Chemical Biology
1S2T

Inorganic Molecules in Energy Metabolism

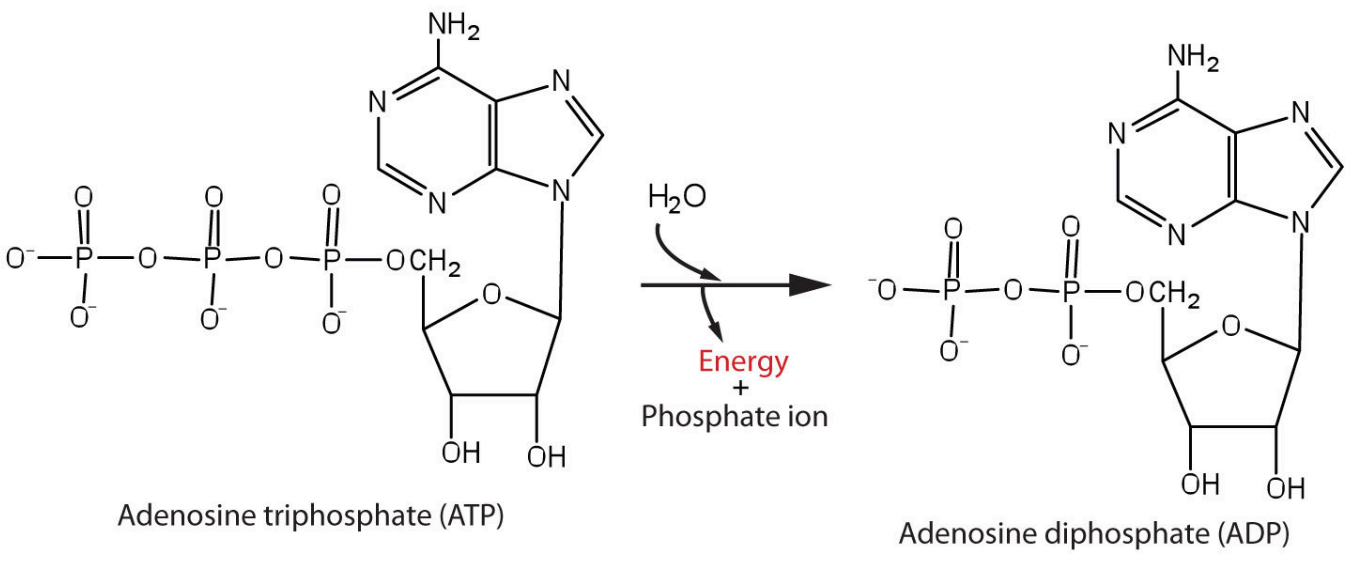
Written Report by Group 3

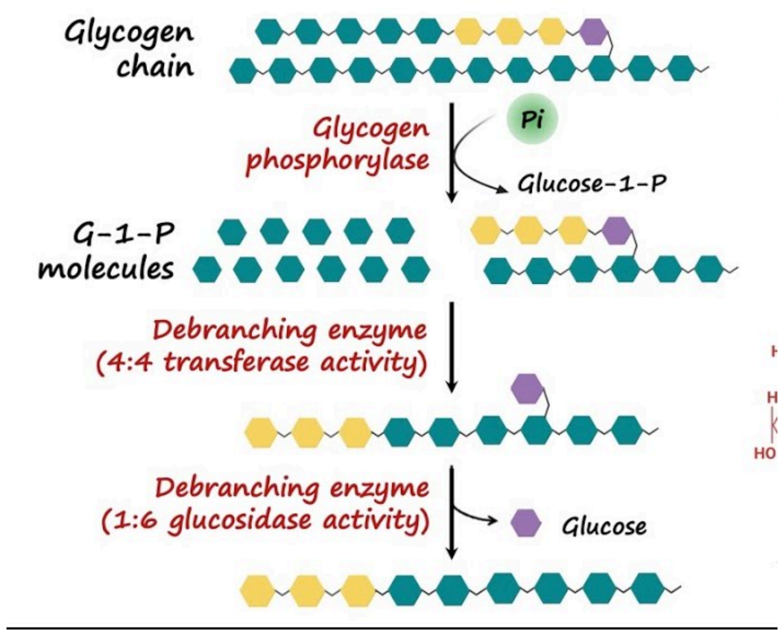
Introduction

Inorganic molecules are essential to the chemical reactions that support life. While organic chemicals like glucose and fatty acids are well known as fuel sources, a closer look reveals that inorganic molecules play an active role in the breakdown, transmission, and regulation of cellular energy. These molecules serve a variety of important functions, including acting as reactants in hydrolytic cleavage of high-energy bonds, final electron acceptors in respiratory chains, contributing to physiological pH balance, improving oxygen delivery to active tissues, driving otherwise irreversible biosynthetic reactions, and even serving as alternative energy substrates when conventional fuels are limited. Beyond energy production, several inorganic compounds aid in nitrogen assimilation, transforming surrounding nutrients into important biomolecules like amino acids and nucleic acids. Others play a role in regulating metabolic pathways like glucose absorption and lipid metabolism, as well as avoiding pathological processes including aberrant mineral deposition. This paper investigates the critical roles of these inorganic compounds in energy metabolism, emphasizing how their chemical characteristics permit efficient ATP generation, metabolic flexibility, and overall cellular homeostasis.

Water

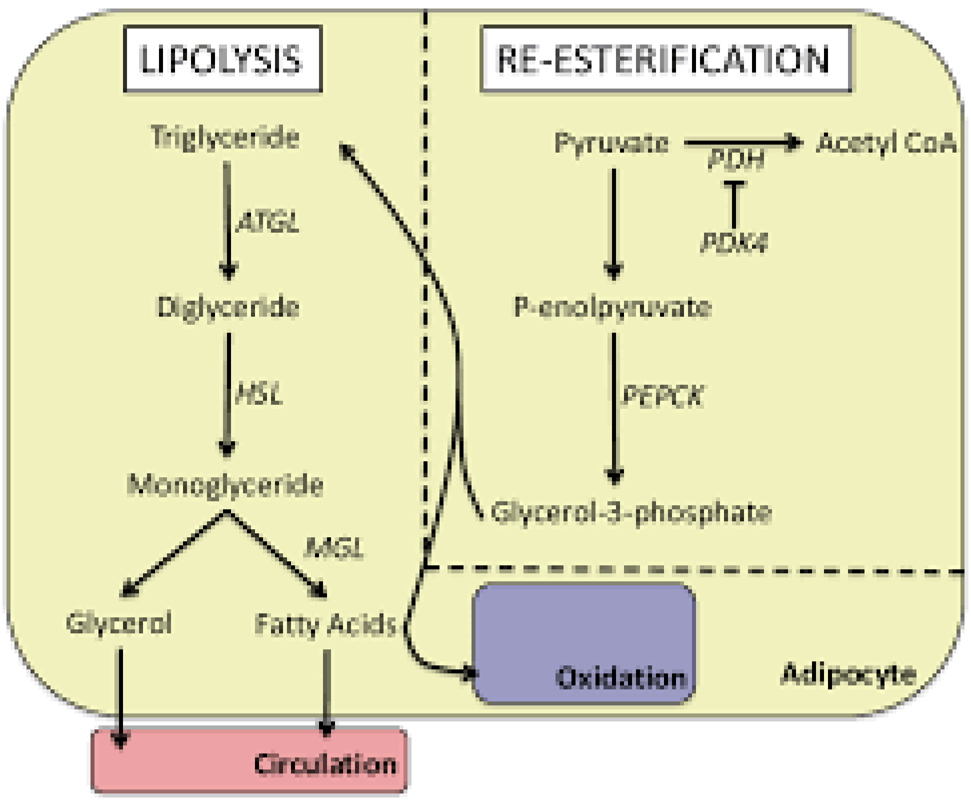
Hydrolysis as a component ATP conversion and Glycogenolysis





Hydrolysis is a key chemical reaction in metabolism that breaks macromolecules into simpler absorbable monomers by the addition of water. Hydrolysis is primarily utilized in breaking down Adenosine Triphosphate (ATP) into Adenosine Diphosphate (ADP) by adding a water molecule to break the high energy terminal phosphoanhydride bond and releases one phosphate group these releases −57 kL/mol of free energy that fuels cellular activities. Additionally, hydrolysis is crucial in breaking down storage molecules like glycogen into glucose for energy. Water molecules break down the branched *a*-1,6-glycosidic bonds in glycogen and release free glucose molecules.

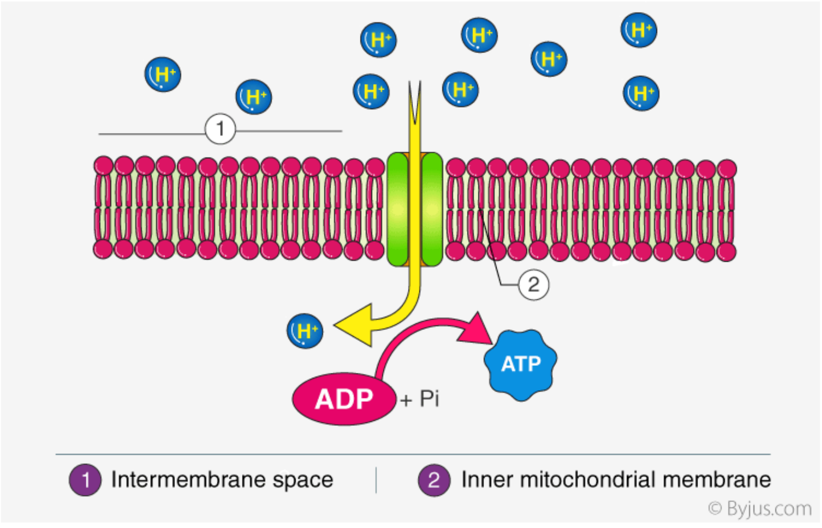
Lipolysis



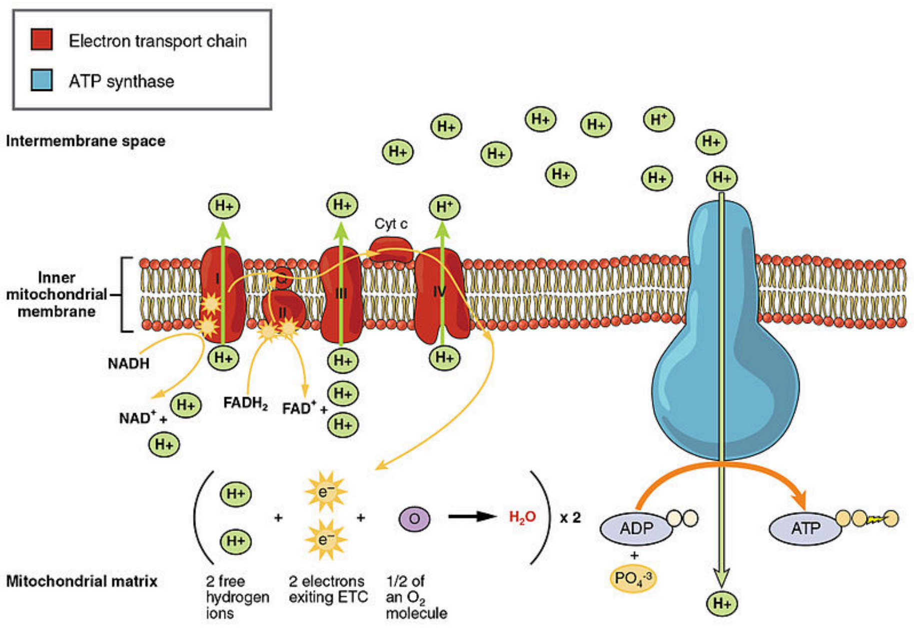
Water is essential in lipolysis, which is a metabolic process where triacylglycerols are broken down via hydrolysis and converted into fatty acids and glycerol. Fatty acids are essential fuels for the body, especially in times where the body is fasting and relies on the fat stored in the adipose tissue. Additionally, glycerol produced by lipolysis is a source of carbon for gluconeogenesis in the liver; produces glucose from non-carbohydrate precursors.

Oxygen

In energy metabolism, inorganic molecules like Oxygen play a crucial role as the final electron acceptor in cellular respiration, allowing cells to efficiently produce energy in the form of ATP. Oxygen enables the complete breakdown of nutrients such as glucose, making energy production much higher compared to anaerobic conditions. One key process that uses oxygen is Oxidative Phosphorylation, where electrons are transferred through the electron transport chain in the mitochondria, and oxygen accepts the electrons at the end to form water, helping drive the production of large amounts of ATP.



Cellular respiration



Oxygen serves as an essential molecule for ATP generation through oxidative phosphorylation. This is the final stage of ATP generation which occurs in the electron transport chain (ETC). Oxygen serves as the final electron receptor in the ETC. 2 free hydrogen ions are utilized with 2 existing electrons and ½ of an oxygen molecule are used to generation one water molecule. This happens twice in the mitochondrial matrix and produces 2 water molecules which can be later utilized for other processes like hydrolysis.

Carbon Dioxide

Carbon dioxide (CO_2) is the fully oxidized inorganic form of carbon derived from organic nutrients such as glucose. It is produced during key stages of aerobic respiration within the mitochondrial matrix:

- **Pyruvate Oxidation:** Pyruvate undergoes oxidative decarboxylation by the pyruvate dehydrogenase complex, releasing one CO_2 molecule and forming acetyl-CoA.
- **Citric Acid (Krebs) Cycle:** Two additional CO_2 molecules are released during the conversion of isocitrate to α-ketoglutarate and succinyl-CoA.

These reactions are coupled with the reduction of NAD^+ to NADH, indicating that CO_2 production reflects the cell's ability to capture high-energy electrons for ATP synthesis.

Physiological Functions of Carbon Dioxide

1) *Acid-Base Balance*

CO_2 is chemically active and plays a major role in maintaining acid–base balance in the body. It diffuses into the bloodstream and reacts with water to form carbonic acid (H_2CO_3), which dissociates into H^+ and HCO_3^-, catalyzed by carbonic anhydrase.

This reversible equilibrium acts as a buffer system:

- Increased CO_2 → increased H^+ → decreased pH (respiratory acidosis)
- Decreased CO_2 → decreased H^+ → increased pH

The body regulates this balance through respiration, adjusting breathing rate to maintain homeostasis

2)D*elivering of Oxygen (Bohr Effect)*

CO_2 functions as a molecular signal that enhances oxygen delivery to active tissues (Malte & Lykkeboe, 2018).

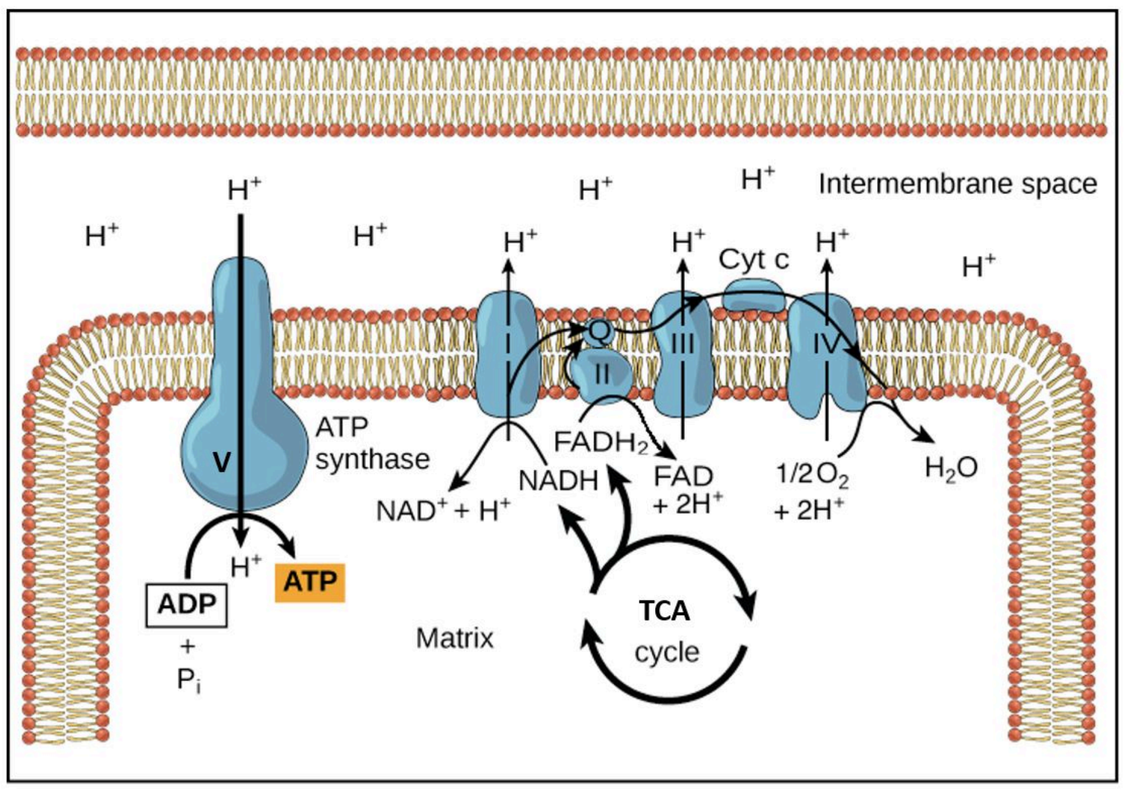
In metabolically active areas (e.g., contracting muscles), CO_2 levels are elevated:

- CO_2 binds to hemoglobin and contributes to a lower pH environment.
- This causes a structural change in hemoglobin, reducing its affinity for oxygen.

As a result, oxygen is more readily released into tissues, supporting continuous ATP production (Malte & Lykkeboe, 2018).

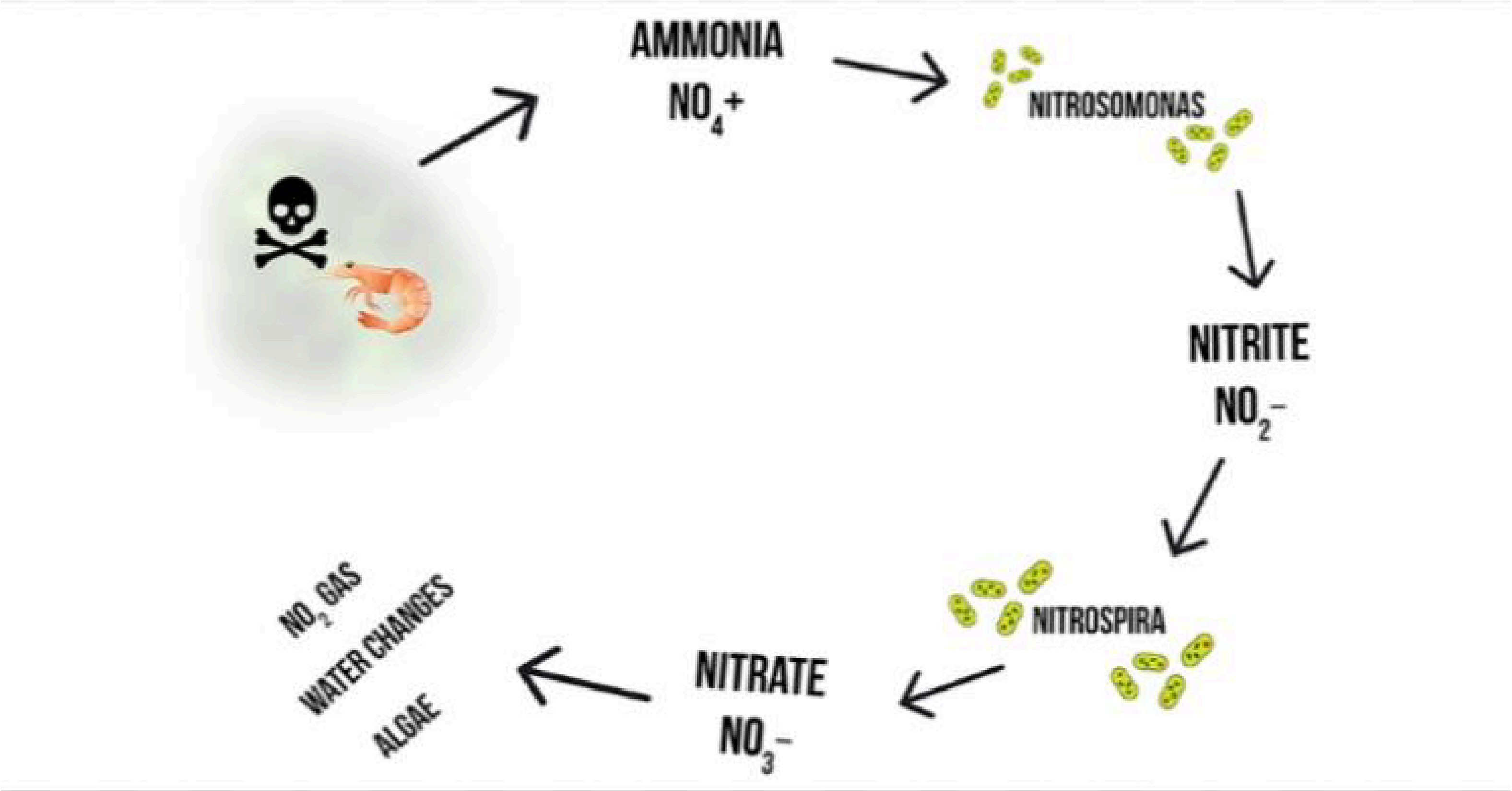
Inorganic Phosphate/Phosphate ion

ATP production



Phosphate ions have an essential role in ATP production and metabolic regulations. In the electron transport chain, phosphate ion is essential in the conversion of ADP into ATP via oxidative phosphorylation. Reduction of oxygen can generate high-energy phosphate bonds that forms ATP. It is a series of oxidation-reduction reactions that involve electron transfer from the NADH and the FADH2 to oxygen via the electron transport chain which generates the ATP molecules utilizing the ATP synthase.

Ammonia and Nitrate



In the nitrogen cycle, ammonia (NH_3) present in the soil is converted into forms that plants can easily absorb through a biological process called nitrification. This process is carried out by nitrifying bacteria, which are specialized microorganisms that obtain energy by oxidizing ammonia (Kuypers, Marchant, & Kartal, 2018).

Nitrification Process

Nitrification is a two-step biological oxidation process carried out by specific soil bacteria that convert ammonia into nitrate, a form that plants can readily absorb.

- **Ammonia Oxidation** – Nitrosomonas bacteria oxidize ammonia (NH_3) into nitrite (NO_2^-). This step releases energy that the bacteria use for their metabolic processes.

- **Nitrite Oxidation** – Nitrobacter bacteria convert nitrite (NO_2^-) into nitrate (NO_3^-). This second oxidation step completes the nitrification process and produces nitrate, the form of nitrogen most commonly absorbed by plants.

Nitrogen Assimilation in Plants

Once nitrate (NO_3^-) enters the plant through the roots, it undergoes nitrogen assimilation, a process that converts inorganic nitrogen into organic compounds needed for growth.

Inside plant cells:

- **Nitrate Reduction** – Nitrate reductase converts nitrate (NO_3^-) into nitrite (NO_2^-).
- **Nitrite Reduction** – Nitrite reductase converts nitrite (NO_2^-) into ammonium (NH_4^+).

The produced ammonium (NH_4^+) is then incorporated into amino acids, which serve as the fundamental building blocks of proteins (Taiz et al., 2022).

These amino acids are assembled into proteins, which are essential for plant growth, enzyme activity, and cellular structure. Nitrogen is also incorporated into nucleic acids (DNA and RNA), which are required for genetic information storage and protein synthesis. Through this pathway, nitrogen derived from ammonia becomes part of the biomolecules that support plant growth and development (Kuypers et al., 2018).

Water (H_2O)

Water (H_2O) is an important inorganic molecule in energy metabolism because it serves as the main medium where metabolic reactions occur, allowing enzymes and substances to interact efficiently; it is involved in hydrolysis, where it helps break down ATP into ADP to release energy and also breaks down food molecules like carbohydrates, fats, and proteins into smaller units for energy production; it supports processes such as glycogenolysis and lipolysis that provide fuel for the body; and it is also produced as a final product of cellular respiration in the mitochondria, showing its role in efficient ATP generation.

Hydrogen Sulfide

Hydrogen sulfide (H_2S) is a colorless, combustible, and highly poisonous gas with the distinct odor of rotten eggs. It occurs naturally in crude oil, natural gas, volcanic gasses, and hot springs. High doses can induce immediate unconsciousness and death, although low amounts can irritate the eyes, nose, and throat.

Substrate for Cellular Respiration (At Low Concentrations)

H_2S, at low quantities, can give electrons to the ETC. It functions as a substrate for mitochondrial sulfide:quinone oxidoreductase (SQR). Electrons from H_2S oxidation are fed into the ETC, contributing to the proton gradient and ATP production. H_2S can serve as an alternate energy source, enabling cells to create energy even when glucose or fatty acids are limited (Szabo, 2021).

Enhancing Glucose Uptake and Glycolysis

H_2S affects sugar processing in cells by activating AMP-activated protein kinase (AMPK), a key energy sensor. AMPK boosts catabolic pathways (which break down molecules for energy) while inhibiting anabolic pathways. It increases glucose absorption in muscle and fat cells by facilitating the translocation of GLUT4 (glucose transporter type 4) to the cell membrane (Li et al., 2023).

Regulating Fat and Lipid Metabolism

H_2S stimulates lipolysis in adipose tissue and boosts fatty acid oxidation in the liver and muscles. It lowers cholesterol levels in the liver, guarding against fatty liver disease. It also causes browning of white adipose tissue, which increases energy expenditure (thermogenesis) (Soriano et al., 2018; Wu et al., 2015).

Inorganic pyrophosphate

Inorganic Pyrophosphate (PPi) is an inorganic compound composed of two phosphate groups linked by a high-energy phosphoanhydride bond, with the chemical formula $P_2O_7^{4-}$. It is produced during many biochemical reactions in living cells, especially when nucleotides such as Adenosine triphosphate are hydrolyzed to support biosynthesis. In many anabolic reactions, ATP is converted into AMP and pyrophosphate, allowing energy to be released and transferred for cellular processes. Because of this, inorganic pyrophosphate serves as an important intermediate in metabolism and contributes significantly to the energy economy of the cell (García-Contreras et al., 2024)

One of the major biological roles of inorganic pyrophosphate is to help drive biosynthetic reactions forward. During DNA replication, RNA transcription, protein activation, and lipid synthesis, pyrophosphate is released as a by-product. This molecule is then rapidly hydrolyzed by pyrophosphatase enzymes into two inorganic phosphate molecules. The hydrolysis of PPi releases additional free energy, making many biosynthetic reactions essentially irreversible and thermodynamically favorable. This mechanism is essential because it prevents the backward reaction and ensures efficient synthesis of important biomolecules (Kajander et al., 2013)

In addition to its intracellular role in metabolism, inorganic pyrophosphate also functions in physiological regulation. It helps prevent abnormal mineral deposition by inhibiting calcium crystal formation in tissues such as blood vessels, joints, and bones. Proper regulation of PPi concentration is therefore necessary for maintaining mineral balance, and abnormalities in its metabolism have been associated with calcification disorders and connective tissue diseases (Terkeltaub, 2001) Overall, inorganic pyrophosphate is a small but highly important molecule because it participates in energy transfer, biosynthetic reactions, and tissue mineral regulation

Magnesium

Magnesium plays an essential role in cellular energy metabolism. It functions primarily by binding to adenosine triphosphate (ATP) to form a biologically active magnesium-ATP complex. This complex is necessary because ATP must be chelated with magnesium to be properly recognized and utilized by enzymes involved in energy transfer. In this form, ATP can be efficiently hydrolyzed to release energy for various cellular processes. Magnesium is therefore required for all reactions that depend on ATP, including those that drive muscle contraction, active transport, and biosynthesis.

Cofactor for numerous enzymes

Beyond its role in ATP binding, magnesium acts as a critical cofactor for numerous enzymes, including kinases, phosphatases, and ATPases. These enzymes are responsible for key metabolic pathways such as glycolysis, oxidative phosphorylation, and glycogen breakdown. By stabilizing the negative charges on ATP's phosphate groups and inducing conformational changes in enzyme active sites, magnesium enables these enzymes to catalyze reactions efficiently. Without adequate magnesium, ATP remains functionally inactive, and energy metabolism is severely impaired. Thus, magnesium is not merely a supporting element but a fundamental requirement for the body to extract and utilize energy from food at the cellular level (Wathar & Verbruggen, 2026).

Conclusion

As a conclusion, inorganic molecules are active and necessary drivers of energy metabolism, rather than passive participants. They allow stored energy from ATP and macromolecules to be released via hydrolysis. They help to generate ATP more efficiently under aerobic conditions by transporting electrons. They also help to regulate the body's pH and transport oxygen to metabolically active areas. Certain inorganic compounds in biological systems act as crucial intermediates, propelling biosynthetic reactions along and ensuring that energy-intensive processes like DNA replication and protein synthesis run smoothly. Others show extraordinary adaptability, acting as alternative energy sources or modulators of metabolic pathways under various situations. Furthermore, the incorporation of inorganic nitrogen into organic compounds demonstrates how ambient inorganic molecules are absorbed into the fundamental building blocks of life. Taken together, these findings demonstrate that energy metabolism cannot be properly understood without acknowledging the critical and complex roles played by inorganic molecules, from mitochondria to the organism as a whole.

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