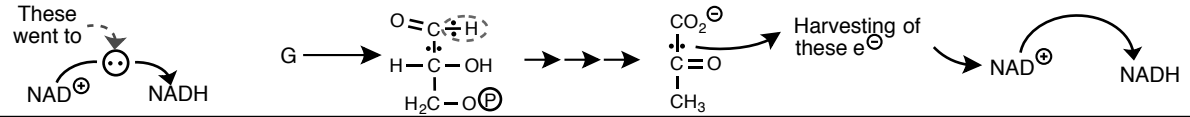
Think retro-synthetically



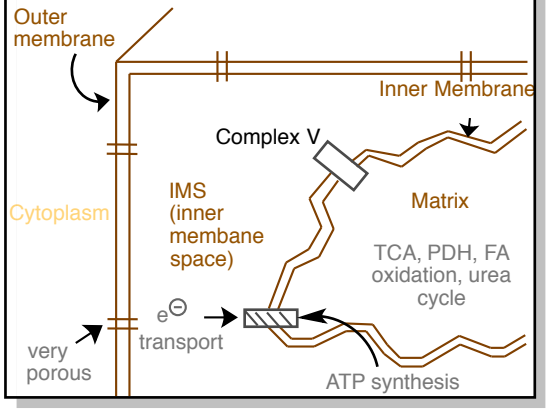

## A Respiration: Oxidative metabolism of all metabolic fuels (carbohyrates, fats) via Acetyl CoA

-- Mitochondrial reactions
-- Require $O_2$ (or another $e^{\ominus}$ acceptor)
-- We can metabolize carbohydrates anaerobically or aerobically
-- We can only metabolize lipids aerobically

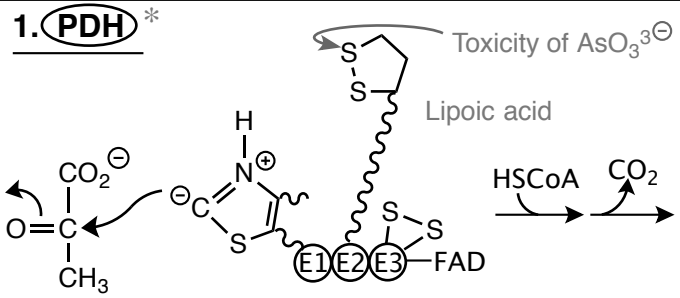
Stages:

1. PDH: P ⟶ AcCoA + NADH
2. TCA: AcCoA ⟶ $CO_2$ + ATP/GTP + NADH + $FADH_2$
3. Electron transport and oxidative phosphorylation } Oxidation of $FADH_2$ and NADH ⇨ Energy ⇨ ATP

### Introducing: The Mitochondrion




## B 1. PDH *

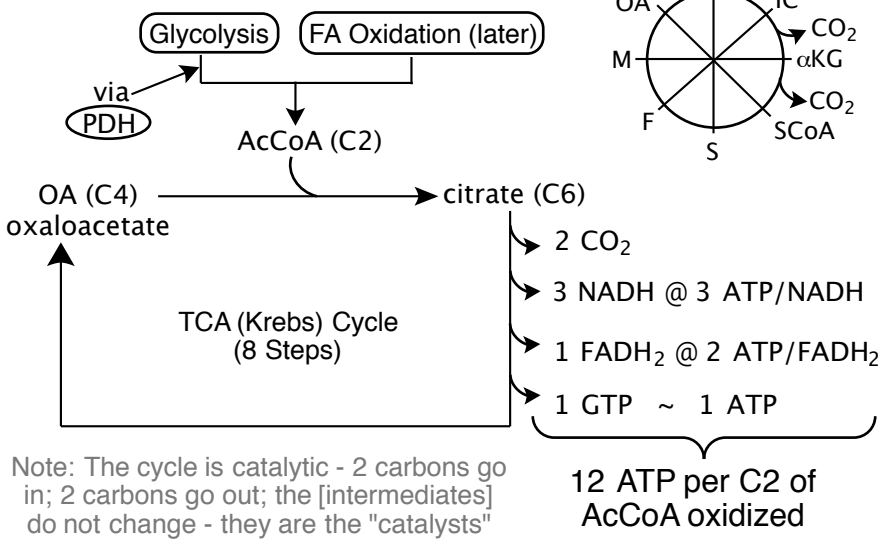



* Reaction mechanism is strikingly similar to αKGDH (below).

Basically, the pair of electrons move left to right across PDH (E1 E2 E3) and reduce FAD ⟶ $FADH_2$. Then, in a redox-challenged last step, $FADH_2$ gives its electrons to $NAD^{\oplus}$ to yield NADH. The NADH is oxidized by the electron transfer chain (later.)

## C 2. TCA Cycle - Overview

-- receives Acetyl CoA from PDH







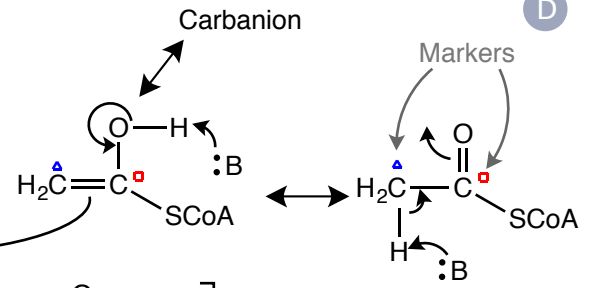
Note: The cycle is catalytic - 2 carbons go in; 2 carbons go out; the [intermediates] do not change - they are the "catalysts"

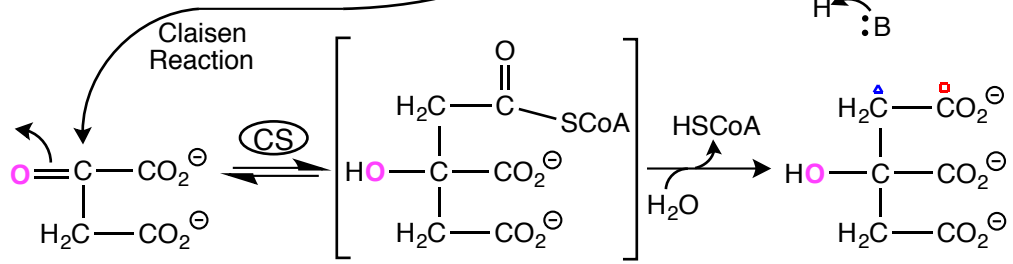
## The Chemistry

**Citrate Synthase**

CS is stereospecific. AcCoA attacks from top ($S_i$) face only. More detail on this later.

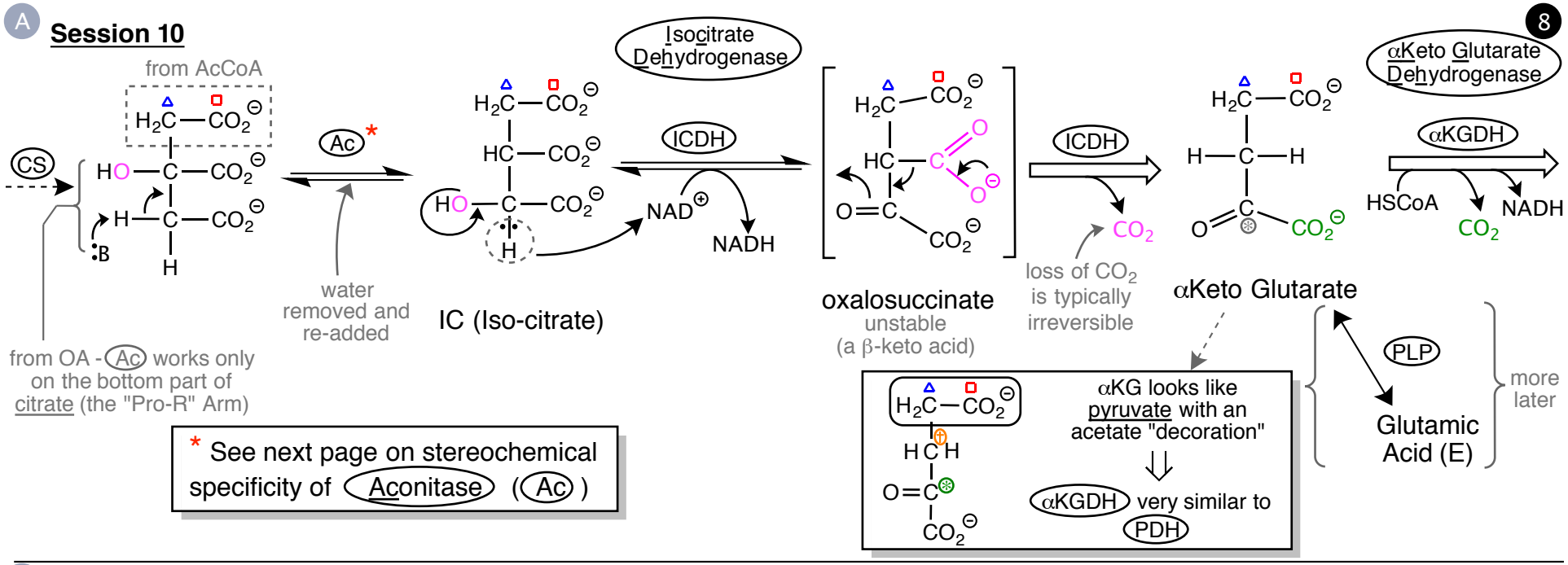
## D



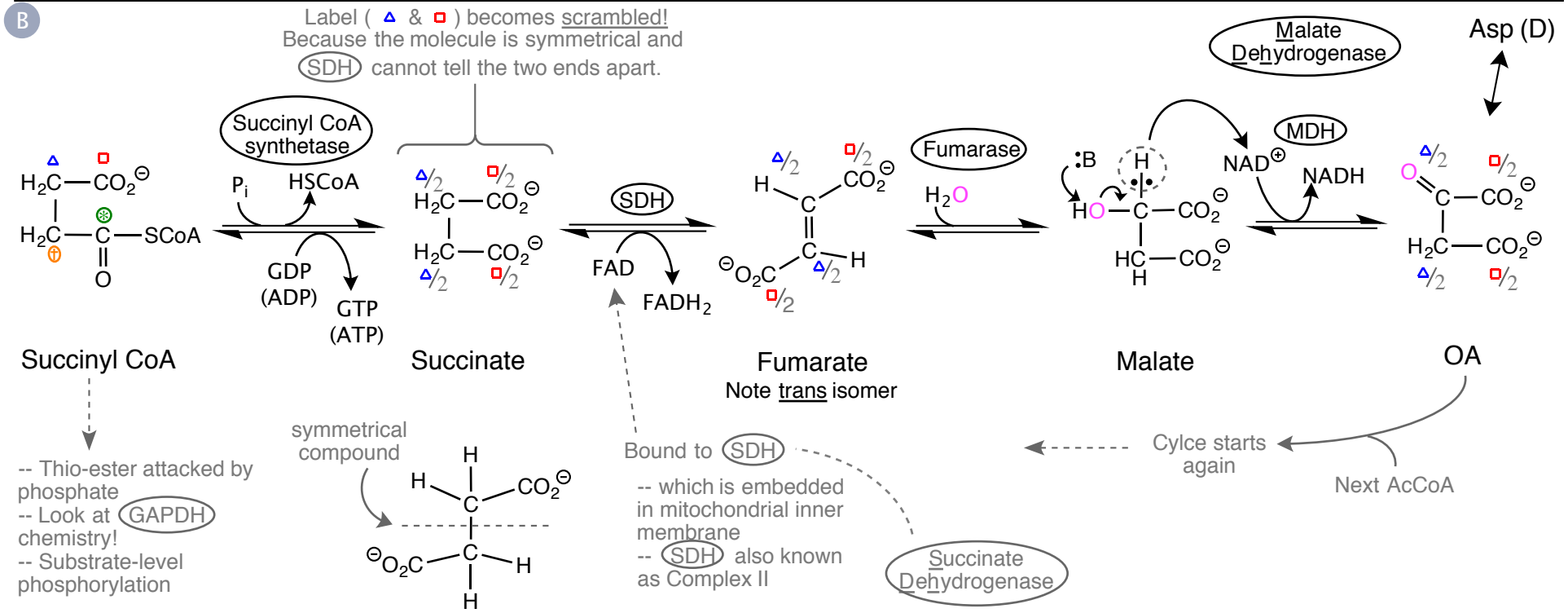



A

## Session 10



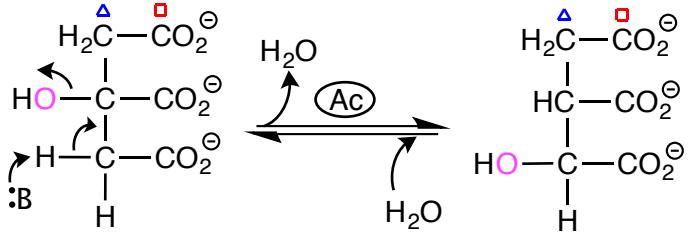

B



## Detail on Stereochemical Specificity of (Aconitase)

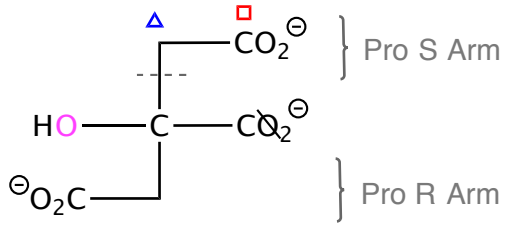
A

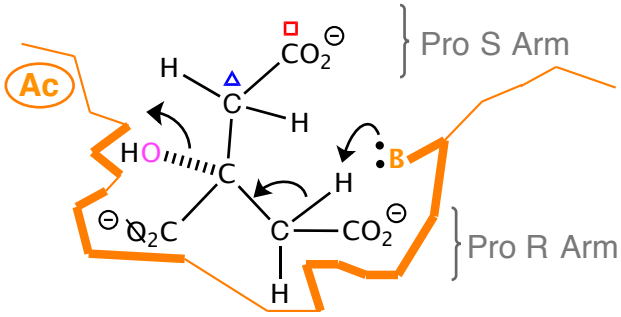
-- The hydroxyl group always moves to the ProR arm and never to the ProS, even though they are chemically identical, because (Ac) can distinguish the two arms (based on pro-chirality).




C (Citrate) IC (Iso-citrate)

B




-- The stereochemistry defined by (CS) generates only one isomer - where the -OH, $C\mathbb{O}_2^{\ominus}$ and $\wedge CO_2^{\ominus}$ fit in a specific way in three docking locations on (Ac).

-- The -OH, $C\mathbb{O}_2^{\ominus}$ and $\wedge CO_2^{\ominus}$ make contact with (Ac) at three sites.

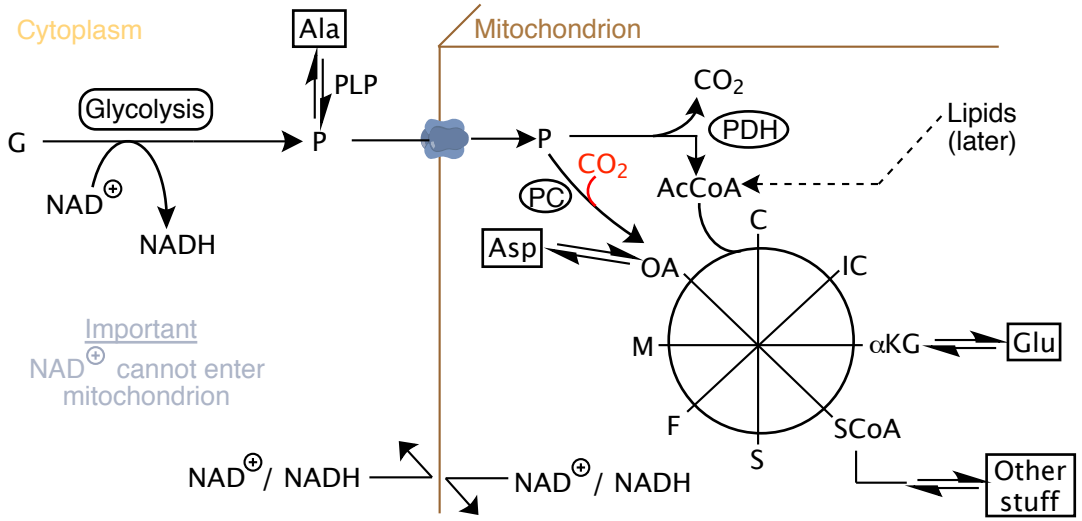
## Anapleurotic Pathways

-- We know three Pathways -- look at Interactions

-- Definition: anapleurotic ≡ "filling up"

-- Pathways that maintain catalytic amounts of TCA cycle intermediates

- Today we'll add more detail to this network
- Start with problem of how different life forms avoid running out of cytoplasmic $NAD^{\oplus}$



# 5.07SC Biological Chemistry I
Fall 2013