

Ways to regulate the flow of carbon through a pathway:

(1). Metabolic Channeling:

- *Localization of metabolites and enzymes in different parts of a cell that influence pathway activity.*

Compartmentation:

- *One of the most common mechanisms of metabolic channeling.*
- *Differential distribution of enzymes and metabolites among separate cell structures or organelles.*
- *Makes possible the simultaneous, but separate, operation and regulation of similar pathways*

Example:

- *Fatty acid oxidation located within the mitochondrion*
- *Fatty acid synthesis occurs in the cytoplasmic matrix*

If two pathways in different compartments require NAD for activity, the pathway with access to the most NAD will be favored.

Enzyme Regulation

- *In order to achieve a balanced metabolism, enzymatic activities need to be regulated.*
- *Regulation is also required in order for bacteria to adjust to changing environmental conditions.*

Two levels of Regulation:

There are two levels of enzyme regulation,

- *first the bacteria can modulate the activity of the enzyme (enzyme level regulation),*
- *or the bacteria can modulate the synthesis of the enzyme by gene level regulation.*

*Enzyme level regulation occurs by activation or inhibition of the catalytic activity of an enzyme. This is best achieved by substances called **inhibitors**, and there are two types.*

(1).

- ***Competitive inhibitors*** *are compounds that have a similar structure to the normal substrate. These compounds are able to bind to the active site, but will not react. When an inhibitor is bound, the normal substrate does not have access to the active site and consequently, the reaction will not proceed.*
- *The inhibitor essentially competes with the substrate for access to the active site.*
- *The inhibition can be released by increasing the concentration of the actual substrate and effectively diluting out the inhibitor.*

- *It is important to emphasize that competitive inhibition is reversible, and the enzyme is not altered.*
- (2).
- ***Noncompetitive inhibition*** *is an irreversible process that occurs when an inhibitor combines with the enzyme at a place other than the active site. This interaction changes the three dimensional conformation of the enzyme and distorts the active site so that it can no longer recognize the proper substrate.*
 - *In contrast to competitive inhibition, **noncompetitive inhibition is not reversible,** and chemically alters the enzyme.*

Allosteric Regulation:

- ***Allosteric enzymes*** *are those which contain both regulatory and active sites.* (figure 8.21)
- ***Effector or Modulator:***
*A small molecule called an **effector**, binds to the regulatory site of an allosteric enzyme and alters the enzymatic activity.*
 - *Effector binds to AE and causes a change in enzyme conformation that results in an alteration in the shape of the active site. Active site binds more effectively to the substrate.*

Effector molecules *may either be*

- ***Inhibitors (negative effector)*** - *which turns off activity or decreasing activity.*
- ***Activators (positive effector)***
Turns on activity therefore increasing enzymatic activity.

Feedback Inhibition or End-Product Inhibition

It is common for a cell to regulate the pathway as a single unit. One mechanism for doing this is called feedback inhibition.

- ***Feedback inhibition*** *occurs when the endproduct of the enzyme pathway “feeds back” into the pathway as an inhibitor of the first enzyme in the pathway.*
Example: *the biosynthesis of the amino acid threonine*
- *Such a feedback loop regulates itself in order to maintain a constant level of the end-product in the cell.*
 - *If end product becomes too concentrated, it inhibits the regulatory enzyme and slows its own synthesis.*
 - *As end-product decreases, pathway activity increases and more product is formed.*

Pacemaker enzyme:

- *Catalyzes the slowest or rate limiting reaction in the pathway*
- *Every pathway has at least one*

- *Usually the first step in a pathway is a pacemaker reaction catalyzed by a regulatory enzyme and the end-product often inhibits the regulatory enzyme.*

Chapter 9

Metabolism: Energy Release and Conservation:

Metabolism:

- *the sum of all of the biochemical reactions that occur in a living cell.*

Two Parts to Metabolism:

Catabolic/Catabolism Reaction Pathways

- *Some enzyme pathways break large complex molecules into very simple molecules*
- *Release energy in the process.*

Anabolic/Anabolism Pathways:

- *Start with the simple compounds and synthesize large and complex molecules.*
- *These reactions consume energy*

Essentially the cell captures the energy released from the catabolic reactions and stores it for later use in anabolic reactions. The cells have an energy bank account where deposits and withdrawals are constantly being made.

Electron Acceptors for Microorganisms:

- ***Fermentation*** *metabolism occurs when the final electron acceptor molecules are **organic** molecules.*
 - *Uses **substrate level phosphorylation** reactions to generate electrons (reducing power)the oxidation of pyruvate to lactate is an example of a fermentation*
- ***Aerobic Respiration*** *Respiratory metabolism occurs when the final electron acceptors are oxygen or inorganic molecules.*
 - *These reactions use both substrate level phosphorylation, as well as the electron transport chain.*
- ***Anaerobic respiration*** *is a metabolism unique to the bacteria. These pathways are defines as the oxidation of organic compounds where an external molecule, other than oxygen, serves as the final electron acceptor. ie nitrate (NO_3^- , SO_4^{2-} , or CO_2)*

Carbohydrates and other nutrients serve two functions in the metabolism of heterotrophic mos:

1. *Oxidized to release energy*
2. *Supply carbon or building blocks for synthesis of new cell components.*

Amphibolic (both sides) pathways:

- *Functions both catabolically and anabolically*
- *Glycolytic and Tricarboxylic acid cycle*
- *Rxns are freely reversible and can be used to synthesize and degrade molecules*

Breakdown of Glucose to Pyruvate

- *The major enzyme pathway in most organisms is the **Embden-Meyerhof** enzyme pathway, which is also known as **Glycolysis**.*
- *Energy-yielding process in which organic molecules serve as both electron donors and acceptors.*

Catabolism of Glucose and other Sugars by MOs:

- *Sugar to pyruvate and similar intermediates*
- *Focus on three pathways*
 1. *Glycolysis*
 2. *the Pentose Phosphate Pathway*
 3. *Entner-Doudoroff pathway*

Glycolytic Pathway:

Figure is on page A-13, in Appendix !!

- ***You are accountable for the structures, enzymes, substrate, products, and number of ATP and NADH of the glycolytic pathway***
- *Embden-Meyerhof: most common pathway for glucose degradation to pyruvate.*
- *Found in all major groups of mos*
- *Functions in the presence of O₂*
- ***Located in the cytoplasmic matrix*** *of prokaryotes and eucaryotes.*
- ***EMP is a pathway of 10 enzymes which sequentially break 1 glucose down into 2 pyruvate molecules, and in the process generate a net gain of 2 ATP.***

The reaction can be subdivided into three steps.

- The **first series of reactions** are preparatory in nature, rearranging the substrates to facilitate the formation of high energy bonds
- The **second reaction series** are the oxidation reactions in which ATP is made.
- The **third reactions series** is the reduction, where the excess electrons are transferred to terminal acceptor compounds

During the course of this pathway, glucose is oxidized to pyruvate.

1. Glucose is **Phosphorylated** twice which requires use of 2 ATP, every time a phosphate is added to the compound.

- 2 ATP are hydrolyzed to 2 ADP + 2 Pi and (consumed)

Steps in the cycle:

- Glucose to Glucose 6 phosphate
- Fructose to Fructose 1,6 bisphosphate
- Enzymes:
- 6 carbon stage
- There is no energy yielding in this stage
- Using 2 ATP
- Phosphate will be used to make ATP later on.

Entering the 3 Carbon stage of Glycolysis:

Now 6 carbon compd is cleaved into 2-- 3 carbon compds each containing a phosphate.

Two three carbon compounds are:

- **Glyceraldehyde 3 phosphate and Dihydroxyacetone phosphate.**
- Dihydroxyacetone phosphate can easily be converted into **Glyceraldehyde 3 phosphate** therefore utilizing the entire components of fructose 1,6 bisphosphate
- **Glyceraldehyde 3 phosphate** is converted directly to pyruvate in a 5 step process.
 - **Glyceraldehyde 3 phosphate** is oxidized with NAD⁺ as the electron acceptor becoming NADH and yielding a Phosphate making a **HIGH ENERGY MOLECULE**
 - 1,3 bis-phosphoglycerate which yields ATP.
 $Pi + ADP \rightarrow ATP$

Substrate level Phosphorylation:

- Synthesis of ATP
- ADP phosphorylation is coupled with the breakdown of a high energy molecule.

Another **Substrate level Phosphorylation** generating a second ATP:

- Phosphate group on 3-phosphoglycerate shifts to a 2- phosphoglycerate with the loss of water, you get Phosphoenolpyruvate (Another High energy molecule).
- PEP donates its phosphate to yield pyruvate and ATP, another substrate level phosphorylation.
- Pyruvate is the final product of the pathway.

Overview of Glycolytic Pathway:

- Degrades 1 glucose to get 2 pyruvates
- What energy is produced? ATP and NADH

Calculation of How many ATPs and NADHs are produced.

- 1st stage (6 C) use 2 ATPs
- 2nd stage (3 C)

2 -- G 3 P

Each G3P → 2 pyruvates

During the transformation to pyruvate:

1 NADH

2 ATP

Therefore:

2 NADH and 4 ATPs

Now:

Subtract of the 2 ATPs used in the 1st stage you

Have 2 NADHs and 2 ATP.

