BOLK'S COMPANIONS

FOR THE STUDY OF MEDICINE

BIOCHEMISTRY

from a phenomenological point of view

Christa van Tellingen, M.D.

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About the author

Christa van Tellingen, M.D. (born in Holland in1949) has been a family physician in California since 1982. From the beginning of her medical studies she has recognized the importance of a new approach to science for understanding the human being in health and disease. In her practice she has found the goethean phenomenological method of observation to be of great value in understanding and treating patients. She has taught medical students and physicians in the United States, Canada, and Europe.

In 1998 she was one of the originators of "Renewal of Medical Education", a project to produce a complement to the current biomedical scientific approach of the human being.

About the Project

The project "Renewal of Medical Education" aims to produce modules which demonstrate how the facts of current biomedical science can be understood differently by using Goethe's phenomenological method. This results in new concepts in biomedical science. These new concepts recapture an understanding of biochemical, physiological and morphological factors in living organisms and their development in time and space. This enables one to see, for instance, the relations of consciousness, psychology and behavior to the shape of the body.

BOLK'S COMPANIONS FOR THE STUDY OF MEDICINE complement current medical education, specifically revealing human qualities in the biomedical sciences of today.

Contents

Preface

This module of **BOLK**'S COMPANIONS FOR THE STUDY OF MEDICINE is presented in an effort to aid medical and other science students in their study of the biochemistry of functioning organisms, and to help them remember it better in later study and work.

It is meant as a supplementary text in biochemistry to assist in gaining an overview of the whole of the subject by using an innovative study and research approach known as the goethean method. At the Louis Bolk Institute in Holland, where this work was written, this method is used extensively in research in the fields of agriculture, nutrition and medicine. Its aim is to connect details with one another meaningfully. Since the detailed knowledge we have of biochemistry derives from coherent organisms, it is possible to draw the details together again and thus augment our understanding of the functioning of organisms.
In the goethean method phenomena are gathered and characterized. This is done, for instance, by demonstrating where certain processes are typical in the living world. Comparing a prototypical process with others within the organism or elsewhere in living nature enables us to draw conclusions as to its role or meaning in the whole of the organ or organism. Thus a greater overview of the subject is gained.
Therefore, in addition to studying the details of biochemistry texts, the study of this module will aid in finding the coherence between organs, organisms, and living nature.
We dedicate this work to all students who need to learn the facts of biochemistry and who also want to gain a greater understanding.
We want to emphasize that this module does not replace studying biochemistry textbooks. The information contained here is compact and presupposes the knowledge contained in such textbooks. But it hopes to make studying and remembering the texts (even) more interesting.

The originator of this new approach to science is the author and scientist Wolfgang von Goethe. For further information on this method we refer to the book by Henri Bortoft, 1986.

Acknowledgements

This module was written at the Louis Bolk Instituut, Driebergen, Holland. It is the result of a stimulating exchange of ideas among colleagues. I am most grateful to Reinout Amons, Harry Scholberg, Maria Linder, Tom Scheffers, Willem Jan van Mierlo, Edmond Schoorel, Guus van der Bie and many others for their valuable comments, and look forward to our further collaboration. The next subject will be the molecular basis of cell biology.

This project was made possible financially by gifts from Iona Stichting, Stichting Phoenix, Pharma Natura (S. Africa), Stichting ter Bevordering van de Heilpedagogie, Stichting Triodos and individual people.

Christa van Tellingen, Driebergen, September 2001

Introduction

How can we do justice to life itself when studying the life sciences?

Biochemistry is the area in the life sciences which pre-eminently offers insight into the continuous and manifold changes that occur in organisms. It shows substances to be not static but ever changing, in structure as well as function. The cell, including the cell membrane, as well as tissues and organisms, are structures in flux.

The flow of organisms is related to their metabolism. While on the level of tissues and organs an organism may seem relatively stable, its biochemical compounds are more or less constantly involved in a process of metabolism. Metabolism is the continual conversion of compounds that takes place in cells and tissues. It builds up to larger molecules (anabolism) or breaks down to smaller ones (catabolism). The rate and kind of metabolism of tissues varies minute by minute according to tissue function, time of day, time of life, mental state. Biochemistry is concerned with the chemistry of *living* organisms. Organisms function as a whole and biochemical reaction processes are interrelated as a consequence. *If we can relate the individual processes to the whole of the organism, we remain aware of the coherence of the substance flow and do more justice to the laws of life.*

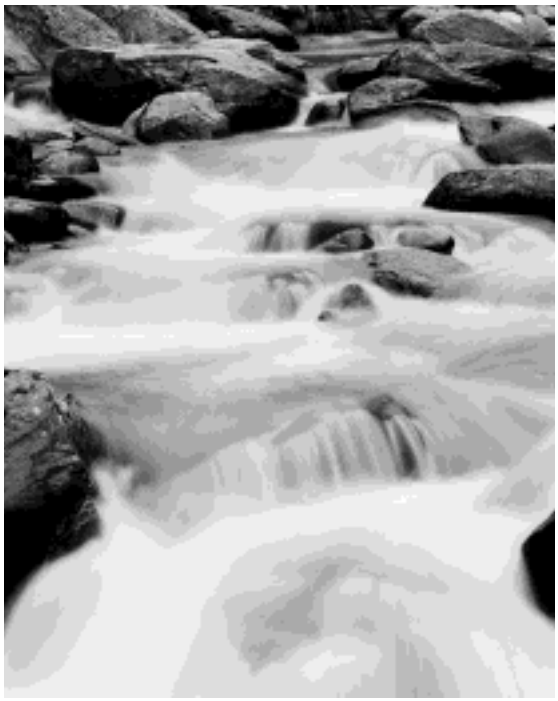
Biochemistry can teach us to see the human body as a standing wave in a creek. The standing wave occurs when irregularities in the creek bed (a rock, for instance) cause the water to form a wave. The standing wave has a more or less constant shape while new water is flowing through it all the time. The unique pattern of the creek bed and the properties of water determine the shape of the standing wave. At the same time, the creek bed is changed by the flow of water in the standing wave. The shape of the standing wave and the unique pattern of the creek bed are interdependent.

Similar to the interdependence of water flow and the shape of the creek bed, the flow of metabolic reaction processes in an organism and the type and shape of the organism are

interrelated. The flow of these processes is unique for each organism. This is true for *living* organisms. Reaction processes in *inorganic* chemistry can be carried out separately; they stand more on their own.

We will try to find if the different groups of compounds in biochemistry and their reaction processes have a *prototypical* place and function, and where and how they fit into the whole of the metabolic flow. For instance: all living organisms have a carbohydrate metabolism; we will demonstrate where in the human organism and in living nature carbohydrate processes have been perfected and play a special role.

We will find this by *making an inventory* of the specific reaction processes, appearance and occurrence of metabolic compounds, and by then *characterizing* them to indicate the type of process we are dealing with. To find relations within the metabolic flow we will use the *comparative* method, which will demonstrate how the various processes are integrated within living organisms.



The result is a coherent view of the facts and a greater understanding of the flow of metabolic processes. Experience has taught that an overview of the whole makes remembering the details easier. Studying this module will make biochemistry more interesting and easier to remember as well as increase our respect for nature.

The questions posed within the boxes do not have definitive answers yet. They are meant to stimulate further research.

1. Metabolism

Introduction

Metabolic flow is based on anabolic and catabolic reactions. Metabolism begins with the ingestion of food that is foreign to the organism (containing a varying amount of smaller and larger compounds), which is broken down in the digestive tract to smaller molecules by hydrolysis.
An anabolic phase occurs when the smaller molecules are taken up into the organism's bloodstream and become part of the organism. Catabolic reactions constantly break down the organism again for its functional needs.
We will demonstrate the connections of processes in organs and organisms as well as the interconnectedness of organisms within the whole of living nature.

1.1. Anabolic and catabolic processes and energy transfer

The flow of substances in metabolism in principle has two opposite directions.

1. Anabolic:
In the anabolic stream of metabolism, larger compounds are formed from smaller ones. Chemical *reductions* play a predominant role in these reactions. An example is the formation of complex carbohydrates from lactate or carbon dioxide.

2. Catabolic:
Catabolism is the opposite type of process, the breakdown of more complex compound into smaller ones. Chemical *oxidation and*

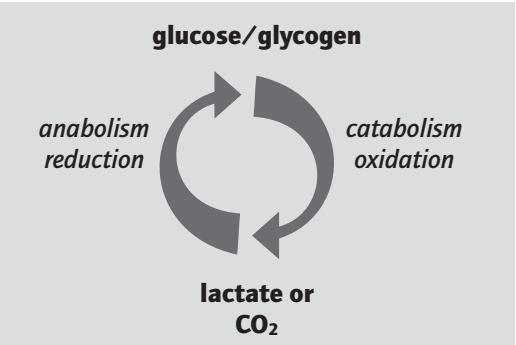
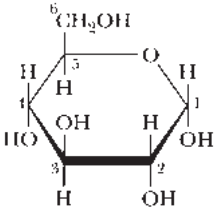
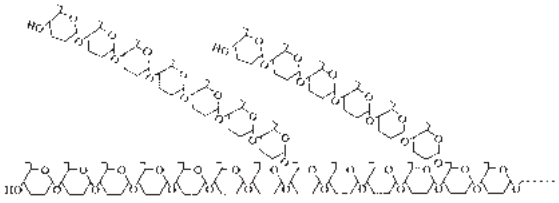


Fig 1.1 Anabolic and catabolic processes in carbohydrate metabolism

dehydrogenation play an important role in these reactions. An example is conversion of glucose or glycogen to carbon dioxide.



α-D-Glucose



Glycogen (from Campbell, 1999)

The effect of *anabolic reactions* is the formation of larger molecules, which will contribute to the organism's seemingly constant structures. Anabolic reactions usually *require energy* to carry out the process. The energy is needed for the reaction process as well as to hold together the structure of the more complex compound that is formed. The *energy captured* in the structure of compounds is stored, potential energy. This energy is expressed, for instance, in the linkages between molecules. Examples are:

- all covalent bonds including the glycosidic linkages in complex carbohydrates and the peptide bonds of the primary structure of proteins;
- the different bonds that hold together the three dimensional structure of proteins like peptide bonds, hydrogen bonds, disulfide bonds;
- the hydrophobic interactions and van der Waals bonds in lipid structures.

Catabolic reactions break down substances in the organism, and the resulting *energy is freed* for other aims. The freed up energy may be used to move muscles (bio-mechanical energy), to facilitate conduction in the nervous tissue (bio-electrical energy), to enable

synthesis of biochemical substances, and to effectuate active transport of substances.

Anabolic reactions incorporate bond energy into the larger compounds, which are in turn part of cellular or tissue structures, for instance cellular membranes, connective tissue fibers, or glycogen in the liver. Catabolic reactions effectively free up this energy. The structuring substances of organisms therefore have the additional function of being a source of potential energy in situations of need.

In trauma, or extreme situations like hunger states, the needs of the organism are met by breaking down more and different structural compounds. Eventually the substance of every organism ends up in its surrounding again, either in the form of energy, for instance as the effect of muscular action, the fluorescent light of certain fishes, etc., or as substance, as excretory products or when the living organism finally dies.

> ***QUESTION:*** *Are different types of bonds prototypical for different types of compounds? Are different types of energy stored in the different types of bonds?*

> ***QUESTION:*** *Where does the energy come from that we use for mental processes like thinking, emotions, or intentions? Is that also released from structures in the organism that are broken down?*

1.2. Biochemical cycles in metabolism

Anabolism and catabolism are opposite processes, and yet one is not simply the reverse of the other. Usually several key reactions of the anabolic pathway need different enzymes and/or produce different intermediate compounds than those used in catabolism. Anabolism and catabolism can take place in the same cell, but they often take place in

different cell compartments (such as lipid anabolism in the cytosol and lipid catabolism in the mitochondrion) and probably at different times. Anabolism and catabolism are not simply opposites but have a cyclic interaction, whereby the one follows the other and prepares for the other. There is no catabolism without there first being something built up that can be broken down. There is no anabolism without there being energy from catabolism to be built into larger structures.

1.2.1. A biochemical cycle in the organism as a whole

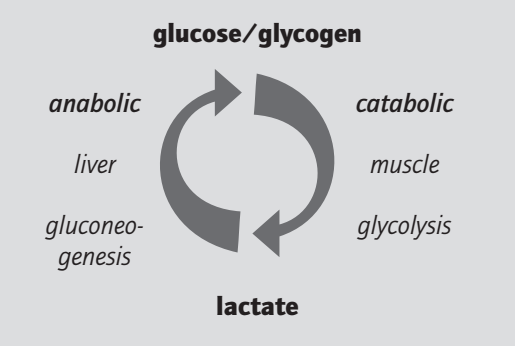


Fig.1.2 An example of anabolic and catabolic processes as a cycle in the organism as a whole: the Cori Cycle

The metabolism in anaerobic exercise provides an example of a metabolic cycle between organs. The so-called Cori cycle comprises glycolysis in the exercising muscle and gluconeogenesis in the liver.

In strenuous exercise, glucose in the skeletal muscle is broken down anaerobically to lactate (glycolysis) for extra directly available energy. The blood transports lactate to the liver. In the liver, glucose can be built back up from lactate (gluconeogenesis). This can be stored as glycogen or transported back to the muscle by the blood to be used as an energy source for muscle contraction again.

Anabolic and catabolic metabolism can alternate cyclically between organs in the human organism.

1.2.2. A biochemical cycle in nature

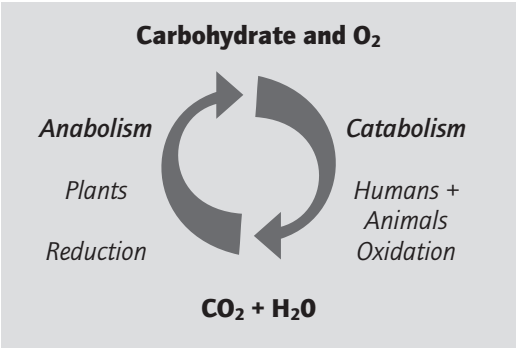


Fig.1.3 An example of coupled anabolic and catabolic processes in nature

A carbohydrate metabolic cycle occurs *between organisms in nature.*

Green plants reduce carbon dioxide and water to carbohydrates and oxygen in the process called photosynthesis. They build up their organism with the carbohydrates formed in photosynthesis and release oxygen. This is a reductive, anabolic process in the plant using external sunlight as the energy source.

The oxygen and the plant carbohydrates produced in photosynthesis are used up by higher organisms in oxidative processes that break down the carbohydrates in the digestive process. The metabolic cycle that exists between plants on the one hand, and humans and animals on the other, involves different organisms in nature.

The overall role of animal and human metabolism in nature is catabolic. Plant metabolism plays a *prototypically* anabolic role in nature and provides the energy required by the overall catabolic metabolism of higher organisms.

1.2.3. The citric acid cycle

The aerobic part of metabolism begins in the mitochondrion. In the eight steps of the citric acid cycle, which takes place in the mitochondrion, the metabolites of carbohydrates, proteins and lipids are finally oxidized to carbon dioxide and water. This catabolic process results in the formation of large amounts of biochemical energy in the form of adenosine triphosphate (ATP). To complete this process, some energy-carrying compounds that are formed in the citric acid cycle have to go through oxidative phosphorylation in the inner

mitochondrial membrane to convert the energy to ATP with the help of the reduction of O_2 to H_2O. These are for instance NADH (the reduced form of nicotinamide adenine dinucleotide) and $FADH_2$ (the reduced form of flavin adenine dinucleotide). The citric acid cycle is also the starting point for gluconeogenesis. And it provides intermediates for the synthesis of proteins and lipids and for the heme group of hemoglobin. In the citric acid cycle anabolic and catabolic pathways connect. Cycles interconnect with other cycles with the citric acid cycle at the center.

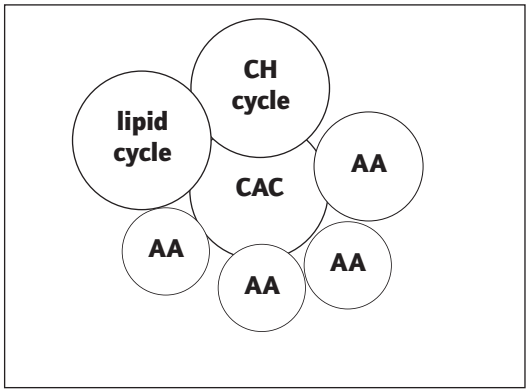
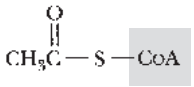


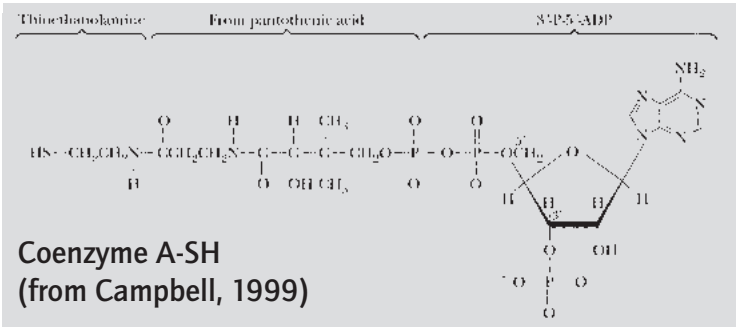
Fig. 1.4 The central place of the citric acid cycle (CH= carbohydrate; AA= amino acid cycle; CAC= citric acid cycle)

Acetyl-CoA and the citric acid cycle

Acetyl-CoA is the molecule that starts the citric acid cycle by binding to its "end" product oxaloacetate. All metabolites of carbohydrates and lipids enter this cycle as acetyl-CoA, and it is the link to ultimate oxidative breakdown for many amino acids.



Acetyl-CoA ↓



Coenzyme A-SH
(from Campbell, 1999)

Acetyl-CoA is possibly *the* key molecule in metabolism (see also sections 2.1.3 and chapter 5). In addition to being the starting molecule for the citric acid cycle it is also the starting point of fatty acid and cholesterol synthesis.

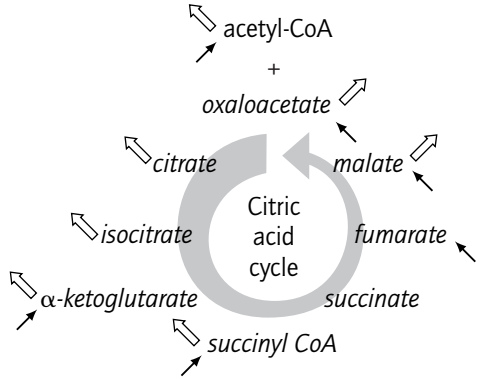
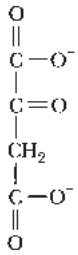


Fig. 1.5 The citric acid cycle and its anabolic (⇦) and catabolic (→) connections. + indicates the condensation of AcCoA with oxaloacetate.

In bacteria and plants, acetyl-CoA can be converted to oxaloacetate and other intermediates of the citric acid cycle via the glyoxylate pathway and as such can become the starting point for the synthesis of both amino acids and carbohydrates. The glyoxylate pathway is not available in mammals, which precludes them from converting fats to carbohydrates. This is the reason that mammals can not exist on a diet that contains only fats. Many bacteria use just acetic acid via a conversion to acetyl-CoA for the synthesis of their organism's compounds.



Oxaloacetate must be kept at specifically sufficient levels in the mitochondrion to allow acetyl-CoA to enter the citric acid cycle. Oxaloacetate is *also* the starting point of gluconeogenesis.

Oxaloacetate

1.2.4. Biochemical cycles in time

The emphasis on either anabolic or catabolic processes in biochemical cycles is different at different times of the day (circadian rhythm) and at different times in the life cycle of an organism.

Photosynthesis in plants

Photosynthesis mainly occurs in the leaves of green plants. It actually represents two processes, the light reactions and the dark reaction.

1. The light reactions:
The light reactions occur under the influence of light which is absorbed by chlorophyll (chlorophyll is a biochemical compound in plants similar to hemoglobin in the blood of higher organisms). The light reactions involve the oxidation of water to produce oxygen.

$$H_2O \rightarrow 2H^+ + \tfrac{1}{2}\, O_2$$

The energy freed in this *catabolic* process is captured in the plant, via the conversion of $NADP^+$ to NADPH, by the photophosphorylation of adenosine diphosphate (ADP) to ATP, a conversion that is coupled to the oxidation of water. The second light reaction is:

$$ADP + P_{inorganic} \rightarrow ATP$$

ATP is an energy-carrying compound and it represents a biochemical form of directly available energy (see also section 3.3.). Under normal circumstances the light reactions of photosynthesis are daytime processes. The light reactions use solar energy to free the

energy that holds together the water molecule, which in turn is converted via NADPH to ATP.

The light reactions convert sunlight to biochemical energy in the plant.
Light drives the transfer of protons from one substance to another in a thermodynamically uphill direction.

2. The dark reaction:
The second process of photosynthesis is the *dark reaction.* It involves the fixation of CO_2 for the production of sugars:

$$6\ CO_2 + 12\ H^+ \rightarrow [C_6\ H_{12}\ O_6] + 3\ O_2$$

The energy for this *anabolic* process comes from the ATP formed in the light reactions. The dark reaction results in the formation of disaccharides and polysaccharides (starch and cellulose). As the name indicates, this reaction is not *directly* dependent on sunlight, only *indirectly*.

The *overall equation* for photosynthesis is:

$$6\ CO_2 + 6\ H_2O + \text{sunlight} \rightarrow \text{carbohydrate}\ (C_6\ H_{12}O_6) + 6\ O_2$$

Chlorophyll in the plant absorbs the sunlight during the day and makes it directly available for the light reactions and indirectly, converted to chemical energy, for the dark reaction of photosynthesis. Plants are our example for using solar energy!

The plant builds up its organism in the dark reaction of photosynthesis, it grows visibly as a result of it. The light reactions do not result in visible growth but in energy production, which is invisible to the naked eye. The visible growth of the plant takes place where the light does not shine. The growth of plants towards the sun and the intricate process of the turning of the sunflower's head towards the light are based on more intensive growth on the side of the plant turned away from the sun, i.e. where the dark reaction can take place.

On the illumined side of the plant, solar energy is converted to biochemical energy as water is oxidized.

The light reactions of photosynthesis cannot take place at night unless an artificial light source is provided. Plant metabolism is linked to the cycle of day and night. The inner time clock of plants is normally set by the rhythm of the sun's light. Plant rhythms can be easily influenced by changing their exposure to light as is done in artificially lit greenhouses.

> ***QUESTION:*** *When does the plant grow more, during the day or at night?*

Metabolism of higher organisms in time

In human beings and higher animals anabolic processes predominate after eating. Anabolism also predominates during periods of growth. At the beginning of life, when growth is more pronounced, metabolism has a stronger anabolic quality than later in life. Humans can produce catabolic states by fasting. During illness catabolism predominates.

In animals and humans the rhythm of the inner time clock moderates the metabolic flow. Light plays a role in setting the inner time clock here too. Animals and humans have a metabolic circadian rhythm (rhythm of day and night). A metabolic circadian rhythm has been demonstrated very early on in the embryos of birds, as well as in human newborns.
In the adult human organism the solar diurnal rhythm has shifted, as in the rhythm of sleeping and waking and in metabolism.

1. The ergotrope phase: Between 3 AM and 3 PM.
Hildebrandt et al (1998) demonstrated that one 2000-calorie meal taken during this time results in a weight decrease of over 500 grams in 5 days. They also measured oxygen consumption when equal, small, low protein meals were given frequently during day and night (every 2-4 hours). Oxygen use is 50% higher during the ergotrope phase (120% of average daily oxygen consumption). Catabolism predominates during this phase.

2. The trophotrope phase: Between 3 PM and 3 AM.
The same one meal taken during the trophotrope phase of the human organism results in a weight gain of more than 500 grams within a week. Oxygen consumption is 80% of the daily average. Anabolism dominates the metabolism during this phase.

In the adult human metabolism the solar diurnal rhythm has shifted to a 3 AM/3 PM rhythm.

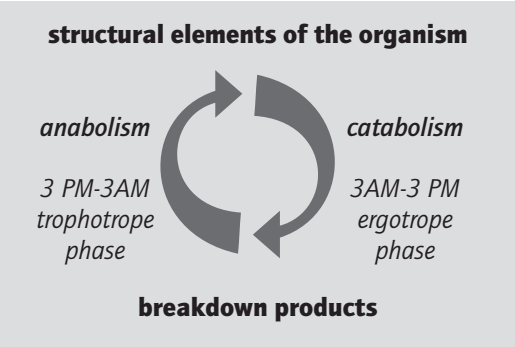


Fig.1.6. Time rhythms in metabolic processes

The human time clock has a resistance to change; it is harder to influence than the time clock of plants (Hildebrandt et al, 1998). It may take human beings 1-3 weeks to adjust physiologically after air travel across time zones. After jet lag many internal rhythms need to shift their phase. Some rhythms adjust to the day and night rhythm of the new time zone on the day of arrival, others take weeks to synchronize. In general, the inner time clock can change 1-2 hours/day after travel across time zones.

1.2.5. Ontogeny, phylogeny and time rhythms

Hildebrandt et al describe different rhythms in organisms:

A. Long wavelength rhythms:
- the circannual rhythm, a yearly rhythm
- the circalunar rhythm, a monthly rhythm
- the circaseptan rhythm, a 7-day rhythm
- the circadian rhythm, a diurnal rhythm

B. Median wavelength rhythms:
hourly and minute rhythms, which we find in organs, as for instance in the rhythms of peristalsis and of breathing.

C. Short wavelength rhythms:
rhythms of seconds or parts of seconds. These are predominant in cells and tissues (as seen for instance in electroencephalogram (EEG) rhythms of the brain).

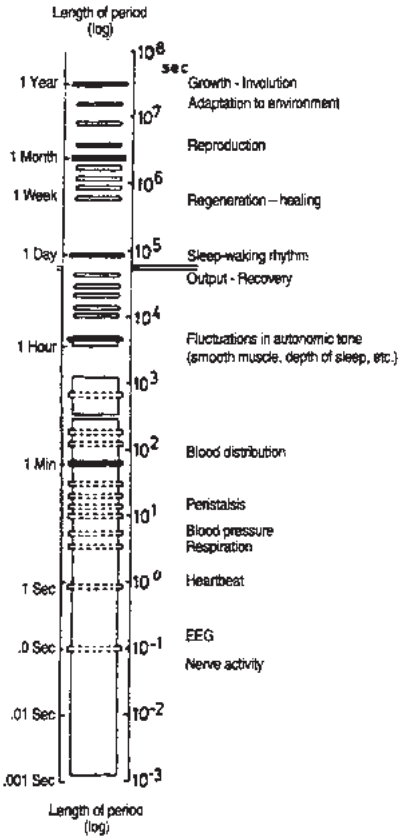


Fig. 1.7 From: Hildebrandt, 1998

In general long wavelength rhythms are more *exogenous rhythms*, which means they are dependent on outside influences, for instance on solar and lunar rhythms. In plants long wavelength rhythms (i.e. circannual and circalunar) are predominant. Plants do not have strongly developed inner rhythms, which makes it easier to change their inner time clock from without, as happens for instance in greenhouses with artificial light.

The shorter wavelength rhythms, such as organ rhythms, are usually *endogenous rhythms*. They are dependent on the inner time clock only. Endogenous rhythms are more developed in animals. The more highly developed the animal the more it develops a whole spectrum of rhythm frequencies, down to the very short ones.

Human beings have pronounced endogenous rhythms. Jet lag is a result of having a strong endogenous rhythm. Human beings have also developed an important additional attribute in relation to time cycles -- we are able to *emancipate* ourselves progressively from exogenous long

wavelength rhythms (such as from sun and moon). These exogenous time rhythms are internalized in the human organism and may then function with a shift in phase. Besides the above-mentioned shift in the solar diurnal rhythm another example of this is the female period in relation to lunar rhythms. Human beings can be relatively free from exogenous rhythms, and more self-dependent in relation to time rhythms.

1.3. Summary and conclusion

Metabolic processes

The metabolic process of the human organism normally starts with breakdown products from the intestines that become available for anabolic or catabolic reactions. Anabolic reactions build up the substances of the organism. Anabolic reactions enable the organism to 'get substance' and take form. The organism becomes visible like a standing wave in a creek.

Larger compounds contain bond energy that holds together the compounds' structure. This energy can be made available by catabolic reactions for those functions of the organism, which require directly available energy. The metabolic flow of living organisms ends with the catabolism of its substance, which frees energy for the organism's functions (such as anabolic biochemical processes, bio-electrical, bio-mechanical and active transport needs).

The citric acid cycle, which takes place in mitochondria, is at the center of oxidative breakdown and can also be the starting point for the reductive synthesis of large compounds in the organism. Acetyl-CoA plays a major role at this center of metabolic activity.

The metabolic cycle in plants begins with the breakdown of *water*. Green plants obtain their energy from breaking down water with the help of solar energy. The oxidation of water provides the energy required in the plant to build up its organism. Plants in turn are an important part of the food cycle in nature. They supply animals and humans with

nutrients, as well as being the source of oxygen for breakdown processes that are required to make foodstuff into usable energy and metabolites. Thus the energy for the functioning of higher organisms is indirectly derived from the breakdown of water by sunlight in the plant.

Characterization
The two opposite metabolic processes of anabolism and catabolism are actually part of *cycles* that involve different biochemical reactions, cell compartments, organs, and/or organisms, and time rhythms.

Biorhythms

Sunlight provides the energy in plants to break down water and also the diurnal rhythm of this process: light exposure is the dominant factor in setting the inner time clock in plants, and animals and humans as well. The human organism has an inner time clock that dominates the metabolic cycle with a cyclically changing emphasis on either anabolism or catabolism in a *shifted* diurnal rhythm (ergotrope and trophotrope phase), indicating that the solar rhythm has been internalized.

Characterization
The wavelength frequency of the metabolic cycle is related to the span of activity of the relevant process in the organism. Plants have longer wavelength rhythms, animals have more endogenous rhythms than plants, and humans can be free from exogenous rhythms.

Because we have encountered a fundamental difference here between animals and humans, specifically that humans can be relatively free from exogenous time cycles, we will research the human organism separately from now on.

> ***QUESTION:*** *What is the relation between the phase of metabolic process (anabolic or catabolic) and state of consciousness?*

Conclusion: *Metabolism plays an important role in the coherence between living organisms and their environment. Metabolic processes function in interlocking cycles and are also cyclic in time. The solar diurnal rhythm plays an important role as an exogenous influence on metabolic rhythms. The prototype of this is found in the plant. Living organisms have their own endogenous time cycles, which are more pronounced in higher animals. Humans have an additional prototypical capability: they can be relatively free from exogenous time cycles.*

2. Structure and bonding of carbohydrates, proteins and lipids

2.1. Polymers, monomers, and bonding

Carbohydrates, proteins, and lipids are primary nutritional ingredients for humans. The breakdown of nutrients (carbohydrates, proteins and lipids) in the intestines results in small compounds (metabolites) that can pass through the wall of the intestines into the blood. Complex carbohydrates and proteins are polymers that break up into a large number of smaller similar compounds, the monomers. Lipids do not have monomer and polymer forms. *All complex compounds in an organism are produced within the organism itself and are also specific to it.*

2.1.1. Complex carbohydrates/polysaccharides

There are three main complex carbohydrates in nature. All three are polysaccharides (see also section 3.2.). *Starch* and *cellulose* are both typical plant products. They are polymeric forms of glucose, and glucose is considered the monomer of starch and cellulose. Even though they are both complexes of glucose in plants, starch and cellulose have a different shape and a different function. *Glycogen* is the glucose polymer in animals and humans. Each of the three breaks down to become a large number of D-glucose molecules.

The glucose molecules in these polysaccharides are linked together by α- or β-*glycosidic linkages*. Glycosidic bonds are special covalent bonds. The special nature of these bonds determines much of the shape of the more complex compound, largely because these linkages inhibit the rotation of specific molecules toward each other.

Starch, cellulose, and glycogen are homopolysaccharides because they contain only one type of monomer, glucose. There are heteropolysaccharides which contain more than one monomer, such as the peptidoglycans in bacterial cell walls. Mostly there are not more than two different kinds of monomer in carbohydrate polymers. We will find that carbohydrates are less differentiated in their polymer structure than proteins (section 2.1.2.).

Fig. 2.1 Starch (from Campbell, 1999)

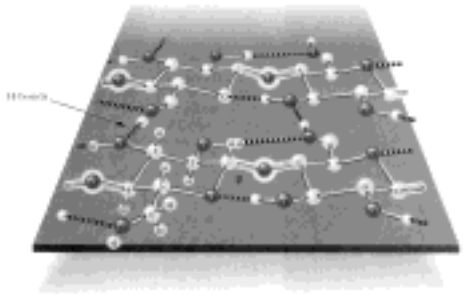


Fig. 2.2 Cellulose (from Campbell, 1999)

Starch

Starch occurs as granules in plant cells. It breaks down to become a large number of α-D-glucose molecules. Starch has α-glycosidic bonds to link glucose molecules. The preferred conformation of amylose, the simplest form of starch, is a helix. The energy that holds together the helical shape and the glycosidic linkages comes free when it is broken down in plants or in the digestive tract of animals and humans. Its role is to be a major energy source in the living world. Enzymes in plant, animal and human organisms can easily break down the α-glycosidic linkages of the starch helix to yield glucose, and glucose can be broken down further to yield energy (section 3.3.). The α-linkage between the glucose molecules in starch also determines its function as an energy storage compound.

Cellulose

Cellulose is the main component of the cell wall of plants. Cellulose is formed from

β-D-glucose with β-glycosidic linkages. The β-glycosidic linkages of cellulose allow for additional hydrogen bonding between linear polysaccharide chains. This results in a strong planar shape which can neither be broken down easily in plants nor in the digestive tract of humans and many animals. The typical β-linkages of cellulose, and the possibility of hydrogen bonding which this allows, make cellulose a structural carbohydrate in plants. The cell wall around the cell membrane of plants consists mainly of cellulose, giving plants their stability. Woody plants contain more cellulose.

Further compounds with β-glycosidic linkages

Structural carbohydrates in non-plants have amino acids or contain amino acid sequences as monomers. Plant cell walls contain relatively little protein or peptide.

Carbohydrates with β-glycosidic linkages can be found in some invertebrates such as insects, shrimp, or lobster. Their exoskeleton contains chitin, which is the polymer of *N*-acetyl-β-D-glucosamine, a monosaccharide with an amine group added onto the sugar. In chitin, individual strands are held together by hydrogen bonds as in cellulose. Accordingly, chitin has a structural function. It is also found in the cell walls of yeasts, fungi and algae.

β-Glycosidic linkages also connect the two amine-group-containing monomers in bacterial cell walls: *N*-acetyl-β-D-glucosamine and *N*-acetylmuramic acid. The strands are cross-linked by amino acid residues, forming a peptidoglycan. Peptidoglycans form a strong structure that is the target of certain antibiotic agents.

Glycogen

Glycogen is found in granules in certain types of cells in animals and humans, like liver and muscle cells, but not normally in heart and brain cells in the human organism. α-Glycosidic linkages connect the glucose molecules in glycogen. As in starch, the α-glycosidic linkages allow for glycogen's function in energy storage because glucose can readily be cleaved off.

2.1.2. Proteins

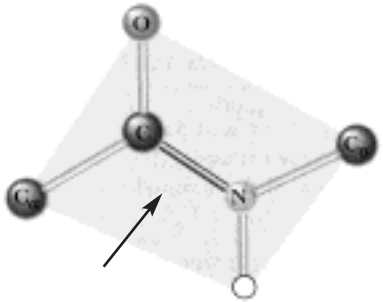


Fig. 2.3 The peptide bond (from Campbell, 1999)

When proteins are hydrolyzed this results in a large number of amino acids. Unlike the monomers of polysaccharides, the amino acids in proteins are of many different forms. Twenty different amino acids are found in human protein in varying quantities and combinations. They are linked together by peptide bonds to form the *primary structure* of proteins. Peptide bonds in proteins are also specialized covalent bonds, like the glycosidic bonds in carbohydrates. And, like glycosidic linkages, peptide bonds inhibit rotation of specific molecules in the amino acids around each other and therefore play a role in the final shape of proteins.

However, the final shape of proteins is not exclusively determined by the sequence of amino acids and the peptide bonds linking them together (the protein's primary structure of covalent bonds). The conformation of proteins is also subject to intricate folding processes connected to different types of bonds such as hydrogen bonds and disulfide bonds. The primary structure of proteins, though, determines their ability to form a secondary and tertiary structure, which is required for proteins to be biologically active in the organism.

The *secondary structure* of proteins is based on the hydrogen-bonded arrangement of the protein's amino acid backbone. It is responsible for α-helix and β-pleated sheet sections in the protein chain. Hydrogen bonds are important in the final structure of collagen, a structural protein (see section 4.2.2.).

The *tertiary structure* of proteins adds to their actual three-dimensional structure with the help of covalent disulfide bonds between sulfide-containing amino acid side chains, hydrogen bonding between amino acid side chains, electrostatic forces of attraction and hydrophobic interactions. Proteins can exhibit a rod-like fibrous or a compact globular conformation, depending not only on the bonding forces mentioned above but also on the conditions under which the protein is formed (sections 4.2.2. and 4.2.3.).

Proteins can also have a *quaternary structure*, which involves several different polypeptide chains. The bonds involved to hold this protein structure together are noncovalent.

The conformation of a protein is specific to it and determines its function and its functional ability.

2.1.3. Lipids

Acetyl-CoA can be considered an important common component of lipids. In the group of lipids, fatty acids and cholesterol are both ultimately synthesized from acetyl-CoA. The open chain lipids contain one or more of the fatty acids, and the fused ring lipids, the steroids, are conversions of cholesterol. Fatty acids are also oxidized to acetyl-CoA. Cholesterol derivatives are not broken down in the human body but are excreted (section 5.4.1.).

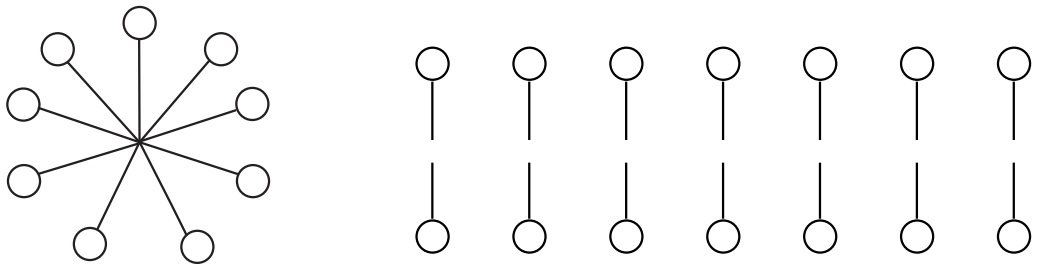
Lipids have the tendency to form clusters in the watery milieu of the body because they have long nonpolar tails which are hydrophobic. The hydrophobic fatty acid tails are "hidden" inside the cluster, sequestered from water, and at the periphery of the cluster the water-soluble hydrophilic side, connected to the head group, is exposed (see fig. 2.4.). Hydrophobic interactions occur spontaneously in aqueous surroundings. In terms of thermodynamics, this type of interaction does not require added energy when hydrophobic side chains or tails are present in the watery milieu of the body. This is in contrast to the types of bonding described earlier, which do require extra energy to occur (see section 1.1.).

Lipid clusters can take on either micelle or membrane-like forms to allow sequestering of their hydrophobic portions from watery surroundings. The *micelle form* occurs, for instance, when lipids are taken up into and transported in the body. Micelles have a single layer of lipids in their structure. They get a high degree of complexity in low-density lipoprotein (LDL) particles, for instance, in which a mosaic of cholesterol and phospholipids bound to a protein (apoprotein B-100) forms the outer structure around many molecules of cholesteryl esters. LDL particles play an important role in the transport of cholesterol in the blood stream.

The triacylglycerols (triglycerides) are the energy storage form of lipids and accumulate as *fat globules* in the cells of adipose tissue (see section 5.2.1.).

All lipids except for triglycerides can be found as components of *membranes*.

Membranes: Lipids are necessary for the formation of membranes because of their hydrophobic property, and the consequent clustering that occurs. Membranes are bilayers



The micelle form **The membrame form**

Fig. 2.4 The micelle and membrane forms of lipids. (○ indicates the hydrophilic backbone of the lipid, | indicates the hydrophobic tail of the lipid). The micelle can be large and have an inner space that is sequestered from water in which lipids can be transported, as in LDL particles. Membranes are actually also round structures and enclose an inner space, the interior of cells or cell compartments.

of lipids. They divide water into compartments, which is essential for the functioning of all organisms. In single-cell organisms it makes the formation of organelles possible and separates the organism from its (mostly aqueous) environment.

Membranes are semi-permeable mainly as a result of the presence of proteins, which function as channels in between the lipids. This allows for the transportation of compounds across the membrane and ensures the connection between the watery milieu inside the membrane with that outside the membrane. Semi-permeable membranes allow for the possibility of a different intracellular milieu from the environment. This makes the single cell into an organism. In multi-cell organisms, membranes make differentiated functioning possible. Cells can have different functions and yet have the same extracellular environment. Metabolism mainly occurs in the intracellular milieu. The extra-cellular milieu has an important role in transportation of metabolic substances and connecting the cells in the organism to form a whole. In vertebrates, the separation of intracellular and extra-cellular milieu makes functions such as the contraction of muscles and conduction of electrical impulses in the nervous system possible.

The presence of the fused-ring lipid, cholesterol, which is rather rigid in its structure, and of unsaturated fatty acids, which have kinks in their tail portion, influences the fluidity of membranes in opposite ways. The membranes of prokaryotes (such as bacteria) are the most supple of all since they hardly contain steroids. Plant membranes contain phytosterols (a steroid similar to cholesterol) and have less fluidity. The many unsaturated fatty acids in plant membranes make them more fluid than membranes in animals and humans, which contain cholesterol.

Lipids (possibly except for the triacylglycerols) occur in specific structured forms in organisms. Lipid structures such as micelles and membranes could perhaps be seen as the polymer form of lipids. The defining interaction in these structures is the spontaneously occurring hydrophobic interaction, supported by weak and changeable van der Waals bonds. Hydrophobic interactions induce the relative immobility of the lipid components toward each other.

However, all components of membranes are in flux, as the seemingly constant shape of organisms is always in movement.

2.2. Summary and conclusion

Carbohydrates and proteins can occur as polymers, which can be broken down to monomers. Lipids do not have polymer forms but form clusters in the watery milieu of the organism.

Compound structures

In *carbohydrates* the polymer forms have mostly not more than two different monomers in their structure. Glucose is the only monomer in the most common polysaccharides - starch, cellulose and glycogen. The difference in functions among polysaccharides results from the different types of glycosidic bond. Starch and glycogen have α-glycosidic linkages, and they function as a source of energy of plants or animals and humans respectively. Cellulose, chitin, and peptidoglycans have β-glycosidic linkages, and they serve as a structural element in plants and lower animals.

Proteins are more differentiated polymers. In the human organism they may contain as many as 20 different amino acids. The three-dimensional conformation of proteins takes on specific forms that achieve the protein's ability to function.

Lipids have no monomer or polymer forms as such; they all have the energized form of acetate as acetyl-CoA at the beginning of their anabolic pathway. They have the possibility to form secondary structures in the form of membranes or micelles.

Characterization

Carbohydrate, protein, and lipid structures can vary in complexity of form, from storage forms, such as granules or globules in cells, to functionally important helix or planar forms in carbohydrates and proteins, fibrous or globular conformations of proteins, or micelle and membrane lipid structures. In multi-cellular higher organisms, storage forms will occur

in cells that are related to the stored compound, i.e. glycogen in liver and muscle cells, lipids in fat cells. *All complex compounds in an organism are produced within the organism itself and are also specific to it.*

Bonds

Covalent bonding is the predominant type of linkage in the structure of carbohydrates (including the glycosidic linkage) and the primary structure of proteins (including the peptide bond). The basic form of lipids is also based on covalent bonding. *Covalent bonds are important in the basic structure of compounds.* It is the main type of bonding in starch.

Additional *hydrogen bonding* is necessary for the final shape of structural polysaccharides such as cellulose and the structural protein collagen and it allows for the formation of α-helices and β-pleated sheets in the secondary structure of proteins. *Hydrogen bonds give additional stability to the structure of compounds.* This renders them essential in structural compounds. More basic forms of life rely on hydrogen bonds in carbohydrates for their structure. Together with covalent *disulfide bonds*, *electrostatic forces of attraction,* and *hydrophobic interactions,* hydrogen bonds enable the specific conformations of proteins that determine the proteins' functional ability.

Hydrophobic interactions allow for micelle and membrane formation, the typical organic forms of lipids. Hydrophobic interactions are not based in the first place on the principle of attraction, as are all other linkages, but on the principle of repulsion. They take place spontaneously in the watery milieu of the body without the addition of extra energy. *Hydrophobic interactions in lipids allow for the organically essential division of aqueous fluids in living organisms, into compartments.* This makes differentiated functioning of organisms possible. There is a degree of hydrogen bonding and electrostatic forces of attraction in lipids, as well as *van der Waals bonds*.

Characterization

Covalent bonding is prototypical in carbohydrates. Hydrogen bonding allows for more stable structures both in structural carbohydrates as well as in proteins. Hydrophobic interactions are not actually bonds; they are based on the principle of sequestering rather

than bonding and occur spontaneously. They play a prominent role in lipid structures and allow for the most complicated, and yet most basic, structuring principles of living organisms.

QUESTION: *Do different types of linkages represent different types of energy? (see also Chapter 6.)*

Conclusion: *Linkages hold potential energy and they determine the structure and function of compounds in organisms.*

3. Carbohydrate metabolism and activity

Introduction: Nutritional Ingredients

The primary nutrients are used by the organism in a variety of ways. Their breakdown in the digestion results in metabolites that can be utilized for further metabolic processes in the organism. They can be used for the formation of large compounds that contribute to the structure of the organism (like the carbohydrates in the cell wall of plants, proteins in collagen, or the lipids in membranes). The metabolites can also be converted to substances that regulate the organism and its functions (as for instance in immune recognition, neurotransmission, or as enzymes). And they can be oxidized further to provide energy for the above processes and bio-mechanical and active transport needs through their ultimate breakdown, as happens for instance with glucose.

Carbohydrates, proteins, and lipids can each be used for a variety of different functions; within limits they can also be converted one into the other with the help of intermediates in the citric acid cycle, which interconnects their anabolic/catabolic cycles. And they each have an area of characteristic activity, which will be discussed in the following chapters for the respective compounds. This chapter deals with carbohydrate metabolism and function, chapter 4 discusses protein metabolism and activity and chapter 5 the metabolism and activity of the lipids.

3.1. Carbohydrates and water

In section 1.2.4 we found how the breakdown of water stands at the beginning of the synthesis of carbohydrates in photosynthesis. This is one important process that shows the relationship between carbohydrates and water. Water is oxidized to convert sunlight into biochemical energy for the synthesis of carbohydrates from CO_2:

$$6\ CO_2 + 6\ H_2O + \text{light} \rightarrow C_6\ H_{12}\ O_6\ \text{(carbohydrates)} + 6\ O_2$$

Animals and humans breathe in the O_2 and use it to break down carbohydrates to CO_2 and water in the citric acid cycle and oxidative phosphorylation (section 1.2.2.). This oxidative catabolic process, together with the reductive anabolic process of photosynthesis, forms a cycle in nature between plants and the organisms of animals and human beings (see fig. 1.3) in which water is alternately oxidized and formed.

The water/carbohydrate connection is also found when sugar is burnt without the addition of oxygen, i.e. made into carbon. This happens when sugar is heated up in a closed container so that no oxygen can enter. The result will be carbon and water, the latter escaping as steam. This phenomenon would imply that the general formula for carbohydrate monomers could be written as $C_n\ (H_2O)_n$. This is the reason they were originally given the name *carbo-hydrate*. The general formula for glucose for instance is $C_6\ H_{12}\ O_6$.

Carbohydrates have a relation to water both in their structure and in their metabolic processes. In the formation of polysaccharides, as in forming the peptide bonds in proteins, one water molecule is released from glucose in forming the glycosidic bond with every addition of a glucose molecule.

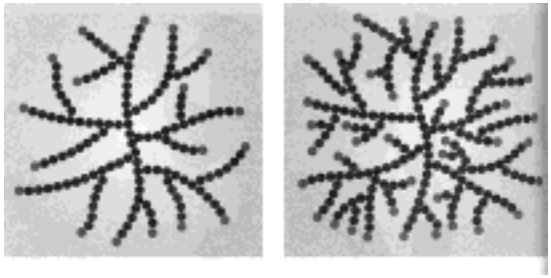
3.2. Functions of carbohydrate polymers

Carbohydrate polymers, like all large compounds, hold within their structure *potential energy* that becomes available at their breakdown as metabolic and other energy for the organism. Many common carbohydrates are polysaccharides.

Polysaccharides are polymers of sugars (see section 2.1.1.). The most commonly occurring monomer is glucose (section 3.3.). Carbohydrates also have structural functions.

Storage function

Glycogen and starch are storage forms for glucose. Glycogen is usually more branched than starch, which allows for the glucose to be cleaved off at more points at the same time. Therefore glycogen, which is the main glucose polymer in higher organisms, can give a greater rate of supply of glucose in demand situations than starch, which exists in plants only, would be able to. Animals and humans have more glucose quicker at their demand than plants. As mentioned before in section 2.1.1. glycogen does not occur in heart and brain cells. It occurs mainly in liver and muscle cells, but only the liver can convert lactate to glucose. Muscle cells are dependent on the liver for gluconeogenesis (see the Cori cycle, section 1.2.1.) and the serum glucose level is primarily buffered by the liver. *The liver's carbohydrate function is prototypical in higher animals and humans*.



Amylopectin **Glycogen**
(Campbell, 1999)

Glycogen has no structural support function in higher organisms and therefore can be broken down without affecting their structure. Glycogen stores in the liver form an ideal energy supply for the organism. However, human glycogen stores are estimated to be depleted after 10-15 hours of fasting and therefore need constant replenishing.

Structural function

Cellulose is a structural glucose polymer in plants (see fig. 2.2.). Structural carbohydrates in non-plants have amino acids or contain amino acid sequences as monomers to form chitin or peptidoglycans (section 2.1.1.). The breakdown of cellulose does affect the structure of the plant, as does the breakdown of peptidoglycans by antibiotics affect the structure of bacteria, and the breakdown of chitin affects the structure of invertebrates that carry it in their exoskeleton.

Glucose cannot be cleaved off of cellulose without the presence of special enzymes called cellulases, which are found in bacteria and in the digestive tract of, for instance, cattle. Humans do not have cellulases in their digestive tract. Cellulose is the main insoluble part of dietary fiber (bulk or roughage) in our diet, which stimulates peristalsis and binds some of the potentially toxic substances in food.

3.3. Glucose and Energy

Glucose is the most abundant of the carbohydrate monomers in nature. Glucose metabolism is central to the energy supply of living organisms. It can be transported in the body to the place where energy is required.

Anaerobic breakdown of glucose in glycolysis yields pyruvate or, under lasting anaerobic conditions, lactate and 2 molecules of ATP per glucose molecule. Its further aerobic breakdown occurs in the citric acid cycle (section 1.2.3.), which can yield 30 more ATP molecules. The catabolism of glucose releases energy, which results in the phosphorylation of ADP to ATP. ATP is the carrier of immediate energy for organisms. It contains two phosphoanhydride bonds linking the phosphates. These bonds hydrolyze easily, with a consequent immediate release of the energy (less than 1 minute). As such, it is directly available biochemical energy, which must, however, be used "right away". It can be used to convert the biochemical energy to bio-mechanical energy (as in the case of the exercising muscle), bio-electrical energy (as in the nervous system), light (as in phosphorescent bacteria), active transport, etc.

The freed up energy from glycolysis and oxidation in the citric acid cycle can also be used in the form of ATP for reductive anabolic processes that result in compounds such as proteins and lipids. Glucose is a reducing sugar. When glucose is oxidized, another compound can be reduced in an anabolic reaction with the energy that becomes available (transferred via ATP).

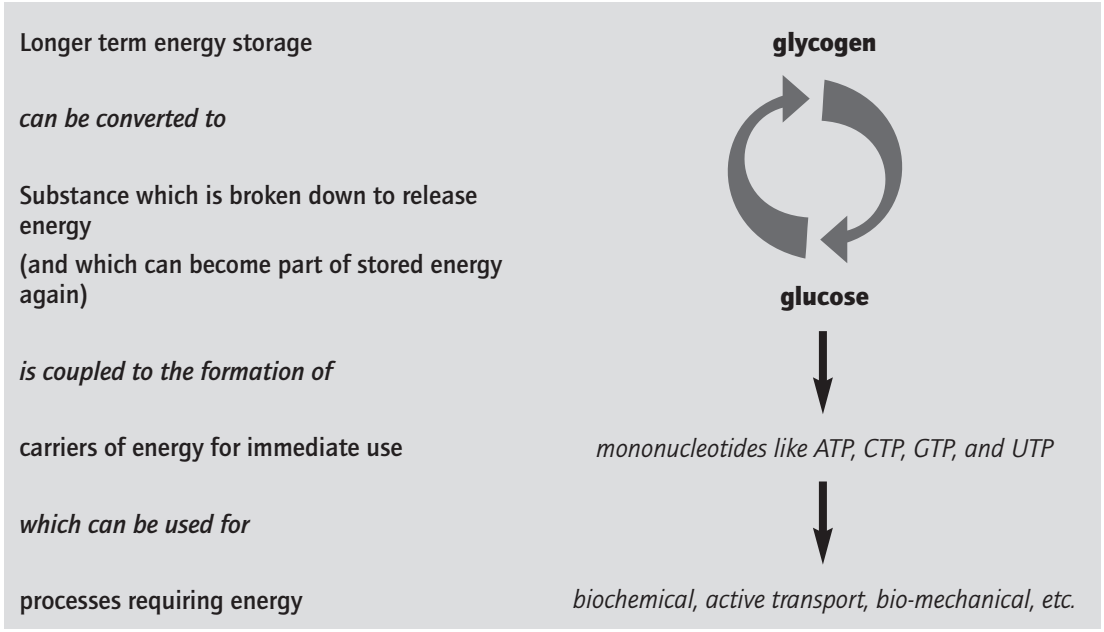


Fig. 3.1 The conversion of energy-carrying compounds to energy-requiring processes

Since it is not needed in the structures of the organism, glucose and glycogen can be broken down without consequences for the structure of the body. Thus glucose becomes the main supplier of energy for living organisms. *The prototypical function of glucose in organisms is to provide energy.*

3.4. Summary and conclusion

Carbohydrate functions

Carbohydrates can be used for a variety of functions in organisms. They serve different functions in plants than in higher organisms. Plants are the only organisms that use homopolysaccharides to build up their structural components, as well as using starch and glucose for an energy source. In lower animals carbohydrates can also have structural

functions. Then their conformation includes amino acids or amino acid derivatives. In higher organisms carbohydrates only provide energy for the metabolic needs of the organism. They do not provide structural support. *Carbohydrates serve different functions in plants than in higher organisms.*
The prototypes of carbohydrate polymer appear in plants, in the form of starch and cellulose. Glycogen in the liver is the prototypical appearance of carbohydrate polymer in higher animals and humans.

Starch in plants and glycogen in animals and humans, can freely release their store of potential energy through their breakdown without disturbing the structural integrity of the organism they are part of. *This makes these carbohydrates the ideal energy source.* Glycogen is broken down to glucose. Glucose is an intermediate energy-carrying compound. Its breakdown yields the energy carrying compound ATP, which needs to be used right away because it hydrolyzes readily. The energy can be used for organism functions, varying from anabolic biochemical to transport to bio-mechanical processes.

Glucose is a reducing sugar in that its oxidation also provides the organism with the energy needed for reductiveprocesses that build up the organism. It makes the synthesis of compounds, tissues, organs, and organisms possible.

Characterization: water, carbohydrates and plants
Water plays an important role in carbohydrate structure and processes. The role of water can be compared to the role of carbohydrates in organisms and the role of plants in nature.

The relation between water and carbohydrates becomes visible in the process of photosynthesis. The oxidation of water by sunlight in photosynthesis stands at the beginning of the synthesis of carbohydrates in plants. The oxygen that is released in this process is essential for the function of higher organisms.

$H_2O \rightarrow H^+ + O_2 \rightarrow$ carbohydrate synthesis + higher organism function

The role of carbohydrates in the metabolism is to make energy available through carbohydrate breakdown for anabolic processes and the functions of the organism.

carbohydrates → ATP and CO_2 → organism synthesis and organism function

The place of the plant in the whole of nature became visible in section 1.2.2. Plants are an important part of the nutrient cycle in nature. They are the most important food supply of many species. The typical function of plants in nature is to help make energy available in higher organisms through their breakdown in the digestive system of higher animals and humans.

plants → metabolites and CO_2 → higher animal and human organism structure + function

Conclusion: *The breakdown of water, which is accompanied by the conversion of sunlight to biochemical energy, provides indirectly for the energy required in living organisms. The function of water in plants is similar to the function of carbohydrates in higher organisms is similar to the function of plants in the whole of nature. Water is basic to all life. Carbohydrate metabolism in organisms is "plant-like."*

4. The metabolism and activity of protein

All proteins contain nitrogen in their basic structure in addition to the carbon and water (= hydrogen and oxygen) which are typically found in polysaccharides. Proteins are polymer forms of the nitrogen containing amino acids. We will characterize their specific area of activity by looking at their properties, and will compare this to similar processes in nature to give us a view of their role in nature.

4.1. Protein metabolism and nitrogen

4.1.1. The nitrogen balance

The catabolism of proteins in organisms is not an expedient way to provide energy to the organism since the catabolism of larger amounts of protein would result in a structural breakdown of chiefly muscle proteins. This becomes visible in the nitrogen balance of organisms. Under physiological conditions the amount of nitrogen excreted must equal the amount taken up in nutrition.

4.1.2. Nitrogen metabolism in nature

The nitrogen that is in amino acids and proteins ultimately comes from the air, which contains 80% N_2. Yet it cannot be taken up directly from the air by most living organisms. It first enters the soil through nitrogen fixation by special bacteria that form the root nodules of legumes. Through this process N_2 is first converted to ammonia and subsequently incorporated in α-ketoglutarate, a citric acid cycle intermediate, to form the amino acid glutamate. The amine group of glutamate is transferred in transamination

processes to further citric acid cycle intermediates and other metabolites of carbohydrates and lipids (acetyl-CoA and acetoacetyl-CoA). Complicated conversion processes can ultimately lead to the formation of all 20 amino acids.

Plants take up the organic nitrogen-containing compounds of bacteria in the soil into their organism.

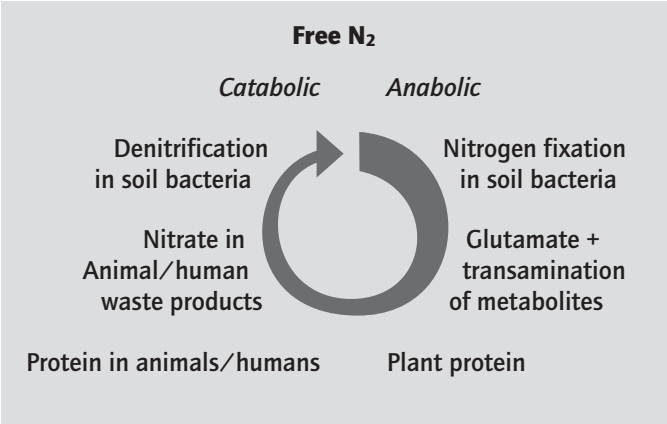


Fig. 4.1 The cycle of nitrogen metabolism in nature

Higher organisms get their nitrogen from the plants through their food. Their waste products contribute nitrogen to the soil again.

Denitrification reactions in bacteria in the soil render the nitrogen back into the atmosphere.

In humans, 10 of the 20 amino acids cannot be synthesized in sufficient quantity, especially in growing children, and must be taken up in the diet to prevent structural breakdown.

4.1.3. The urea cycle in organisms

Nitrogen metabolism in organisms is also cyclic. In the *urea cycle,* glutamate donates ammonia to ornithine through de-amination in the mitochondrion, which leads to the formation of citruline. This passes to the cytosol and via two more steps is converted to arginine, which gives off urea to form ornithine again. The urea cycle is linked to both anabolic and catabolic processes in nitrogen metabolism. The urea cycle has two links

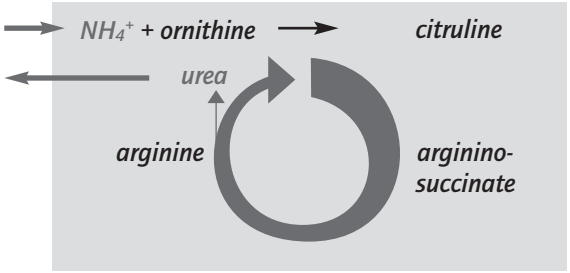


Fig.4.2 The urea cycle, the nitrogen cycle in organisms

with the citric acid cycle, via oxaloacetate and fumarate.

The secretion of urea requires the presence of water, therefore many mammals excrete it in their urine as a waste product. Sufficient quantities of water are needed to be able to excrete it properly.

Nitrogen metabolism is a controlled mechanism with limits on the supply and the excretion sides. It is controlled by *negative feedback* systems. When the amount of end product reaches a certain level it inhibits its own synthesis. Feedback systems function as control cycles. They are characteristic for nitrogen metabolism because of the latter's inherent tight supply and demand limits.

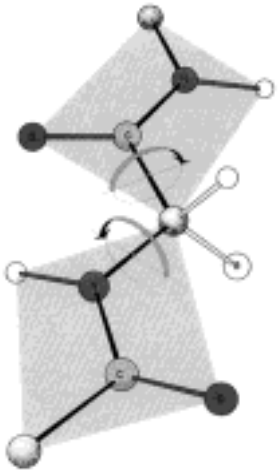


Fig. 4.3 Polypeptide chainformation (from Campbell, 1999)

4.2. Protein structure as the basis for protein function

4.2.1. The specificity of protein structure

Protein primary structure consists of varying combinations of 20 different amino acids in long polypeptide chains (section 2.1.2.). Protein conformation is more differentiated and more complicated than carbohydrate structure. Proteins have three possible levels of conformation beyond their primary structure of amino acid chains (polypeptide chains).

Secondary structure involves the formation of α-helical forms and β-pleated sheets (see also section 2.1.2.). Helices and planar forms in separate compounds also exist in carbohydrates. In protein they exist in the same compound. Tertiary structure is the overall folding of the protein on itself, which results in the typical three-dimensional arrangement that allows its function. Quaternary structure exists when several polypeptide chains (subunits) together form an interacting molecule such as hemoglobin.

The variety of amino acids creates the potential for differentiated polypeptide chains, which allows for many different proteins. The proteins in an organism are very varied and they can perform a large number of functions. Proteins, in contradistinction to carbohydrates, are also highly specific to the function they fulfill. The alteration of one or more amino acids in the polypeptide chain can give them a different function (as for instance in myoglobin, in relation to the hemoglobin α and β chains) or render them dysfunctional (as in hemoglobin S in sickle-cell anemia).

Protein conformation can be *fibrous* or *globular*. *Membrane proteins* are situated in the membranes of cells. They can have different forms, varying with their function. *Glycoproteins* are proteins with carbohydrate residues.

Fig. 4.4 Collagen (from Campbell, 1999)

4.2.2. Fibrous proteins

The overall shape of fibrous proteins is a long rod. Fibrous proteins are *non-soluble in water*.

Examples of typical fibrous proteins:

• *Collagen*, is the prototype of fibrous proteins and the most frequently occurring protein in vertebrates. Collagen consists of three helical polypeptide chains wrapped around each other to form a superimposed

triple helix. Hydrogen bonds hold the three strands together. Collagen is located extracellularly in bone and connective tissue. The polypeptide chains consist mainly of a relatively simple triad of three amino acids: glycine, proline and hydroxyproline. Every third amino acid is glycine, the second is proline or hydroxyproline, and the first amino acid is mostly also proline or hydroxyproline or can be another amino acid. Collagen has an important structural function. It is the main fiber in connective tissue: the tissue between organs and other tissues in which cells and organ parts are embedded.

• Another example of fibrous conformation in proteins is *keratin* in wool and hair. It is mostly α-helical. The fibers of *fibroin*, the main protein in silk, has largely β-sheets.

• The *muscle proteins,* actin and myosin, are also mainly fibrous proteins. They are the principal constituents of muscle fibers, but do also occur in other kinds of cells. These proteins are always located intracellularly. Their structure is relatively simple, albeit more complex than that of collagen. Myosin has a globular head that is instrumental in muscle contraction. It provides the power stroke for the contraction by interacting with actin. In action, the interlocking of actin and myosin components intensifies and the muscle contracts, thus moving the body in part or as a whole and altering the relation of the organ or organism to its surroundings. These proteins are structural proteins in the resting state as well as functional proteins when in action. Muscle fibers also affect movement within cells.

Fibrous proteins provide structural elements to the animal and human organism.

4.2.3. Globular proteins

Globular proteins are compact *functional* proteins. The overall shape of a globular protein is spherical, as the name indicates. Their tertiary and quaternary structures are complex. Globular proteins are *water-soluble*.

Examples of globular proteins

- Most *enzymes* are globular proteins and are principally only functional. They catalyze reaction processes between molecules. In the lock and key model of enzyme function they bind substrate and catalyze a specific reaction, then let go of the reaction products. Their configuration changes reversibly with their activity. Otherwise they are unchanged by the process they catalyze.

Fig. 4.5 Myoglobin, a globular protein (from Campbell, 1999)

Enzymes catalyze numerous metabolic reactions throughout the organism. Reactions catalyzed by enzymes will proceed up to 10^{14} times faster than non-catalyzed reactions. Each reaction process has a specific enzyme that catalyzes it. This diversity of form in proteins becomes possible through the configuration of their primary structure with 20 different amino acids, which subsequently enables the formation of their specific secondary, tertiary, and possibly quaternary structures. The amino acid sequence has to be exact for the protein to be biologically active.

- Other examples of globular proteins include myoglobin and hemoglobin.

4.2.4. Membrane proteins

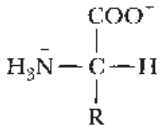
Membrane proteins are an important component of membranes. 20 - 80 % of the membrane weight of animal and human cells consists of protein. These proteins have a structural function, but their major role is functional. They form channels through the membrane that allow the passage of specific compounds under certain conditions, they

effect active transport of certain compounds across the membrane, and they function as receptors on the membrane's inner and outer surface for compounds such as neurotransmitters. They can also be enzymes themselves.

4.2.5. Glycoproteins

Glycoproteins play a role as antibodies in immune recognition and as antigenic determinants in human cell membranes. The use of glycoproteins for the typing and matching of blood groups and grafts is exemplary of the specificity of proteins in organisms. Even though close matches can be found, for instance in twins, the perfect match is only found in proteins within an individual organism. *Proteins emphasize the singularity of organisms* and play an important role in recognizing the distinction between self and non-self, which is the function of the immune system.

4.3. Amino acids



General amino acid structure

Protein breakdown in the metabolism does not specifically yield energy-carrying substances, even though amino acids yield energy when they are broken down. Amino acids are important as metabolites that can be used by the organism in anabolic processes to build up its own proteins. The energy for this process comes from the catabolism of carbohydrates.

4.3.1. Amino acid activity

Many amino acids are themselves biologically active in the organism (such as glutamate or glycine) or with small structural changes (such as the monoamine serotonin, which is formed from tryptophan, and the catecholamines, which are derived from tyrosine) or as

peptides (small amino acid chains). They are active as neurotransmitters in nervous tissue, where they connect nerve cells functionally by transmitting the electrical impulse chemically from the axon to the receptors on the axon or cell body of the next cell. Some have an important function as bile salt (glycine in glycocholic acid), in methylation reactions (methionine), or in inflammation (histamine from histidine). Thyroxine is a derivative of tyrosine, and functions as a hormonal substance important for the rate of metabolism. Oxytocin, vasopressin and insulin are peptide hormones, which effect contraction of smooth muscles in the uterus, contraction of smooth muscles in the blood vessels, and carbohydrate metabolism respectively.

Many of these compounds are also known to influence consciousness. Serotonin and histamine released from a bee sting provoke a strong sensation of pain as well as local inflammation. In schizophrenia we find increased levels of serotonin and catecholamines, including dopamine. In endogenous depressions, a lack of serotonin and catecholamine metabolism is found. The stimulating effect of coffee on consciousness is due to its stimulating influence on monoamine metabolism. Stimulants of consciousness such as cocaine and LSD mimic the central nervous system action of catecholamines and serotonin respectively. The rate of monoamine metabolism varies with the rhythm of sleeping and waking in the healthy organism. Serotonin and dopamine are secreted in the area of the brainstem that is active during waking (see Elsas, 1994).

4.3.2. Amino acid metabolism

Most amino acids are *glucogenic*. Their degradation after de-amination yields pyruvate or oxaloacetate. This gives the possibility for them to be converted to glucose through gluconeogenesis and enter carbohydrate metabolism, or they may be used up in the citric acid cycle. Amino acids can therefore provide energy for the organism like the carbohydrates, but they do so less efficiently. When body energy requirements need protein degradation in larger quantity, as in hunger states or malnutrition, this happens at the expense of other tasks of proteins and amino acids in the organism, both structural as well as functional (section 4.1.1.).

The amino acid leucine is only *ketogenic*, meaning it can only be broken down to acetyl-CoA or acetoacetyl-CoA and its breakdown may lead to the formation of ketone bodies or fatty acids. It can be used in the citric acid cycle but cannot be converted to glucose. Isoleucine, lysine, phenolalanine, tryptophan and tyrosine are both ketogenic and glucogenic.

Amino acids also contribute to the synthesis of nucleic acids and the pyrrole ring of hemoglobin.

4.4. Summary and conclusion

Nitrogen

Nitrogen is fixed from the atmosphere by soil bacteria and taken up by leguminous plants. When animals and humans eat the plants, the nitrogen-containing substances enter their organism. The nitrogen becomes part of the urea cycle in organisms, which has links to both anabolic and catabolic processes as well as to the citric acid cycle. Once the nitrogen is excreted as urea it enters the larger cycle in nature again and can be either taken up by plants again or denitrified by soil bacteria to become part of the nitrogen in the air in an even larger cycle. Nitrogen metabolism in organisms is controlled by extensive negative feedback mechanisms to support the tight nitrogen balance. Nitrogen intake has to match excretion to prevent structural breakdown.

The breakdown of protein in the digestive tract yields amino acids, which are important as metabolites for the organism to build up its own proteins in anabolic processes. The energy for these processes comes from the catabolism of carbohydrates. When proteins are broken down for energy in the organism as happens in hunger states, this means structural as well as functional breakdown of the organism. Proteins have a structural function in animals and humans, and they cannot be used as the regular energy source. We found that carbohydrates take on the structural function in plants, and also have a major role in the structural components of bacteria and invertebrates. In the latter two the

structural element contains amine or amino acid derivatives. They may be seen as transitions to the structural proteins. This makes proteins *characteristic in animal structure*.

Conformation of proteins

The conformation of proteins is fibrous or globular. Proteins usually have 20 different amino acids in varying sequences in their polypeptide backbone. The polypeptide chain may consist of several hundred amino acids. But a change as small as one amino acid may render the protein dysfunctional. Protein conformation is *as diverse as it is specific*. The primary structure of proteins, the amino acid sequence, determines their ability to form the secondary and tertiary (and sometimes quaternary) structure that is required to be biologically active in organisms. Amino acids and proteins have a large array of functions and structures, but these are *as specific as they are diverse*. Carbohydrates have the specific function of energy storage and supply. In section 2.1.2. we found that proteins have the whole array of bonds, where specialized covalent bonds are typical for carbohydrates.

The most abundant protein in higher organisms is collagen, the *fibrous protein* in connective tissue and bone. It has mostly just three different amino acids in its triple helix conformation. As the main fiber of connective tissue it provides the structure in which organs and cells are embedded. Another form of fibrous protein occurs in muscle. Muscle fibers at rest contribute to the organism's structure. In action, they enable movement of the organism and its parts. Fibrous proteins are insoluble in water and are mainly *structural* proteins.

Enzymes are *the* examples of *globular proteins*. Most globular proteins are enzymes. They affect the relations between reaction substrates by catalyzing reactions. Their configuration changes only temporarily and reversibly with their activity. Enzymes catalyze numerous metabolic reactions throughout the organism, and each reaction process has a specific enzyme that catalyzes it. The diversity and specificity of proteins becomes exemplary in enzymes. Globular proteins are water-soluble and principally only *functional*.

Membrane proteins play a role in the transmission of signals and compounds across membranes. *Glycoproteins* play a role in immune recognition. The function of the immune system is to recognize the distinction between self and non-self. As such glycoproteins emphasize the singularity of organisms and promote individualization.

Many protein monomers - the amino acids, and their derivatives - are biologically active in the organism. They facilitate the conduction in the nervous system, metabolic processes, and they affect smooth muscle contraction.

Characterization
The typical difference between plants and animals is that animals have the ability to move themselves with the help of muscle activity and conduction in the nervous system. This makes animals more individualized than plants. They form a diverse array of inner organs as a result, which have specialized functions in their organism. Plants form only external organs, such as flowers. Individualization also necessitates new ways to relate to the environment to avoid isolation. Muscles, nerves, and senses serve animals in sustaining a relation to their environment. Animals characteristically learn from behavioral feedback.

Amino acids and proteins	Animals
Diverse structures are typical	Diverse inner organs are typical
Specialized enzyme functions	Specialized organ functions
Are muscle proteins	Have muscle action
Immune function of glycoproteins	Individualization
Are neurotransmitters	Have nervous system function
Feedback characteristic	Characteristically learn from feedback
Structural compound in animals	Use proteins for their structure

Table 4.1 The relation between proteins and animals

The characteristics we have indicated for animals are related to characteristics of proteins and amino acids as shown in table 4.1. The diversity in structures and functions of amino acids and proteins can be summarized as one comprehensive idea: *amino acids and proteins serve to enhance the connections within organisms and of organisms with their environment.*

Connective tissue is the structural prototype and enzymes are the functional prototype of this.

Conclusion: *Amino acids and proteins have functions in organisms that are related to the characteristic functions in animals. Amino acids and proteins are "animal-like." Their comprehensive characteristic is that they enhance connections.*

5. Lipid structure and metabolism

Lipid structure is characterized by a relative lack of oxygen. This renders lipids richer in calories, as they have further to go in the oxidation process. Lipids consist almost exclusively of carbon and hydrogen and have a preponderance of nonpolar groups. This means they do not mix well with water, they are hydrophobic.

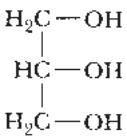
Acetyl-CoA is the starting point of the anabolic pathway of fatty acids and cholesterol and it is the end product of the breakdown of all long-chain lipids (the steroids are not broken down, they are excreted). Acetyl-CoA can be considered an important common component of lipids. Acetyl-CoA also functions as the starting molecule for the citric acid cycle (see also sections 1.2.3 and 2.1.3).

5.1. Classification of lipids

5.1.1. Structure of lipids

Structurally there are two main groups of lipids:

- The first group has *open chains*. This group consists of lipids with a (largely polar) head group and nonpolar tails of varying size. This group includes triacylglycerols (triglycerides), glycolipids, phosphoacylglycerols, and sphingolipids. The nonpolar tails make these lipids hydrophobic.
- The second group, the steroids, has *fused-rings*. It includes cholesterol. There is just one hydrophilic group



Glycerol

in cholesterol, which makes it very hydrophobic (section 5.4).

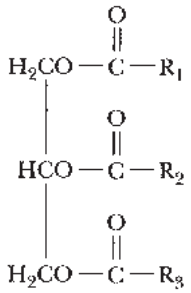
5.1.2. Lipid function

Another way of classifying lipids is according to function rather than according to chemical structure:

- *Energy supply*
  The first of these groups of lipids accumulates in adipose tissue and is directly available for the energy needs of the organism. These lipids also play a role in the padding of certain vital organs, for instance the eyes, heart, and kidneys. This group comprises triacylglycerols and fatty acids only.
- *Formation of membranes*
  The lipids of the second group have an important structural role because they are an essential component of cell membranes. Their components can be converted to a variety of further compounds that have functional properties, such as prostaglandin, leukotriene, and thromboxane, which are derivatives of arachidonic acid, a fatty acid found in the membrane lipids. The second group comprises the other open chain lipids and cholesterol.
- *Directing organism functions*
  The third group of lipids comprises the other fused-ring lipids: the steroid hormones, bile acids, and the fat soluble vitamin D_3, which are all derivatives of cholesterol and have different directing functions for maintaining the organism but no direct structural role.

We will discuss the lipids as three groups:

- The *triacylglycerols and fatty acids* (we will look at these separately from the other open chain lipids because of their different function)
- The *other open-chain lipids*
- The *fused-ring lipids*



5.2. Triacylglycerols and fatty acids

Triacylglycerols consist of three fatty acid chains bound to a backbone of glycerol. The triglycerides have a relation to carbohydrates in more than one way as will be explained in section 5.2.1.

5.2.1. Metabolism of triacylglycerols and fatty acids

Glycerol becomes available from glycolysis as glyceraldehyde-3-phosphate, and its breakdown yields glucose. Synthesis of triacylglycerols (and all other lipids) takes place in the cytosol, catabolic metabolism in mitochondria. Triacylglycerols are found in adipose tissue and are the lipid form of energy storage in animals and humans.

The *catabolism* of fatty acids is a main source of energy production. Fatty acids are broken down to acetyl-CoA through β-oxidation in the mitochondrial matrix. For a complete breakdown of fatty acids, acetyl-CoA must enter the citric acid cycle. This will yield a large amount of ATP for the energy requirements of the organism. One molecule of an 18-carbon fatty acid yields 120 molecules of ATP when it is completely oxidized to CO_2 and water.

Acetyl-CoA needs the availability of oxaloacetate to enter the citric acid cycle. Oxaloacetate is produced from pyruvate, the usual end product of glycolysis. Thus fatty acid breakdown in animals and humans needs products from glycolysis, notably pyruvate, to be accomplished completely and to yield the energy stored in the fatty acids.

The *anabolic* pathway of fatty acids starts from acetyl-CoA, which can be converted from pyruvate. Further acetyl-CoA molecules are added to form the lipid chain of fatty acids.

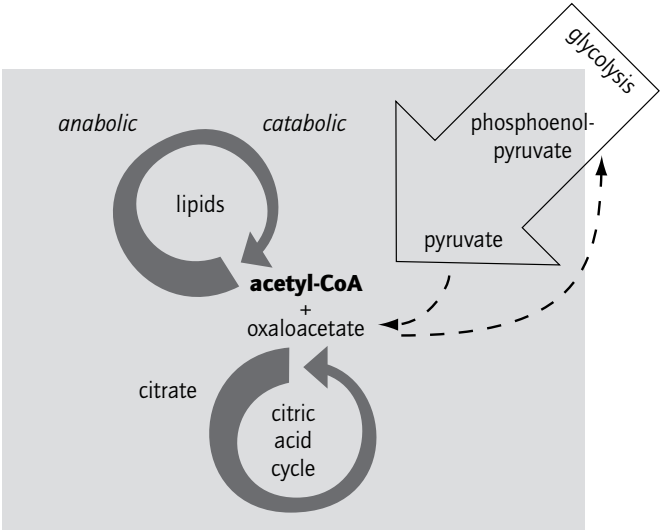


Fig. 5.1 The interconnections of lipid metabolism, carbohydrate metabolism and citric acid cycle (+ indicates the site of condensation of acetyl-CoA with oxaloacetate)

Triacylglycerols in fat cells are a long-term storage form of energy, far longer than glycogen in higher organisms. They can make more energy available per unit of weight than carbohydrates.

5.2.2. Fatty acid metabolism in fasting and diabetes mellitus

Carbohydrates are the preferred form of energy supply for the numerous anabolic and functional activities of the organism, but glycogen stores in the liver are estimated to be not more than 10-15 hours worth of glucose energy (which equals a long night's sleep) (see section 3.2.). The organism then uses the oxidation of lipids for its energy supply.

In prolonged fasting, glycolysis does not yield sufficient oxaloacetate for condensation with acetyl-CoA to accomplish complete oxidation of fatty acids (see fig. 5.1.). Oxaloacetate may then be formed from the breakdown of muscle protein. The amino acids that are released from muscle protein enter gluconeogenesis and yield the needed oxaloacetate (mainly from glutamine and alanine). Formation of oxaloacetate from amino acids also happens physiologically when an organism has a relatively high fat intake as

compared to carbohydrates. Then the amino acids for gluconeogenesis are yielded by the breakdown of proteins in the diet.

When there is a relative or absolute *shortage of carbohydrate metabolism*, such as in fasting, there is an excess of acetyl-CoA from β-oxidation and 2 molecules of acetyl-CoA will condense to acetoacetate. The latter in turn can either be reduced to β-hydroxybutyrate, or decarboxylated to yield acetone. These "ketone bodies" can be used very efficiently in energy supply. They are the major regular source of energy for the heart, which is embedded in adipose tissue and does not store glycogen.

The ketone bodies are also an important nutrient for the brain, especially when there is a shortage of carbohydrates. This means that *heart and brain cells, which do not contain glycogen, have all or a major portion of their energy supplied by lipids rather than carbohydrates*.

In *diabetes mellitus*, fatty acid breakdown is not matched with glycolysis, and acetyl-CoA cannot enter the citric acid cycle directly. This results in the pathological formation of ketone bodies from acetyl-CoA, which is the cause of the dangerous state of ketoacidosis in diabetics.

5.3. Other open-chain lipids and membranes

5.3.1. Membrane components and function

The other open-chain lipids, the phosphoacylglycerols, sphingolipids, and glycolipids, have an important characteristic in common: they are all part of membranes. Because the other open-chain lipids have a nonpolar hydrophobic group on one end and a polar hydrophilic group on the other end, they can form lipid bilayers, and this is what membranes actually are (see section 2.1.3.). Lipids are essential for membranes. Membranes allow aqueous liquids to be separated into compartments. They separate single cell organisms from their

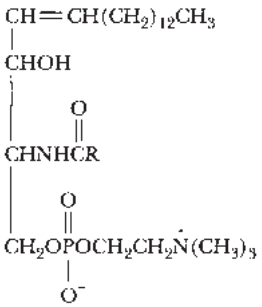
environment. They separate cells in organisms and various cell organelles from the surrounding cytoplasm.

The other main component of membranes is protein (see section 4.2.4.). Membrane proteins constitute about half of the plasma membrane compounds. They have a structural function, but they also provide the channels through which many compounds can enter or leave the cells, and in addition they function as receptors on the membrane's inner and outer surface.

Phosphoacylglycerols are found in all membranes of the body and are similar to triacylglycerols. They have a phosphoric acid molecule and some other alcohol instead of one of the fatty acids bound to a glycerol backbone. Sphingolipids and glycolipids are only found in the membranes of the nervous system.

5.3.2. Membranes in the nervous system

Both the sphingolipids, which include ceramides and sphingomyelins, and the glycolipids, which include gangliosides and cerebrosides, are special membrane lipids that occur only in the nervous system, primarily in the cell membranes of nerve and brain cells. Their backbone is sphingosine, which contains an amine residue. Glycolipids contain carbohydrate residues.



Sphingomyelins are found in abundance in myelin sheaths around the axons in the white matter of the brain, which derives its name and color from the amount of lipid it contains. Myelin sheaths consist of plasma membranes wrapped many times around the axon to form a many layered structure. Myelin contains very little protein in the lipid bilayer and is essentially just lipid. The myelin sheath around the axon permits a much faster transmission of the electrical impulse in the nervous system. A defect in myelin

sheaths may cause serious neurological defects, which we find in multiple sclerosis.

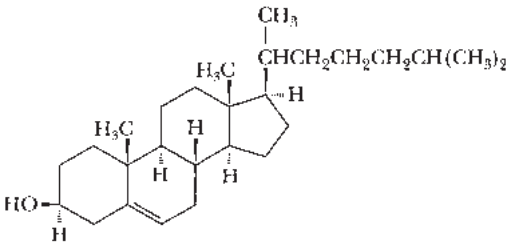
5.3.3. Membranes as "storage places"

An important function of membranes that is central to recent research is that they have a special type of storage function. Membrane constituents can be released under certain circumstances to yield important biologically active ingredients. A well-known example is the release of prostaglandins, leukotrienes, and thromboxane in injury, which are responsible for the inflammation that occurs at the injury site, but can also affect distant organs such as lungs, uterus, or functions such as the blood pressure. Arachidonic acid in membranes is the fatty acid precursor of these compounds. Prostaglandins and thromboxane form rings in the conversion from arachidonic acid.

5.4. Fused-ring lipids

The fused-ring lipids are *cholesterol* and the *steroids* that are derived from it. Cholesterol is the precursor of all other steroids that are produced in the human organism.

5.4.1 Cholesterol



Cholesterol is built up from acetyl groups from acetyl-CoA and forms 4 rings. Most of the cholesterol is formed in the liver. Cholesterol is very hydrophobic since it has only one hydrophilic group. The catabolism of cholesterol yields *bile acids*. Bile acids aid and regulate the uptake of lipids in the intestines. A large amount of this cholesterol metabolite in the digestive tract

will cause more lipids to be taken up into the bloodstream. This is an example of a positive feedback mechanism.

The presence of cholesterol, which is rather rigid in its structure, influences the fluidity of membranes (section 2.1.3.). The membranes of prokaryotes are the most supple of all since they hardly contain steroids. Plant membranes contain phytosterols (a steroid similar to cholesterol) and have less fluidity. The many unsaturated fatty acids in plant membranes make them more fluid than membranes in animals and humans, which contain cholesterol.

Cholesterol is the precursor of signal molecules (see section 5.4.2.).

Cholesterol is present in blood plasma, and it has been linked to the formation of atherosclerotic plaques in arteries. (Linder, 1997).

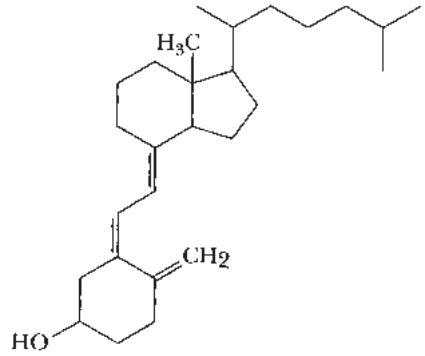
5.4.2. Steroid hormones

Steroids are derivatives of cholesterol. Most of them are signal molecules. They include:

- the *glucocorticoids,* such as cortisone, which play a regulating role in carbohydrate metabolism, suppress signs of inflammation and regulate how the organism deals with long term stress,
- the *mineralocorticoids,* such as aldosterone, which regulate the electrolyte balance (esp. sodium) in the organism, and
- the *sex hormones*, which arise from the conversion of cholesterol to pregnenolone and progesterone. They regulate the generative functions.

Hormones have regulatory functions in organisms. They aid the organism in maintaining homeostasis. They are themselves regulated by negative feedback mechanisms.

5.4.3. Vitamin D



Vitamin D_3

Cholesterol is also precursor to the fat soluble Vitamin D_3. Its function is regulating the balance of the plasma calcium concentration.

5.5. Summary and conclusion

Acetyl-CoA

Acetyl-CoA is the compound from which all lipids are synthesized. It is an important gateway to the citric acid cycle, which is central in all metabolic processes. It is possibly the key molecule in metabolism.

Three groups of lipids

Lipids were considered in three groups.

- The first group consists of the *triacylglycerols* and *fatty acids*. They are the long-chain fatty acid components of adipose tissue, and their main function is *energy storage*. They also have a structural function and support vital organs like heart, kidneys, epidermis, and the mammary glands, which are embedded in a layer of adipose tissue. The amount of adipose tissue also affects the structure of organisms!
  They are related to carbohydrates in more than one way. In their structure they carry glycerol as their backbone, which comes from glycolysis. In their function as energy providers for the animal and human organism they fulfill a typical carbohydrate function. Their metabolism has many connections to and is dependent on carbohydrate metabolism. The triacylglycerols ensure the availability of energy to the organism in times of temporary carbohydrate shortage since they can store energy over long periods of time. Triacylglycerols ensure a steady supply of energy to the organism in case of need.

- The second group is the other open-chain lipids, which form biological *membranes* through their bipolar nature. Membranes give the possibility of creating a sensitive balance between intracellular and extracellular processes.

  The other open-chain lipids are the *phosphoacylglycerols, sphingolipids, and glycolipids.* Phosphoacylglycerols are found in all cell membranes. Sphingolipids and glycolipids are only found as part of the cell membranes in nervous tissue. Sphingomyelins are abundant in the many lipid bilayers that form the myelin sheaths around axons. The white matter of the brain derives its name from its high lipid content. Myelin sheaths accelerate the speed of conduction of the electrical impulses in the nervous system, and they contain almost no protein.

  Proteins complement the open-chain lipids in biological membranes. Membrane proteins play a role in making the connection of the cell to its surroundings.

  Membranes can have a specialized storage function. Derivatives of the fatty acids of the membrane lipids such as the prostaglandins, leukotrienes, and thromboxane play a role in inflammation, blood pressure, blood clotting, etc. As such, they help to re-establish or maintain homeostasis in the organism.

- The third group of lipids is the *steroids*, the fused-ring lipids. The principal fused-ring lipid is cholesterol. It is synthesized from acetyl-CoA. Cholesterol plays an important role in determining the stiffness of animal and human cell membranes. Cholesterol is the precursor of all other steroids. The hormones and the vitamin derived from cholesterol *regulate metabolic processes* and as such bring homeostasis to the functions of the organism.

Lipid characterization

Triacylglycerols enhance the functioning of organisms by refining the possibilities of energy supply. This group of lipids is, in function, metabolism and structure, "carbohydrate-like." It is the long-term energy storage form of the body, and at the same time these lipids provide more energy per weight unit and a more efficient energy supply

than carbohydrates. In the form of ketone bodies they are the main energy source for the heart and an important energy source for the brain, both of which belong to the most highly developed organs in humans.

The second group of lipids enables more differentiated functioning in the body by forming bilayers, which are basic to the membranes throughout the organism. The other open chain lipids have a relation to the proteins and their function of enhancing the connections within organisms and of organisms with their environment. Two classes in this group are only found in the nervous system, the sphingolipids and the glycolipids. They promote conduction in the nervous system as myelin sheaths and as such enhance the function of the nervous system. They are so abundant in the central nervous system that white brain matter derives its color from them.

The third group of lipids makes cell membranes tougher and thus more stable and has a characteristic regulating function. Cholesterol is the prototype of this group as well as being the precursor to the others.

We described the three characteristic functions of the three lipid groups as

- enhancing the functioning of organisms by refining the possibilities of energy supply (which is related to carbohydrate metabolism),
- enabling a more differentiated functioning in the body and enhancing the function of the nervous system (these lipids are related to the proteins), and
- regulating metabolic processes and as such contributing to the maintenance of homeostasis in the organism.

Humans typically may

- enhance and refine energy supplies in the economic process,
- enable more differentiated functioning by enhancing social life, and
- regulate processes in nature by cultivating, so that homeostasis is maintained.

These are all tasks that animals cannot fulfill. Human functioning in nature has similar qualities to the functioning of lipids in organisms. Humans are also free to influence these natural processes or not.

The characteristic aspects of lipids are developed in the human organism to the highest possible degree in the functioning of endocrine, heart, and nervous systems.

Conclusion: *Lipid function in organisms is "human-like." Characteristic lipid functions are developed most highly in humans.*

6 Review and conclusions

We used the *goethean scientific method* for the study of biochemistry. This enabled us to draw conclusions regarding the role or *meaning of processes* in the whole of the organ or organism.

6.1. Cycles and rhythms

In the previous chapters we looked at phenomena in biochemistry. We worked out the cyclic nature of metabolic processes and saw how the cycles span cells, organs, organisms, and nature as a whole. We found that they interconnect and that they are subject to time rhythms. The span of time rhythms includes long solar rhythms, as in plant growth, as well as the short millisecond rhythms of the nervous system. Long exogenous rhythms are predominant in plants; animals have the whole array of rhythms; humans can be relatively free from exogenous rhythms. The longest rhythm of an organism is its life span. By studying biochemistry organisms became visible like the standing waves in a creek, through which water is constantly flowing, while the shape changes only slowly and sometimes imperceptibly. *Cycles are characteristic for life itself* - in inorganic chemistry processes have the linear quality of cause and effect, rather than being cyclic.

6.2. Carbohydrates, plants, and light

In Chapter 3 we found that carbohydrates are *typically energy carrying compounds*. The oxidation of water under the influence of sunlight in photosynthesis provides the energy for carbohydrate synthesis.
Carbohydrate metabolism in organisms can be described as "plant-like," since it has a similar function in organisms as plants have in nature. Carbohydrate metabolism provides prototypical examples of cyclic processes.

The primary nutrients that feed into the cycles of organisms each have a characteristic way of bonding. Covalent bonding is characteristic in carbohydrates. Photosynthesis revealed that the energy for covalent bonding in carbohydrates originally came from sunlight.

Monosaccharides have a relation to light in that they can polarize it. This property disappears when polysaccharides are formed. The glycosidic bond involves the chiral C-atom of monosaccharides, which is also implied in the ability to polarize light. In many other small compounds with mainly covalent bonds (such as the amino acids) we find the ability to polarize light again. With the formation of the peptide bond in proteins this ability also disappears. *The ability to polarize light becomes the ability to make specific covalent bonds, such as the glycosidic linkages in carbohydrates.*

6.3. Proteins, animals, and mathematical and musical laws

In Chapter 4 we described the functions of proteins and amino acids. These compounds all contain nitrogen from the air. They are as diverse as they are specific. Proteins characteristically encompass the whole array of bonding types in their structures, including covalent bonding, hydrogen bonding, disulfide bonds, electrostatic bonds, and hydrophobic interactions. We described protein metabolism as "animal-like," since the function it has in organisms is similar to the function animals have in nature (section 4.4.).

The comprehensive characteristic of proteins and amino acids is *that they enhance connections.* Connective tissue is the structural prototype and enzymes are the functional prototype of this.

Enzymes are as diverse and specific in their connections as are the notes in a piece of music. Each note has to be in the correct relation to the others for us to be able to hear the dynamic structure of a piece of music. We can see the same lawfulness in mathematical calculations, and for that matter in chemistry itself, where the correct

relation between compounds is essential for the function of organisms. The cyclic nature of carbohydrate metabolism undergoes further refinement in protein metabolism. Complicated negative feedback mechanisms that are characteristic of nitrogen metabolism are set up to accomplish this. We can characterize *protein metabolism as dominated by mathematical/musical laws.*

6.4. Humans, lipids, and the ability to say "no"

Chapter 5 focused on the lipids and we described their task as *enhancing and refining the energy supply* of organisms; *enabling more differentiated functioning* in the whole organism and specifically the nervous system by their ability to form and perfect membranes; and *regulating processes* so that homeostasis is maintained. Humans have similar tasks in nature and it is significant that the characteristic functions of lipids are developed to the highest possible degree in humans. Lipid metabolism in organisms is "human-like," since it has a similar function in organisms as humans have in nature.

In lipids, cycles become structural in the forms of micelles and of the membranes around cells and cell organelles.

Hydrophobic interactions are characteristic in lipids. These interactions are based on the principle of repulsion, rather than the principle of attraction which predominates in all other bonds. The development of the child has a characteristic phase at age two that is sometimes described as the "terrible two's." During this time the toddler learns what it is like to say "no," sometimes to the exasperation of those around it! Hydrophobic interactions in the typically watery, organic milieu of organisms leads to membrane formation in a spontaneously occurring reaction and membranes enable individualized life forms. The ability to say "no" also enables individualization. The "terrible two's" culminate in the capability of the child to say "I" to him- or herself. *Lipid metabolism lays the basis for individualization.*

The ability to say "no" can be found physiologically in the way human beings develop. They stay immature longer than any animal, and the possibility to develop continues for the whole of life, albeit culturally rather than physiologically after 18 years of age (see Verhulst, 1999).

The ability to say "no" is necessary for the development of free actions. Freedom is based on the ability to hold back and choose, not on the ability to do whatever comes around as a possibility! The human being's partaking in nature is increasingly free from natural laws. This creates a situation that is as precarious as it is hopeful, for not only is this creative interaction the basis for our cultural development, it is also the source of exhaustion of our natural resources. The development of free individuality brings the need to take responsibility. We may understand our responsibility better by learning about the coherence in nature and the relation between our environment and ourselves. This is where goethean science can be an enhancement for natural science.

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