Energy Metabolism and Life

Introduction

When you put a drop of milk onto a coffee, the milk will gradually diffuse into coffee to make milk coffee without any artificial shaking. However, roll back of the film will never happen such that the diffused mild is concentrated back to the initial stage as a milk drop.

The factor determining the direction of changes occurring in the nature is called entropy, although this quantity is not easily measured and thus is not easy to substantially understand.

The entropy is explained in some case as the degree of randomness or complexity. It is much easier to imagine. Actually, in the above case, the milk condensed in a spot is highly concentrated and thus highly ordered, but after became more randomly distributed in the coffee as time progressed.

Likewise, the reactions occurring in the nature always accompany with the increase of entropy as defined as the second law of thermodynamics.

An effort is necessary for the existence of the creature.

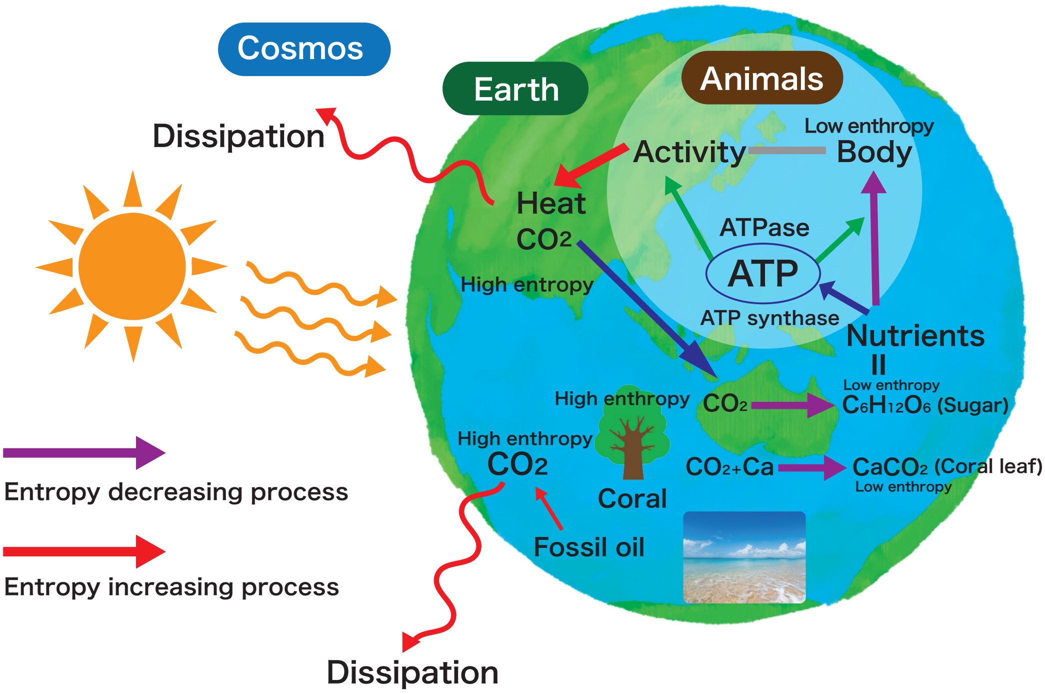
Creatures living on earth appear not to follow this low. They have highly ordered structure (body) and system constructed with complex molecules such as nucleic acids, protein, membrane and polysaccharides and those molecules themselves are in the state of low entropy compared to their building block atoms like carbon and hydrogen.

Since the process to form such highly ordered large molecules and cell structures is accompanied with the decrement of entropy, input of energy is necessary to drive such anabolic reactions against the thermodynamic low. Unless constant energy input, cells have the fate to decompose and fractionated into small pieces of chemicals and atoms.
Against this trend, creatures living on the earth incorporate low entropy substances as nutrients, alternatively, creatures uptake negative entropy (negentropy) to keep the system in highly ordered structure.

Carbon recycling on the earth.

Creatures on the earth are also called “organisms” because they are made of carbon. Therefore, the life activity of creatures becomes a part of carbon recycling on the earth. The carbon-recycling system plays a crucial role for maintaining the structure and activity of organisms as low entropic system, and is the backbone of ecosystem on the earth.

Organisms and Carbon recycling on the earth

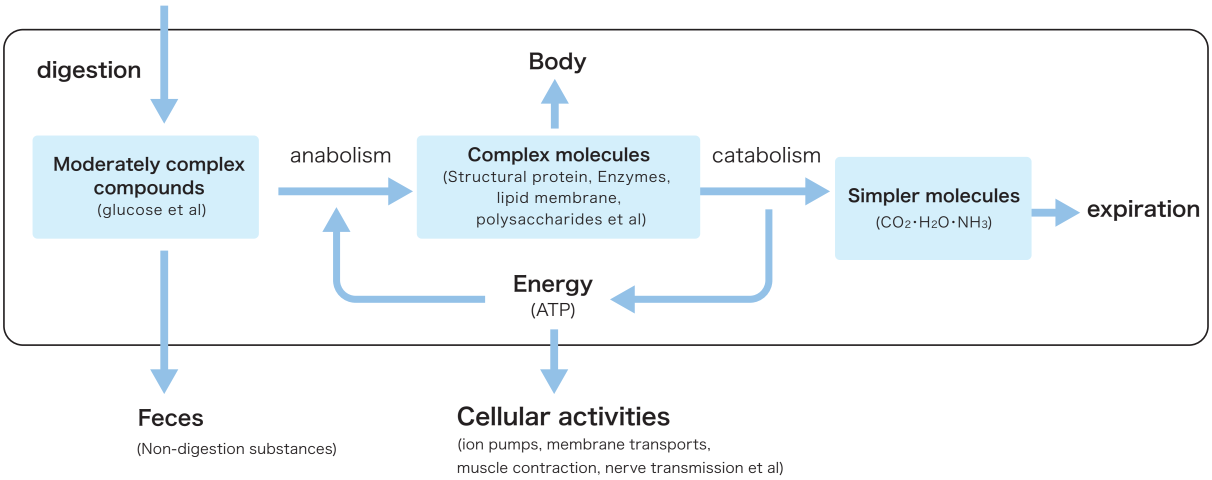


In the carbon-recycling system, atmospheric carbon dioxide is primary fixed with water in plants or other photosynthetic creatures by the use of solar energy. In the sea, choral organisms play a major role in assimilation of carbon dioxide. The photosynthetic synbiotes of choral forms hard backbone shell made of Ca carbonate as the major component, and also synthesize glucose using solar energy as well as in plants on the gland. Glucose is the primary organic molecule produced by photosynthetic creatures and is not only used as the substrate of energy production but also converted to other complex organic molecules necessary for sustaining life activity, that is, the structures and functions of creature. These organisms being able to sustain their life by themselves are called autotrophs.

On the other hand, creatures like animals including human do not have ability to produce glucose by themselves, and thus have to intake glucose or glucose originated low entropic organic compounds from outside as nutrients. From the nutrients, they extract energy and building block substrates necessary for performing living activity and constructing structure. These creatures are thus called heterotrophs.

The glucose and other complex organic compounds taken as nutrients are processed by complex metabolic path to extract energy and stored in the battery molecule ATP, and then used to maintain their structure (body) and energy for the activity. The process related to the production and usage of energy is called energy metabolism. Therefore, the global ecosystem is sustained primary by plants that assimilate low entropy organic compounds from high entropic carbon dioxide and water using solar energy. Therefore, from the carbon recycling, we can understand the characteristics of global ecosystem.

Anabolism and catabolism: metabolic balance

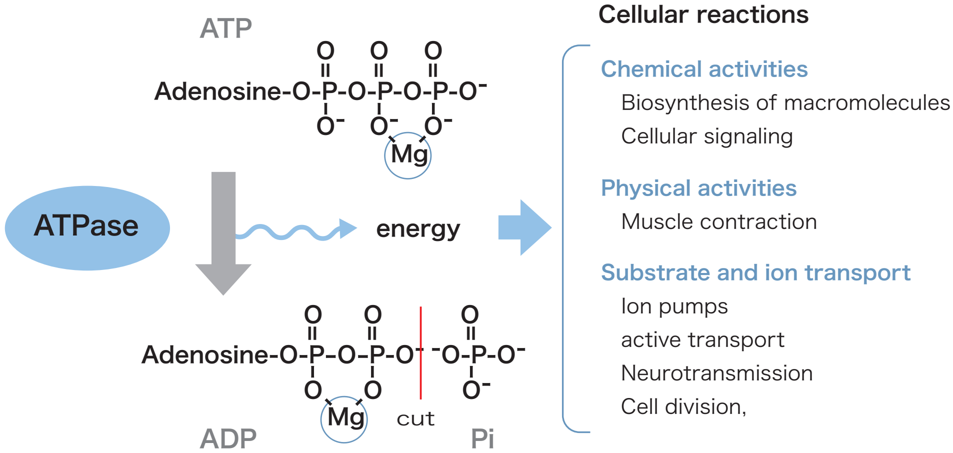


Metabolism is the biochemical processes occurring in the creatures to maintain their body and activity. The process is consisted of two processes called anabolic and catabolic metabolisms. The former is the process converting glucose to more complex organic compounds such as proteins and nucleic acids, and the latter is the process to extract energy for life activities by decomposing glucose and other low entropy substrates. Coupled cycling of anabolic and catabolic metabolisms is essential to keep the entropy of living system in low, and thus the life is in the dynamic equilibrium between synthesis and degradation.

ATP is the energy currency in living system.

In organisms, a chemical compound named ATP is used as a source of energy for driving necessary chemical and physical reactions for living. ATP releases energy occasionally as a battery when is hydrolyzed by the enzyme called ATPase. ATP is often called energy currency of biological system because it supports economic expenditure of energy in living system.

ATP-Mg as the battery for cellular activity



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The works done using ATP includes many processes such as transport of ion and substrates, maintaining ionic balance between inside and outside of cell, concentrating ion or substrate in subcellular organs, synthesis of large molecules such as protein and DNA from smaller building brock molecules, synthesis of physiological mediator molecules including hormone, cellular signaling, muscle contraction, and neurotransmission, et al. Therefore, ATP depletion directly relates to the death of living system. The energy metabolism related to synthesis and hydrolysis of ATP is a basic system to sustain the life.

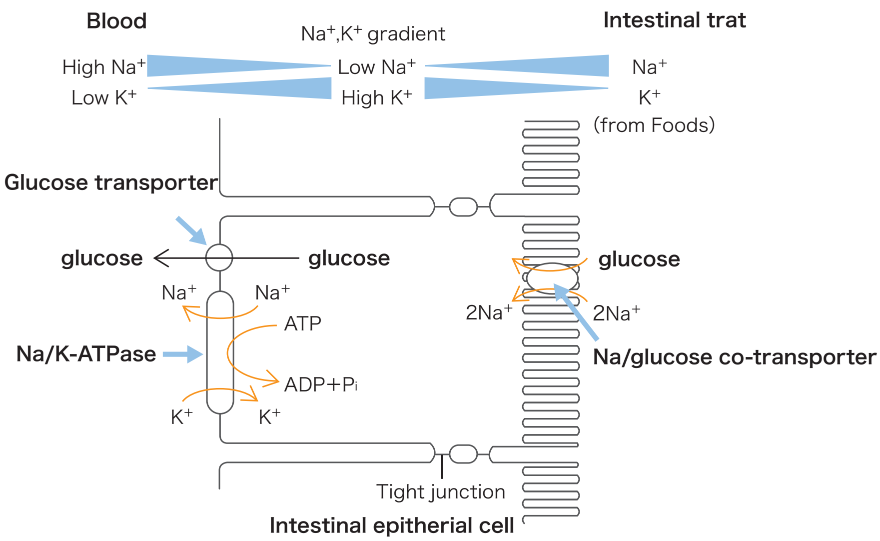
ATPase is the enzyme necessary for using ATP as energy currency.

There are two types of enzyme using ATP as the substrate. One is kinase and the other is ATPase. Kinase is the enzyme mediating phosphorylation of specific protein and other substrate as cellular signals using ATP as phosphate source. On the other hand, ATPase is the enzyme linked directly to the production or usage of ATP as battery. There are several types of ATPase differing the functional mechanism and structure. Almost all ATPase, except acting on muscle proteins actin and myosin, are membrane bound and the chemical energy stored in ATP is used to drive mechanical works such as protein conformation change or rotation associated with such as muscle contraction or substrate and ion transport.

Na/K-ATPase is an essential ion pump for the cell.

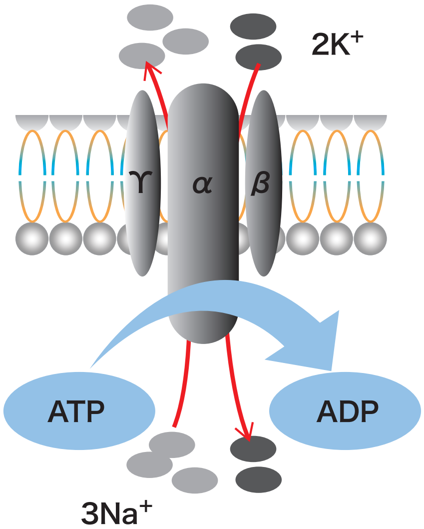
Cell functions are basically controlled by the electrochemical potential created by transmembrane movement of ions. Therefore, the ATPase functioning as ion pump is the basic device for maintaining cell physiology. Na/K-ATPase is the one that plays basic and essential role in cell physiology.

Cells maintain high K^+ and low Na^+ concentrations inside so as to create certain membrane potential called resting membrane potential under physiological condition. This potential is created by K^+ outflow through K^+ channel presenting in plasma membrane that is driven by the concentration gradient across the membrane. Change of the membrane potential associates with cellular functions such as cell excitation and transport of substrates or ions. The high diffusion potential of Na^+ also facilitates cellular uptake of necessary substrate such as glucose through co-transporter protein.



Creation and maintenance of large concentration gradient of K^+ and Na^+ is attained by the Na/K-ATPase that pumps in three K^+ equivalent from outside in coupled with pumping out of two Na^+ equivalent from inside to outside using energy produced by hydrolyzing ATP. This ATPase forms phosphorylated intermediate during pumping ion, and thus this type of ATPases are called P-type ATPase.

This ATPase pumps out Na^+ from the cell and pumps K^+ into the cell to create membrane potential using the energy produced by ATP hydrolysis.



●**Motive force of membrane transport (electrochemical energy)**

Membrane potential (electric energy)
Concentration gradient (chemical energy)

Type	Examples of Channel and transporter
Passive transport	K^+-channel, Ca-channel, aquaporin
Facilitated transport	GLT2、GLT4
Active transport	Na/K-ATPase, H/K-ATPase, Ca-ATPase, Na/glucose co-transporter

There are many other types of ATPase functioning in cells. Ca-ATPase is the one that regulates Ca^+ concentration as cellular signal molecule, or more directly as a coupled ion of certain substrate transport or mechanical works at cell membrane, mitochondria, and in muscle endoplasmic reticulum. Other ATPases such as H^+-ATPase functioning in gastric juice excretion, and Na^+/H^+-ATPase functioning in Na^+ reabsorption in kidney, are playing critical roles in maintaining physiological state of cells together with transporter or channel proteins.

Mg is the essential mineral for ATP related reactions.

$Ca2^+$ and $Mg2^+$ are the essential minerals for ATPase reaction. ATPase is a protein complex having two domains, that is, channel forming domain and catalytic domain. The former domain has two structures named channel and valve. The ion or substrate is selected by the valve and transported through the channel across the membrane. Catalytic domain, on the other hand, has ATP binding site. ATP bound to the site is subjected to hydrolytic reaction to release energy. For proper binding of ATP to the site, ATP needs to form a chelate complex with Mg ion. Mg and also Ca have another function such that regulates the direction of the reactions progressing in the ATPase enzyme. Mg is, thus, the essential mineral for energy metabolism.

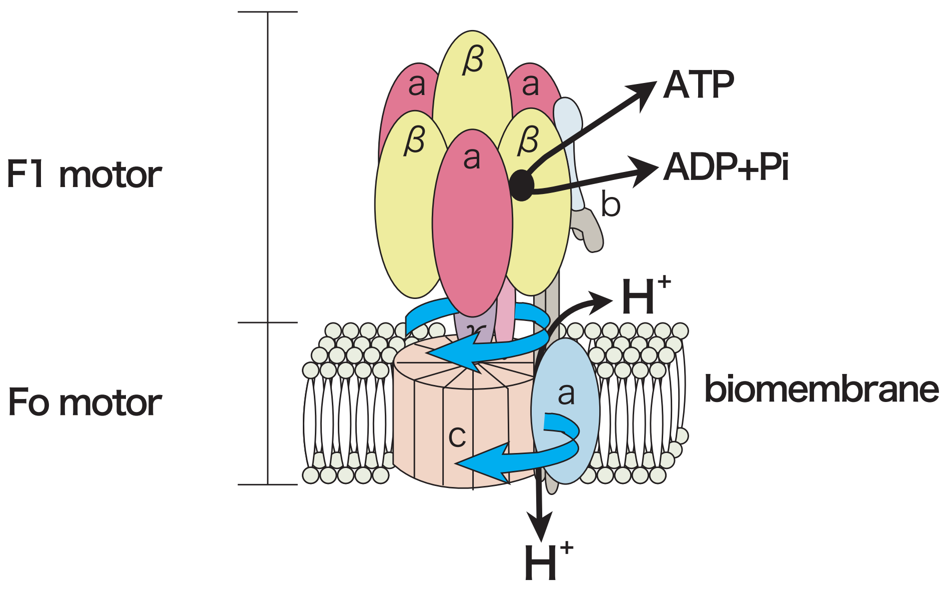
Mitochondria are the cellular energy plant for ATP production.

ATP is produced in part in the process of anaerobic glycolysis in cytoplasm but is produced mainly at cell organelle named mitochondrion, and thus mitochondria are called cellular energy plant to provide necessary energy for living.

ATP is produced by ATP synthase enzyme complex in mitochondria.

ATP synthase is the enzyme to produce ATP in mitochondria. The driving force of ATP synthesis is the electrochemical potential formed by the function of electron transport chain located in the inner mitochondrial membrane. ATP synthase has two major subunits named Fo and F1, respectively. Fo is located in the membrane to form a proton channel and F1 is located on the membrane surface. Fo functions as a mechanical motor, which rotates when protons flow through the channel. This rolling is mechanically transferred to F1 subunit as catalytic site to rotate so as to the bound ADP reacts with Pi to produce ATP. This reaction is reversal. Therefore, F1 can hydrolyse ATP to ADP and Pi to create proton electrochemical potential, and this process is actually happening in H^+-ATPase. This type of ATPase is called F1-type ATPase.

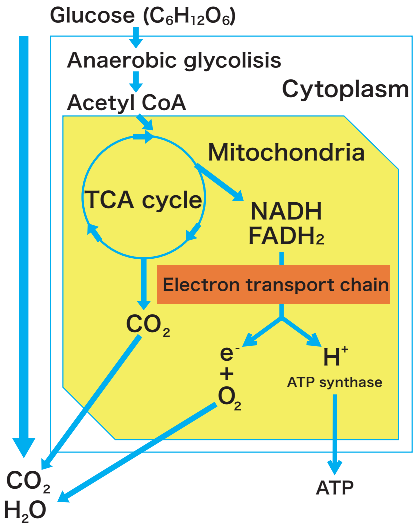
Structure and function of ATP synthetase

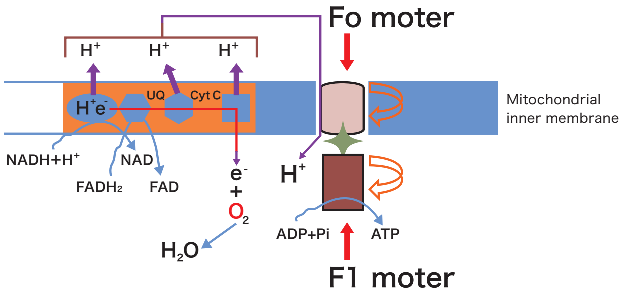


Overview of cellular energy metabolism.

Glucose as nutrient is metabolized in the process called anaerobic glycolysis. During the process, the negative entropy (negentropy) stored in the nutrient is converted to reducing substrates, NADH or $FADH_2$. Then, proton and electron are extracted from these substrates by the redox enzymes forming electron transport chain. The electrons extracted are transferred through electron transport chain components to oxygen to produce H_2O. On the other hand, the protons are expelled into intra-mitochondrial membrane space to create electrochemical potential to use for driving ATP synthase enzyme to produce ATP. Therefore, glucose as nutrient is decomposed back to the original building blocks, CO_2 and H_2O, via glycolysis - TCA cycle - electron transport chain reactions. By these processes, the energy stored in the nutrients are gradually converted to ATP as fuel battery usable for life activity. It is easy to understand that this energy metabolism is quite unique and clever system for using energy included in nutrients, because simple decomposition by burning produces only heat as energy that is useless to drive reactions in living system.

Cellular glucose metabolism to produce ATP





Glucose is metabolized to afford NADH and $FADH_2$ as the substrates for mitochondrial energy production. Electron transport chain consisting of 4 enzyme complexes and 2 redox molecule located in mitochondrial inner membrane extracts electron and H^+ from the substrate that are used to create electrochemical potential to drive ATP synthetase and reduce oxygen to H_2O.

Minerals and antioxidant intake are important for maintaining living system.

Even though the energy metabolism select this silent oxidation mechanism, the l living system still faces to oxidative stress. During electron transport chain reaction, so called active oxygen species are exclusively produced, and thus living system developed inherent antioxidant protection system in that antioxidant enzymes function such as superoxide dismutase and glutathione peroxidase. From the standpoint of energy metabolism, in addition to intake the substrate nutrients for energy production, we need to care about proper intake of natural antioxidants and minerals. Those play critical roles in driving and maintaining the energy metabolism in living system.

(Tetsuya Konishi 2019/01/10)

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