Lecture:6

Substrate Cycling

A substrate cycle is a set of metabolic reactions, arranged in a loop, which does not result in net consumption or production of the metabolites. The cycle operates by transforming a cofactor, e.g. oxidizing a reducing equivalent.

Substrate cycles can be shown, theoretically, to be **one of a series of mechanisms** for improving sensitivity of enzymes, enzyme-systems or transport processes to changes in the concentrations of effectors.

The reason this cycle was called "futile" cycle was **because it appeared that this cycle operated with no net utility for the organism**. As such, it was thought of being a quirk of the metabolism and thus named a futile cycle.

Futile cycles are **processes in which the only net change is energy dissipation**. A common example of a futile cycle is carboxylating PEPC activity countered by decarboxylating PEPCK activity.

A futile cycle, also known as a substrate cycle, occurs when two metabolic pathways run simultaneously in opposite directions and have no overall effect other than to dissipate energy in the form of heat. The reason this cycle was called "futile" cycle was because it appeared that this cycle operated with no net utility for the organism. As such, it was thought of being a quirk of the metabolism and thus named a futile cycle. After further investigation it was seen that futile cycles are very important for regulating the concentrations of metabolites. For example, if glycolysis and gluconeogenesis were to be active at the same time, glucose would be converted to pyruvate by glycolysis and then converted back to glucose by gluconeogenesis, with an overall consumption of ATP. Futile cycles may have a role in metabolic regulation, where a futile cycle would be a system oscillating between two states and very sensitive to small changes in the activity of any of the enzymes involved. The cycle does generate heat, and may be used to maintain thermal homeostasis, for example in the brown adipose tissue of young mammals, or to generate heat rapidly, for example in insect flight

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muscles and in hibernating animals during periodical arousal from torpor. It has been reported that the glucose metabolism substrate cycle is not a futile cycle but a regulatory process. For example, when energy is suddenly needed, ATP is replaced by AMP, a much more reactive adenine.

Examples of substrate cycling are cycling of gluconeogenesis and glycolysis pathways and cycling of the triglycerides and fatty acid pathways. Rates of substrate cycling may be increased many-fold in association with hypermetabolic states resulting from severe burns, cold exposure.

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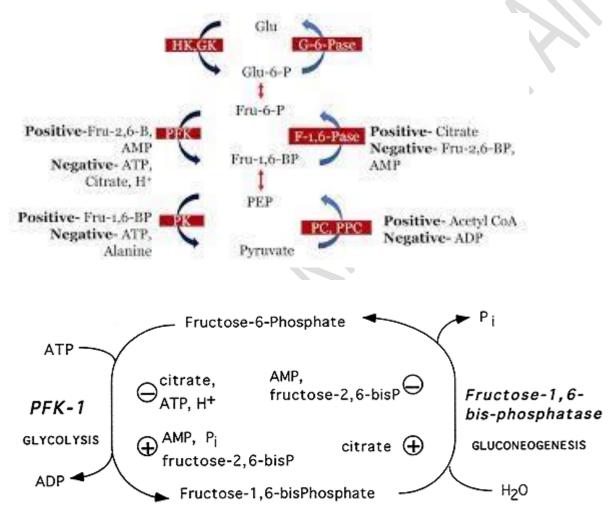
The Cori cycle is futile because each round produces two skeletal muscle ATP molecules and consumes six in the liver, for a net consumption of 4 ATP equivalents. Cori cycling is energetically supported by fatty acid oxidation in the liver for gluconeogenesis, as well as in the muscle to support muscle ATP demand

Substrate cycles, also known as futile cycles, are cyclic metabolic routesthat dissipate energy by hydrolysing cofactors such as ATP. A popular example is the conversion of fructose 6-phosphateto fructose 1,6-bisphosphate and back.

Substrate cycles, also known as futile cycles, comprise pathways with a cyclic flow that result in the dissipation of energy but do not perform any anabolic or catabolic transformation. In the simplest case, substrate cycles correspond to the interconversion between two substrates. The driving force of these cycles is an exergonic process usually involving the permanent hydrolysis of energy-rich cofactors such as ATP. The function of these cycles is not yet completely understood, although the experimental observation of these cycles has allowed various hypotheses to be put forward: thermogenesis in brown adipose tissue as well as in muscles of bumble-bees, improved regulation, and substrate cycles as a buffering mechanism in metabolic precursor supply as well as in

thermodynamic buffering .Typical examples of substrate cycles occur in carbohydrate catabolism and can be found in important pathways such as glycolysis and an aplerotic reactions . Pairs of kinase and phosphatase reactions

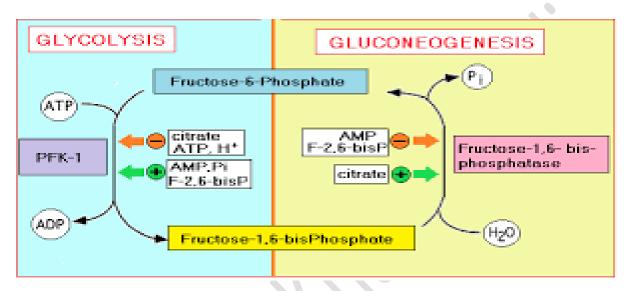
such as hexokinase/glucose 6-phosphatase (glucose6-phosphate cycle) and phosphofructokinase-1/fructose 1,6-bisphosphatase (fructose 1,6-bisphosphatecycle) are often found in many organisms and cell types,including human hepatocytes and adipocytes .



a cycle of sucrose synthesis and degradation exists in sugar cane, involving up to five reactions.

The simultaneous carrying out of glycolysis and gluconeogenesis is an example of a futile cycle, represented by the following equation:

For example, during glycolysis, fructose-6-phosphate is converted to fructose-1,6-bisphosphate in a reaction catalysed by the enzyme phosphofructokinase 1 (PFK-1).



ATP + fructose-6-phosphate → Fructose-1,6-bisphosphate + ADP

But during gluconeogenesis (synthesis of glucose from **pyruvate** and other compounds) the reverse reaction takes place, being catalyzed by fructose-1,6-bisphosphatase (FBPase-1).

Fructose-1,6-bisphosphate $+ H_2O \rightarrow fructose$ -6-phosphate $+ P_i$

Giving an overall reaction of:

$$ATP + H_2O \rightarrow ADP + P_i + Heat$$

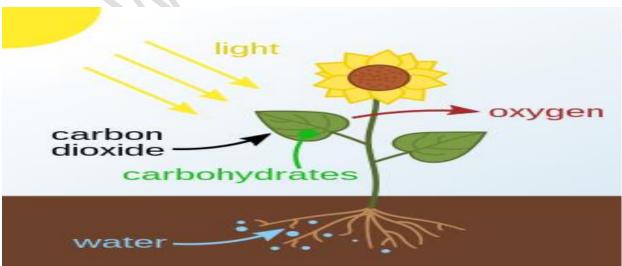
That is, hydrolysis of ATP without any useful metabolic work being done. Clearly, if these two reactions were allowed to proceed simultaneously at a high rate in the same cell, a large amount of chemical energy would be dissipated as heat. This uneconomical process has therefore been called a futile cycle.

Futile cycles have held the interest of microbial physiologists for decades as a form of energy spilling and as a potential energy management mechanism. Futile cycles are processes in which the only net change is energy dissipation.

Photosynthesis

Photosynthesis is the process by which plants use sunlight, water, and carbon dioxide to create oxygen and energy in the form of sugar.

Photosynthesis is a process used by plants and other organisms to convert light energy into chemical energy that, through cellular respiration, can later be released to fuel the organism's activities. Some of this chemical energy is stored in carbohydrate molecules, such as sugars and starches, which are synthesized from carbon dioxide and water – hence the name photosynthesis, from the Greek "light", and synthesis "putting together". Most plants, algae, and cyanobacteria perform photosynthesis; such organisms are called photoautotrophs. Photosynthesis is largely responsible for producing and maintaining the oxygen content of the Earth's atmosphere, and supplies most of the energy necessary for life on Earth.



Although photosynthesis is performed differently by different species, the process always begins when energy from light is absorbed by proteins called reaction centers that contain green chlorophyll (and other colored) pigments/chromophores. In plants, these proteins are held inside organelles called chloroplasts, which are most abundant in leaf cells, while in bacteria they are embedded in the plasma membrane. In these light-dependent reactions, some energy is used to strip electrons from suitable substances, such as water, producing oxygen gas. The hydrogen freed by the splitting of water is used in the creation of two further compounds that serve as short-term stores of energy, enabling its transfer to drive other reactions: these compounds are reduced nicotinamide adenine dinucleotide phosphate (NADPH) and adenosine triphosphate (ATP), the "energy currency" of cells.

Photosynthesis is vital for climate processes, as it captures carbon dioxide from the air and then binds carbon in plants and further in soils and harvested products.

The general equation for photosynthesis as first is:

CO₂carbon

dioxide + $2H_2$ Aelectron donor + <u>photons</u> light energy \rightarrow [CH₂O]<u>carbohydrate</u> + 2Aoxidized electron donor + H_2 Owater

Since water is used as the electron donor in oxygenic photosynthesis, the equation for this process is:

CO₂carbon

dioxide + $2H_2O$ water + photonslight energy \rightarrow [CH₂O]carbohydrate + O_2 oxygen + H_2O water

This equation emphasizes that water is both a reactant in the $\underline{\text{light-dependent}}$ reaction and a product of the $\underline{\text{light-independent reaction}}$, but canceling n water molecules from each side gives the net equation:

CO₂carbon

dioxide + H_2O water + photonslight energy \rightarrow [CH₂O]carbohydrate + O₂ oxygen

photosynthesis, the process by which green plants and certain other organisms transform light energy into chemical energy. During photosynthesis in green plants, light energy is captured and used to convert water, carbon dioxide, and minerals into oxygen and energy-rich organic compounds.

It would be impossible to overestimate the importance of photosynthesis in the maintenance of life on Earth. If photosynthesis ceased, there would soon be little food or other organic matter on Earth. Most organisms would disappear, and in time Earth's atmosphere would become nearly devoid of gaseous oxygen. The only organisms able to exist under such conditions would be the chemosynthetic bacteria, which can utilize the chemical energy of certain inorganic compounds and thus are not dependent on the conversion of light energy.

Energy produced by photosynthesis carried out by plants millions of years ago is responsible for the fossil fuels (i.e., coal, oil, and gas) that power industrial society. In past ages, green plants and small organisms that fed on plants increased faster than they were consumed, and their remains were deposited in Earth's crust by sedimentation and other geological processes. There, protected from oxidation, these organic remains were slowly converted to fossil fuels. These fuels not only provide much of the energy used in factories, homes, and transportation but also serve as the raw material for plastics and other synthetic products. Unfortunately, modern civilization is using up in a few centuries the excess of photosynthetic production accumulated over millions of years. Consequently, the carbon dioxide that has been removed from the air to make carbohydrates in photosynthesis over millions of years is being returned at an incredibly rapid rate. The carbon dioxide concentration in Earth's atmosphere is rising the fastest it ever has in Earth's history, and this phenomenon is expected to have major implications on Earth's climate.