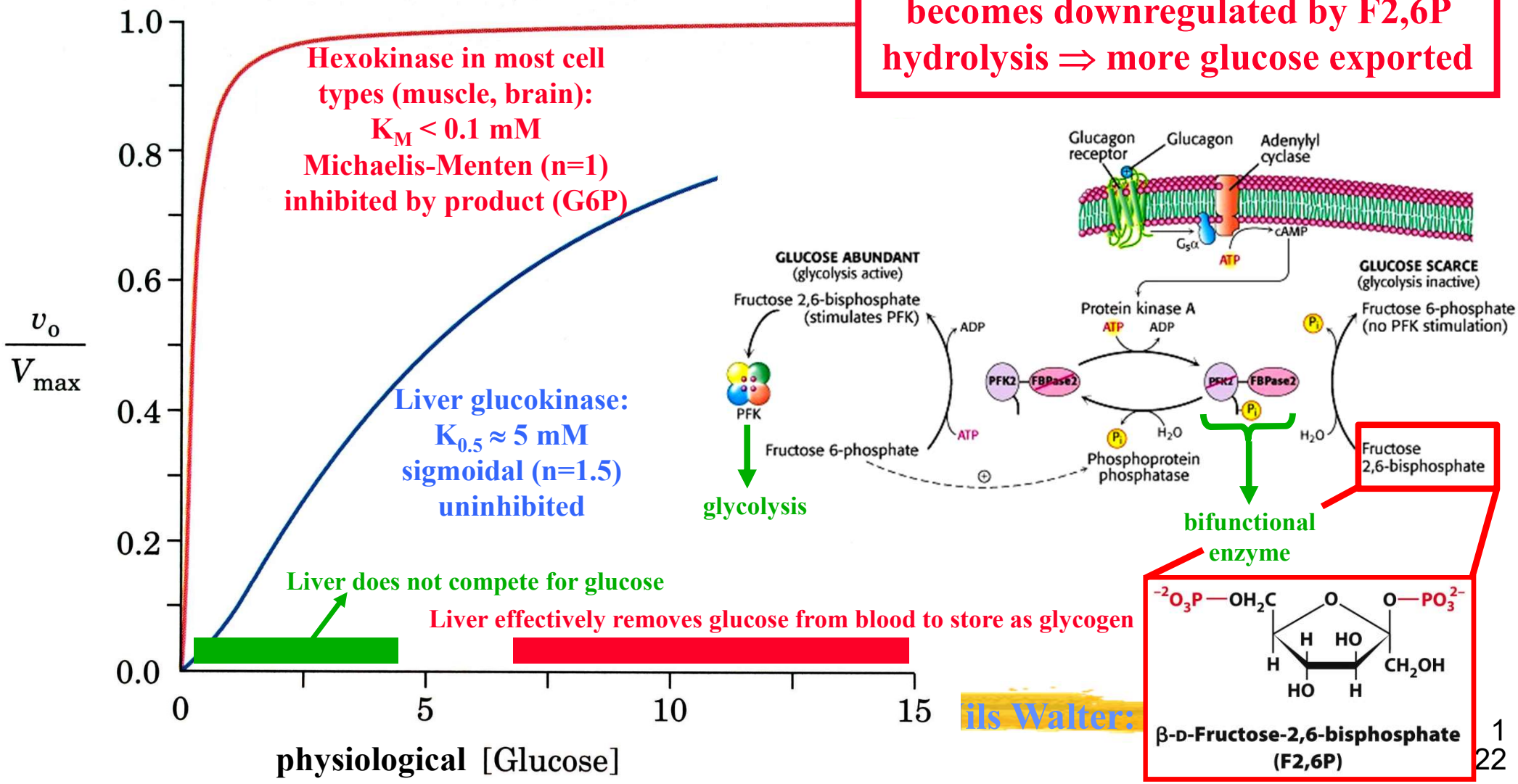
But Wait: How Does This Work so that the Liver Does Not Gobble Up all Glucose?

Trick 1: Liver traps glucose for glycogen synthesis and glycolysis only when abundant

Trick 2: When blood [glucose] low (glucagon!), glycolysis in the liver becomes downregulated by F2,6P hydrolysis ⇒ more glucose exported



ils Walter:

Genetic Glycogen Storage Diseases

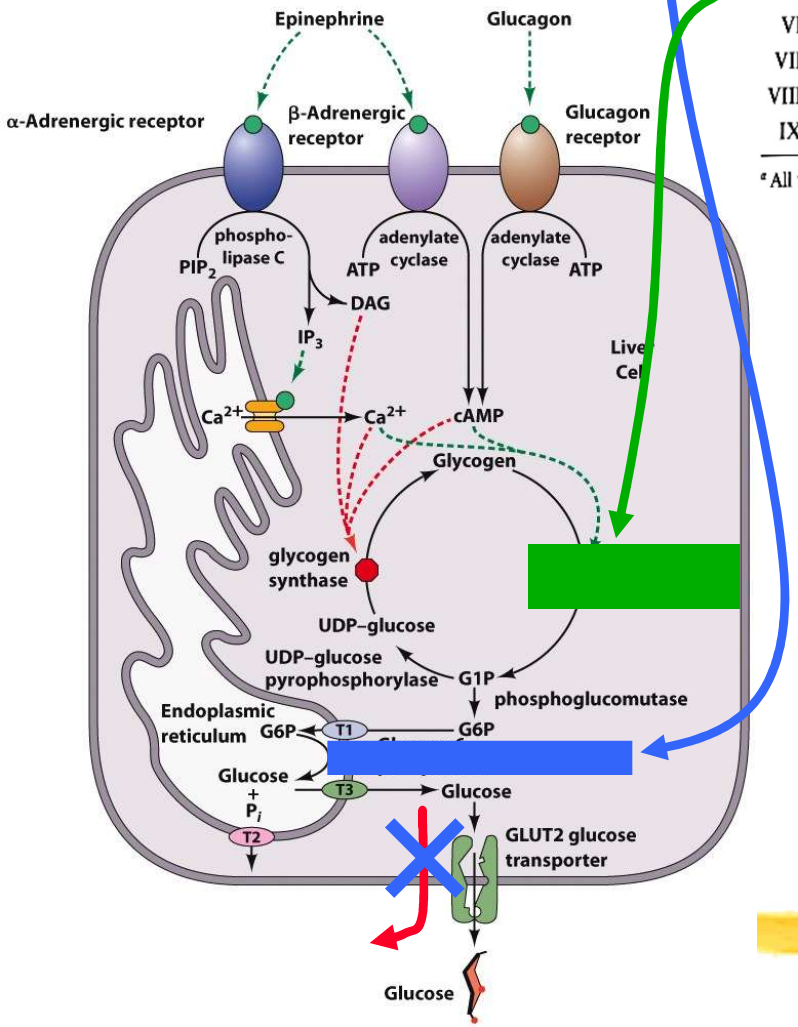


TABLE 17-1. HEREDITARY GLYCOGEN STORAGE DISEASES[a]

Type	Enzyme Deficiency	Tissue	Common Name	Glycogen Structure
I	Glucose-6-phosphatase	Liver	von Gierke's disease	Normal
II	α-1,4-Glucosidase	All lysosomes	Pompe's disease	Normal
III	Amylo-1,6-glucosidase (debranching enzyme)	All organs	Cori's disease	Outer chains missing or very short
IV	Amylo-(1,4 → 1,6)-transglycosylase (branching enzyme)	Liver, probably all organs	Andersen's disease	Very long unbranched chains
V	Glycogen phosphorylase	Muscle	McArdle's disease	Normal
VI	Glycogen phosphorylase	Liver	Hers' disease	Normal
VII	Phosphofructokinase	Muscle		Normal
VIII	Phosphorylase kinase	Liver	Tarui's disease	Normal
IX	Glycogen synthase	Liver		Normal, deficient in quality

[a] All types but Type VIII are autosomal recessive; Type VIII is sex linked.

⇒ In both cases:
Too much glycogen of normal structure

Chapter 18: What have we learned?

☺ Glucose = important fuel, needs to be stored to be "ready"

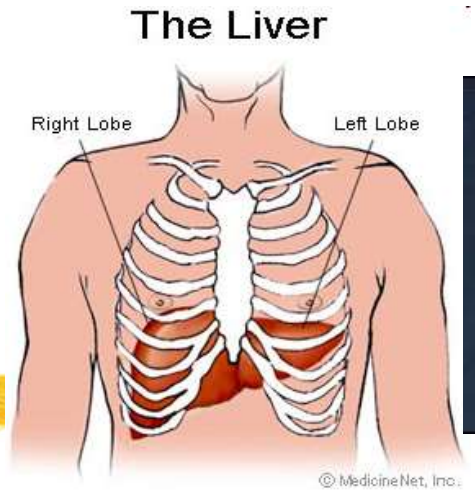
☺ Enzymes required for glycogen breakdown and synthesis, and their mechanisms

☺ Energetics of glycogen breakdown and synthesis

☺ Regulation of glycogen breakdown and synthesis (allosteric and covalent modification; cyclic cascades)

☺ How the liver regulates and maintains blood [glucose]

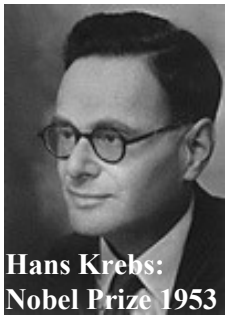
☺ Glycogen storage diseases



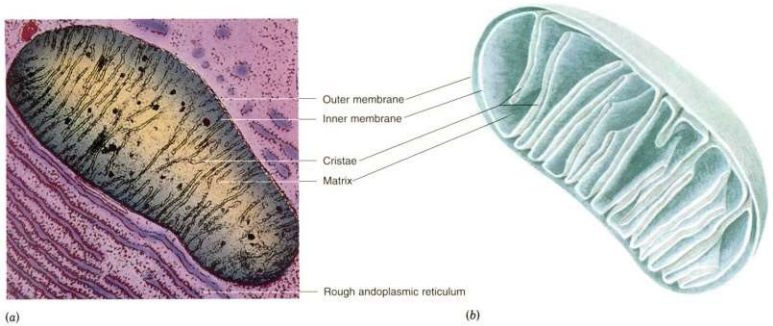
The Citric Acid Cycle

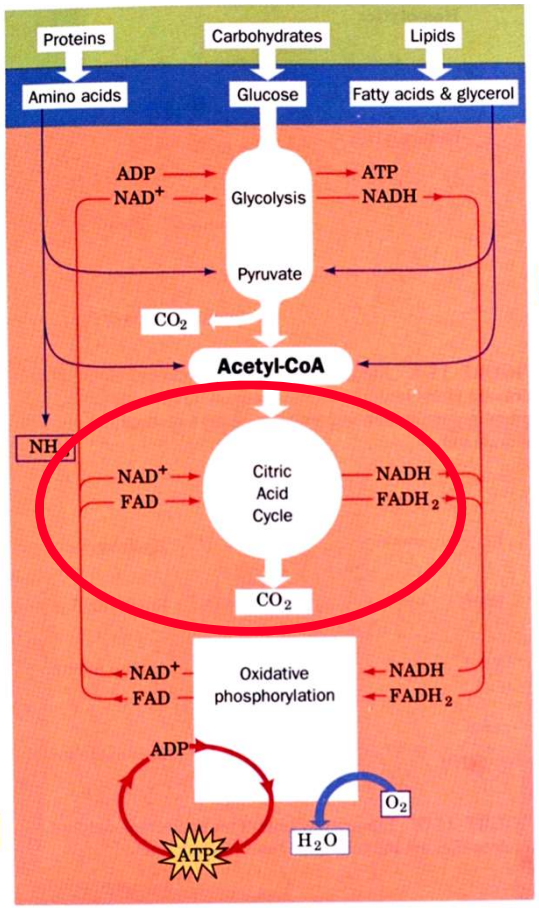
(also Tricarboxylic Acid or Krebs Cycle)

Voet & Voet, Chapter 21

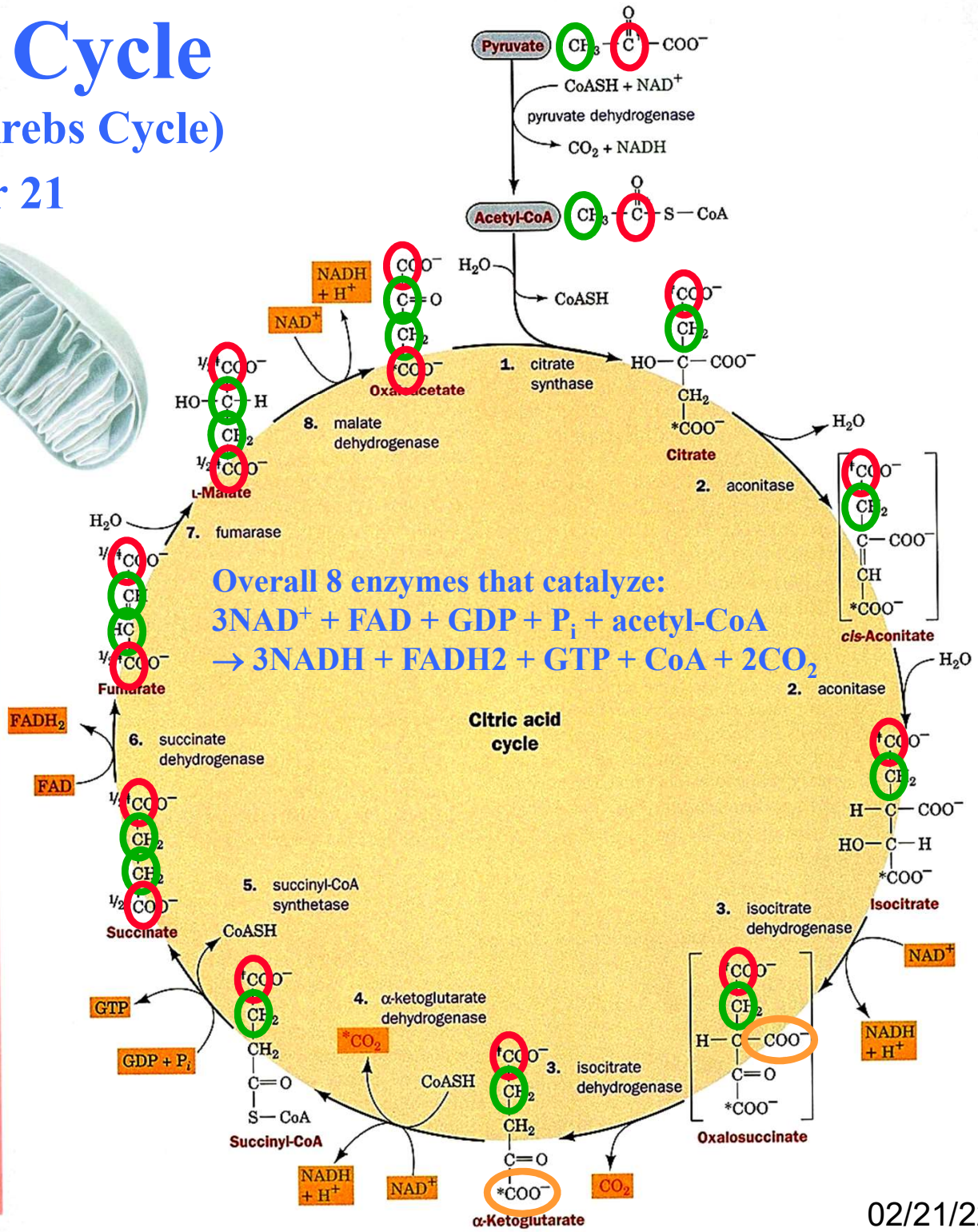


Hans Krebs:
Nobel Prize 1953

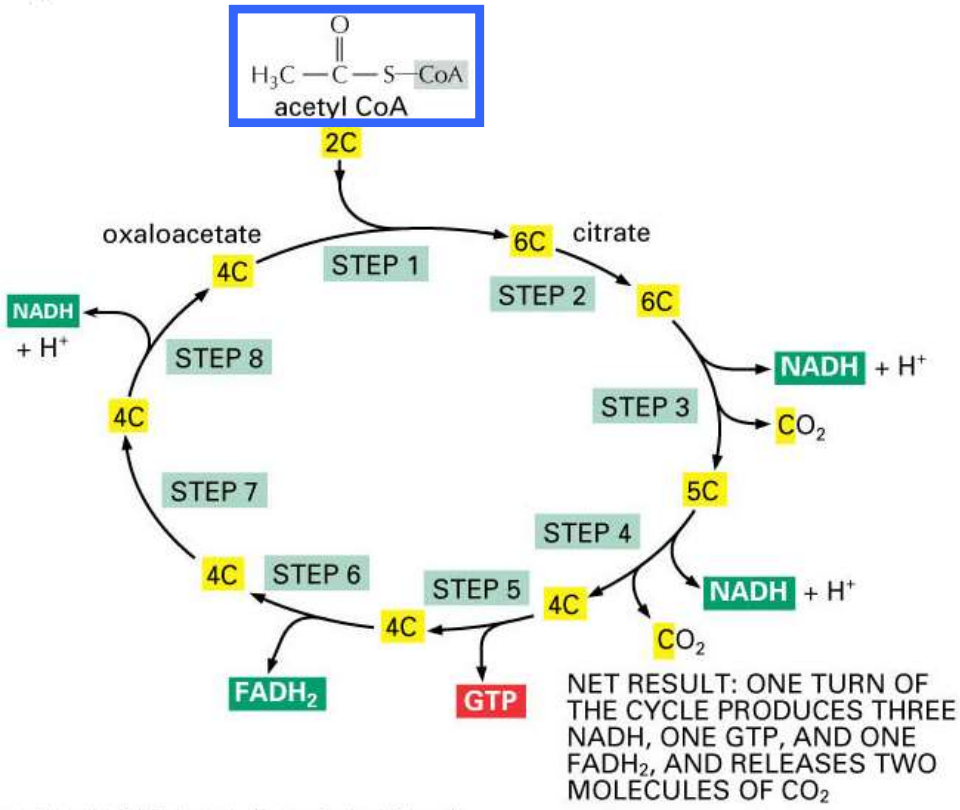


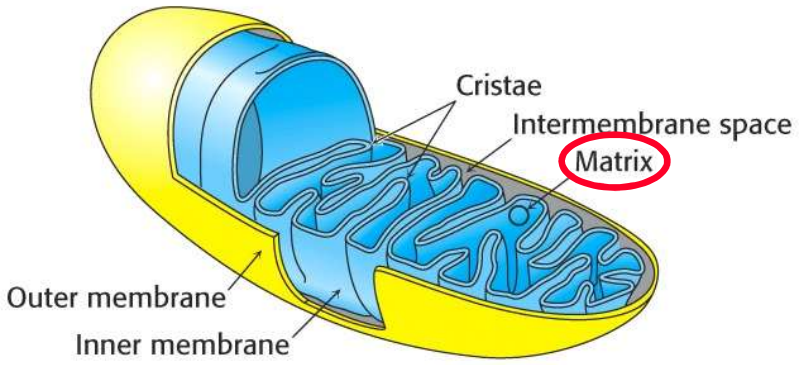


A central and "catalytic" cycle



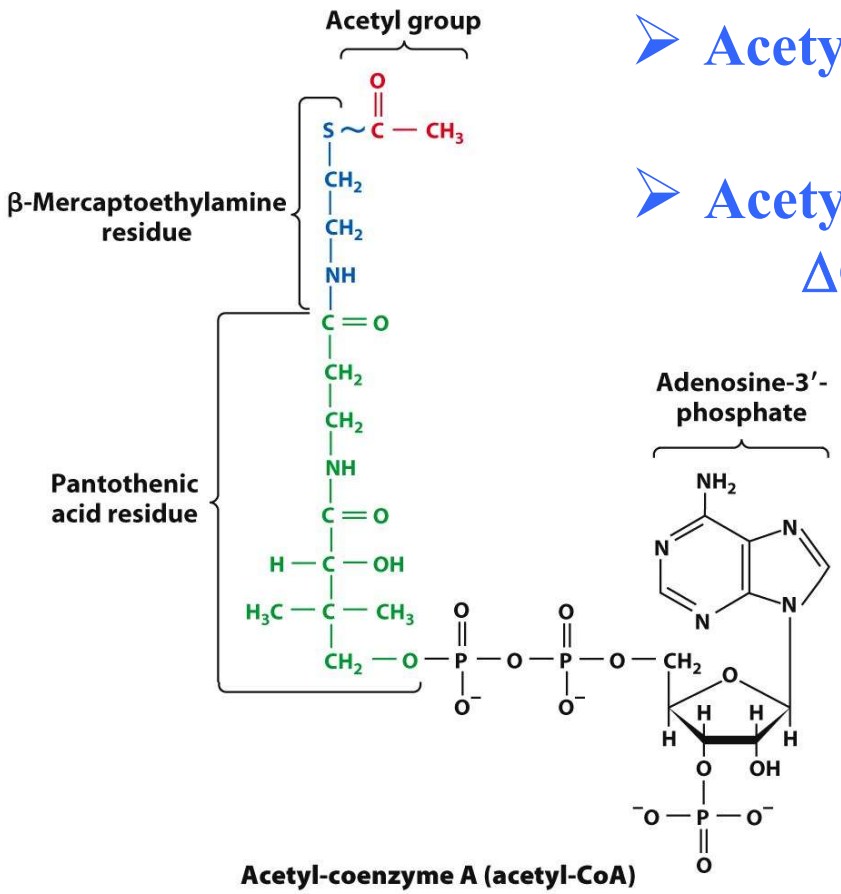
02/21/22



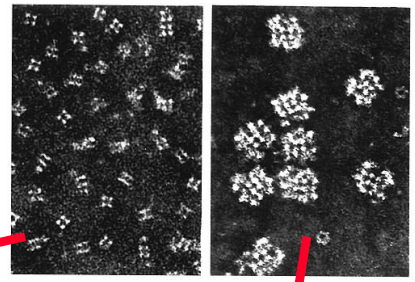


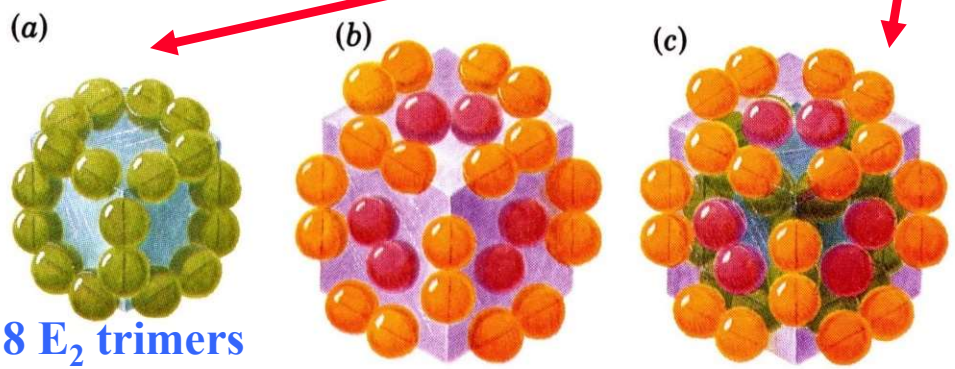
http://www.youtube.com/watch?v=hw5nWB0xN0Y

Acetyl-CoA and Where it is Made



- Acetyl-CoA = a common product of carbohydrate, fatty acid and amino acid breakdown
- Acetyl-CoA = a thioester as carrier of acetyl groups
  $\Delta G^{0'}$(hydrolysis) = -31.5 kJ/mol (> ATP!)
- Pyruvate dehydrogenase, a multienzyme complex (here: *E. coli*, eukaryotic even bigger)

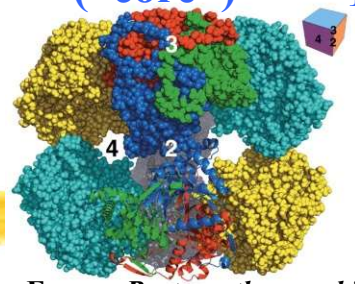




8 E_2 trimers ("core")

12 E_1 dimers, 6 E_3 dimers (outer shell)

Multienzyme complex

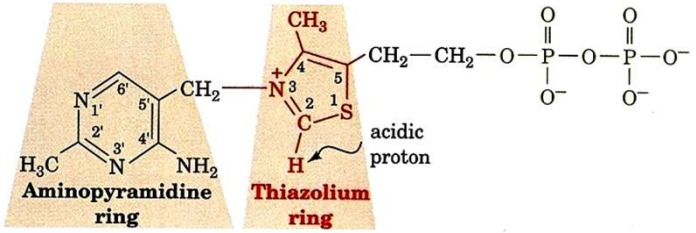


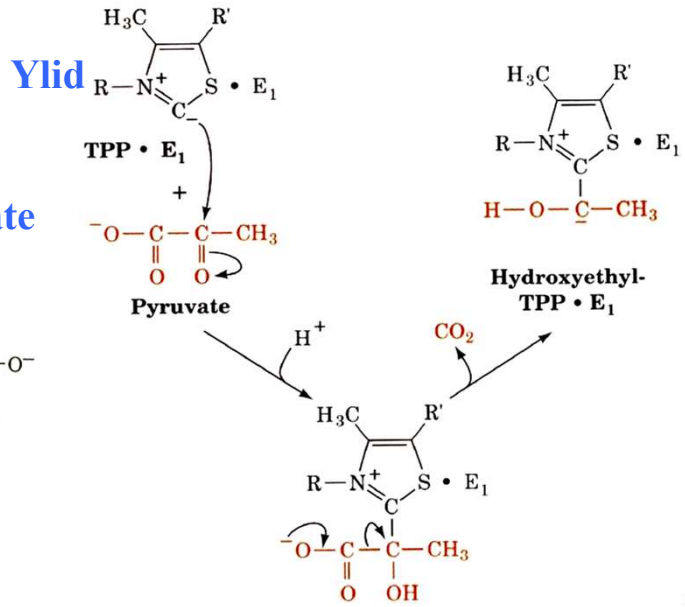
E_2 core *B. stearothermophilus*

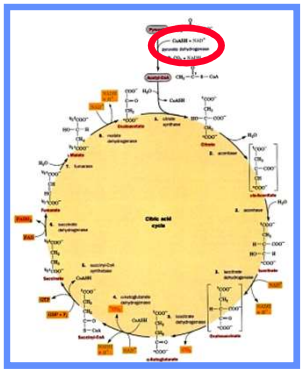
- **Advantages:**
  - Short diffusion distances ⇒ fast rates
  - Channeling ⇒ few side reactions
  - Coordinated control

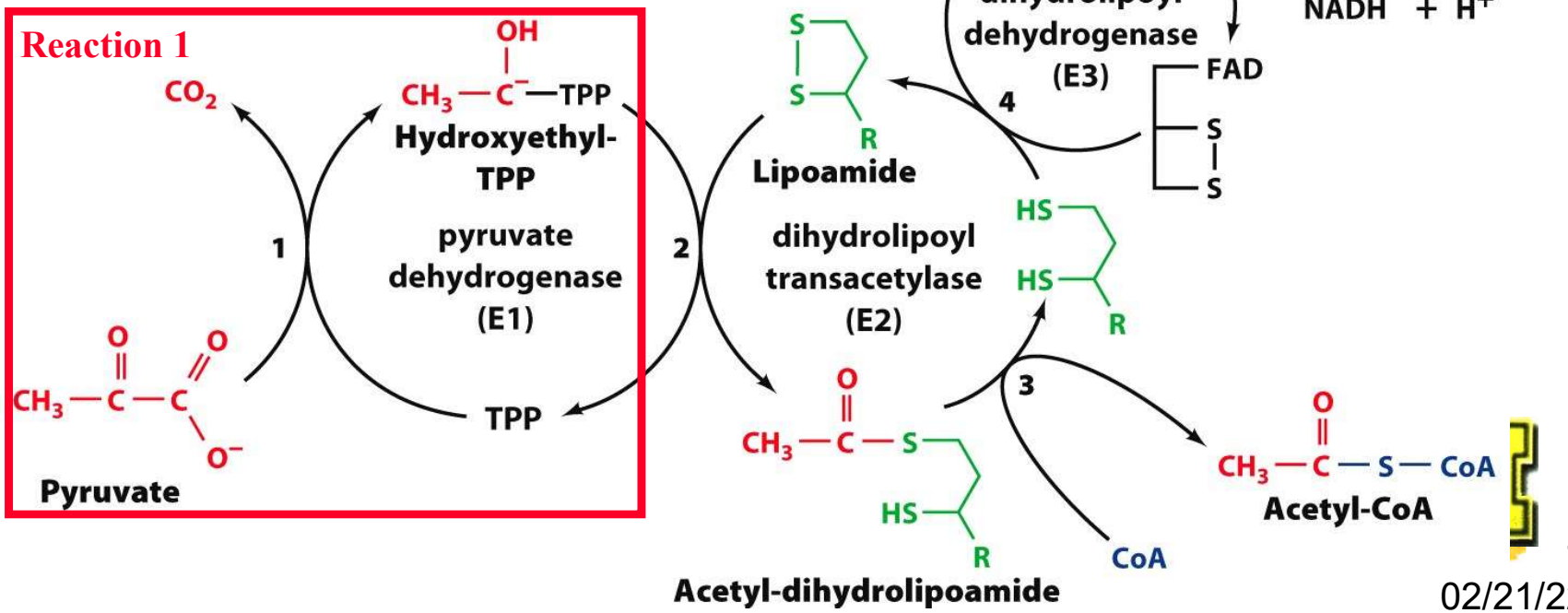
The 5 Reactions of the Pyruvate Dehydrogenase Multienzyme Complex

Thiamin pyrophosphate, also in pyruvate decarboxylase (alcoholic fermentation)

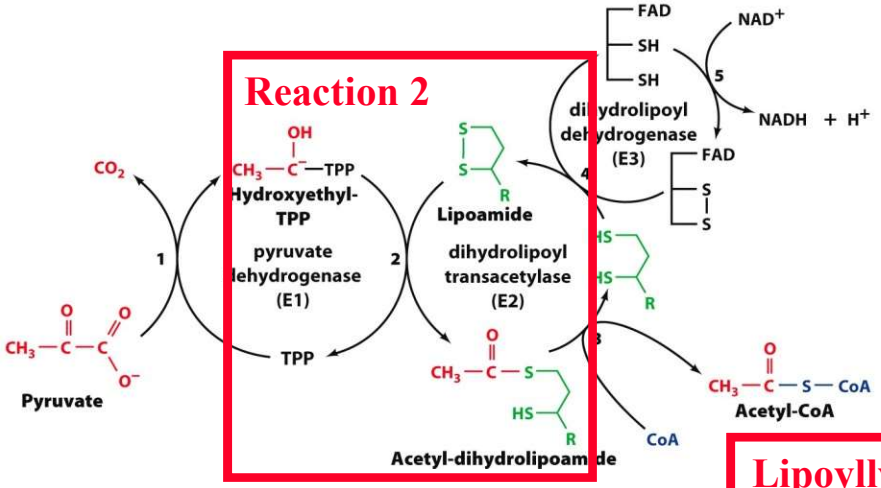


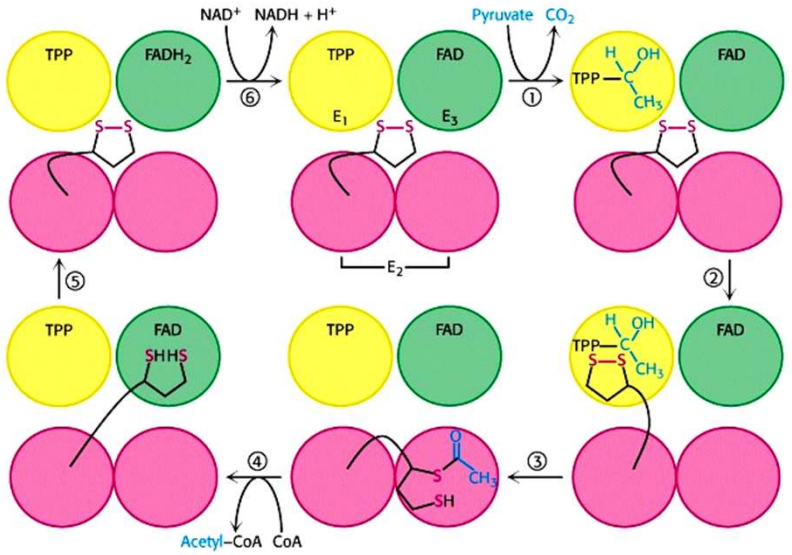






Pyruvate Dehydrogenase (E_1) transfers the Hydroxyethyl Group to Lipoamide on E_2





Lipoyllysyl: A flexible arm