Chem 30B Handout: Metabolism

Catabolism Flow Chart

FOOD

LIPIDS   CARBOHYDRATES   PROTEINS

Fatty Acids + Glycerols   Glucose + Other Sugars   Amino Acids

Fatty Acids   Amino Acid Catabolism

Pentose Phosphate Pathway

5-C sugars + NAPDH   Glucose 6-phosphate   Glycogenesis   Glycogen

β-oxidation

Glycolysis   2 NADH + 2 ATP

Glycolysis yields 2 pyruvates, so multiply everything below by 2x!

$$H_3C-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-O^-$$

Anaerobic → Lactate

Pyruvate   Aerobic

n NADH + n FADH$_2$

(n depends on carbon length of fatty acid)

CO_2 NADH

$$H_3C-\overset{\overset{O}{\|}}{C}-SCoA$$

Steroids

Ketone bodies

Acetyl-CoA   Protein metabolism

Citric Acid Cycle

1 ATP   2 CO_2

3 NADH, 1 FADH$_2$

O_2

Electron Transport Chain & Oxidative Phosphorylation

H_2O

11 ATP
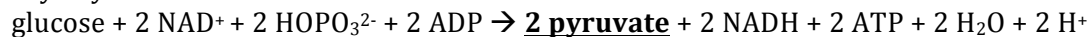(3 ATP/NADH + 2 ATP/FADH$_2$)

Glucose and Fatty Acid Catabolism

I. Glucose Catabolism

A. Steps of Glucose Catabolism

1. Glycolysis:

glucose + 2 NAD^+ + 2 $HOPO_3^{2-}$ + 2 ADP → **2 pyruvate** + 2 NADH + 2 ATP + 2 H_2O + 2 H^+

2. Pyruvate Oxidation:

2 pyruvate + 2 NAD^+ + 2 HSCoA → **2 Acetyl-CoA** + 2 CO_2 + 2 NADH + 2 H^+

3. Citric Acid Cycle:

2 Acetyl-CoA + 6 NAD^+ + 2 FAD + 2 ADP + 2 $HOPO_3^{2-}$ + 4 H_2O → 2 HSCoA + 6 NADH + 6 H^+ + 2 $FADH_2$ + 2 ATP + 4 CO_2
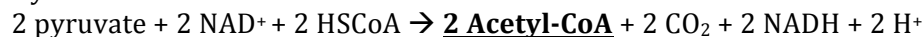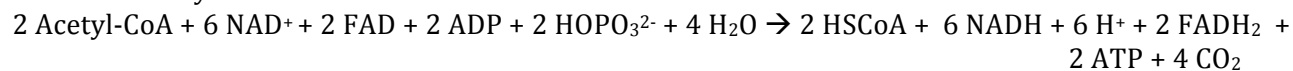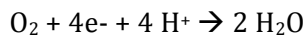
4. Electron Transport/Oxidative Phosphorylation:

Electrons from all the NADH and $FADH_2$ made in the previous steps are used to reduce O_2 to water:

O_2 + 4e- + 4 H^+ → 2 H_2O

The released energy is used to make ATP:

3 ATP made/1 NADH

2 ATP made/1 $FADH_2$

(More accurate: 2.5 ATP/NADH, 1.5 ATP/ $FADH_2$)

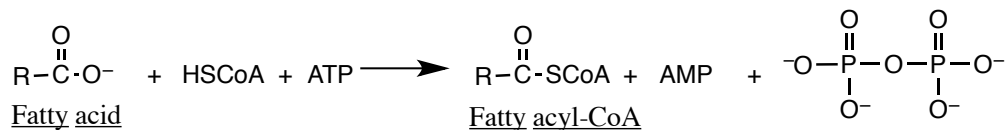### B. Total ATP Count for Catabolism of a Glucose Molecule

- Glycolysis: 2 ATP + 6 ATP (from 2 NADH) = 8 ATP
- Pyruvate oxidation: 6 ATP (from 2 NADH) = 6 ATP
- Citric Acid Cycle: 2 ATP + 18 ATP (from 6 NADH) + 4 ATP (from 2 $FADH_2$) = 24 ATP

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TOTAL: 38 ATP

II. Fatty Acid Catabolism

A. Steps of Fatty Acid Catabolism

1. Activation of fatty acid:

$$R-\overset{\overset{\displaystyle O}{\|}}{C}-O^- \;+\; HSCoA \;+\; ATP \longrightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-SCoA \;+\; AMP \;+\; {}^-O-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}-O-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}-O^-$$

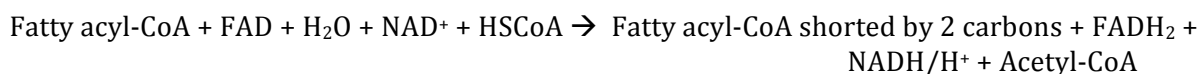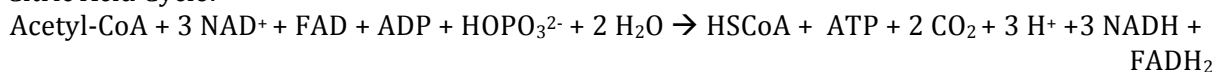Fatty acid   Fatty acyl-CoA

2. Trans-membrane transport of fatty acyl-CoA from cytosol into mitochondrial matrix

3. β-Oxidation of fatty acyl-CoA (Repeat for each 2-carbon unit EXCEPT for the last 2-carbon unit, since the last β-oxidation cleaves 4-carbon chain to give two acetyl-CoA molecules):

For each round of β-oxidation

    Fatty acyl-CoA + FAD + H_2O + NAD^+ + HSCoA → Fatty acyl-CoA shorted by 2 carbons + $FADH_2$ + $NADH/H^+$ + Acetyl-CoA

4. Citric Acid Cycle:
    Acetyl-CoA + 3 NAD^+ + FAD + ADP + $HOPO_3^{2-}$ + 2 H_2O → HSCoA + ATP + 2 CO_2 + 3 H^+ + 3 NADH + $FADH_2$

5. Electron Transport/Oxidative Phosphorylation: 3 ATP made/1 NADH, and 2 ATP made/1 $FADH_2$

B. Total ATP Count for Catabolism of a Fatty Acid Molecule

- **Activation**: −2 ATP [One-time loss for the whole fatty acid molecule]

- **β-Oxidation**:
  2 ATP (per $FADH_2$) + 3 ATP (per NADH) = 5 ATP/ β-oxidation round

$$\frac{5\ ATP}{1\ \beta-\text{oxidation } round} \times \text{No. of β-oxidation rounds} = \text{No. of ATP from all β-oxidation rounds}$$

    *Note: No. of β-oxidation rounds $= \dfrac{No.\,of\ carbon\ atoms\ in\ fatty\ acid}{2} - 1$

- **Citric acid cycle**:
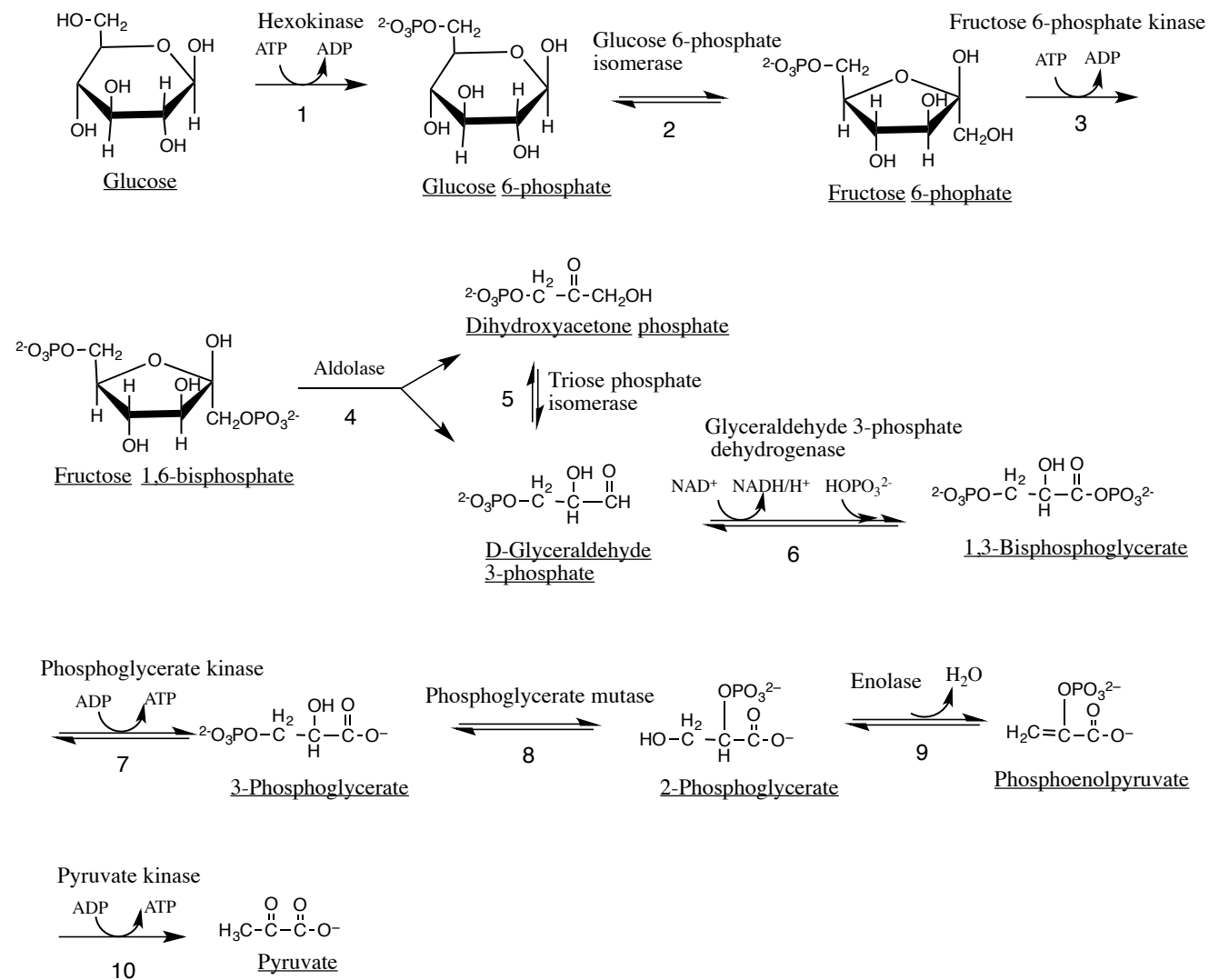 No. of carbon atoms in fatty acid/2 = No. of acetyl-CoA

$$\frac{12\ ATP}{1\ acetyl-CoA} \times \text{No. of acetyl-CoA} = \text{No. of ATP from all acetyl-CoA}$$

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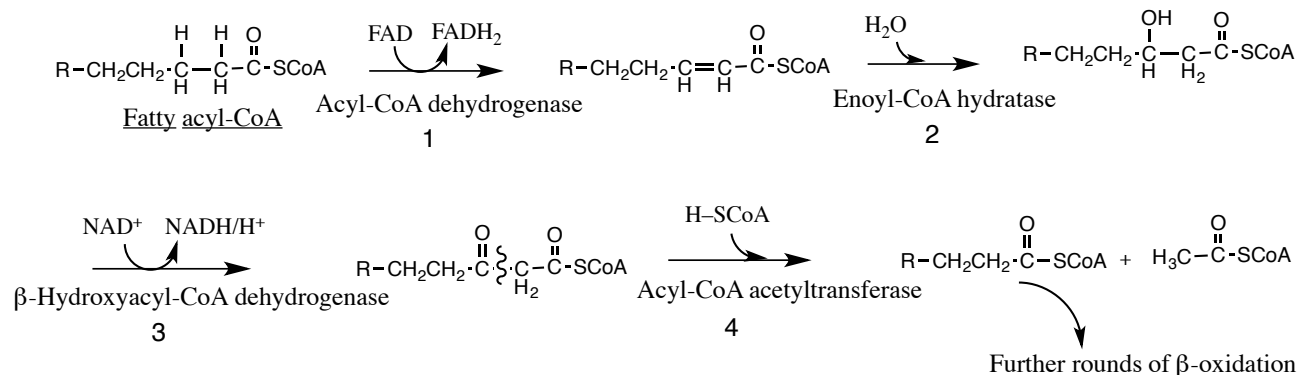**TOTAL**: Net ATP from three steps above.

Three Metabolic Pathways

I. Glycolysis

HO-CH$_2$ ... Glucose

Hexokinase

ATP ADP

1

$^{2-}$O$_3$PO-CH$_2$ ... Glucose 6-phosphate

Glucose 6-phosphate isomerase

2

$^{2-}$O$_3$PO-CH$_2$ ... CH$_2$OH ... Fructose 6-phophate

Fructose 6-phosphate kinase

ATP ADP

3

Glucose — Glucose 6-phosphate — Fructose 6-phophate

$^{2-}$O$_3$PO-CH$_2$ ... OH ... CH$_2$OPO$_3$$^{2-}$

Fructose 1,6-bisphosphate

Aldolase

4

$^{2-}$O$_3$PO-C$\overset{H_2}{}$ -$\overset{O}{\underset{}{C}}$-CH$_2$OH

Dihydroxyacetone phosphate

5 Triose phosphate isomerase

$^{2-}$O$_3$PO-C$\overset{H_2}{}$ -$\overset{OH}{\underset{H}{C}}$-$\overset{O}{CH}$

D-Glyceraldehyde 3-phosphate

Glyceraldehyde 3-phosphate dehydrogenase

NAD$^+$ NADH/H$^+$ HOPO$_3$$^{2-}$

6

$^{2-}$O$_3$PO-C$\overset{H_2}{}$ -$\overset{OH}{\underset{H}{C}}$-$\overset{O}{C}$-OPO$_3$$^{2-}$

1,3-Bisphosphoglycerate

Phosphoglycerate kinase

ADP ATP

7

$^{2-}$O$_3$PO-C$\overset{H_2}{}$ -$\overset{OH}{\underset{H}{C}}$-$\overset{O}{C}$-O$^-$

3-Phosphoglycerate

Phosphoglycerate mutase

8

HO-C$\overset{H_2}{}$ -$\overset{OPO_3^{2-}}{\underset{H}{C}}$-$\overset{O}{C}$-O$^-$

2-Phosphoglycerate

Enolase H$_2$O

9

H$_2$C=$\overset{OPO_3^{2-}}{C}$-$\overset{O}{C}$-O$^-$

Phosphoenolpyruvate

Pyruvate kinase

ADP ATP

10

H$_3$C-$\overset{O}{C}$-$\overset{O}{C}$-O$^-$

Pyruvate

II. β-Oxidation of Fatty Acid

R-CH$_2$CH$_2$·$\overset{H}{\underset{H}{C}}$-$\overset{H}{\underset{H}{C}}$-$\overset{O}{C}$-SCoA

Fatty acyl-CoA

FAD FADH$_2$

Acyl-CoA dehydrogenase

1

R-CH$_2$CH$_2$·$\overset{H}{C}$=$\overset{H}{C}$-$\overset{O}{C}$-SCoA

H$_2$O

Enoyl-CoA hydratase

2

R-CH$_2$CH$_2$·$\overset{OH}{\underset{H}{C}}$-$\overset{O}{\underset{H_2}{C}}$-$\overset{O}{C}$-SCoA

NAD$^+$ NADH/H$^+$

β-Hydroxyacyl-CoA dehydrogenase

3

R-CH$_2$CH$_2$·$\overset{O}{C}$-$\overset{}{\underset{H_2}{C}}$-$\overset{O}{C}$-SCoA

H–SCoA

Acyl-CoA acetyltransferase

4

R-CH$_2$CH$_2$·$\overset{O}{C}$-SCoA + H$_3$C-$\overset{O}{C}$-SCoA

Further rounds of β-oxidation

III. Citric Acid Cycle

H. Kim for Chem 30B