

BI/CH 422/622

Announcements:

Its a Monday schedule today; OH are as they would be on Mon (4:30-5:30)

Getting vaccinated today: Wed lecture could be all remote on zoom; may not get recorded

Exam 1 is tomorrow in Morse at 7:00 pm

OUTLINE:

Glycogenolysis

Glycolysis

Introduction & overview; 2 phases

Phase I

Phase II

Summary: logic, energetics, labeling studies

Other sugars

Pasteur: Anaerobic vs Aerobic

Fermentations

Lactate-lactate dehydrogenase

Ethanol-pyruvate decarboxylase & alcohol dehydrogenase

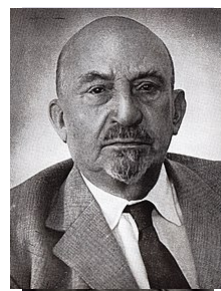
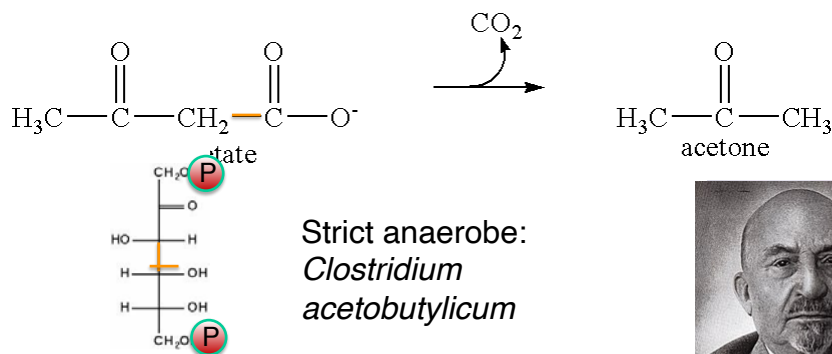
Acetoacetate decarboxylase

Exam-1 material

Pyruvate

pyruvate dehydrogenase

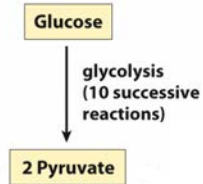
Fermentation: Acetoacetate decarboxylase



In 1916, the enzyme, *acetoacetate decarboxylase*, was discovered by Chaim Weizmann..... on to serendipity!

Dr. Kornberg: Lecture 02.01.17 (33:24-48:02)-Weizmann (15 min)

Fates of Pyruvate

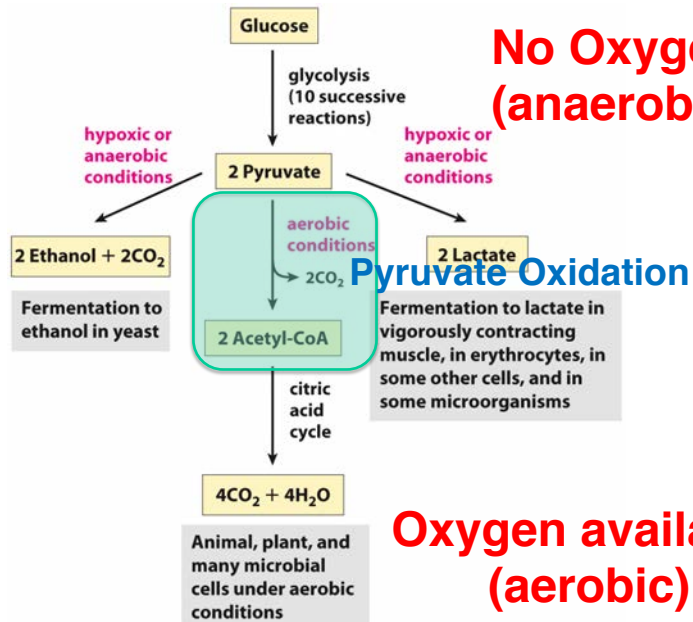


**No Oxygen
(anaerobic)**

Pyruvate Oxidation

**Oxygen available
(aerobic)**

Fates of Pyruvate



**No Oxygen
(anaerobic)**

Pyruvate Oxidation

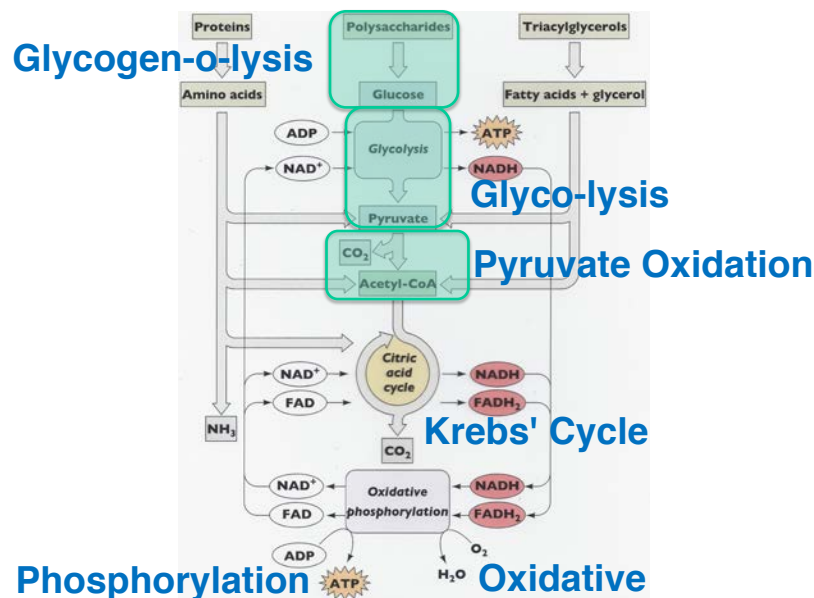
**Oxygen available
(aerobic)**

Pyruvate Oxidation

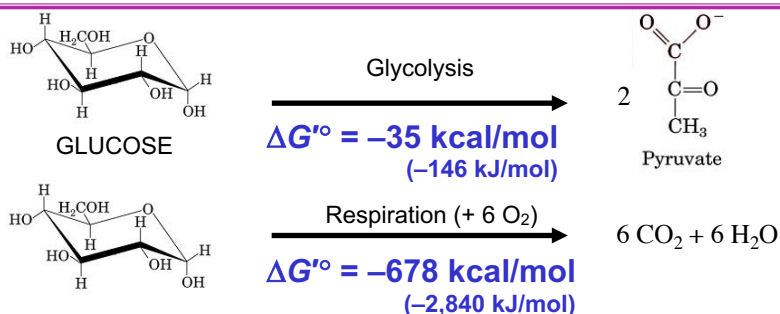
ONLY when O₂ is present

- This is why its called cellular respiration.
- The end result will be the COMPLETE oxidation of carbon to CO₂

Pyruvate Oxidation



Pyruvate Oxidation



Occurs in three major stages:

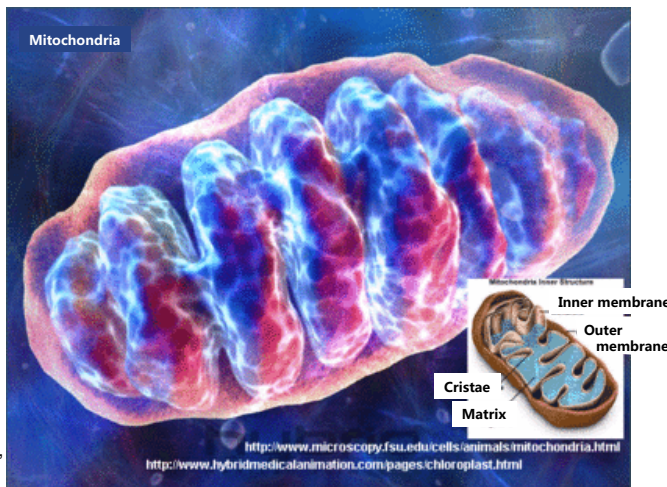
- Process in which cells consume O₂ and produce CO₂
- Provides more energy (ATP) per glucose than glycolysis
- Process is slower than glycolysis
- Evolutionary origin: developed about 2,500 mya
- Used by animals, plants, and many microorganisms
- Other fuel sources (lipids and AA) converge on respiration.

- 1) Pyruvate oxidation (acetyl CoA production)
- 2) acetyl CoA oxidation (CO₂ production)
- 3) electron transfer and oxidative phosphorylation (H₂O production)

Pyruvate Oxidation

Localization: In Eukaryotes, Respiration is Localized to the Mitochondria (Compartmentation)

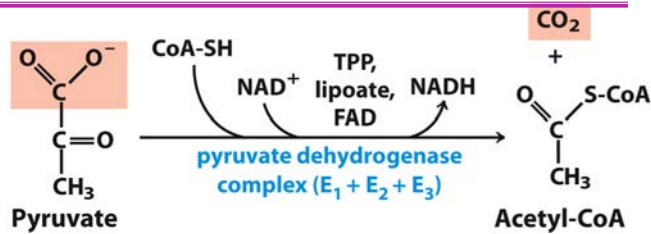
- Glycolysis occurs in the cytoplasm.
- Pyruvate Oxidation and Citric Acid Cycle occurs in the mitochondrial matrix.[†]
- Fantastic example of *Compartmentation*.
- Oxidative phosphorylation occurs in the inner membrane.



[†]Except succinate dehydrogenase, which is located in the inner membrane

Pyruvate Oxidation

Conversion of Pyruvate to Acetyl-CoA

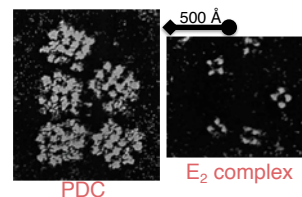


- Net reaction:
 - oxidative decarboxylation of pyruvate
 - Means pyruvate will get oxidized as the carboxylate leaves (as CO₂)
 - first carbons of glucose to be fully oxidized (C3 & C4)
- Fairly simple reaction done by a complicated process.
- Highly thermodynamically favorable/irreversible ($\Delta G^{\circ} = -8$ kcal/mol); mostly due to the loss of CO₂
- Catalyzed by the **Pyruvate Dehydrogenase Complex (PDC)**
 - Three main enzyme, each with multiple subunits: **E₁**, **E₂**, **E₃**
 - Regulatory subunits: PD kinase & PD phosphatase
 - Overall structure of **E₁₉₆**, **E₂₂₄**, **E₃₂₄**
 - requires 5 coenzymes
 - **TPP**, **lipoic acid**, and **FAD** are prosthetic groups.
 - **NAD⁺** and **CoA-SH** are co-substrates.

Pyruvate Oxidation

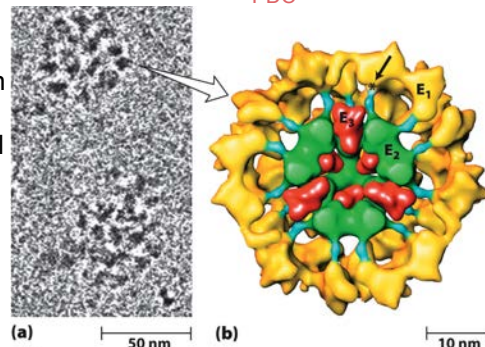
PDC is a large (up to **10 MDa**) multienzyme complex.

- **pyruvate dehydrogenase (E₁)**
- **dihydrolipoyl transacetylase (E₂)**
- **dihydrolipoyl dehydrogenase (E₃)**

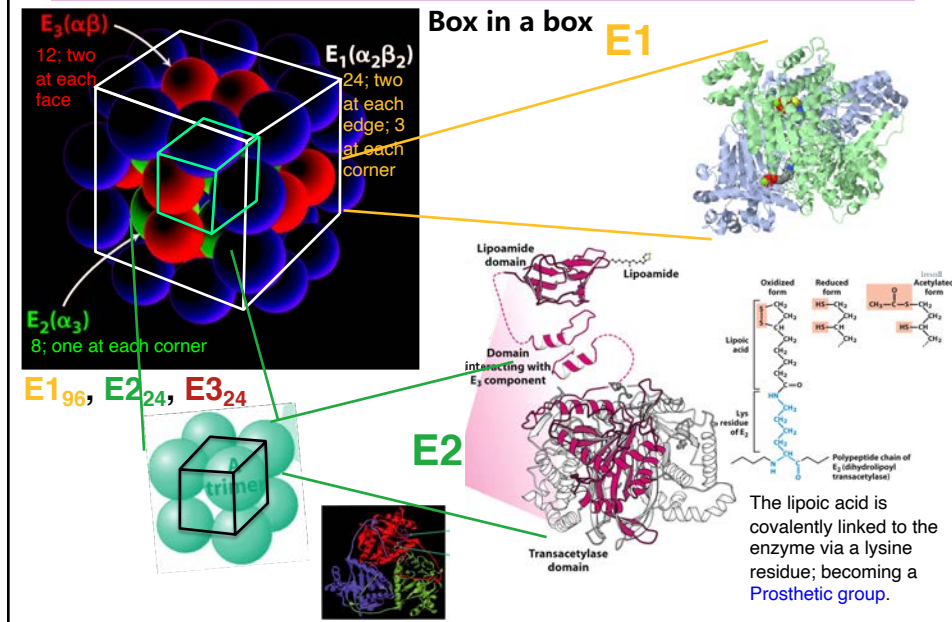


Cryoelectronmicroscopy

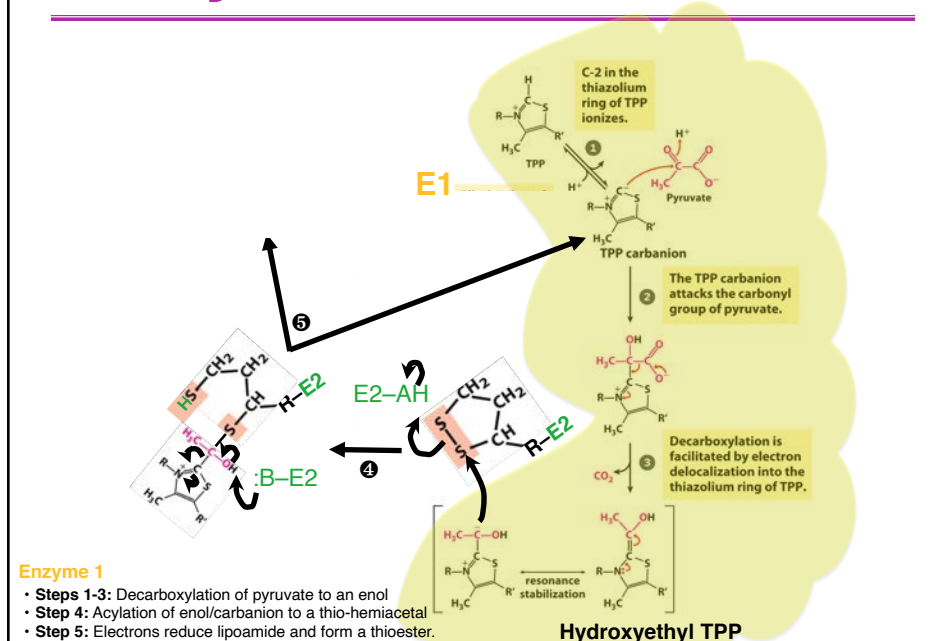
- Samples are in a near-native frozen hydrated state.
- Low **temperature** protects biological specimens against **radiation** damage.
- Electrons have a smaller wavelength and produce much **higher-resolution** images than light.
- No need for a crystal.



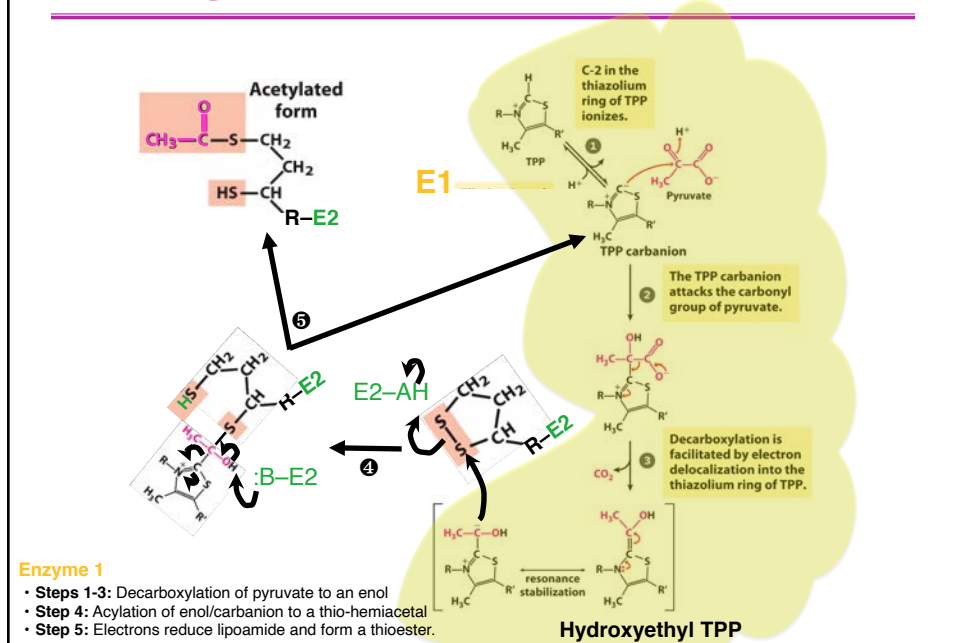
Pyruvate Oxidation



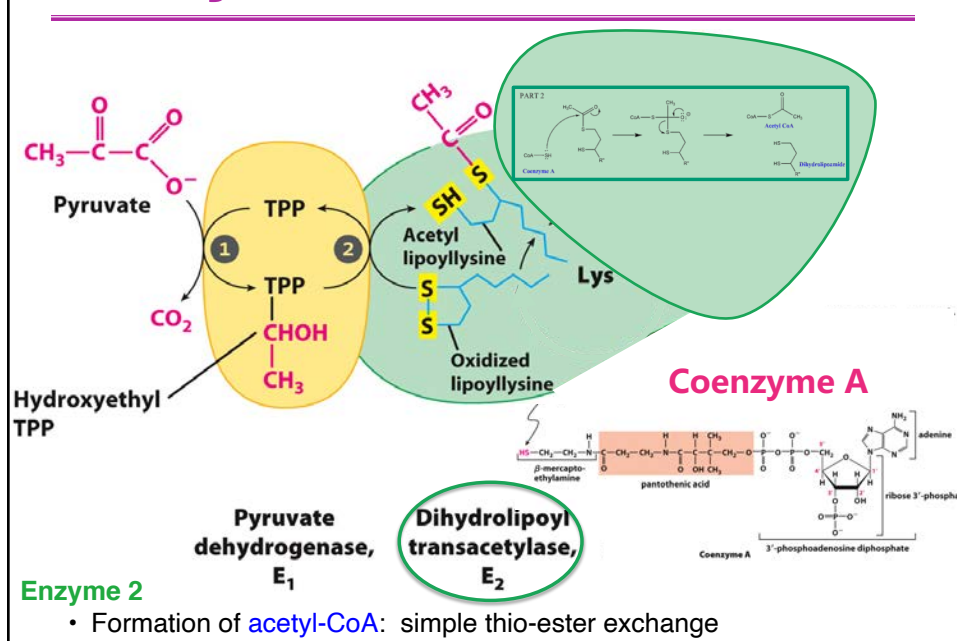
Pyruvate Oxidation



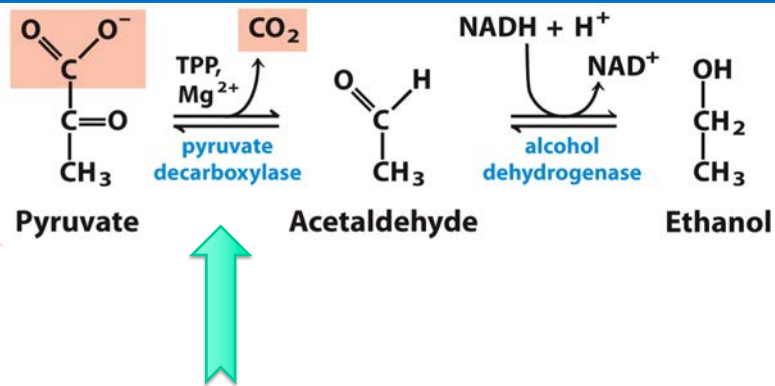
Pyruvate Oxidation



Pyruvate Oxidation



Fermentation: Ethanol



Humans are missing
the gene for this
enzyme.

Dr. Kornberg: Lecture
01.30.17 (30:56-34:08)
&
(45:37-46:10)
(4 min)