Biochemical reactions in metabolic pathway

Today's class

- Biotransformation overview

- Some representative processes in metabolic pathways
  - Hydrolysis
  - Processing of simple organics
  - Citric acid cycle

Mineralization vs. Transformation

- Mineralization: conversion of organic compounds to inorganic end products

- Transformation: conversion occurred, but a portion still remains as organic

  ex) reductive dechlorination of trichloroethylene (TCE)

$$C_2HCl_3 + H_2 \rightarrow C_2H_2Cl_2 + H^+ + Cl^-$$

TCE — DCE (dichloroethylene)

Useful general rules of biotransformation

- Simple carbohydrates and amino acids are very biodegradable; fats and oils may be more difficult to degrade because of solubility limitations
- Hydrocarbons are more difficult to oxidize than alcohols, aldehydes, or acids. Aldehydes are generally more toxic than alcohols or acids. Unsaturated aliphatic compounds are more readily degraded than saturated aliphatics.
- Ketones are more difficult to degrade than aldehydes.
- Ethers are difficult to biodegrade.
- Tertiary and quaternary carbons and nitrogens are much more difficult to degrade than primary or secondary carbons or nitrogens. Quaternary nitrogen compounds are very toxic to bacteria.

(continued)

- Hydrolysis of esters, amides, and carbamates, among others, is generally fast and easily carried out by microorganisms.
- Adding a chlorine atom or a nitro group to a benzene ring increases its resistance to biodegradation and its toxicity.
- Meta substitution to a benzene ring generally makes it more difficult to degrade than to the ortho or the para positions.
- Polycyclic aromatic hydrocarbons (PAHs) with more than three rings are very resistant to biodegradation.

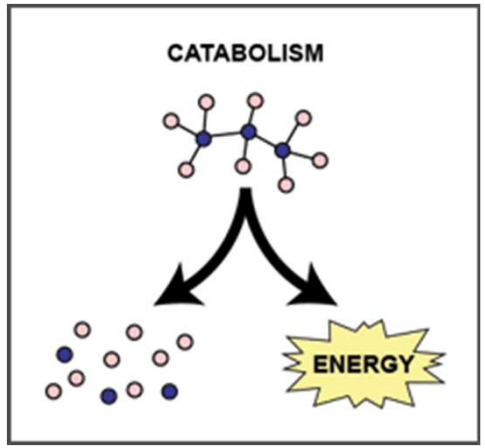
(ref: Sawyer, McCarty, and Parkin; Chemistry for Environmental Engineering and Science, 5th ed.; p. 323)

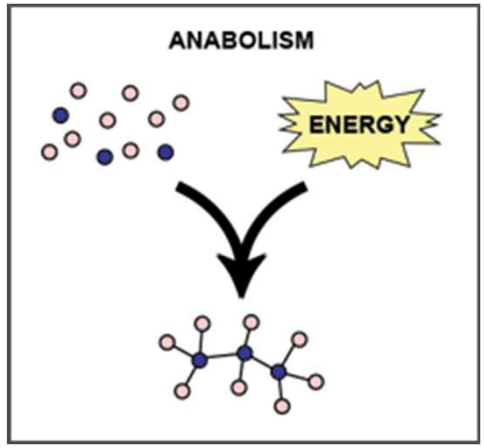
Transformation rxns mediated by bacteria

- **Oxidation**. Release of electrons during transformation
- **Reduction**. Addition of electrons during transformation
- **Hydrolysis**. Addition of water
- **Substitution**. Exchange of one group for another
- **Elimination**. Removal of atoms from adjacent carbons, leaving a double bond between them
- **Dealkylation**. Removal of an alkyl group
- **Deamination**. Removal of an NH_2 group
- **Condensation**. Production of a larger molecule from smaller molecules
- **Isomerization**. Conversion of one isomer into another
- **Ring cleavage**. Opening of an aromatic ring structure, generally for the purpose of further biotransformation

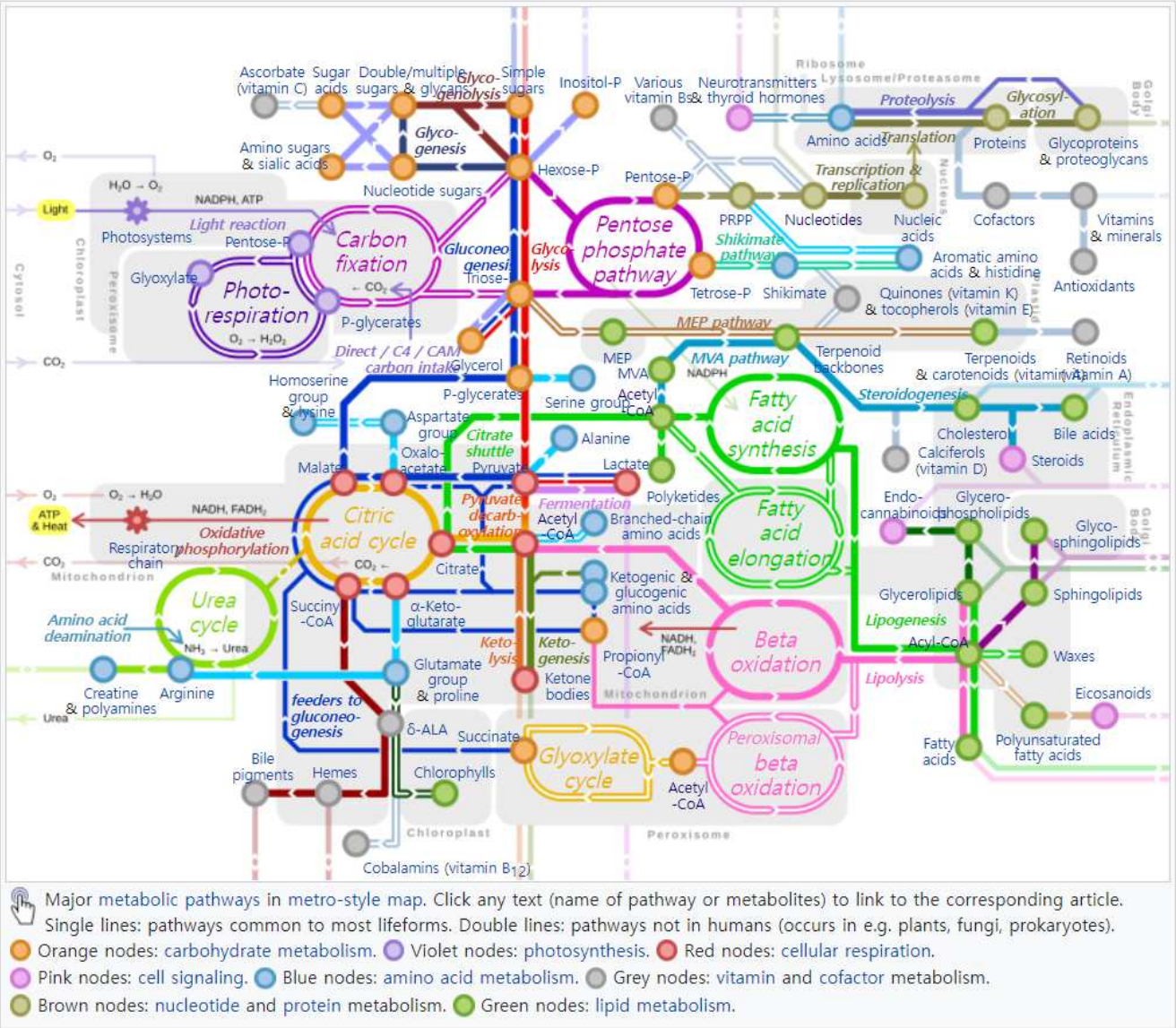
Metabolism

- Life-sustaining chemical transformations within cells of living organisms
- Catabolism: process to break down molecules into smaller units to generate energy (ATP)
- Anabolism: process to construct macromolecules from smaller molecules (consumes ATP)





Metabolic pathway within a cell



Major metabolic pathways in metro-style map. Click any text (name of pathway or metabolites) to link to the corresponding article.
Single lines: pathways common to most lifeforms. Double lines: pathways not in humans (occurs in e.g. plants, fungi, prokaryotes).
Orange nodes: carbohydrate metabolism. Violet nodes: photosynthesis. Red nodes: cellular respiration.
Pink nodes: cell signaling. Blue nodes: amino acid metabolism. Grey nodes: vitamin and cofactor metabolism.
Brown nodes: nucleotide and protein metabolism. Green nodes: lipid metabolism.

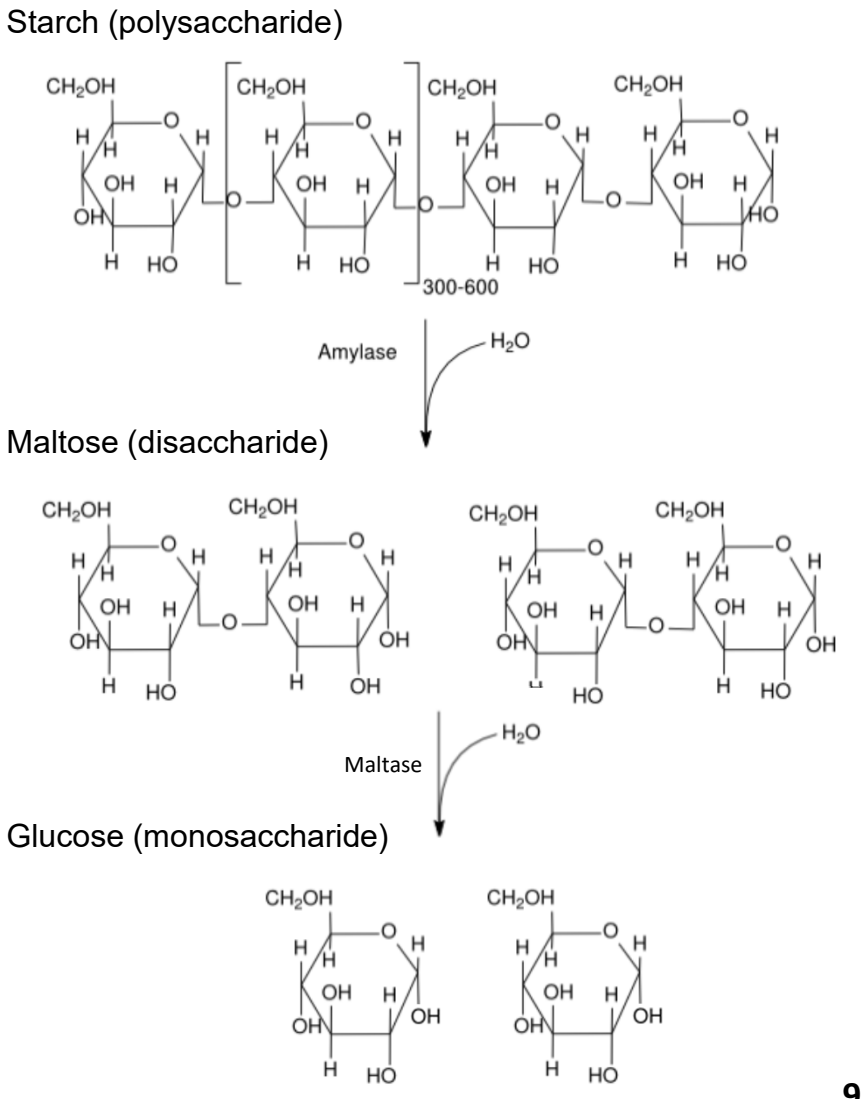
Breakdown of macromolecules

- By hydrolysis, mediated by extracellular enzymes

Carbohydrates
----> monosaccharides

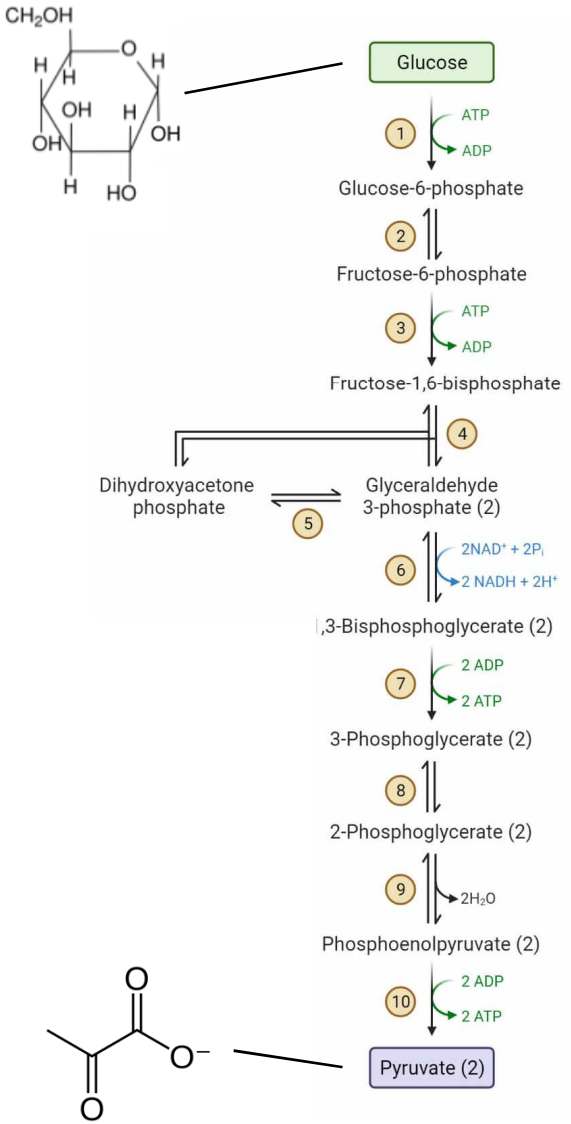
Proteins
----> amino acids

Fats
----> glycerol + fatty acids



Processing of simple organics

- Transformation of monosaccharides to pyruvate



ENZYMES	
1	Hexokinase
2	Phosphoglucose isomerase
3	Phosphofructokinase-1
4	Aldolase
5	Triosephosphate isomerase
6	Glyceraldehyde 3-phosphate dehydrogenase
7	Phosphoglycerate kinase
8	Phosphoglyceromutase
9	Enolase
10	Pyruvate kinase

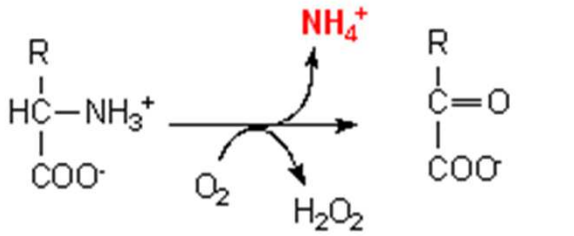
PRODUCTS	
2 ATP	2 Pyruvate
2 NADH	

Pyruvate
: key intermediate in catabolism and anabolism in most organisms

Processing of simple organics

- Deamination of amino acids

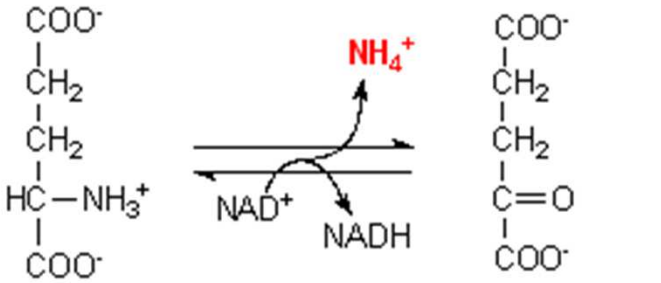
D- and L-amino acid oxidases



amino acid

keto-acid
(oxo-acid)

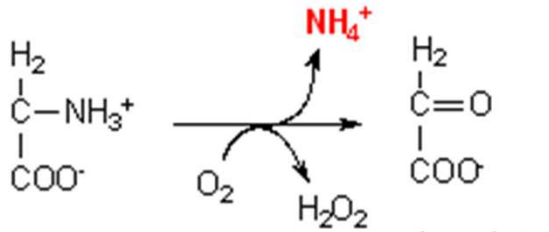
glutamate dehydrogenase



glutamate

ketoglutarate
(oxo-glutarate)

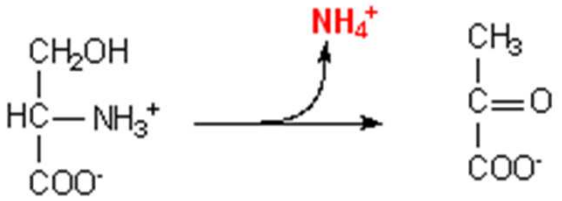
glycine oxidase



glycine

glyoxylate

serine deaminase

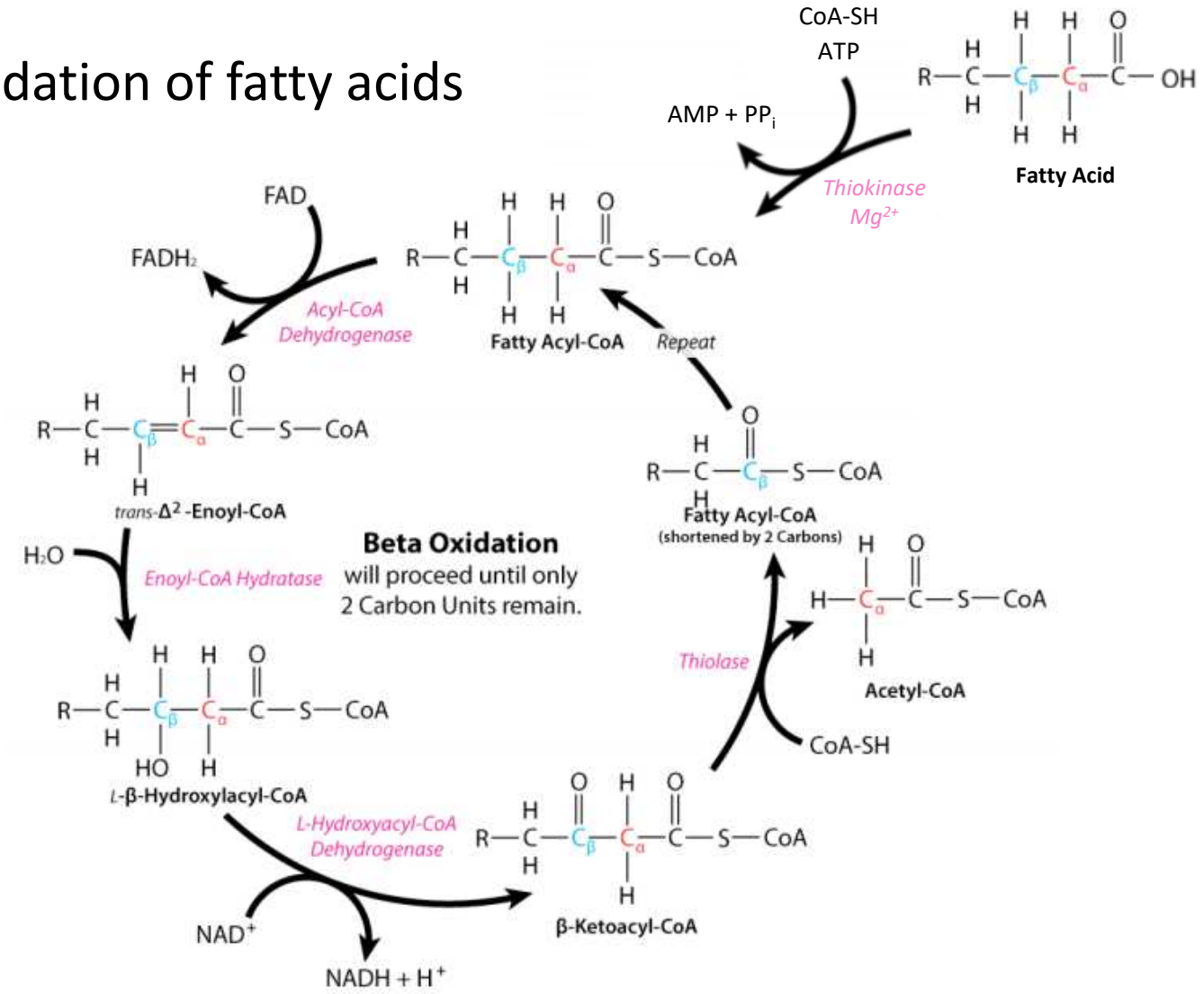


serine

pyruvate

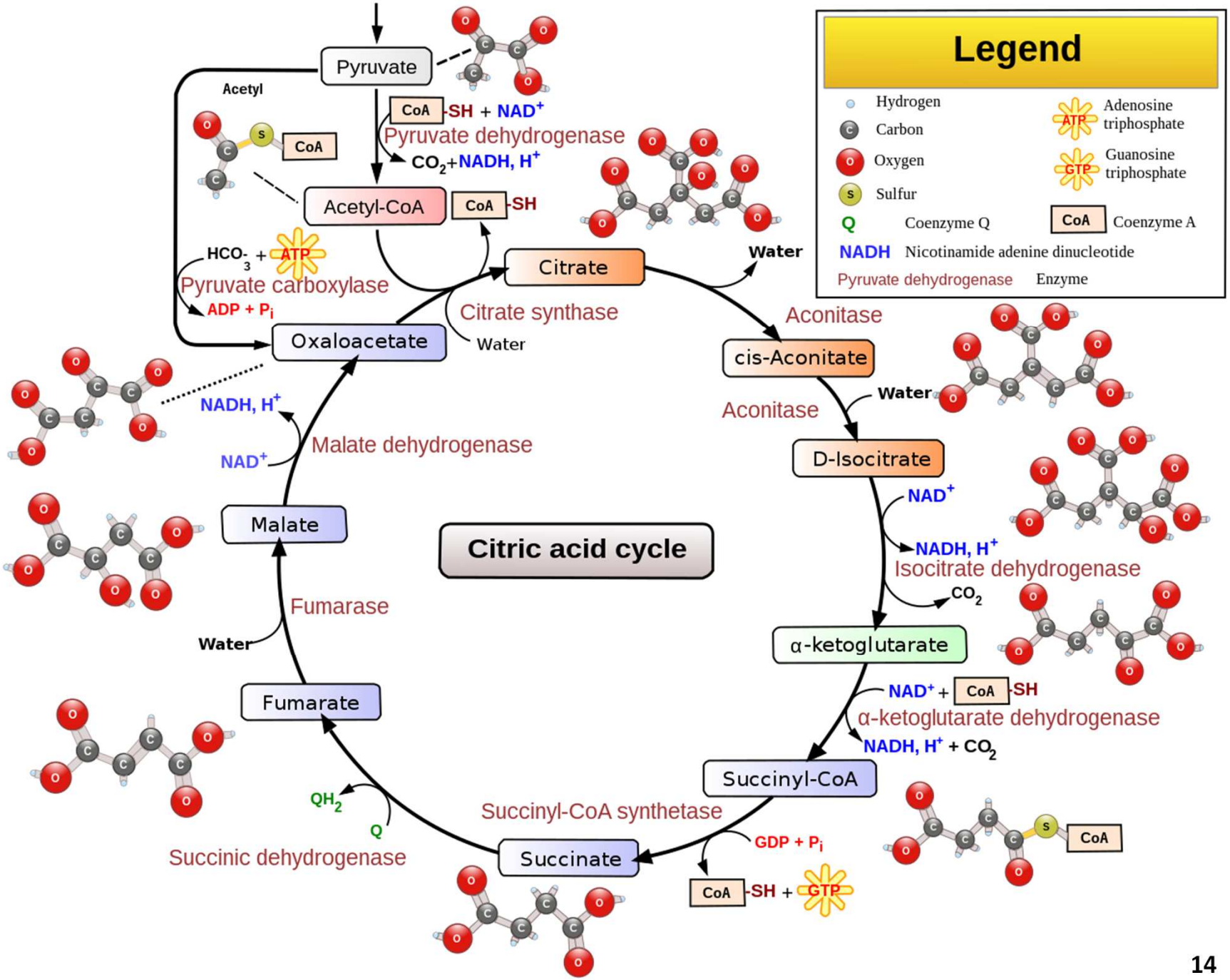
Processing of simple organics

- β-oxidation of fatty acids



Citric acid cycle

- a.k.a. tricarboxylic (TCA) cycle or Krebs cycle
- A series of chemical reactions to release energy through the oxidation of acetyl-CoA
  - Acetyl-CoA is derived from carbohydrates, fats, or proteins
- Used by organisms that respire (both aerobically and anaerobically) to generate energy
  - Fermentation does not take this route
- Provides precursors of some amino acids and the reducing agents NADH and $FADH_2$

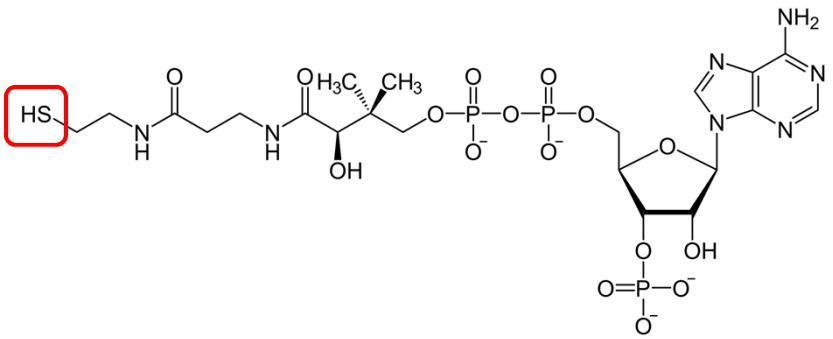

Legend
Hydrogen
Carbon
Oxygen
Sulfur
Coenzyme Q
Nicotinamide adenine dinucleotide
Pyruvate dehydrogenase
Enzyme
Adenosine triphosphate
Guanosine triphosphate
Coenzyme A
Pyruvate
Acetyl
CoA
Acetyl-CoA
Citrate
Water
Aconitase
cis-Aconitate
D-Isocitrate
Isocitrate dehydrogenase
α-ketoglutarate
α-ketoglutarate dehydrogenase
Succinyl-CoA
Succinyl-CoA synthetase
Succinate
Succinic dehydrogenase
Fumarate
Fumarase
Malate
Malate dehydrogenase
Oxaloacetate
Citrate synthase
Pyruvate carboxylase
Pyruvate dehydrogenase
Citric acid cycle

Citric acid cycle – overall reaction

$$Acetyl - CoA + 3NAD^{+} + FAD + GDP + P_i + 2H_2O$$

$$\longrightarrow \quad CoA - SH + 3NADH + FADH_2 + GTP + 2CO_2$$

- GDP/GTP = guanine di-/tri-phosphate. GTP can be used to form ATP by [GTP + ADP → GDP + ATP]
- CoA-SH = coenzyme A with in its intact form



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- Overall reaction

$$Acetyl - CoA + 3NAD^+ + FAD + GDP + P_i + 2H_2O \longrightarrow CoA - SH + 3NADH + FADH_2 + GTP + 2CO_2$$

GDP/GTP = guanine di-/tri-phosphate. GTP can be used to form ATP by [GTP + ADP → GDP + ATP]

Degradation of amino acids: What happens after deamination?