Biochemistry

METABOLISM

DONE BY

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"HEAL US TO HEAL OTHERS"

METABOLISM

Introduction

- Chemical reactions taking place in the living system are collectively referred to as metabolism.
- Occurs through enzyme catalyzed reaction that organized into discrete pathways - metabolic pathways that convert nutrients, necessary to nourish living organism into energy.
- Proceed in a stepwise fashion, transforming substrate into end products.
- The precursor is converted into a product through a series of metabolic intermediate – metabolites.
- Overall process through which living systems acquire & utilize free energy need to carry out various functions.

PURPOSE

- Generation of energy to drive vital functions
- Synthesis of biological molecules

Metabolism consists of two contrasting process

- Anabolism
  - **Synthesis of cellular components are called anabolic pathways. Greek meaning is "Up".**
  - **It is an endergonic reaction, *ie,* energy requiring process, generally in the form of ATP.**
  - **Anabolism is also called as biosynthesis, in which the small and simple precursors are built up into larger and more complex biomolecules including crabohydrates, lipids, proteins and nucleic acids.**

Catabolism

- **Breakdown or oxidation of cellular components are called catabolic pathways. Greek meaning is "Down".**
- **It is an exergonic reaction, *ie,* energy liberating process.**
- **Catabolism is the degradative phase of metabolism in which organic nutrient molecules (carbohydrates, fats & lipids) are converted into smaller, simpler end products such as lactic acid, CO_2, NH_3.**

Catabolic pathways play two roles in cell:

- They release the free energy needed to drive cellular function.
- They give rise to the small organic molecule or metabolites.

SITE OF METABOLISM

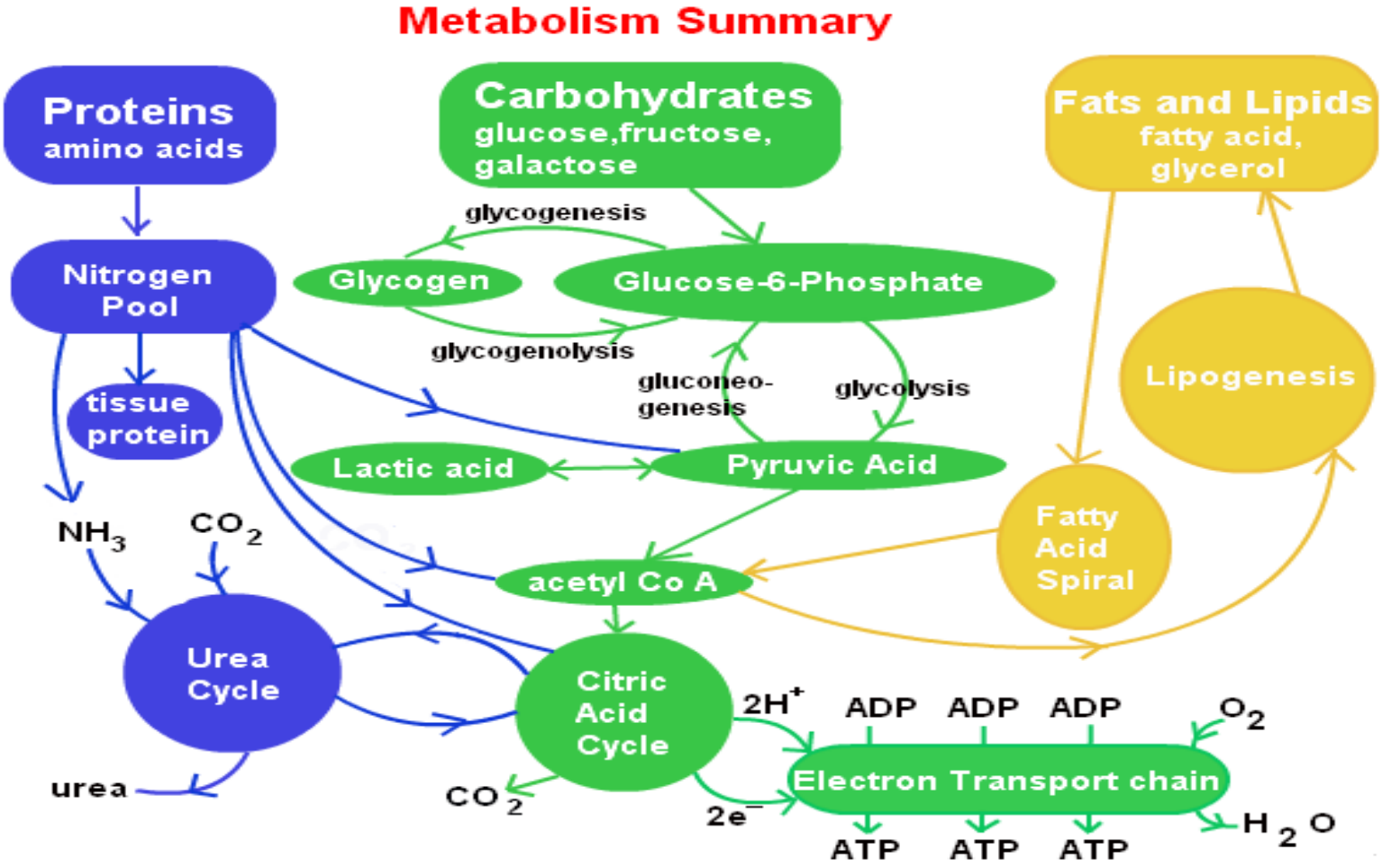
Metabolic pathways in eukaryotic cells occurs in specific cellular locations:

- **Mitochondria** – TCA cycle, electron transport, oxidative phosphorylation, fatty acid oxidation & amino acid breakdown
- **Cytosol** – Glucolysis, HMP shunt, fatty acid biosynthesis & gluconeogenesis.

TYPES OF METABOLISM

- Carbohydrate Metabolism
- Lipid Metabolism
- Protein Metabolism

METABOLISM – OVER VIEW



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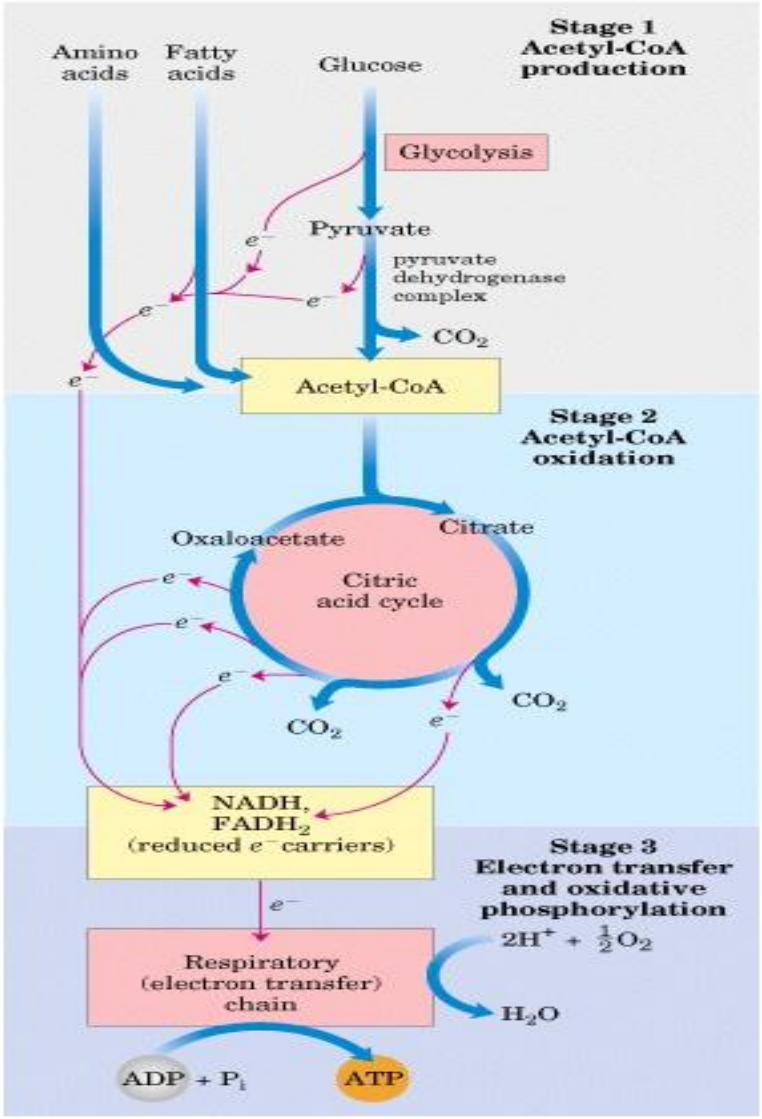
Overview of Energy Metabolism: Glycolysis, TCA Cycle

- **All living cells require energy to carry out various cellular activities. This energy is stored in the chemical bonds of organic molecules (*e.g. carbohydrates, fats, proteins) that we eat as food.***
- **These organic molecules are broken down by enzymatic reactions in cells to generate energy in the form of adenosine triphosphate (ATP).**
- **The ATP generated by these pathways in cells is used to drive fundamental cellular processes such as cell division, cell motility, cell differentiation, cell signaling, organelle movement, etc.**

CATABOLISM – OVER VIEW



In Cytosol

In Mitochondria

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Multiple Stages of Cellular Metabolism - Overview:

- The food we consume is mainly comprised of proteins, polysaccharides (carbohydrates) and fats. These cannot be used by the organism directly.
- Digestive process first have to degrade or broken down them into monomers or smaller units such as proteins into amino acids, polysaccharides into sugars, and fats into fatty acids and glycerol. This process occurs outside the cell.
- The amino acids, sugars and fatty acids then enter the cell and undergo oxidation by glycolysis (in the cytosol) and the citric acid cycle (in the mitochondria) to generate ATP (from ADP and Pi).

- During glycolysis, each molecule of glucose is converted into two molecules of pyruvate generating two molecules of ATP, two molecules of NADH in this process.

- Pyruvate that is generated during glycolysis is enters mitochondria where it is converted to acetyl CoA. Likewise fatty acids and aminoacids are converted to acetylCoA.

- Acetylcoa molecules are major source of energy for aerobic organisms and is the common intermediate of oxidative process. These enter into citric acid cycle to combine with oxaloacetate and through several steps generate 3 NADH, 2FADH2 & 1 GTP molecule.

- Majority of ATP is generated when NADH & FADH2 molecules transfer their electrons to O2 via electron transport chain. This generates a proton gradient that is then used to produce ATP. This entire process is called oxidative phosphorylation.

- The most important form of storage for chemical energy in all cell is ATP.

- Waste products from the generation of organic substances in animal metabolism include CO2, H2O & ammonia NH3.

- In mammals, the toxic substance ammonia is incorporated into urea and excreted in this form.

CATABOLISM OF CARBOHYDRATE FOR ENERGY PURPOSE

OXIDATIVE OR CATABOLIC OR DEGRADATIVE PATHWAYS

- Glycolysis
- Citric Acid Cycle

GLYCOLYSIS

DEFINITION

- **Sequence of ten enzymatic reactions converting one molecule of glucose into 2 molecules of pyruvate or lactate with the generation of 2 molecules of ATP.**

Glycolysis: Derived from Greek words

Glykys = Sweet, Lysis = splitting

- **Glycolysis was the very first biochemistry or oldest biochemistry studied.**
- **It is the first metabolic pathway discovered.**
- **It is the universal pathway in the living cells.**
- **Elucidated by the German Biochemists Otto Warburg, G.Embden & O.Mayerhof.**
- **Also referred to as Embden-Mayerhof or EM pathway.**

- Glycolysis takes place in cytosol, because the enzymes of glycolysis are located in the cytosol.
- Major pathway for ATP synthesis in tissues lacking mitochondria (eg:erythrocytes, cornea etc).
- Very essential for brain which is dependent on glucose for energy.
- During this process one molecule of glucose (6 carbon molecule) is degraded into two molecules of pyruvate (three carbon molecule).
- Free energy released in this process is stored as 2 molecules of ATP, and 2 molecules of NADH.

TYPES OF GLYCOLYSIS

- Aerobic Glycolysis

  This occurs in cells in the presence of oxygen

- Anaerobic Glycolysis

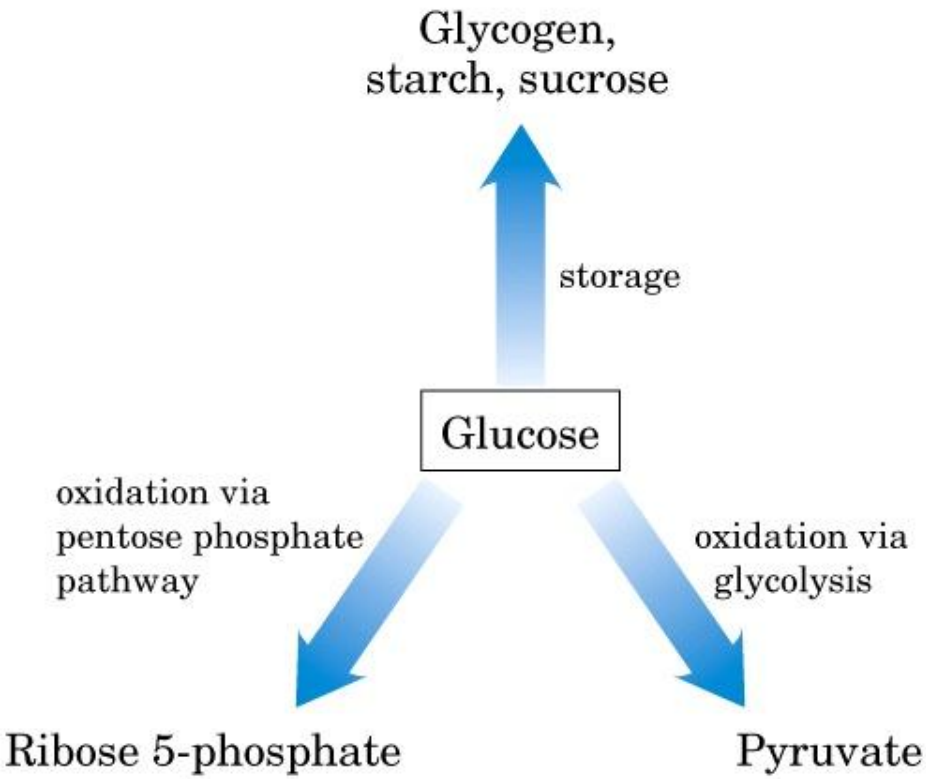
  Occurs in cells under hypoxic conditions. During severe exercise there will be depletion of O2 in tissues. Lactate is formed as the end product.

PHASES OF GLYCOLYSIS

- Energy investment phase or priming stage
- Splitting phase
- Energy generation phase
  - Stage I consumes 2 ATP
  - Stage II produces 4 ATP

Fate of glucose in living systems

5.2% of total free energy that can be released by glucose is released in glycolysis.

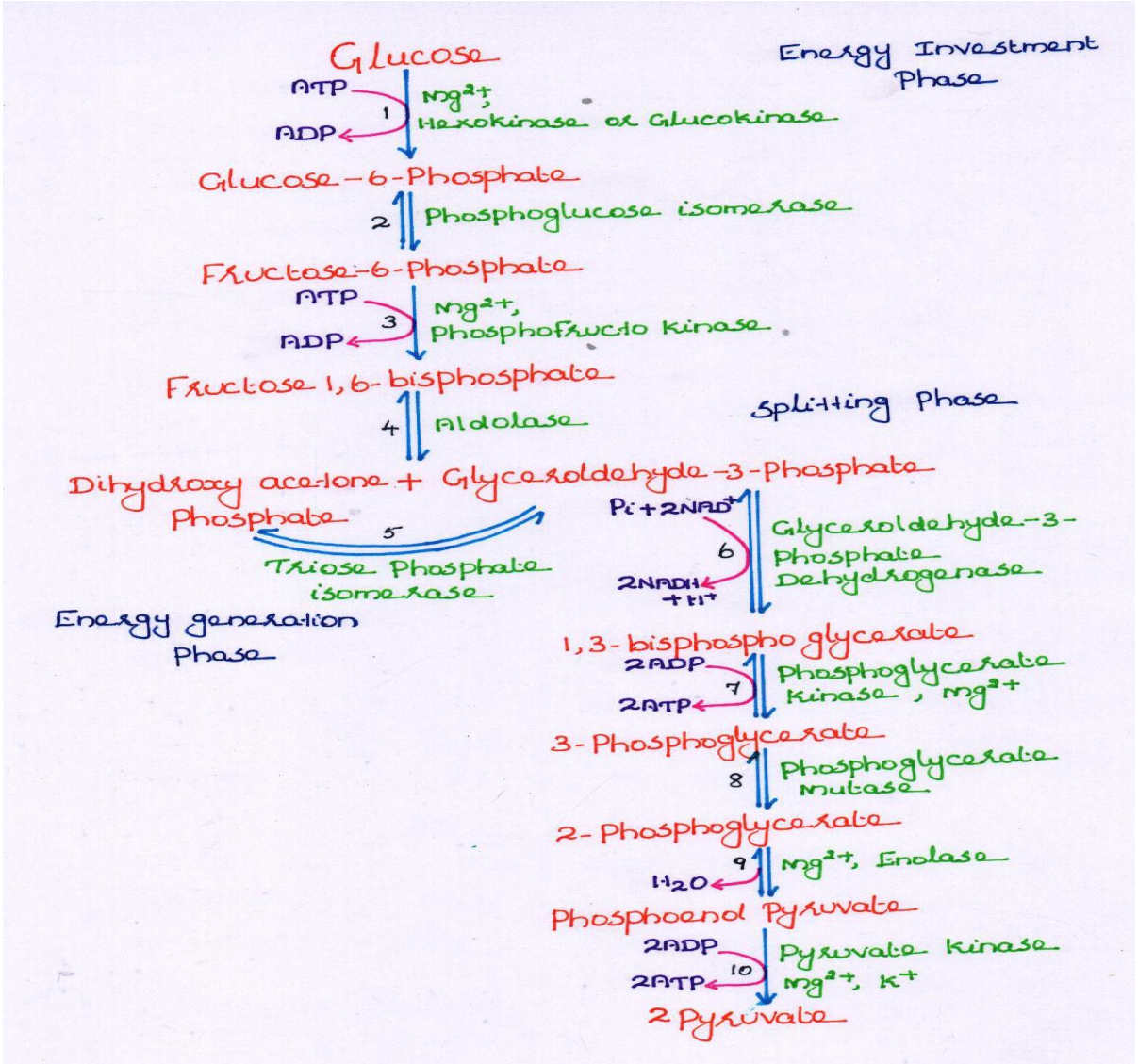


There are 10 enzyme-catalyzed reactions in glycolysis.

Stage 1: Reactions 1-5) A preparatory stage in which glucose is phosphorylated, converted to fructose which is again for phorylated and cleaved into two molecules of glyceraldehyde-3-phosphate. In this phase there is an investment of two molecules of ATP.

Stage 2 & 3: (reactions 6-10) The two molecules of glyceraldehyde-3-phosphate are converted to pyruvate with concomitant generation of four ATP molecules and two molecules of NADH. Thus there is a net gain of two ATP molecules per molecule of Glucose in glycolysis.

GLYCOLYTIC PATHWAY



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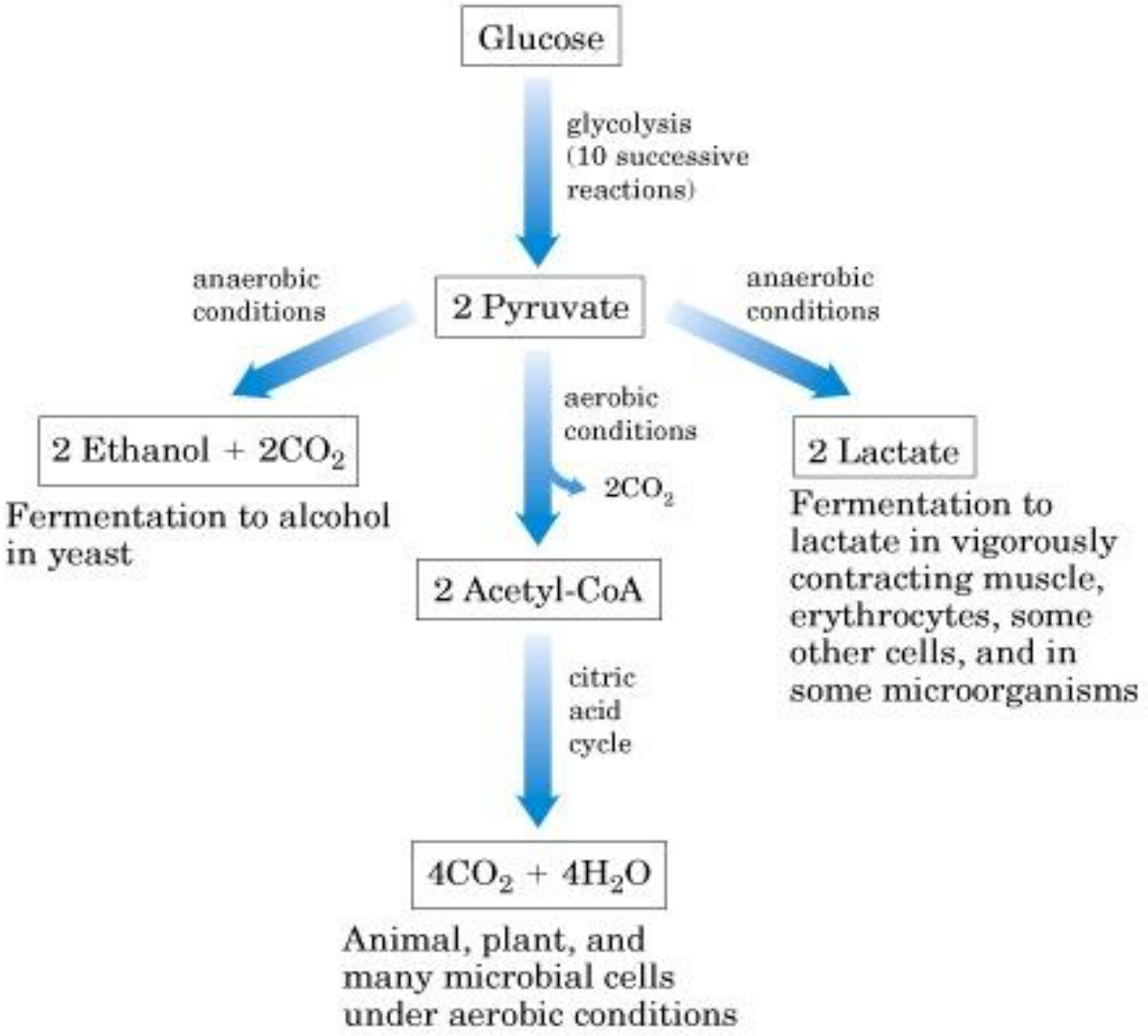
FATE OF PYRUVATE



ENERGETICS

ATP from Glycolysis

Reaction Pathway	ATP for One Glucose
ATP from Glycolysis	
Activation of glucose	-2 ATP
Oxidation of 2 NADH (as $FADH_2$)	4 ATP
Direct ADP phosphorylation (two triose)	4 ATP

Summary:

$$\underset{\text{glucose}}{C_6H_{12}O_6} \longrightarrow 2 \text{ pyruvate} + 2H_2O + 6 \text{ ATP}$$

REGULATION OF GLYCOLYSIS

Two types controls for metabolic reactions:

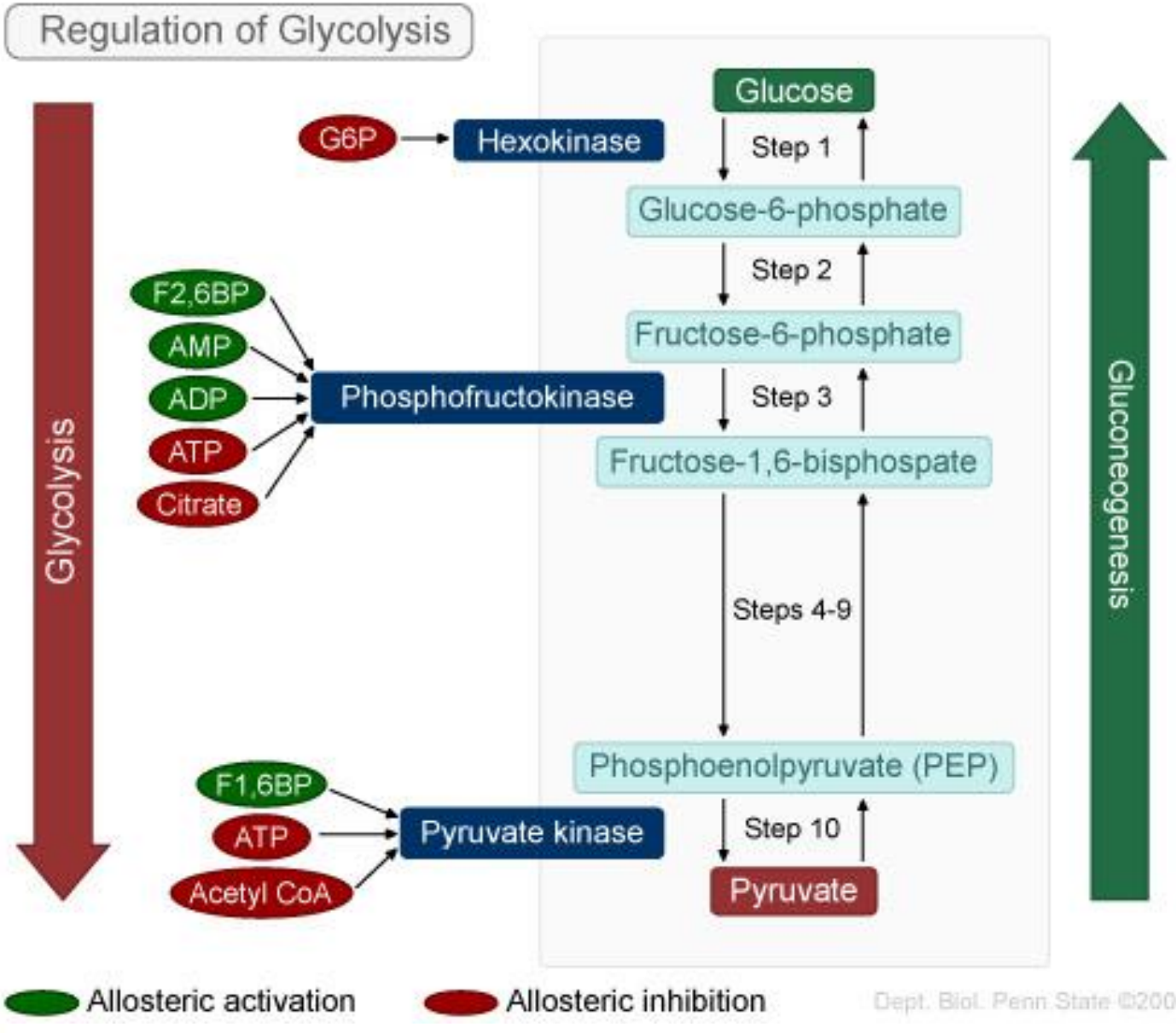
a) Substrate limited : When concentrations of reactant and products in the cell are near equilibrium, then it is the availability of substrate which decides the rate of reaction.

b) Enzyme-limited: When concentration of substrate and products are far away from the equilibrium, then it is activity of enzyme that decides the rate of reaction. These reactions are the one which control the flux of the overall pathway.

Key Enzymes:

Three key enzymes which regulate the flux of glycolysis:

I. **The hexokinase (HK)**
II. **The phoshofructokinase (PFK)**
III. **The pyruvate kinase**



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Definitions

- **Glycosylation : Attachment of carbohydrate moiety is essential for some protein to perform their functions.**
- **Glycolysis : Sequence of reactions converting glucose to pyruvate or lactate, with the production of ATP.**
- **Glycogenesis : Synthesis of glycogen from glucose.**
- **Gluconeogenesis : Synthesis of glucose from non-carbohydrate compounds.**
- **Glycogenolysis : Degradation of stored glycogen in liver and muscle.**

THANK YOU