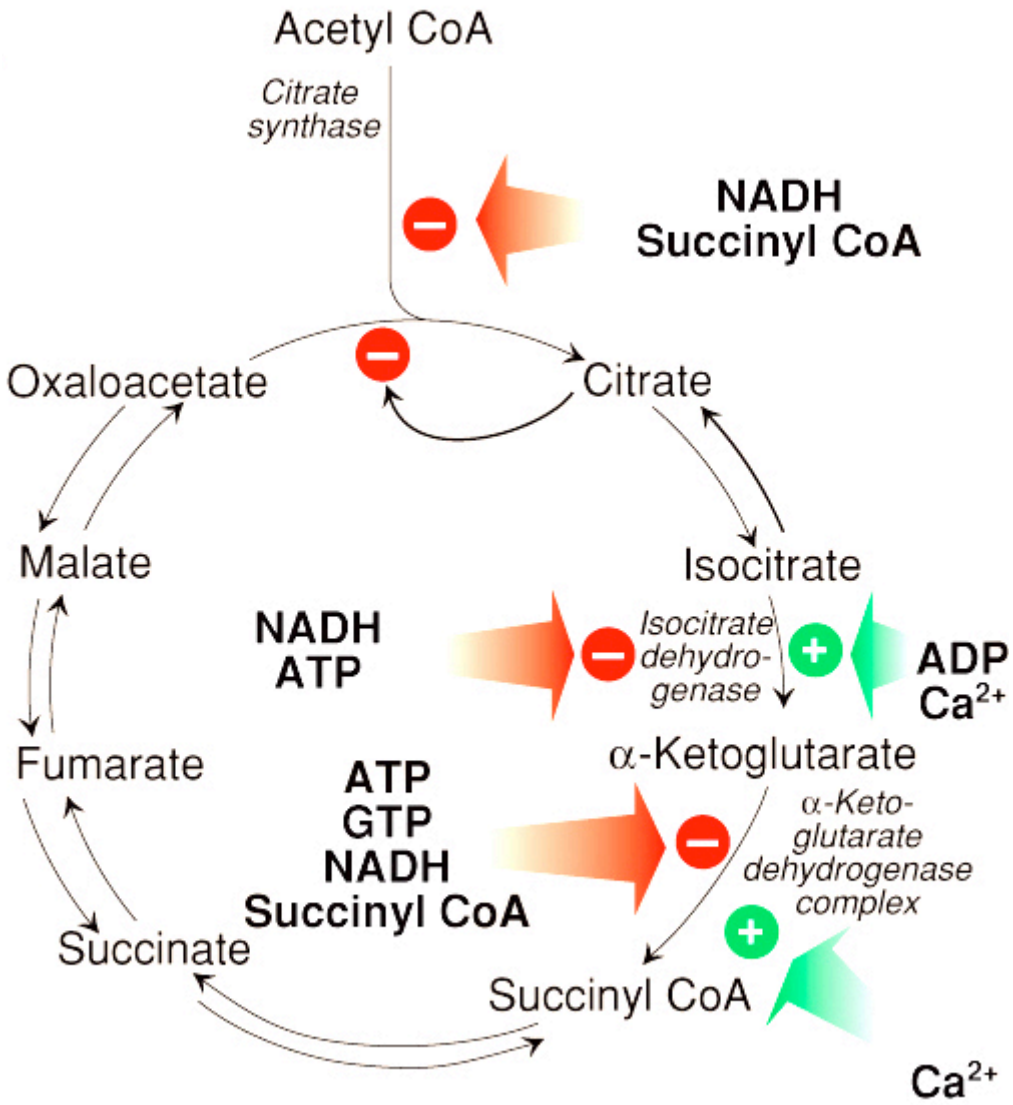


oxidation

hydration


L-Malate
NAD+
Malate dehydrogenase
Reversible oxidation reaction
NADH + H+
e−
(4)
Oxaloacetate

Energy-producing reaction	Number of ATP produced
$3\ NADH \longrightarrow 3\ NAD^+$	9
$FADH_2 \longrightarrow FAD$	2
$GDP + P_i \longrightarrow GTP$	1
	12 ATP/acetyl CoA oxidized


Acetyl CoA
Citrate synthase
NADH
Succinyl CoA
Oxaloacetate
Citrate
Malate
Isocitrate
NADH
ATP
Isocitrate dehydro-genase
ADP
Ca2+
Fumarate
α-Ketoglutarate
ATP
GTP
NADH
Succinyl CoA
α-Keto-glutarate dehydrogenase complex
Succinate
Succinyl CoA
Ca2+

Main Points of the Krebs Cycle

- Occurs in mitochondrion
- All enzymes are hydrophilic and occur in the matrix except for succinate dehydrogenase, which occurs in the inner mitochondrial membrane
- Citrate synthase, isocitrate dehydrogenase and a-ketoglutarate dehydrogenase are the three irreversible reactions
- ICD is the main regulatory enzyme, and it is activated by ADP
- Succinate dehydrogenase is inhibited by malonate and oxaloacetrate