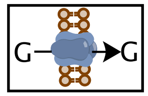
Session 9 & 10

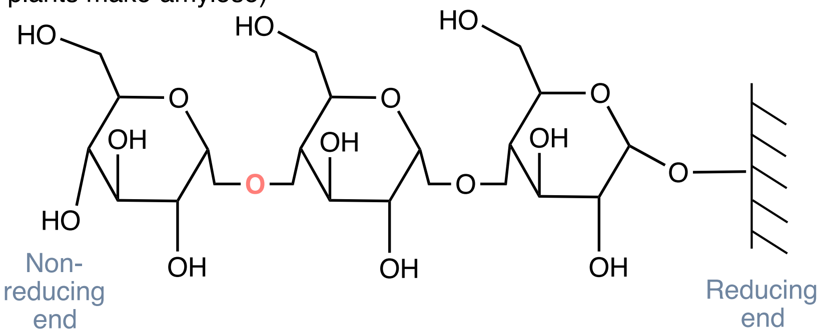
Carbohydrate Catabolism

A

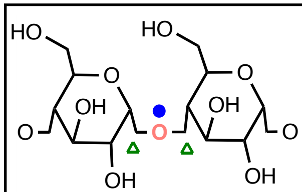
Two sources of glucose:

1.) G from blood via G transporter
2.) G as G1P from glycogen
(animals and bacteria make glycogen, plants make amylose)

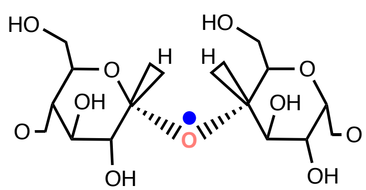




Glycogen (n units of glucose)



The △'s are not carbons. This is a convention used to denote the following stereochemistry:

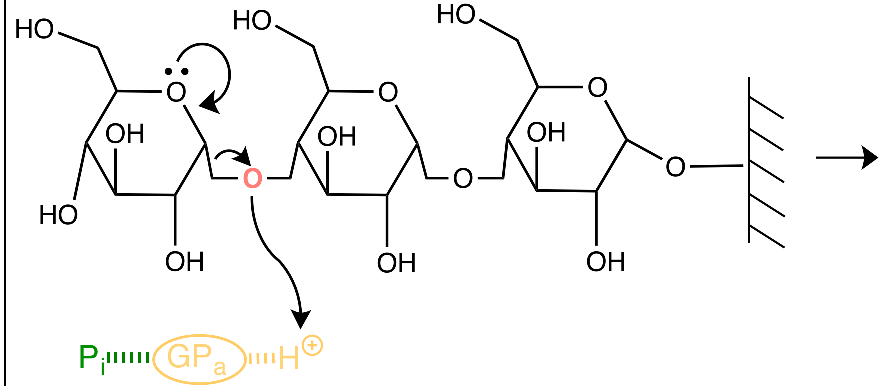


B

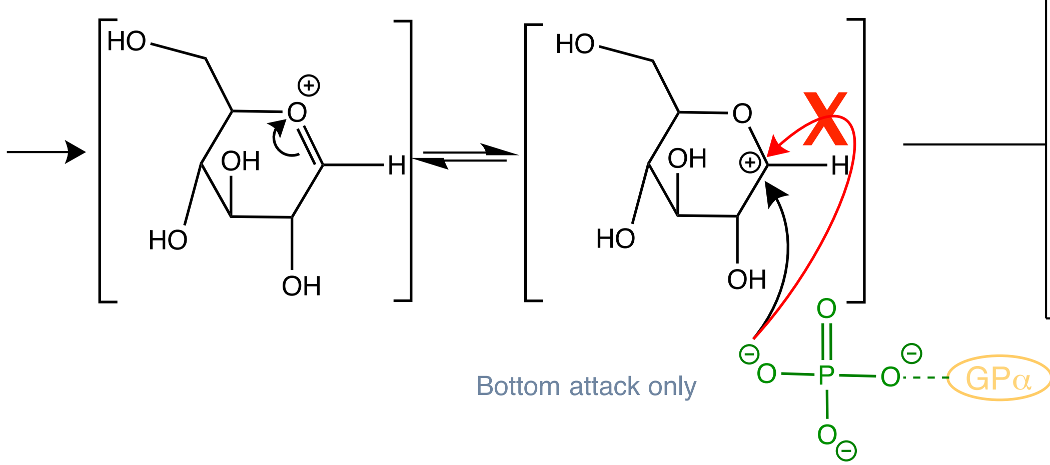
2

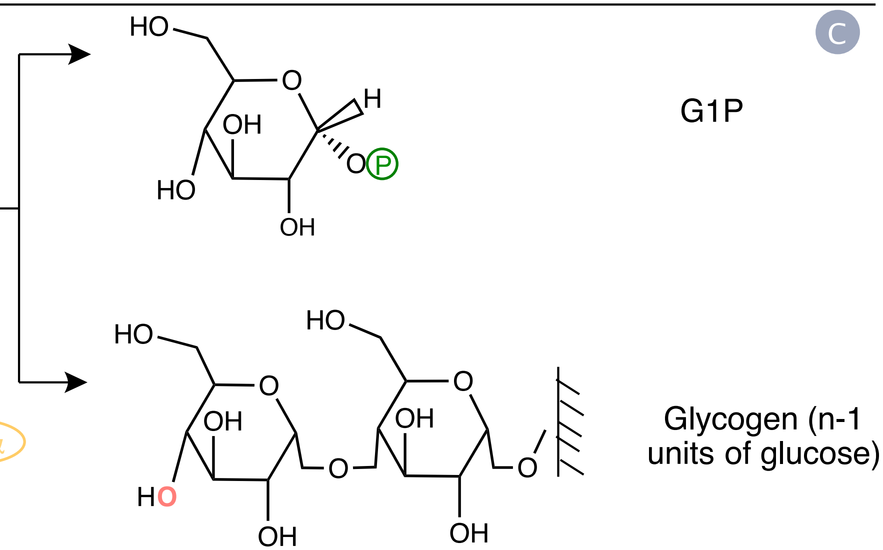
GP Mechanism

Glycogen = [glucose (α1 → 4) glucose] with some (α1 → 6) branches



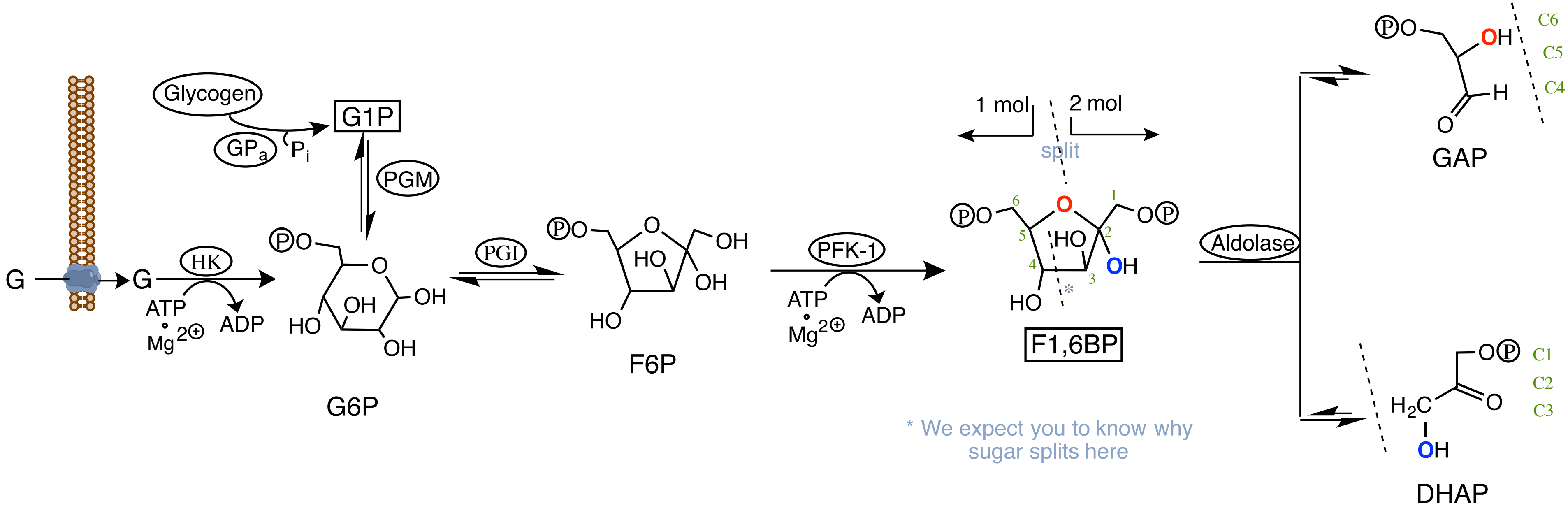
C



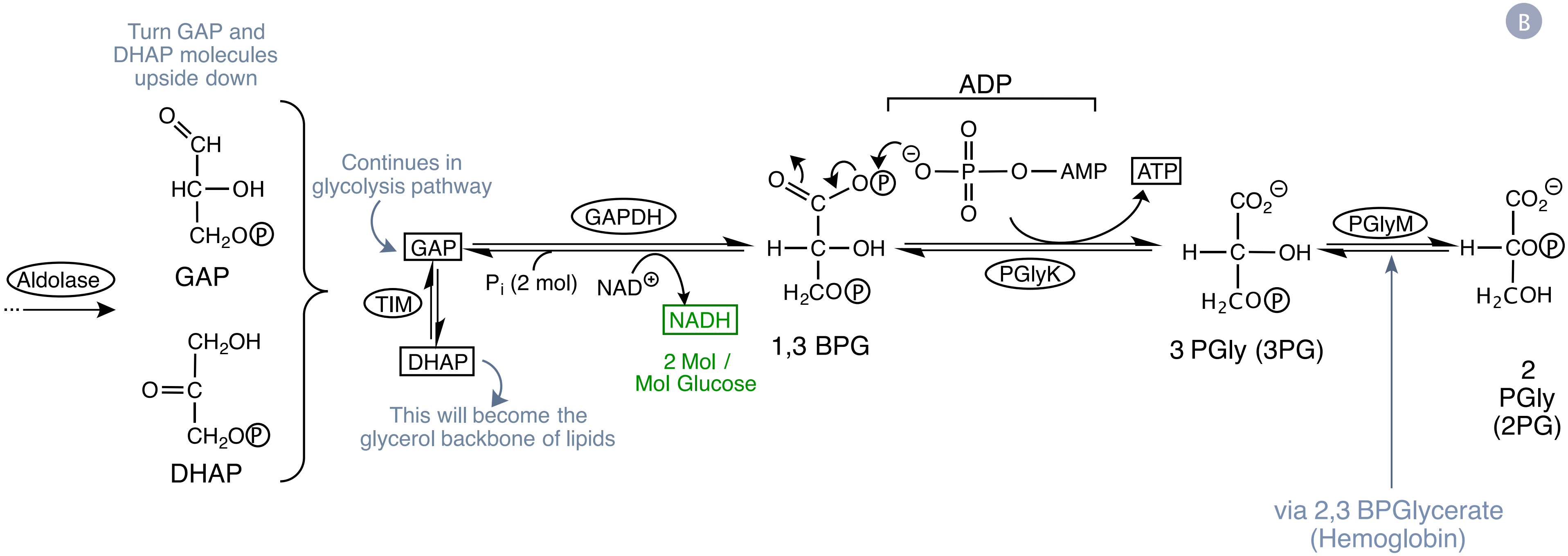


Glycolysis Details: The Classic Carbohydrate Catabolic Pathway

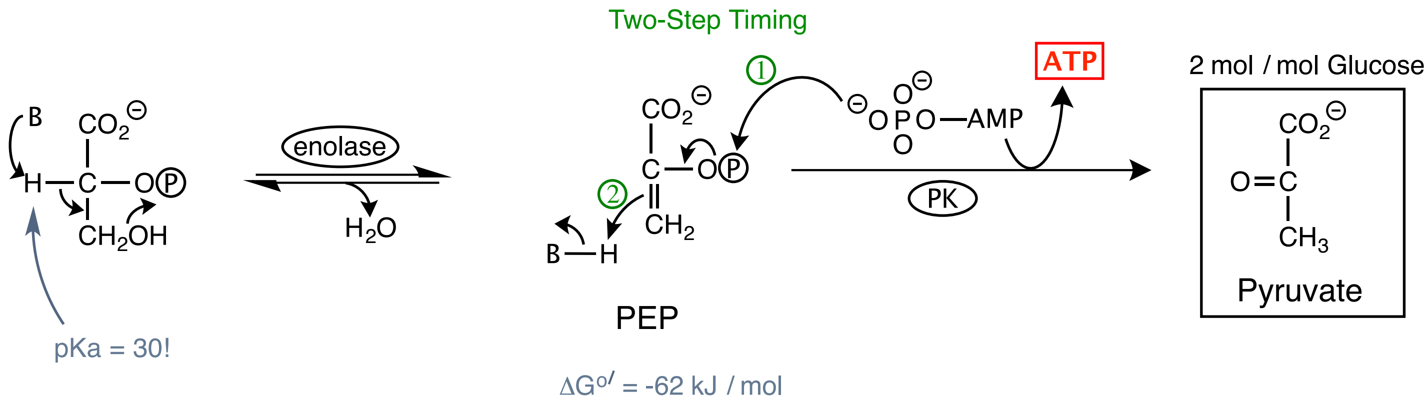
A 3



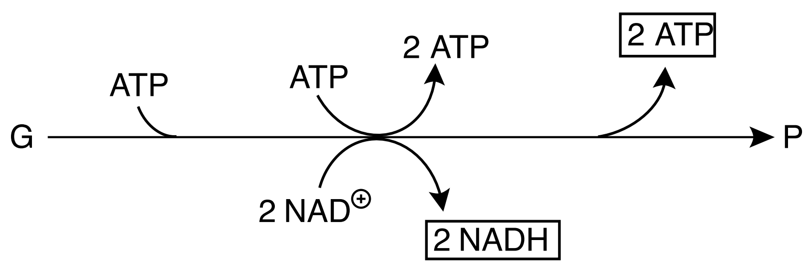
B



Glycolysis Details (continued)



Summary



-- note - we do not have a lot of $NAD^{\oplus}$
-- Needs to be regenerated
-- See notes on "shuttles"

A

Regulation

Glycolysis is regulated at the three irreversible steps:

1. HK
2. PFK-1
3. PK

} control is both allosteric and covalent (enzyme activity altered by covalent modification)

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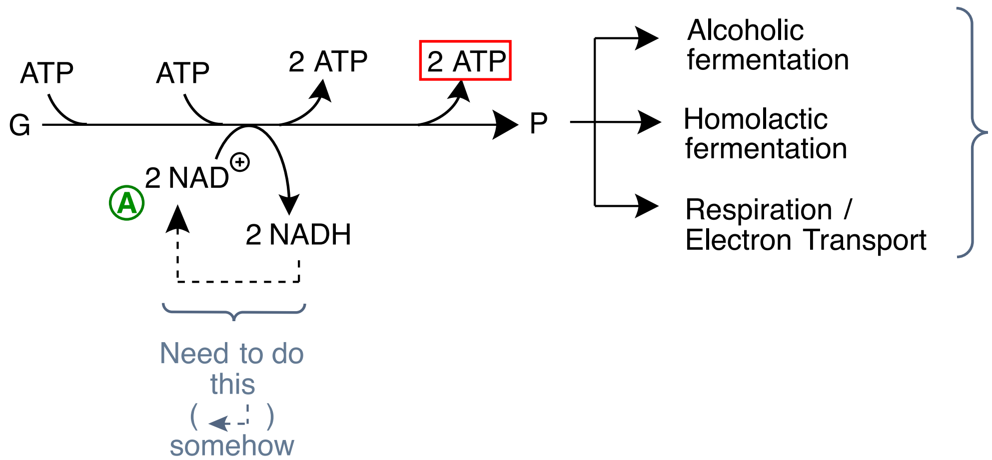
4. As well as GP, which is upstream of glycolysis.

B

5

Nature's problem:

If you do glycolysis as above, you get (2) ATP but you will run out of NAD$^{\oplus}$. Must regenerate it from NADH.

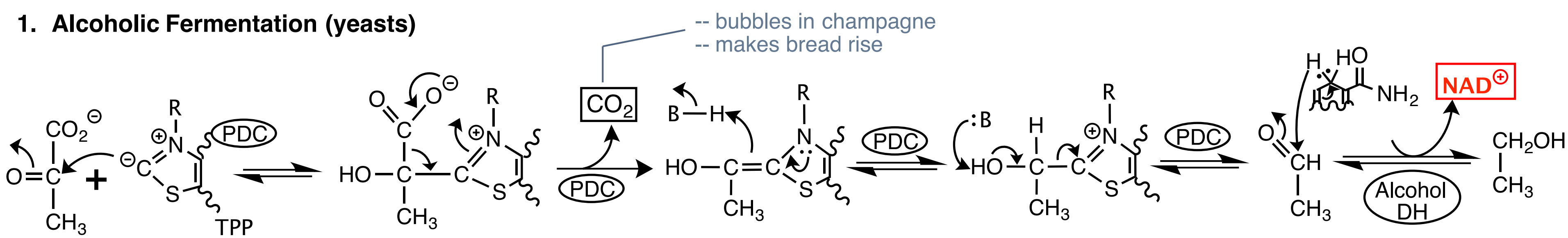


To regenerate NAD$^{\oplus}$, pyruvate must be processed by one of these three "endings of glycolysis." A lot of 5.07 will deal with the needs of the cell to achieve redox balance.

Three ways to achieve redox balance AFTER glycolysis

C

1. Alcoholic Fermentation (yeasts)



Pyruvate

(PDC) = Pyruvate decarboxylase

Acetaldehyde

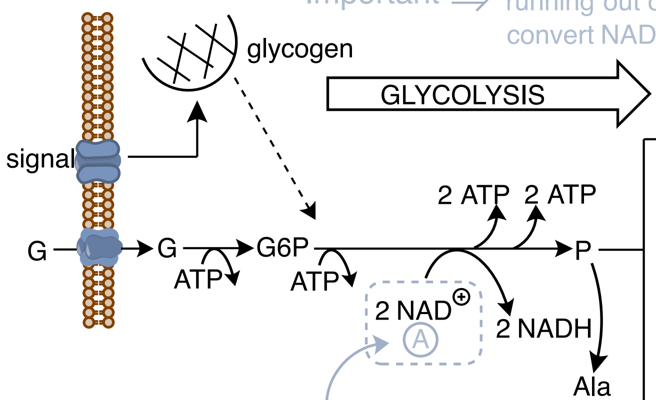
Ethanol

The NAD$^{\oplus}$ produced goes to (A) [previous panel] to keep overall process redox neutral.

Review

(A)

Important ⟹ These endings prevent cell from running out of $NAD^{\oplus}$. They convert NADH ⟿ $NAD^{\oplus}$.



Three Endings

1. Alcohol Fermentation (anaerobic)
2. Homolactic Fermentation (anaerobic)
3. Respiration:
   (a) PDH
   (b) TCA
   (c) ET/Ox Phos

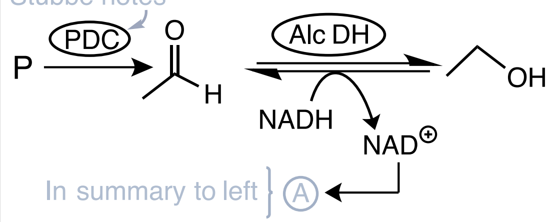
To make glycolysis continuous, cells must find a way to replace the $NAD^{\oplus}$ consumed here.

* Respiration is coupled with "shuttles" - later

(B) (1.) Alcohol Fermentation (anaerobic)

yeasts

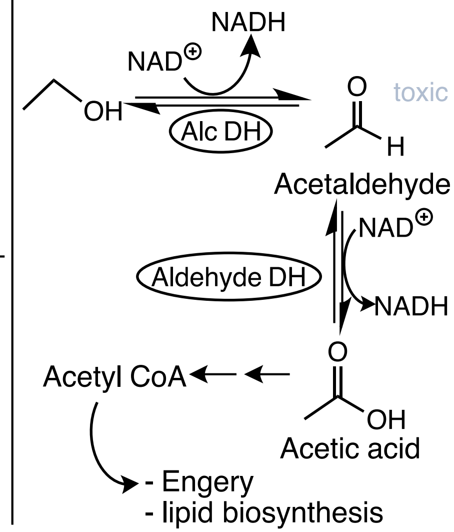
Refer to J. Stubbe notes



East Asians have an active (very) Alcohol Dehydrogenase, (Alc DH), but many have a relatively sluggish (Aldehyde DH). Hence they suffer from acetaldehyde toxicity (hangover) if they drink too much.

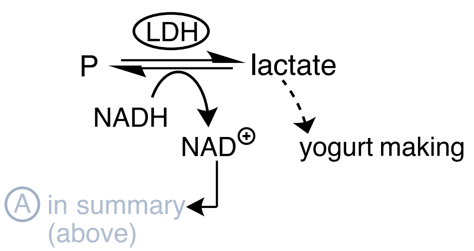
Relevant Digression (C) 6

Metabolism of ethanol in mammals (and yeasts)



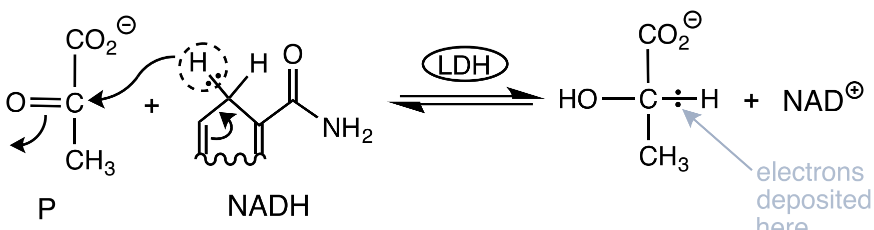
2. Homolactic Fermentation (anaerobic) (D)

lactic acid bacteria; animals



- While fermentations are anaerobic, they can occur in the presence of O_2 - they just do not use O_2

- They are electronically balanced (redox neutral)

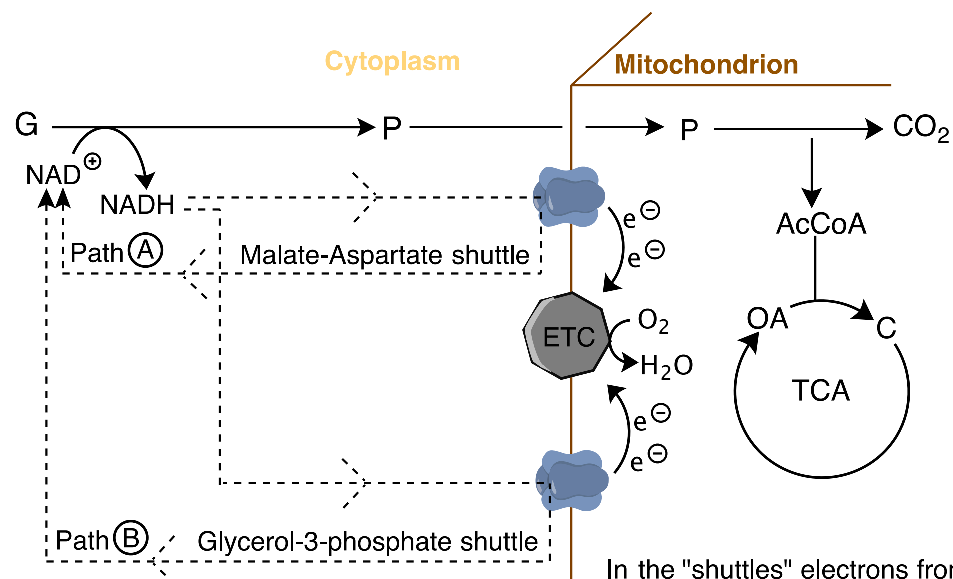


There is a similarity to path (B) to right

Animals working hard (anaerobically) do lactic acid fermentation. But the lactate from muscles can be re-built into glucose by process of gluconeogenesis in the liver. More on this later.

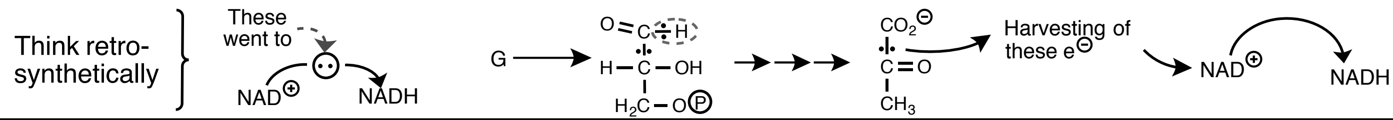
3. Respiration (E)

shuttles will be discussed after we do TCA cycle.



Electrons harvested in cytoplasm reduce oxygen in mitochondrion

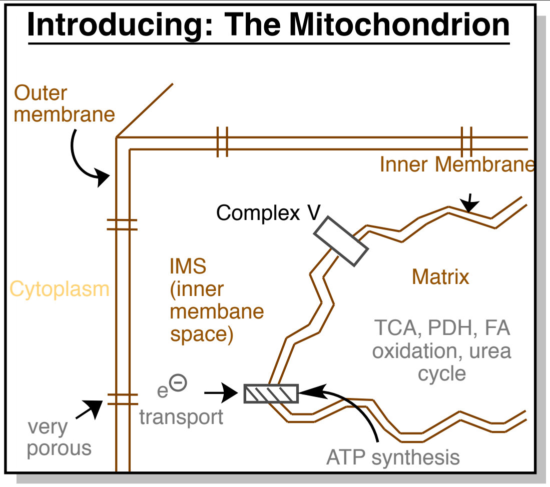
In the "shuttles" electrons from NADH are deposited into the mitochondrial electron transfer chain, ETC.



A Respiration:

Oxidative metabolism of all metabolic fuels (carbohyrates, fats) via Acetyl CoA

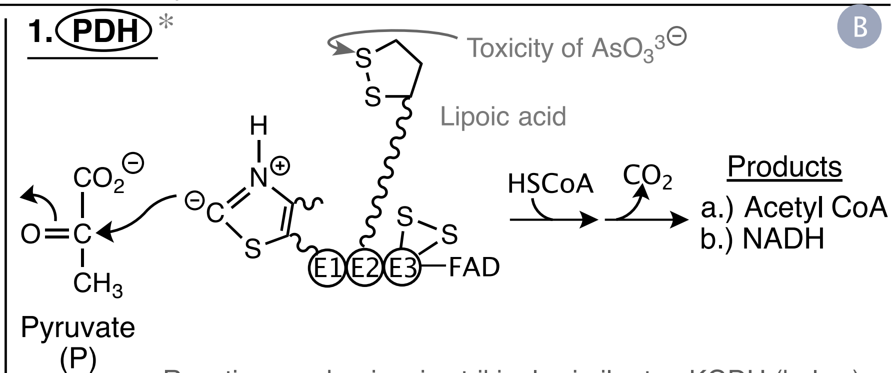
-- Mitochondrial reactions
-- Require O_2 (or another $e^{\ominus}$ acceptor)
-- We can metabolize carbohydrates anaerobically or aerobically
-- We can only metabolize lipids aerobically



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

B 1. PDH *

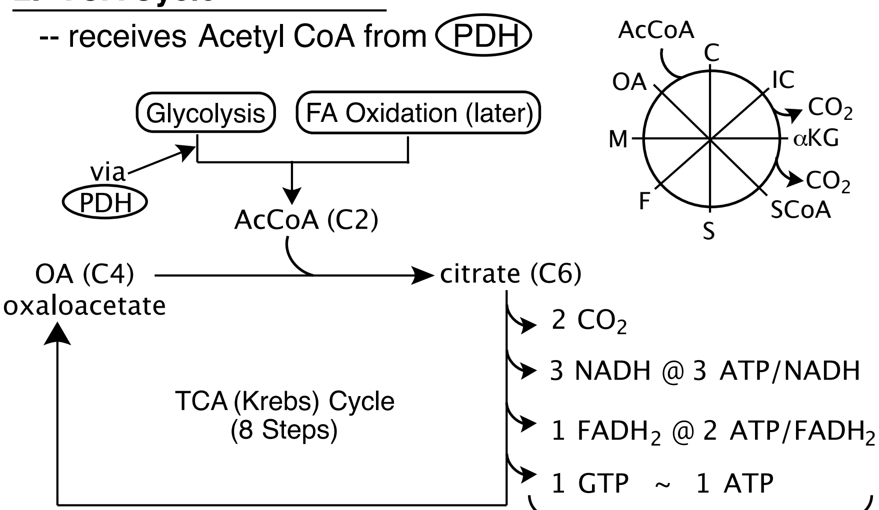


* Reaction mechanism is strikingly similar to αKGDH (below).

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



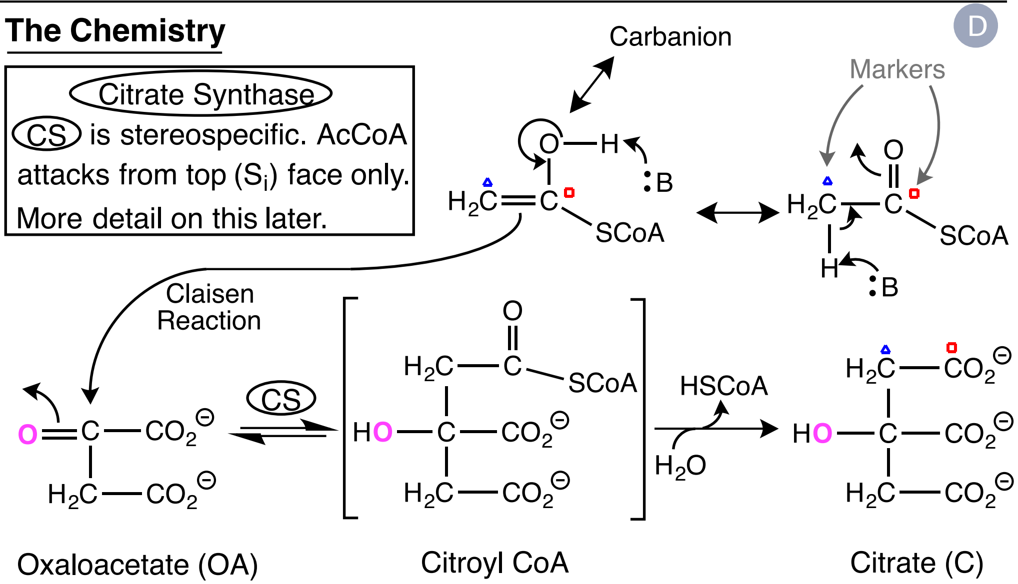
12 ATP per C2 of AcCoA oxidized

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

D The Chemistry

Citrate Synthase

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



One micro-molar concentation ⇨ very precious!

Unstable! $\Delta G^{o\prime}$ = -31 KJ/mol

5.07SC Biological Chemistry I
Fall 2013