MAJOR METABOLIC PATHWAYS

Outline

- Overview of metabolism pathways
  - Catabolism
  - Anabolism
- Bioenergetics
- Important metabolic pathways
  - Catabolism:
    - Glucose catabolism (aerobic pathway, anaerobic pathway)
    - Nitrogen compounds
    - Hydrocarbon
  - Anabolism:
    - Photosynthesis
    - Biosynthesis

Metabolic Pathways

- **<u>Metabolism</u>:** a complete set of chemical reactions that occur in living cells, allowing cells to grow and reproduce, maintain their structures, and respond to their environments.
- Major challenges in bioprocess development:
  - To select an organism that can efficiently make a given product

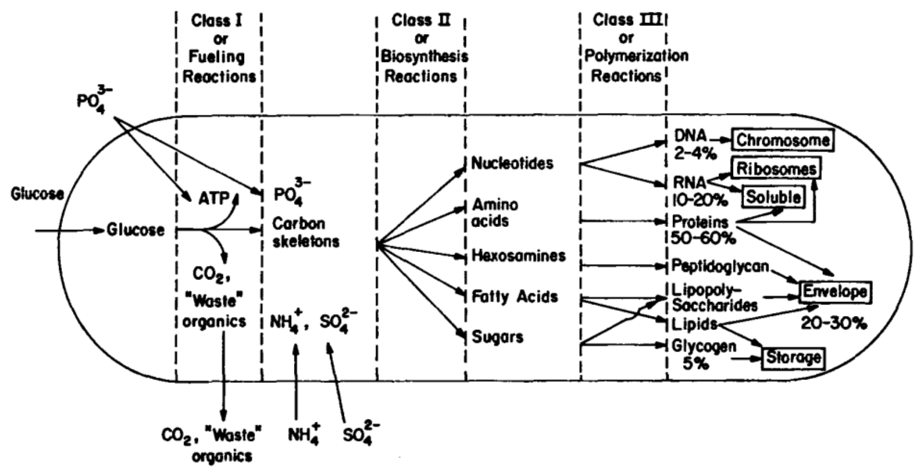
    or
  - digest wastes in the Environment.

It is important to understand the metabolic pathways.

Metabolic Pathways

- Metabolism can be subdivided by:
  - **Catabolism**: The intracellular process of degrading a compound into smaller and simpler products and generating energy.
    - **Example:** Glucose to CO_2 and H_2O, protein to amino acids.
  - **Anabolism**: the synthesis of more complex compounds and requires energy.
    - **Example:** Glucose to glycogen

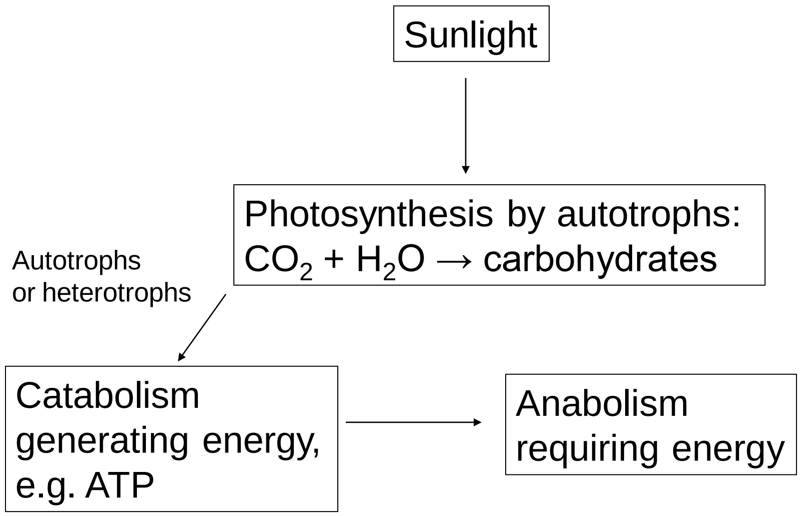
Major Metabolic Pathways in a Bacterial Cell *(M. Shuler, 2002)*



Bioenergetics

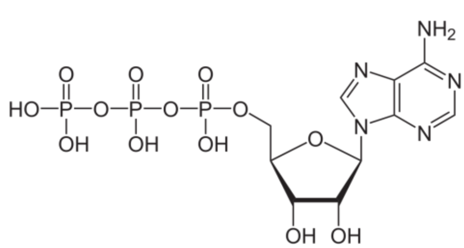
- Living cells require energy for
  - biosynthesis,
  - transport of nutrients,
  - motility, and
  - maintenance.
- This energy is obtained from the catabolism of carbon compounds, mainly carbohydrates.
- Carbohydrates are synthesized from CO_2 and H_2O in the presence of light by photosynthesis.
- The sun is the ultimate energy source for the life processes on earth.

Bioenergetics



Bioenergetics

- Energy in biological systems is primarily stored and transferred via adenosine triphosphate (ATP); contains high-energy phosphate bonds.

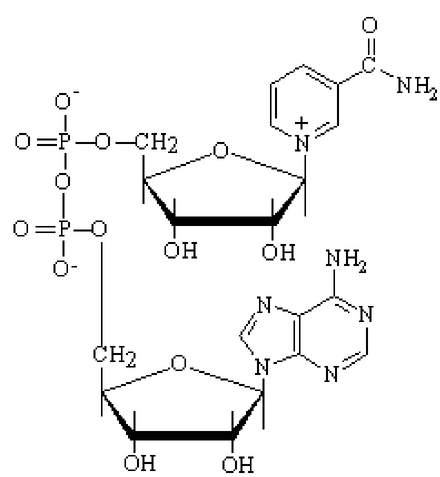


- Other energy carrying compounds include GTP, UTP and CTP.

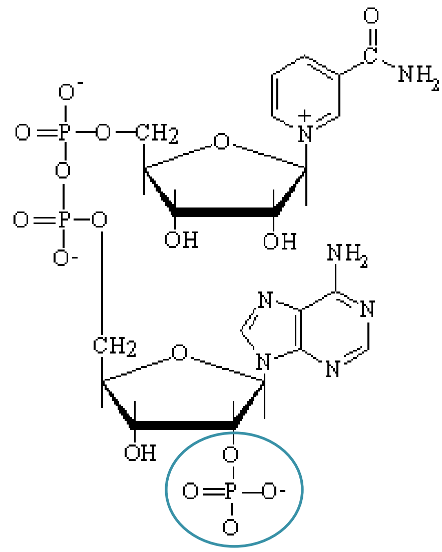
Bioenergetics

- Hydrogen atoms released in biological oxidation–reduction reactions are carried by nucleotide derivatives, especially by nicotinamide adenine dinucleotide (NAD+) and nicotinamide adenine dinucleotide phosphate (NADP+).
- The oxidation–reduction reaction described is readily reversible.
  - NADH can donate electrons to certain compounds and accept from others, depending on the oxidation–reduction potential of the compounds.

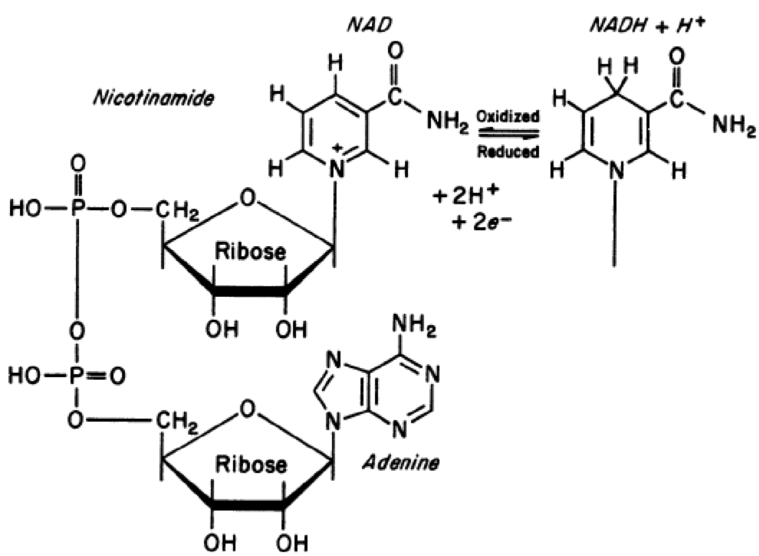
Nicotinamide Adenine Dinucleotide (NAD^+)



Nicotinamide Adenine Dinucleotide Phosphate ($NADP^+$)



NAD undergoing Oxidation–Reduction reaction



Bioenergetics

- NADH has two major functions in biological systems:
  1. Reducing power: NADH and **NADPH** supply hydrogen atom in biosynthesis reactions.
     - Example: CO_2 fixation by autotrophic organisms
       $CO_2 + 4\ H \rightarrow CH_2O + H_2O$
  2. ATP formation in respiratory metabolism:
     - **NADH** is a major electron (or H atom) carriers in the oxidation of fuel molecules and for ATP generation.

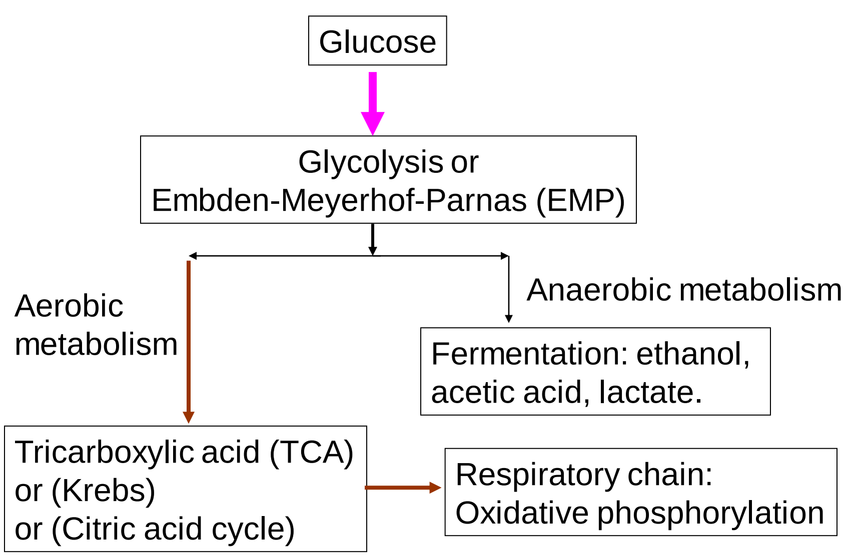
Glucose Catabolism

- Glucose is a major carbon and energy source for many organisms.
- Several different metabolic pathways are used by different organisms for the catabolism of glucose.
- The catabolism of glucose by ***glycolysis***, or the *Embden–Meyerhof–Parnas* (EMP) pathway, is the primary pathway in many organisms.
- Other pathways include *hexose monophosphate* (HMP) and *Entner–Doudoroff* (ED) pathways.

Glucose Catabolism

- Aerobic catabolism of organic compounds such as glucose may be considered in three different phases:
  1. EMP pathway for fermentation of glucose to pyruvate.
  2. *Krebs*, *tricarboxylic acid (TCA)*, or *citric acid cycle* for conversion of pyruvate to CO_2 and NADH.
  3. Respiratory or *electron transport chain* for formation of ATP by transferring electrons from NADH to an electron acceptor.

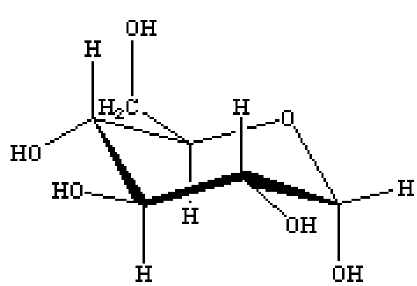
Glucose Catabolism



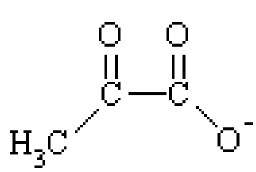
Glucose Catabolism
Glycolysis

- Glycolysis = Embden-Meyerhof-Parnas (EMP) pathway
  - Results in breakdown of a molecule of glucose to two pyruvate molecules.
  - Each step is catalyzed by particular enzyme
  - Generating 2 ATP, 2 NADH and 2 pyruvate (Key Metabolite).
  - Taking place in cytoplasm

http://www.science.smith.edu/departments/Biology/Bio231/glycolysis.html Glycolysis.htm

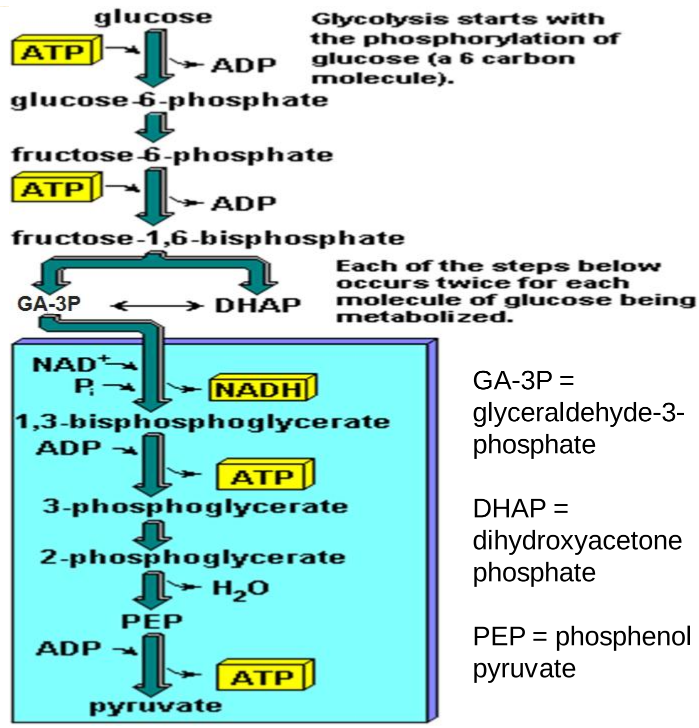


α-D-Glucose



Pyruvate

Glycolysis (EPM)



GA-3P = glyceraldehyde-3-phosphate

DHAP = dihydroxyacetone phosphate

PEP = phosphenol pyruvate

Glucose Catabolism

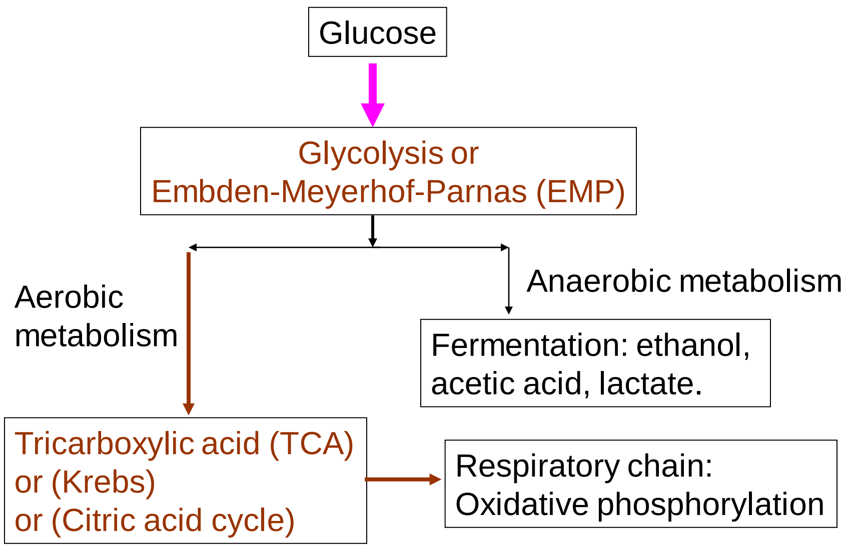
Glycolysis

- The overall reaction in glycolysis is:

Glucose + 2ADP + 2 NAD$^+$ + 2 Pi
→ 2 pyruvate + 2 ATP + 2 (NADH + H$^+$)

- Produce
  - Energy
  - Key metabolite: **pyruvate**

Glucose Catabolism



Glucose Catabolism

Tricarboxylic Acid (TCA) Cycle

- Krebs Cycle = Tricarboxylic Acid (TCA) Cycle = Citric Acid Cycle
- Occurs under **aerobic** conditions
- Taking place
  - in mitochondria in eucaryotes
  - associated with membrane-bound enzymes in procaryotes
- Pyruvate produced in glycolysis (EMP) pathway transfers its reducing power to NAD^+.

http://www.science.smith.edu/departments/Biology/Bio231/krebs.html
krebstca.htm

Glucose Catabolism
Tricarboxylic Acid (TCA) Cycle

- Entry into the Krebs cycle is provided by the acylation of coenyzme-A by pyruvate.

pyruvate + NAD^+ + CoA-SH

→ acetyl-CoA + CO_2 + (NADH + H^+)

- The overall reaction of TCA cycle:

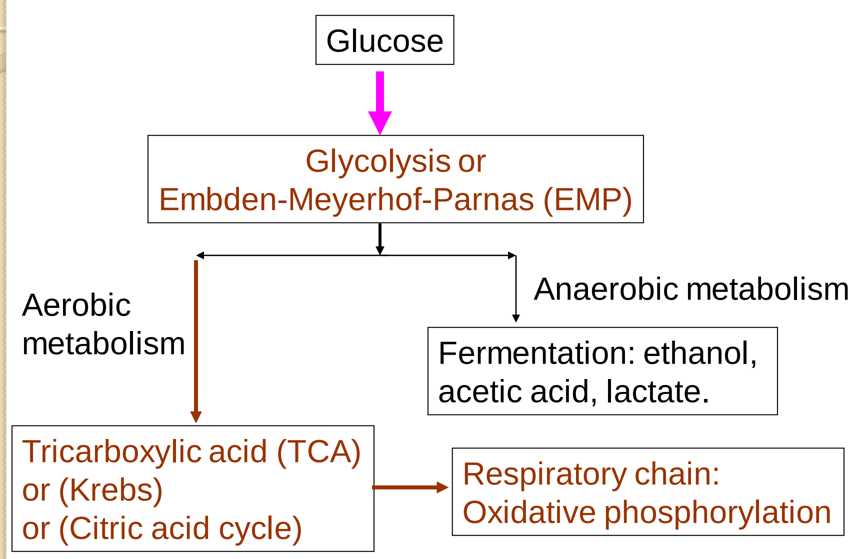
acetyl-CoA + 3 NAD^+ + FAD + GDP+ Pi + $2H_2O$

→ CoA + 3(NADH + H^+) + $FADH_2$+ GTP + $2CO_2$

Glucose Catabolism
Tricarboxylic Acid (TCA) Cycle

- **Major roles of the TCA cycle**
  - (1) to provide electrons (NADH) for the electron transport chain and biosynthesis
    - The reducing power (NADH + H^+ and $FADH_2$) is used for biosynthesis pathway or for ATP generation through the electron transport chain.
  - (2) to supply C skeletons for amino acid synthesis
    - Intermediate products such as oxylacetate and α–ketoglutarate are used as precursors for the synthesis of certain amino acids.
  - (3) to generate energy

Glucose Catabolism



Glucose Catabolism

Respiratory Chain

Respiratory Chain = Oxidative Phosphorylation

"Oxidative Phosphorylation is the electron transport chain that forms ATP as electrons are transferred from NADH or $FADH_2$ to ***oxygen*** *by a series of electron carriers"*

- electron acceptor: oxygen (aerobic condition)
- generate ATP, H_2O
- from NADH or $FADH_2$

- Taking place
  - inside mitochondria in eukaryotes
  - in cytoplasmic membrane in prokaryotes

http://www.brookscole.com/chemistry_d/templates/student_resources/shared_resources/animations/oxidative/oxidativephosphorylation.html

Glucose Catabolism
Respiratory Chain

- Major role of Electron Transport Chain is to regenerate
  - NADs for glycolysis
    - $\frac{1}{2}O_2 + NADH + H^+ \rightarrow H_2O + NAD^+$

      and
  - ATPs for biosynthesis
    - ADP + Pi $\rightarrow$ ATP

Glucose Catabolism
Oxidative Phosphorylation

- In the process of **Oxidative Phosphorylation**

In eukaryotes:

$NADH + H^+ \rightarrow$ 3 ATP

$FADH_2 \rightarrow$ 2 ATP

In prokaryotes:

$NADH + H^+ \rightarrow$ ≤2 ATP

$FADH_2 \rightarrow$ 1 ATP

Summary of NADH, $FADH_2$, and ATP Formation during Aerobic Catabolism of Glucose

	NADH	$FADH_2$	ATP	Total ATP[a]
Glycolysis	2	–	2	6[b]
Oxidative decarboxylation of pyruvate	2	–	–	6
TCA cycle	6	2	2	24
Total	10	2	4	36 mol ATP

In eukaryotes

EMP Glycolysis:

2 NADH → 2 $FADH_2$ → 4 ATP

Entry of pyruvate and TCA cycle:

8 NADH → 24 ATP

TCA cycle:

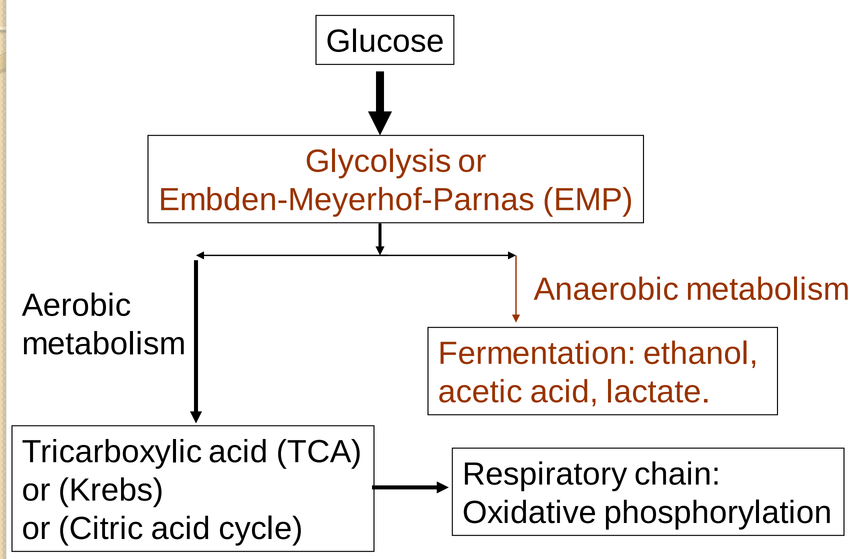
2 $FADH_2$ → 4 ATP

Glucose Aerobic Catabolism Overall Reaction

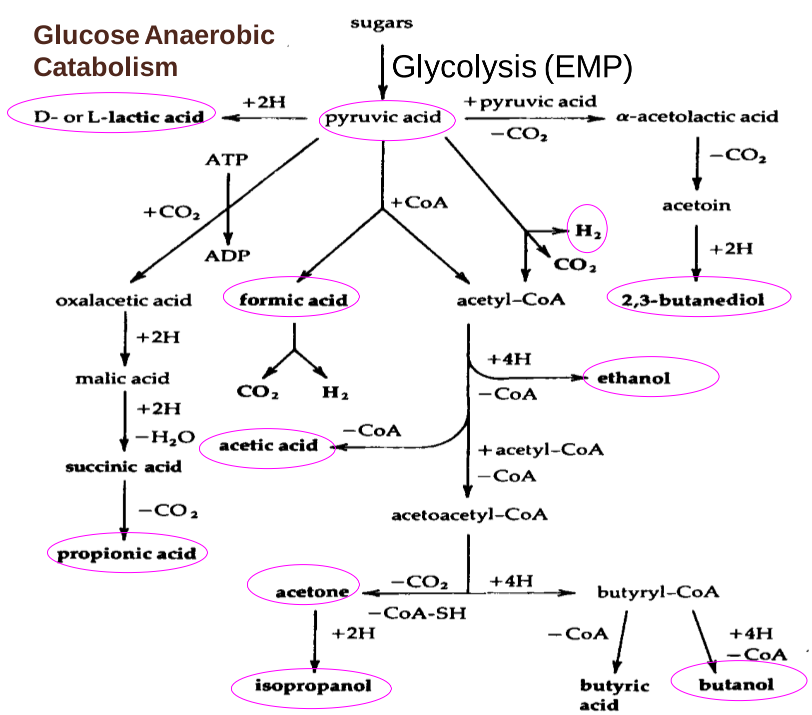
- Overall reaction (assuming 3 ATP/NADH) of aerobic glucose catabolism in eukaryotes

Glucose + 6 O_2 + 36 ADP + 36 Pi → 6 CO_2 + 6 H_2O + 36 ATP

Glucose Catabolism



Glucose Anaerobic Catabolism



Nitrogen Compounds Catabolism

- Nitrogen compounds can be used as
  - Carbon C source
  - Nitrogen N source
  - energy source
- Proteins $\xrightarrow{+H_2O}$ peptides $\xrightarrow{ptoteases}$ amino acids
- Amino acids are converted to other amino acids or organic acids by **deamination** (removal of amino group).
- Deamination reaction may be **oxidative**, **reductive**, or **dehydrative**, depending on the enzyme systems involved

Nitrogen Compounds Catabolism

- Typical oxidative deamination reaction:

$$R-\underset{NH_2}{\underset{|}{CH}}-COOH + H_2O + NAD^+ \longrightarrow R-\overset{O}{\overset{\|}{C}}-COOH + NH_3 + NADH + H^+$$

- Ammonia (NH_3) released from deamination is utilized in protein and nucleic acid synthesis as a nitrogen source, and
- Organic acids (RCOCOOH) can be further oxidized for energy production (ATP), and also used in lipid synthesis.

Nitrogen Compounds Catabolism

- **Transamination** is another mechanism for conversion of amino acids to organic acids and other amino acids.
- A typical transamination reaction is

$$\text{glutamic acid} + \text{oxaloacetic acid} \longrightarrow \alpha\text{-keto glutaric acid} + \text{aspartic acid}$$

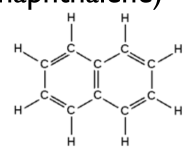
- Amino acids can be used to produce proteins, other amino acids or enter TCA cycle

Nitrogen Compounds Catabolism

- Nucleic acids are utilized in producing
  - ribose/deoxyribose
    - Sugar molecules are metabolized by glycolysis and the TCA cycle, producing CO_2 and H_2O under aerobic conditions
  - phosphoric acid
    - Phosphoric acid are used in ATP, phospholipid, and nucleic acid synthesis.
  - purine/pyrimidine
    - Purines/pyrimidines are degraded into urea and acetic acid and then to ammonia and CO_2.

Hydrocarbon Catabolism

- Hydrocarbon: C & H
  - Aliphatic hydrocarbon (e.g. octane, C_8H_{18}, polyethylene –(HC=CH)–)
  - Aromatic hydrocarbon (e.g. naphthalene)
- Metabolism of hydrocarbon
  - Requires oxygen
  - **Challenges:**
    - low solubility of hydrocarbons in water is a barrier to rapid metabolism
    - Only few organisms *(Pseudomonas, Mycobacteria)* can metabolize hydrocarbons



Hydrocarbon Catabolism

- **Metabolism steps of aliphatic hydrocarbons**
  - Oxygenation by oxygenases
  - Converting hydrocarbon molecules to an alcohol by incorporation of oxygen into the end of the carbon skeleton.
  - The alcohol molecule is further oxidized to aldehyde and then to an organic acid which is further converted to acetyl-CoA
  - acetyl-CoA is metabolized by the TCA cycle.

Hydrocarbon Catabolism

- **Metabolism steps of aromatic hydrocarbons**
  - Oxygenation by oxygenases
    - much slower than oxidation of aliphatic hydrocarbons
  - Cathecol is the key intermediate in the oxidation sequence and can be further broken down ultimately to acetyl-CoA or TCA cycle intermediates
  - **Aerobic metabolism of benzene:**

benzene ⟶ cathecol ⟶ *cis-cis*-muconate ⟶ β-keto adipate

↓

acetyl-CoA + succinate

Overview of Biosynthesis

- **Pentose-phosphate pathway (hexose-monophosphate pathway (HMP)):**
  - provides an array of small organic compounds with three, four, five, and seven carbon atoms (C_3 ~ C_7)
    - These compounds are particularly important for the synthesis of ribose, purines, coenzymes, and the aromatic amino acids.
  - provide the reducing power necessary to support anabolism
  - Cells need to synthesize:
    - Amino acids and Nucleic acids (DNAs, RNAs)
    - Polysaccharides (glycan, glycogen) from glucose
    - Glucose by gluconeogenesis
    - Lipids from fatty acids