

## Bootstrapping the Energy Flow in the Beginning of Life

R. Hengeveld · M. A. Fedonkin

Received: 30 November 2006 / Accepted: 25 April 2007 / Published online: 25 October 2007  
© Springer Science+Business Media B.V. 2007

**Abstract** This paper suggests that the energy flow on which all living structures depend only started up slowly, the low-energy, initial phase starting up a second, slightly more energetic phase, and so on. In this way, the build up of the energy flow follows a bootstrapping process similar to that found in the development of computers, the first generation making possible the calculations necessary for constructing the second one, etc. In the biogenetic upstart of an energy flow, non-metals in the lower periods of the Periodic Table of Elements would have constituted the most primitive systems, their operation being enhanced and later supplanted by elements in the higher periods that demand more energy. This bootstrapping process would put the development of the metabolisms based on the second period elements carbon, nitrogen and oxygen at the end of the evolutionary process rather than at, or even before, the biogenetic event.

**Keywords** Origin of life · Biogenesi · Thermodynamics · Inorganic chemical elements · Redox reactions · Periodic table · Electronegativity

---

R. Hengeveld (✉)  
Institute of Ecological Science, Vrije Universiteit, De Boelelaan 1087, Amsterdam, HV 1081,  
The Netherlands  
e-mail: rhengeveld@wish.net

R. Hengeveld  
Department of Ecology and Environment, Alterra, P.O. Box 47, Wageningen, AA 6700,  
The Netherlands

M. A. Fedonkin  
Paleontological Institute, Russian Academy of Sciences, Moscow, Russia  
e-mail: mfedon@paleo.ru

## 1 Introduction

“Earths from each sun with quick explosion burst,  
And second planets issued from the first,  
Then, whilst the sea at the coeval birth,  
Surge over surge, involv'd the shoreless earth,  
Nurs'd by warm sun-beams in primeval caves,  
Organic life began beneath the waves...  
Hence without parent by spontaneous birth,  
Rise the first specks of animated earth.”  
Erasmus Darwin, 1803

This paper describes how and why the energy flow within living structures only started up slowly, step-by-step developing into the massive flow of energy we observe in modern organisms. The present energy flow is assisted by a homeostatically balanced and finely-tuned, complex system of catalysts. This system had to co-evolve with that of the energy flow. Presently-found compounds are not only formed with the help of catalysts, they also store energy for later use, and channel the thermodynamic degradation of energy. The ability to store energy presumes that processes exist that can bridge periods of energy generation and energy shortage, or processes that use energy over longer and longer periods. This process of energy storage on longer terms needs an abundant energy supply, sufficient for immediate maintenance, growth and reproduction and, on top of this, that part of the energy can be stored away. A system of homeostatic reactions is also needed to allow energy-storing molecules to be formed, and, in the case of energy shortage, to be broken down again (Kooijman 2000). Finally, the continual construction and breakdown of catalysts, particularly energy-hungry macromolecules, such as proteins, put a heavy burden on the energy budget of living structures. It is therefore likely that at the very beginning of the evolutionary development of the highly sophisticated, energy-demanding living systems of the present, the elements and processes required less energy than those that constitute present-day metabolisms. This would have allowed the initial energy flow to be much weaker, despite the fact that the aqueous medium was electron-rich.

These considerations are based on a systems-theoretical approach that assumes a retarded flow of energy through the system. This approach is physical as it is concerned with the generation, storage, transduction, gradual degradation, and the eventual dissipation of energy. It contrasts sharply with the usual, chemical approach to biogenetic analysis which is concerned with the origin of individual chemical compounds within an unstructured primordial soup. Furthermore, such compounds would even have concerned energy-costly macromolecules or their building blocks, such as carbohydrates, amino acids, proteins, nucleic acids, RNA and DNA, and lipids. Moreover, most of these compounds readily hydrolyse in an aqueous medium, so that their maintenance and continual reconstitution also require energy. An earlier paper by one of us, Hengeveld (2007), distinguished this chemical approach to biogenesis from one starting from physical principles, and contrasted the questions they pose.

The present paper is a follow-up of our earlier ones, and concentrates on the systems-theoretical aspects of the origin, build up and maintenance of the energy flow basic to the operation of any system. It attempts to formulate an answer from the perspective of the physical way of looking at questions about biogenesis. We consider the slow, step-by-step build up of this energy flow to be a bootstrapping process. This concerns both its intensity and its chemistry.

## 2 Methodology

In this paper, we follow a few methodological principles. The historical continuity of life in terms of its basic biochemistry and consistency with physics and chemistry allow us to use a bottom-up approach and to test our results against biochemical, geochemical and palaeontological data. Also, we develop a systems approach and describe the development of metabolisms and the environment as complementary and interdependent processes. Moreover, life and its environment are considered both in dynamic as well as in structuralistic terms. This approach allows us to use one language for describing the whole developing hierarchy of the biogeochemical system, and this within an ecological framework; living structures are compartments of their environment. We demonstrate the organising capacity of the energy flow in all stages of biogenesis, giving priority to the dynamic, physical, aspect of the origin of life above the chemical one.

### 2.1 Some Postulates

- Organisms are energy-dissipating structures.
- Along with the evolution at the cellular, organismic and higher levels of the biological hierarchy, the evolution of metabolism is an essential part of evolution (Alves et al. 2002). Life's origin and evolution are physically and chemically constrained (Williams and Fraústo da Silva 2003).
- The initial biochemistry was tightly related to the early geochemistry, which, in turn, was close to cosmochemistry.
- Life initiated in an environment as a low-energy process rich in electrons and protons.
- An inorganic stage of metabolic evolution predated carbon-based life forms. Inorganic catalysts predated enzymes. Components of the biosphere changed irreversibly from those existing when life originated. Chemical conservatism is fundamental in evolution: biochemical reactions based on the structure and function of homologous proteins
- are more conserved than substrate specificity (Alves et al. 2002).
- To remain effective under changing conditions, archaic parts of the biochemistry are protected by metabolic pathways that are superimposed later. The increasing biological complexity reflects the conflict between the ancient biochemistry and the new chemistry of the biotopes. This is similar to backward compatibility from computer science.

- Two kinds of reactions form the essence of life: redox reactions involving electron transfer from metals to non-metal acceptors, and acid–base reactions of phosphates concerning proton transfer. Metals acting as electron donors initiated life as catalysts.
- The structure of the metabolic network and that of enzymes are subject to causal-historical analysis.
- In the living cell, signals are enhanced by biochemical reaction cascades in which one enzyme, as the product of a previously catalysed reaction, in turn catalyses the production of another enzyme, and this one catalyses the next, and so on. Morowitz (1968) suggested that metabolic cascades would recapitulate the biochemical evolution of the cell along with that of the environment (Fedonkin 2003). If so, the bootstrapping evolution of the energy flow through metabolic pathways allows us to reconstruct life's very origin. We do this in historical and physical terms of metabolism, rather than in chemical ones.

### 3 Bootstrapping Processes

Bootstrapping is applied, for example, in starting up the extremely powerful engines of present-day oil tankers. First, a light, starting engine, which can be turned on easily, starts the second, heavier one. This second engine, in turn, starts a third one, and so on, until the last engine but one in the series is able to start the final, very heavy engine that is able to power the ship across the ocean. Again, when mooring, a thin rope is thrown to the quay which pulls a heavier one across, until finally a very heavy hawser attaches the ship to the bollard. Similarly, and more in terms of evolution and complexity, simple first-generation computers made the necessary calculations for building second generation ones, and so on.

The principle in all three cases is that very heavy or complicated tasks cannot be carried out in one go, but have to follow a route of, often stepwise, increasing power or complexity. This process is known as bootstrapping. Thus, without the help of an external force or process, some process internal to the system starts itself up, in its achievements, in its structural complexity, or in both. We can find inspiration in these kinds of processes in order to describe how living structures could have evolved from abiotic conditions and processes. First, primitive structures arose, step-by-step developing into the highly complex and sophisticated biological ones we see around us today.

### 4 Three Broad Phases of Biogenetic Bootstrapping

At the present stage of our knowledge, descriptions of the biogenetic bootstrapping process can only be partial, many details still having to be filled in. We recognise three, broadly defined stages of evolutionary development. The first stage is dominated by heavy non-metals—possibly selenium—, their reaction with

hydrogen being catalysed by certain transition metals forming a mineral crust that envelops a cavity. This hydrogenation–dehydrogenation reaction depends on the exchange of electrons which is known as a redox reaction. The metals and the operation concerned are still found in metal co-factors of many proteins. The second stage would have added reactions of another type, the exchange of protons, which are basic to condensation–hydrolysis cycles and are known as acid–base reactions. These cycles result in condensations—polymerisations—, as well as in the hydrolysis still found throughout the biochemistry of the present cell. These acid–base reactions particularly concern nucleotide coenzymes. Proteins include either these coenzymes or the initial transition metals as their active site. In this stage, lipids could have been inserted into that mineral crust that surrounded the developing system. With the system's growing complexity, fine-tuning and standardisation of catalysis separated out from the nucleotide coenzyme system based on phosphates as RNA and, subsequently, as DNA. The third stage would have built on this already highly complex and integrated system, applying external solar energy for the photolysis, first of  $\text{H}_2\text{S}$  and then of  $\text{H}_2\text{O}$ . Initially, this supplied the system with an over-abundance of energy for which an extensive biochemical storage and release system was later installed with respect to carbohydrates. In all three stages, covalent bonding dominates, which concerns the sharing of electrons; redox reactions occur only in part of the catalytic reactions. The exergonic redox reactions seem to occur particularly in the membranes where energy is generated, whereas the later endergonic metabolic processing and storing reactions—and therefore energy degrading ones—are found primarily in the cytosol.

## 5 Stepwise Intensification of the Energy Flow

Energy must be generated at a certain point within a system, and alternatively be stored or transduced along specific pathways, ultimately leaving the system in a degraded form, that is as heat. Such a process depends on a continual flow of energy, the process never reaching a state of chemical equilibrium. This can only happen within a closed system, which puts aside any pre-biotic evolution in an unstructured primordial soup. From their very beginning, living structures arise by environmental compartmentalisation into oxidised conditions inside some cavity and reducing ones outside: a delimiting, mineral crust must have been the place where the energy was generated and from where it could begin to flow into some closed cavity.

Up to now, Russell and Hall (1997) have supplied the only model presently existing for the formation and operation of such an enveloping mineral crust. Herein, like in a chemical garden, this crust would have formed around a tiny, fine trickle of alkaline water seeping from a porous basalt seafloor into the metal-rich, acidic water. Because the anoxic seawater will have contained iron and nickel, and the seepage, sulphur, the precipitating crust would have been greigite,  $(\text{FeNiS}_2)_n$ . This crust would have initiated a charge gradient similar—or, possibly, evolutionarily basic—to that in modern chemiosmosis, which still generates and drives the energy flow within cells. Of course, the separation of reducing metals outside and

oxidising alkaline compounds inside, will not have been that strict, the seepage—and therefore the water contained within the crust—will have included some metals as well, coming out of the basalt, or loosening from the crust. Thus, reactions between metals and non-metals would have been possible. Apart from these reactions, heterocatalytic ones may have taken place on the inside of the mineral crust.

In this way, the initial processes would have taken place within a thermodynamically closed system, allowing energy transduction to happen, without, however, necessarily exchanging matter (Harold 1986, 2001). This may seem a drawback of the model whereas, in fact, it is not. In the first place, it solves a major problem of open systems like the primordial soup, where chemical equilibrium will soon be reached. Thermodynamically, therefore, it is impossible for biogenesis to have taken place in a primordial soup (Hengeveld 2007); it can only happen within a closed space under a constant energy supply, as in Russell and Hall's (1997) battery model. However, conditional to their model is that the molecules formed, decay at the same rate, thus forming closed loops or reaction cycles (e.g. Morowitz 1968). Phosphates, for example, could have oligomerised—condensed—at the inner surface of the crust and then fragmented—hydrolysed—in the water in the cavity (Hengeveld 2007). At the crust, they would thus capture energy heterocatalytically, then releasing it within the cavity, thereby transmitting energy by oligomerising other molecules. These oligomers, in turn, could have transmitted the energy in the same way, thus forming chains or cycles of energy degradation through a series of condensation–hydrolysis reactions. These reactions happened homocatalytically within the free space of the cavity.

A difficulty of this model, though, is that the greigite crust supplies too little energy for the covalent bonding of phosphates (R.J.P. Williams, pers. comm.), or for nucleotide triphosphates (NTPs) and nucleotide coenzymes that probably evolved later. Moreover, one of the basic requirements of the energetics of system formation is that, to prevent the system from running out of energy, surplus energy can be stored for later use (Ho 1998). Therefore, the formation of a covalent bond is needed that is weaker than that of phosphates. As we will see, selenium may be a candidate in this regard, but this would require different redox conditions than found at present.

## 6 Historical Interpretation of Ecological Gradients

An historical interpretation of biochemical types along environmental gradients can be fruitful with regard to biogenesis. In a biospheric factor space, such types can be asymmetrically distributed; changes in their characteristics with regard to almost every environmental factor result from interactions between long-term geological and short-term biological processes.

Life is asymmetrically distributed along a temperature gradient. In the cell, temperature determines redox potentials, controls catalytic reaction rates and influences the solubility of bio-organic compounds, minerals and gases. For example, compared to the dioxygen dissolved in water at 20°C, less than 2% of that

volume is found at 90°C (Brock 1978). Thus, we can visualise that during the initial anoxic conditions, with temperatures of about 40°C, hardly any free oxygen would have been available. The functional optimum of most prokaryotes and eukaryotes is found between 5°C and 30°C, with an increase in the proportion of prokaryotes at higher temperatures, and one in that of eukaryotes at lower temperatures. The structure of ecosystems simplifies in the geological history with the increasing eukaryotes represented under declining temperatures.

## 6.1 Metal Abundance

The relative abundance of elements in the Earth's crust and in meteorites partly explains their role in the life processes; in both non-living and in living material, elements with an even atomic number are more abundant than those with an odd one. The significance of the metals changes with their availability in the environment, and with their behaviour in living systems. The significance of a metal in living systems concerns either the type of enzyme it is in, its position within a protein molecule, or the composition of the prosthetic group. Furthermore, its significance is also affected by its possible replacement by another metal, its toxicity, and physiological antagonisms between metals, and so on. These various roles can be explained historically.

The early Earth was rich in iron (Fe), and also contained 5–30% nickel (Ni), similarly to iron meteorites. Other types of meteorites, chondrites, for example, may contain more than 10% of Fe–Ni, whereas Achaean komatiites contain large amounts of magnesium (Mg) and tungsten (W) as well (Becker et al. 2004). Significantly, pure nickel can contain large amounts of interstitial hydrogen.

Only few elements with an atomic number higher than 35 are metabolically active. This is partly because of their low abundance in the Earth's crust, although strontium (Sr, 38), niobium (Nb, 41), molybdenum (Mo, 42), iodine (I, 53), barium (Ba, 56), tantalum (Ta, 73), and tungsten (W 74) are exceptions to this rule (Fraústo da Silva and Williams, 1991). These exceptions suggest that early life was based on some heavier metals available on the young Earth, and that it subsequently shifted to lighter ones. The high rate of biological uptake of the lighter metals aluminium (Al), copper (Cu), iron (Fe), manganese (Mn), and zinc (Zn), and their low concentrations in present-day seas may reflect the antiquity of catalytic and metabolic pathways established when the abundance and bio-availability of these metals in seawater were high. Metabolic reactions seem to have been maintained by the metalloproteins containing them. These reactions predated and evolved in the prokaryotes, which could only have happened when new metabolic pathways superimposed them, conserving their archaic biochemistries both structurally and functionally.

As shown by the biological roles of nickel and tungsten (Cammack 1988; Ragsdale 1998), ancient enzymes may at some point have contained more transition metals than present-day ones. Tungsten is an especially interesting case (Kletzin and Adams 1996). So far, it has only been found in prokaryotes, such as the hyperthermophilic archaeobacteria *Pyrococcus furiosus* and *Thermococcus*

*litoralis*, the methanogenic bacteria *Methanobacterium thermoautotrophicum*, the gram-positive bacteria *Clostridium thermoaceticum*, *C. formicoaceticum*, and *Eubacterium acidaminophilum*, the gram-negative anaerobic bacteria *Desulfovibrio gigas* and *Pelobacter acetylenicus*, and the gram-negative aerobic bacteria *Methylbacterium* spec. Yet, only the hyperthermophilic archaeobacteria are obligatory dependent on tungsten; if they are indeed ancient, a very early origin of tungsten catalysts is probable (Fedonkin 2005). Tungsten, although an essential trace element for some prokaryotes, is antagonistic to other metals, such as molybdenum. The occurrence of metals such as nickel and tungsten in modern enzymes may be a biochemical relict of the early Achaean biosphere of about four billion years ago (4 Ga).

Thus, along with iron, other metals seem to have been involved in initiating biogenesis. Their catalytic role was essential, although, as with iron, the role of a particular metal may have changed with time.

## 7 Metal Availability

In the reduced Early Achaean hydrosphere, there were many metals available for biochemical reactions. As some reactions were irreversible, metals became less available, so impoverishing the geochemistry of the hydrosphere. Moreover, most heavy metals sank to the core of the Earth through gravity when it was still young, a period known as the Iron Catastrophe. Recent models based on Hf–W (hafnium–tungsten) chronometry suggest that more than 90% of this core would have already formed less than a hundred million years (>0.1 Ga) after the accretion of the planet (Galimov 1998, 2005; Yin et al. 2002). In that case, the magnetic field of the Earth was present very early in its history, thereby protecting the first life forms from the abundant hard radiation from space.

As radiogenic heat decreased, so did volcanism, reducing the amount of chemical elements entering the biosphere. At the same time, the orbit of the Moon increased, and as a result, its mechanical heating of the Earth lessened (Sorokhtin and Ushakov 1991; see, however, Williams 2000). Despite the 30% smaller luminosity of the Sun during the Early Achaean, the initial temperatures were still high because of warming by greenhouse gases, such as carbon dioxide, and water vapour and methane, methane being 20 times more effective than carbon dioxide.

The huge sedimentary ore deposits of the Precambrian show that large amounts of metals were removed from biogeochemical circulation. These deposits include shales, and uranium and gold conglomerates, bedded iron ores including jaspilites, copper sandstones, lead–zinc mineralisations in shales and carbonates, sedimentary manganese ores, and abundant phosphorites.

In this respect, the history of silica in the biosphere is especially striking. The Precambrian ocean was so saturated with silica that it precipitated as a gel, forming vast siliceous beds. Only since the appearance of taxa that used silica in their skeletons, such as sponges, radiolarians, diatom algae, and silicoflagellates (Broecker, 1971), has the ocean transformed into a siliceous

vacuum. This and many other phenomena show that the chemical composition of the early ocean was quite different from that of more modern times. The removal of metals like iron, nickel, cobalt, and tungsten from circulation as powerful, ancient catalysts, and later as cofactors in many enzymes, reflects this change. This could have determined the way life originated and evolved.

Later on, molybdenum is associated with the polymerisation of some proteins, with the biological breakdown of sulphur and carbon compounds, and still later with oxygen transport in animals. However, in the reduced, anoxic biosphere of the early Earth of about 4 Ga, molybdenum was unavailable, its later function was carried out by other metals, such as tungsten, vanadium, or even by iron. Molybdenum took their place as a cofactor in enzymes when the oxidation of the biosphere made these metals scarce. Today, bacteria with archaic enzymes are still to be found around hydrothermal vents saturated with hydrogen. These vents, inhabited by hyperthermophilic archaeobacteria, are rich in tungsten but poor in molybdenum, which precipitates there as a sulphide. However, at larger distances where oxygen is present, tungsten becomes metabolically unavailable, while molybdenum becomes soluble; this affects the composition of the local microbial communities. Therefore, those organisms using tungsten in their enzymatic apparatus seemed to have occurred on an anoxic, reducing early Earth and those using molybdenum, later. Interestingly, molybdenum replaces tungsten in metabolic processes in many phylogenetic lineages.

Apparently, one of the main trends of the evolution of metabolism concerns the replacement of trace metals in enzymes. Metals that were abundantly available, became replaced by newly available ones.

## 8 The Biogenetic Role of Metals

The transport of electrons and protons is the fuel of life, which is why we propose a thermodynamic rather than a chemical approach to biogenesis. The electron and proton flow as the essence of life, and its persistence over billions of years, suggests that life began in an aqueous medium containing electrons and protons that were easily available. At that time, metals were abundant, providing a rich source of electrons.

Metals play significant roles in life processes, in redox reactions, electron transfer, oxygen transport, gene regulation, structural stabilization of organic compounds, biomineralization, and so on. In some organisms, such as iron bacteria, metals are important in their energetics (Cowen et al. 1986; Myers and Nealsen 1988). Their significance for life is found in their catalytic properties: over 70% of the enzymes known containing metal atoms that function as cofactors. Transition metals, such as iron, nickel, cobalt, tungsten, manganese, molybdenum, vanadium, chromium, copper, and zinc play principal roles as the active site of an enzyme, known as activators, they can enhance the working of enzymes thousands or millions of times.

In cells of marine organisms, the concentration of many metals is several orders higher than that in the surrounding seawater (Morozov 1983). The concentrations in the phytoplankton compared to that in seawater are, iron: 87,000; zinc: 65,000; aluminium: 25,000; nitrogen: 19,000; copper: 17,000; phosphorus: 15,000; manganese: 9400; cadmium: 910; sulphur: 1.7; magnesium: 0.69; and sodium: 0.14 (Bowen 1966). The high figures indicate a significant biochemical role for these elements which could have led to a depletion in the sea water. Abundant and bioavailable elements, like sulphur, magnesium, and sodium, have a low ratio. In modern terrestrial organisms, such as man similar ratios occur in plasma relative to their concentration in seawater: iron 22300/0.5–20; zinc 17200/80; copper 16500/10; molybdenum 10000/100; chromium 55/4; vanadium 200/40; manganese 110/0.7; and nickel 44/5 nmol/l. Such high concentrations again suggest that two important processes have taken place in history. Firstly, the development of storage mechanisms in the cell, and secondly, as a result, an impoverishment of metals in the aquatic environment. Metal concentrations in the ocean are up to six orders lower than those in the soil and the Earth's crust (Di Toro et al. 2001). These huge disproportions suggest that very effective biotic mechanisms both for extracting metals, and for keeping them in the cell.

The universal role of metals as electron donors and their present-day catalytic properties suggest that metals started up the life processes on the early Earth (Fedonkin 2003, 2005). The widespread occurrence of  $(\text{FeS})_n$  clusters in molecular structures, such as in ferredoxins, cytochromes, haemoglobin, myoglobin, and other haemoproteins, points to an ancient, iron-rich environment as a possible cradle of life (Martin and Russell 2003; Russell 2006). The pivotal role of iron in life processes, even in its present low concentrations, is the result of its chemical properties: iron is the most abundant transition metal. Moreover, in the ancient Earth's crust, iron was more abundant, and under the anoxic conditions of the early biosphere more available to life.

## 9 A Biochemical Upstart

### 9.1 Ancient Elements in Modern Biochemistry

As the biosphere became oxidised, the biological role of the metals changed. For example, Fe-Mn superoxid-dismutases (SOD), that are so common in the prokaryotes, were replaced by the Cu-Zn SOD in the eukaryotes. In modern oxidised environments, different metals are involved in varying degrees in various nitrogenases following the Irving-Williams Series:  $\text{Mo} > \text{V} > \text{Fe}$  (Williams and Fraústo da Silva 1999, 2003, 2006).

### 9.2 Nickel

Nickel constitutes about 0.02% of the Earth's crust, which is 500 times less than iron. Nickel enzymes catalyse reactions between hydrogen, nitrogen,

carbon monoxide, and carbon dioxide, gases which could have constituted the atmosphere of the early Earth. Together with iron, nickel dominates in metallic meteorites, whereas its concentration in present-day seawater is very low. The high concentration of nickel in metallic meteorites and in the Earth's crust during the period of its most intense bombardment by meteorites at about 4 Ga, suggests that, also with iron, nickel was abundant and available at the dawn of life. The evolutionary fates of nickel and iron seem to be connected, both elements forming the active centres in such enzymes as hydrogenases and ferredoxins in Archaea, Eubacteria, fungi, algae and higher plants (see Hausinger 1993; Telser 1998; Fontecilla-Camps 1998); these are considered the most ancient, and archaic catalysts. Nickel is found in proteins, such as the hydrogenase Ni-tetrapyrrole (factor F430) in methanogenic bacteria, and in superoxide dismutase, carbon monoxide dehydrogenase, methyl-S-coenzyme M reductase, acetyl-CoA synthase, urease, and so on. (Ragsdale 1998; Ermler et al. 1998; Cammack 1988). The large size of proteins, such as hydrogenase and ureases, suggests the need to protect their archaic active centre from oxidation. However, the porphyrin shell surrounding the nickel ion in certain enzymes suggests that the need for protection of the catalyst is even older.

### 9.3 Iron

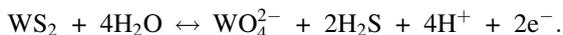
Iron is the fourth most abundant element in the Earth's crust; it is a transition metal and after aluminium, it is the second most abundant metal. Iron is very reactive, binding with halogens, sulphur, phosphorus, carbon, and silicon, and displaces hydrogen from most dilute acids (Microsoft Encarta, Encyclopedia Standard Edition, 2002). Both are important properties with regard to the energy flow in biogenesis; iron plays a pivotal role in the metabolism of hydrogen. Many metals react with water, thereby forming metal oxides and metal hydroxides, whereby hydrogen is released. Iron is no exception, although the reaction needs heat. Under the reducing conditions of the early Earth where iron was abundant, this kind of hydrogen production could have been common, particularly near active, underwater volcanoes. However, the reaction of iron with weak natural acids was probably more effective in generating hydrogen; such acids would have been formed when volcanic gases dissolved, such as when  $\text{SO}_2$ , that results in sulphuric acid, or when anoxic water percolates through sulphide deposits.

Iron is the most important oxygen reagent, such as in photosynthesis, in nitrogen fixation, and in respiration. Haemoproteins, which include haemoglobin, myoglobin, various cytochromes, catalase, some peroxidases and dehydratases, ferredoxins, ferredoxin oxyreductase, and other Fe-S proteins, probably form the largest group of metalloproteins. Interestingly, the haemoproteins do not tolerate  $\text{H}_2\text{S}$ , HCN and CO, compounds that were possibly present, both in the earliest environment and in archaic biochemistries; this suggests their late origin relative to the oxygenation of the biosphere.

## 9.4 Tungsten

Despite its large atomic weight, tungsten is important in the biochemistry of Archaea and Eubacteria, but not in that of the eukaryotes. Most tungsten proteins occur in strictly anaerobic thermophiles and hyperthermophiles, and catalyse very negative redox reactions of less than  $-420$  mV. Tungsten concentrations in aerated seawater are extremely low (1 ppM), although in hydrothermal vents these can be higher than 50 nM because of the high solubility of tungsten sulphide,  $WS_2$ . Together with its relatively high concentrations, that are similar those of nickel, in Achaean volcanic rocks (komatiits), its asymmetric distribution over various taxa and over present-day environments suggests that on the early Earth, tungsten had a more important biological role than it has at present. Tungsten easily donates and accepts electrons, which is conditional for reversible reactions that keep the energy flow going. Because tungsten and molybdenum both occur in group 6 of the periodic table but in one period lower (6) than molybdenum (5), these two elements are chemically similar; this is reflected in their comparable electronegativity, 1.4 and 1.3, respectively. However, biochemically, the two metals are often antagonistic (Kletzin and Adams 1996).

Despite their similar abundance in the Earth's crust, in which tungsten and molybdenum rank as 54th and 53rd, tungsten's concentration in seawater (0.0002  $\mu\text{g}/\text{kg}$ ) is about 500,000-fold lower than that of molybdenum (8.8–13.5  $\mu\text{g}/\text{kg}$ ). However, this could have been just the reverse on the early Earth, since under anoxic conditions, tungsten dominates to the same extent over molybdenum. Typically, tungsten deposits are found in hydrothermal systems. Along with oxygen-rich tungstate minerals, such as scheelite ( $\text{CaWO}_4$ ) and wolframite ( $[\text{Fe}/\text{Mn}]\text{WO}_4$ ), tungsten occurs as the more reduced and rarer, soluble tungstenite ( $WS_2$ ):



Tungsten's great availability in modern hydrothermal systems, which are usually inhabited by communities rich in tungsten-dependent prokaryotes, suggests that on the early Earth with a greater hydrothermal activity these biotopes could have been more widespread. The great diversity of tungsten proteins, such as formate dehydrogenase, formyl methanofuran dehydrogenase, acetylene hydratase, and aldehyde oxidoreductases, has recently been discovered.

## 9.5 Selenium

There are more than 130 mineral species containing selenium in the mineralogical database and reference website <http://www.mindat.org/index.php> contains. The physical and chemical properties of selenide minerals are similar to those of sulphides, the largest group of ore minerals. It is not surprising that they are found together.

Selenium-containing minerals and natural sulphides have common structural types. However, while sulphur forms sulphide minerals with more than forty elements, selenium does so with only a small number of elements, such as lead, mercury, beryllium, silver, copper, cobalt, iron, nickel, zinc, cadmium, and titanium. The commonest of these is lead selenide, PbSe, or clausthalite. Most selenide minerals are rare and occur in low concentrations in sulphide mineral deposits where selenium replaces sulphur. Selenide minerals also occur with sulphate and oxide minerals in relatively oxidized thermal spring deposits where, with the exception of cinnabar, sulphide minerals are unstable (Vikre 2005). The geochemical chalcophilic behaviour of selenium is also shown in its high concentrations in meteorites, of up to 300 mg/kg. Selenium often occurs in sulphide lattices, and is concentrated in oxidized, sulphur-enriched deposits; it is very common, with abundances of up to 5% in native volcanic sulphur, but not in sedimentary sulphur. Selenites ( $\text{Se}^{4+}$ ) and selenates ( $\text{Se}^{6+}$ ) are unstable minerals which are absorbed by clay minerals, iron oxides and iron hydroxides. In oxidized hydrothermal systems, sulphur is oxidized more readily than selenium, so that at high redox values, sulphur separates out as  $[\text{SO}_4]^{2-}$ . Thus, over geological history, the oxidation of the environment reduced the availability of selenium, and increased the biogenetic role of sulphur under the still anoxic conditions of the early Earth.

Selenium and sulphur are both in group 16; with its position in period 4, selenium is a non-metal with slightly metallic properties, whereas sulphur in period 3 is not metallic. Among the elements in the Earth's crust, sulphur ranks as 16th in abundance, occurring both in a free state, as well as in many metal sulphides and sulphates, making sulphur more widely available than selenium. Therefore, the replacement of selenium by sulphur in metal-non-metal clusters was likely, where the lighter, abundant sulphur replaced the heavier, less abundant selenium.

Selenium, being able to both donate and accept electrons, has oxidation states  $2^-$ ,  $4^+$  and  $6^+$ , binding with metals as well as with many organic compounds. It thus produces analogues of sulphur-organic compounds. In selenium-metal bonds, Se is negatively charged, whereas in oxygen-selenium organic bonds it is positive. The multiple oxidation states of selenium have different fates in the environment: its reduced forms, such as selenides, Se(-II) and elemental selenium, Se(0), are formed anaerobically, and seem not to be mobile or bioavailable (Presser and Swain 1990). The reduced selenium species are less soluble than selenite ( $\text{SeO}_3^{2-}$ ) and selenate ( $\text{SeO}_4^{2-}$ ), which are the most soluble of all; they are distributed as a function of pH between the solid and dissolved phase (Hayes et al. 1987). Six of the 17 selenium isotopes are stable, with an abundance ranking as:  $^{74}\text{Se}$  0.87%;  $^{76}\text{Se}$  9.0%;  $^{77}\text{Se}$  7.58%;  $^{78}\text{Se}$  23.52%;  $^{80}\text{Se}$  49.82% and  $^{82}\text{Se}$  9.19% (Ermakov 2004).

We mention the selenides of iron and nickel, ashavalite, FeSe, ferroselite,  $\text{FeSe}_2$ , and blokite,  $\text{NiSe}_2$ , given their importance in ancient catalytic reactions of these metals. Like most selenides, these minerals precipitate during hydrothermal processes because of low redox potentials. In living cells, selenium is important as an antioxidant; there is a large group of Se-proteins or Se-dependent proteins, which almost all occur as seleno-cysteines (Patching and Gardiner 1999; Schrauser 2003).

## 9.6 Hydrogen

The primary sources of hydrogen on the early Earth could have been the outgassing of mantle-based rocks, releasing with neutral and slightly acidic fluids, along with H<sub>2</sub>, some other hydrogen-containing volatiles such as CH<sub>4</sub> and H<sub>2</sub>S (Nealson 2005). A second powerful hydrogen source was the reaction of olivine- and pyroxene-rich rocks with water, serpentinization (Schulte et al. 2006). This process generates the serpentine group minerals and varying amounts of brucite, magnetite, and/or FeNi alloys, liberating molecular hydrogen and electrons used by organisms of various chemosynthetic taxa. The radioactive decay of elements such as uranium, thorium, and potassium releases radiation energy, which, in turn, is used to split water molecules: another source of hydrogen that seemed to be far richer on the early Earth. This mechanism allows bacteria of the division Firmicutes to exist at about 2.8 km deep utilising the energy in water found in pores and cavities in rocks in a gold mine near Johannesburg, South Africa. The bacteria use hydrogen for respiration, thus generating energy. This bacterial taxon is also known from hydrothermal deep sea vents, as well as from deep mineralised groundwater (see also Lin et al. 2006).

Hydrogen is central to microbiological systems, not only as a component of water; this element constitutes 60% of the cell contents. The cell uses hydrogen gradients to generate ATP by chemiosmosis; the function of most microbial enzymes concerns the transfer of hydrogen. Moreover, the formation of hydrogen bonds is crucial for the stability of the most important macromolecules. Hydrogen, being a 2-electron transfer currency of the cell, is a primary fuel for living structures, and the most abundant building block of the Universe. Fe–Ni crusts may have acted as a hydrogenase, catalysing the most ancient reactions with hydrogen, thereby starting up the energy flow found in all living structures up to the present day.

## 10 Biogenesis and Systems Theory

Characterising systems for the initial stages of biogenesis is difficult, since this characterisation should point to the uninterrupted continuity of life. Moreover, living systems interact with their environment without which the organism cannot exist; in fact, as these interactions are part and parcel of the system we call an organism, they should also be taken into account. How we can recognise systems, and how do their properties put constraints on which chemical elements can be thought to have constituted them? Of course, not all elements are equally available, not only because of their relative abundance, but because of the physical and chemical conditions of the environment, such as redox potential and acidity.

Concerning inorganic chemistry in relation to life processes, Fraústo da Silva and Williams (1991) and Williams and Fraústo da Silva (1996, 1999, 2006) have given the basic information and understanding. Surprisingly, though, these authors treat the subject from a chemical viewpoint rather than from a physical one based on the energetics of systems (see Hengeveld (2007) for this distinction). The physical viewpoint puts the chemistry involved into a physical framework, which directly

gives an insight into how living structures and systems originated. It also shows how the chemical constituents and mechanisms of operation of the systems subsequently shifted in accordance with shifts in the physical properties of their chemical environment. (Proto-)cells as compartments of the environment cannot be analysed separately from this environment.

### 10.1 Systems, Energy, and the Selection of Elements

Systems can be defined as sets of dynamically interacting components, and their evolution concerns shifts, either in the dynamics of these interactions, in the nature of the components themselves, or in both. Moreover, as in any system, biological systems are structured, and their origin and maintenance result from a flow of energy they generate themselves, which dissipates from them in a degraded form. The interactions thus form mechanisms for energy generation and transduction, which, in turn, define which chemical elements or compounds fit these mechanisms, and which do not. In other words, the origin and maintenance of a structure primarily requires an energy flux, and the nature and intensity of this flux defines the selection of elements and subsequently that of the compounds they constitute. During, and well after biogenesis, the system is therefore primarily physically defined, after which, first, chemical processes and later, biological ones were added for its continued operation. The chemical processes concerned biochemical pathways and cycles, for example, and the biological ones interactions between cellular compartments, or communication within and among multicellulars.

The first systems must have been mechanisms for a directed energy degradation. These mechanisms would have been partly dependent on the abundance, availability and chemical activity of the elements, and partly on the flow of energy through a thermodynamically closed compartment of the environment. According to Russell and Hall's (1997) model, the initial energy flux concerned redox reactions with a flow of protons and electrons from outside the cavity into it. Although keeping to the basics of their model, we suggest this crust to have consisted not of greigite,  $(\text{FeNiS}_2)_n$ , but instead, of Fe–Ni–selenides.

### 10.2 Life as an Emergent Property of Matter

In a modern metaphor, life can be considered as an emerging property of inanimate matter. Thus, similar to water that has specific, “emerging” properties not found in individual molecules, but that result from their specific interactions (e.g. boiling and melting point), living structures and life processes can also show emerging properties; this distinguishes them from non-living ones. Unlike in water, though, the interactions between the molecules of living structures are not static but dynamic, the elemental and molecular interactions being activated by the energy flowing through the structure. Yet, as specific properties determine these interactions: just as they do in water, they connect the two levels of variation, that of quantum-mechanical properties of elements and molecules with the level of a

biochemical structure. Without any contradiction, therefore, living structures reveal their own, biochemical or biological behaviour, whilst retaining their physico-chemical basis. However, the growing network of interactions between a multitude of atoms and ever more species of molecules by their sheer number soon becomes intractable in practice, although in principle this should be possible (Elsasser 1987). Kaufmann's emergent, self-organisation (2000) does not allow for the specificity of these reactions; his models assume connections between chemically unidentified, non-specific units. It is precisely the specificity of the evolving interactions at the elemental and molecular level, and this in relation to the evolution of the environment, that determines the type of system that will emerge.

### 10.3 Closed Systems

The first steps of biogenesis must have been made within a thermodynamically closed space which generated a chemical non-equilibrium. Thus, a structured energy flow was started up, which has continued uninterruptedly up to the present day for almost four billion years, without chemical equilibrium ever being reached. It is very well possible that the degradation of the energy that flowed through the system did not result in waste products, because the initial reactions were fully reversible; this allowed the system to be thermodynamically closed. Furthermore, as soon as several processes became tuned to each other, they had to remain separate from the environment, becoming constrained and channelled, operating in an increasingly structured and coherent way. This means that in living structures, energy degradation is partitioned into an increasingly larger number of consecutive steps. These steps, moreover, formed temporal hierarchies of homeostasis, according to chemical activity and reaction rates, and to the degree of stability of the compounds. The phosphates as energy carriers, after having obtained their nucleoside bases, became more powerful and specific in their operation with the increase in complexity. They finally assumed their homeostatic standardisation function, first as various species of metabolic RNA, later as genetic macromolecules, and finally as DNA.

Also, within the initial cavity enclosed by the mineral crust, reactions took place in micro-compartments (Ho 1995), such as membranes or parts thereof. Much later, in the eukaryotes, the reactions occurred in spatially delimited compartments (e.g. Williams and Fraústo da Silva 1999). Processes requiring different conditions concerning pH or oxidation state, for example, thus ran isolated from each other. Still later, particularly from the end of the Proterozoic, calcium and sodium, as well as the newly added transition metals, such as copper and zinc, metalloids and some halogens operated mostly extracellularly, thereby obtaining communication and mechanical functions. This spatio-temporal structure also ordered and tuned the processes, which implies the elaboration of homeostasis, as well as specificity of the reactions that were taking place. Thus, a biochemical superstructure arose, imposed onto the energy flux underlying it; at the same time the energy flow determined the structure and selected its constituent elements and compounds. These systems show the bootstrapping processes at the level of the system in their basic operation and in

their various forms of sophistication. As far-from-equilibrium, spatio-temporally structured systems, they could only develop within a closed space, this would have been impossible in an open, primordial sea. The structuring energy flow was the result of this initial compartmentalisation of the environment into proto-cell and its environment, and its evolution in turn involved a refinement of this structuring.

#### 10.4 Biochemical Cycles

At some stage, an initial hydrogenation–dehydrogenation process may have taken place, resulting in an ever broadening chain of selenium-based compounds, together forming reaction chains or cycles of a certain extent. Thus, hydrogen and selenium may have formed selenium hydride,  $\text{H}_2\text{Se}$ , which, in turn, could have formed other selenium compounds, which together formed an ancient selenium-based biochemistry. In this way, homeostatic systems—chains or cycles—could have formed and been extended, step by step following a structural bootstrapping process within the context of a growing and intensifying reaction system. At first, growth concerned the intensification of the system, only later being supplemented by system extensification, that is by multiplication.

In a similar way, phosphates on the inner surface of the mineral crust may have oligomerised with the release of water, condensation, the surface operating as in heterocatalysis (compare Wächtershäuser 1988). After these oligomers detached from the crust, the water in the cavity could have hydrolysed them again, whereby condensation energy gained at the crust would be transmitted in a next-condensation-reaction of the phosphate monomers into oligomers. Next, the monomers or dimers thus formed in the cavity can condense again at the crust, closing a cycle consisting of three components only. The energy released in the cavity would eventually leave it as heat. Therefore, phosphates would have acted as energy carriers, transporting energy into the cavity from the electron charge and pH gradient around the crust. Various stages of system build up are retained in metabolic pathways, as well as in the co-enzymatic operation of metalloproteins and in the genetic system underlying chemical homeostasis. This is similar to the initial homogeneous catalytic operation of metals in the solution in the cavity, in addition to heterocatalysis at the crust. In this way, complex homeostatic systems of multi-component reaction chains or metabolic cycles could have been formed (compare Morowitz (1968); Gánti (2003) for a general model).

#### 10.5 Putting Carnot Cycles in Series

Thus, either a first hydrogenation–dehydrogenation or a hydrolysis–condensation cycle can be imagined to have occurred, but this implies a decay process only, tending towards ever increasing entropy. To obtain complex molecules and systems, living structures have put several of them in series, each next one assembling several units of free energy released by the previous cycle (H.J.M. de Groot, pers. comm.). Cycles like these are known as Carnot cycles. Putting them in series is well

known from photosynthesis in plants where two photosystems together forming the Z-scheme pass on the energy from two light quanta such that one electron is passed on from a water molecule with a high redox potential of +820 mV, meaning that it holds on its electrons tightly, to NADP<sup>+</sup> with a low one of −320 mV. Moreover, this leaves enough energy to pump one proton across the thylakoid membrane to enable the production of one molecule of ATP.

Thus, by putting two units in series, a thermodynamic uphill process becomes possible, after several repetitions eventually allowing complex carbonate molecules to be formed storing energy for later use. This series of Carnot cycles can eventually form, either linear pathways such as the glycolytic pathway, or cyclic ones, such as the TCA cycle. In fact, this build up represents one form of bootstrapping recognisable in living structures and allowing life to exist. The first such process may be expected to have occurred immediately after the first hydride formation with selenium. At present, the energetics of these processes is under investigation.

## 10.6 Minimal Energy Loss

Ho (1995, 1998) observed that in non-living systems, energy is used directly, whereas in living ones, it is stored temporarily at one or more places between its capture and its eventual release. In fact, storage of energy seems to be the first process after its generation before it is used in processes such as growth, maintenance, reproduction and mobility (Kooijman and Hengeveld 2005).

Moreover, special processes, reactions or structures are found that minimise the leakage of energy during its transfer and utilisation; living systems are highly efficient in their energy use, because they store it and minimise leakage. Thus, energy is retained by the formation of chemical transfer compounds in, for example, the energy transfer of ATP. First, one phosphate binds to the substrate, after which this transition compound reacts with water instead of hydrolysing directly without the interference of the substrate. There are several sources of energy release in the liberation of one phosphate from ATP, among which that from the possible rearrangement of the configuration of the bonds in the substrate molecule. This new configuration consequently leads to a more stable, new molecule. The point here is that enzymatic reactions always involve the formation of one or more transition compounds, which—often alternately—release or absorb a large part of the energy from a previous bond. This only occurs internally, and therefore with a minimum of energy leaking into the environment.

Part of the energy released in a reaction is transferred through rearrangements in the configuration of a substrate molecule to the new bonds of the reaction products. This principle, developed in phosphates and nucleotide coenzymes, subsequently became evolutionarily refined to the highest degree with the development of the apozymatic proteinaceous macromolecules added to the catalytic metals and RNAs. Since nucleotide bases and amino acids contain carbon, nitrogen and oxygen, and because proteins are structurally and dynamically exceedingly large and complex macromolecules requiring much energy for their formation and maintenance, proteins could only have evolved after an intricate, forceful energy-generating and

processing system was established. This also holds for the various forms of RNA and for DNA as evolutionary, polymeric end products of the phosphates (White 1976, 1982; Hengeveld 2007). The refinement of the catalytic operation of proteins can be found in their structural rearrangements, that reduce the energy barrier between substrate and product to almost nil.

For modern catalytic systems, Lumry (1994) described how the charge of the apozymatic part of the protein changes from one step to the next, to which its configuration responds. These changes in configuration either release, or demand energy; the amounts released and demanded compensate each other at each step of hydrogen tunnelling or in a chemically catalytic process. Both processes result in a redistribution of charges throughout the molecule and, hence, in a change in its configuration (e.g. Hammes-Schiffer 2006, Hammes-Schiffer and Benkovic 2006, Hammes-Schiffer and Watney 2006). Thus, the energy transactions within each step are accounted for precisely by the apozymatic part of the protein. In this way, the often large apozymatic, proteinaceous part of the enzyme could have been a later addition to either the metal or the RNA cofactor, making it energetically efficient. Moreover, each protein is highly specific: each step within a spatially and temporally ordered process is reflected in another molecular configuration, that ties in energetically with this process. (NB. It is unimaginable that proteins could ever have been formed in a primeval soup, without specific functional interactions involving stepwise deformations and reformations relative to a particular molecule, and this under certain pH and temperature conditions or a specific network of biochemical reactions, and this quite apart from the energy needed for their costly formation and maintenance.)

## 10.7 Environmental Conditions

A proper functioning of the dynamics of the proteinaceous, apozymatic part of an enzyme heavily depends on the conditions set by its chemical environment. Responding to changes in charge, the operation requires a specific pH and temperature. The pH determines the strength of many bonds, and that of hydrogenbonds, etc. and, hence, the configuration of the complex molecule. As a measure of, for example, vibration, temperature determines both the reaction rates of molecules as well as their stability and internal configuration. Together, pH and temperature determine the degree of tuning within a hierarchy of interdependent reactions. It is conceivable that during the earlier stages of evolution, both fluctuated but that their range of variation within the system gradually narrowed down, particularly during the time of the formation of highly sensitive proteins.

The tendency towards a compulsory standardisation of tuning of reactions is a function of the intensity and extent of interactions between the various reactions making up the system; they cannot interact properly when their optimal conditions lie far apart. Thus, compounds and their biochemical reactions will have been selected, such that only those operating under similar or identical conditions remained. Particularly when polymers would have begun to be formed, each with a specific folding and internal dynamics, pH and temperature must have stabilised

within narrow limits for their biologically optimal functioning. And as systems kept operating the same way over billions of years, it is safe to assume that present-day optimal values of pH and temperature reflect those during or soon after biogenesis. These would have been at neutral pH and somewhere between 30 and 40°C, conditions that have been kept ever since. (At a later evolutionary stage, hyperthermophiles among the archaeobacteria developed ionic bonds between the folds of proteins as a special adaptation to prevent their degradation by high temperatures (Jaenicke 1996; Rice et al. 1996)). Therefore, internal to the system the conditioning of the processes also followed a bootstrapping process.

Thus, it is the structuring of components with specific properties into a system, which has to co-evolve with changing external conditions. Together, they generate and channel the flux of energy through the system, shaping and directing its operation. Each step in this adaptive process of a living, structured system forms the platform from which the next step can be taken. It is, in short, a bootstrapping process.

## 11 A Bootstrapping Scenario of Biogenesis

### 11.1 A Scenario for the First Steps

From a systems-theoretical viewpoint, we have to concentrate on a flow of energy that must have been started up for biogenesis to take place. Therefore, looking at mechanisms to achieve this, we need to know how elements were selected and compounds were formed. Energy transfer from one element or compound to the next could in the first instance have been achieved by electrons, and the build up of compounds, by protons or hydrogen atoms. In this way, by starting from a systems-theoretical viewpoint and by translating this physically into an energy flow as the basis of the origin and maintenance of any system, we obtain a unifying criterion for selecting, first, elements, then compounds, and finally whole biochemical systems and cell organelles. Fraústo da Silva and Williams (1996) in their *The natural selection of the chemical elements* did supply us with information and insight into the chemical properties of elements and inorganic compounds found in various parts of biological systems, but not with an exact selection criterion with regard to biogenesis. They described how existing biological systems select chemical elements, whereas within a biogenetic and evolutionary perspective, we need to know the criteria for selecting elements that made these systems possible in the first place. It is this criterion from which their historical insertion into these systems, and their functioning within them, could follow.

Biological systems still operate within an environmental context from which they obtain their energy and with which they interchange matter. It will particularly have been the far-from-equilibrium condition between both sides of a mineral crust or membrane from which living systems initially drew their energy. This far-from-equilibrium condition, dependent exclusively on an enveloping crust or membrane, initiated the structuring energy flux, which has been kept up biologically from its physical beginnings ever since. This far-from-equilibrium condition determines the

ecological basis of all life processes, without which it is impossible to understand them. Starting from a non-compartmentalised primordial soup, or considering the evolution of processes within an existing (proto-)cell only, leads to nothing. Because of its fundamentally physical mechanism, the early evolution of life integrated environmental with (bio)chemical conditions and processes. In fact, it has done so ever since, up to the most complex, modern life forms.

Hydrogenase, which is basic to most of the metabolic system, and possibly having been involved in the upstart of the energy flow essential for life processes, could have been achieved by metals which may still have the same effect in present-day metalloproteins (e.g. Cammack et al. 2001). In fact, hydrogen occurs between the lattices of many metals, such as nickel, where it forms interstitial nickel hydride. These and other metal hydrides could transfer protons further to other elements, firstly, selenium and subsequently to sulphur, and then to ever stronger non-metal oxidisers. Thus, in principle, protons and electrons could have reduced selenium as an initial, covalently bonding element to hydrogen. In this way, selenium hydride,  $H_2Se$ , would have been formed, in effect forming the chemical cradle of life.

In these initial reactions, electron or proton tunnelling, respectively, can be thought to have played a role from the early beginning when energy may have been particularly short in supply. Both types of tunnelling depend on the quantum theoretical dualism of matter and energy, wherein matter is described in terms of a probability wave of quantised energy. Depending on “particle” size, the period of these waves differs, the larger the particle, the smaller the period. Electrons and protons are small enough to account for tunnelling, their periods often being larger than the distance between two molecules and, hence, they are able to bridge it. Thus, in a hydrogen world, the probability of an electron or proton being part of molecule A, at the same time also occurring in molecule B, is high enough for it to stay in B when the distance between the molecules increases again through vibrational motion, that is it tunnels or hops from A to B. (In a deuterium world instead of a hydrogen world, life may not be possible because, according to Ball (2004), the wave periods are too small to cover the distances often enough.) Quantum tunnelling, not requiring energy, may have been relatively prominent from the initial stages of biogenesis onwards, as it still is in the operation of many modern proteins (Dutton et al. 2006).

## 11.2 Hydrogenases as Archaic Catalysts

Several experimental field studies show that hydrogen is a main energy source, particularly in hydrothermal microbial communities (Chapelle et al. 2002). In this respect, methanogens with a hydrogen/carbon dioxide metabolism, and those taxa using a hydrogen/sulphite metabolism are especially interesting. Molecular data suggest that both kinds of metabolism, common on the seafloor around hydrothermal vents, occurred on the early Earth.

The significance of hydrogen relates to the dominance of water in the cytosol, in which hydrogen bonding stabilises macromolecules, many microbial enzymes affect proton transfer, whereas within the proton gradients ATP is generated. Moreover,

$H^-$  serves as a two-electron transfer currency in the cell (Wackett et al. 2004). The assumption that hydrogen is indeed the oldest, universal fuel for life, points to the hydrogenases as ancient catalysts, equilibrating  $H^+$  and  $H_2$ . These enzymes therefore catalyse the reversible oxidation of molecular hydrogen (Vignais et al. 2001).

The diversity and taxonomic distribution of hydrogenases can be interpreted historically:

- Most hydrogenases are found both in the Eubacteria and in the Archaea, and very few are known from eukaryotes, thus reflecting the antiquity of the hydrogen metabolism;
- The great majority of hydrogenases are metallo-enzymes, indicative of the initial role of metals in the origin of biological catalysis. Metal-free hydrogenases, as found in some methanogenic Archaea (Buurman et al. 2000), need to be studied both in terms of their structure and molecular sequence;
- Iron and nickel form the core of the active site of the majority of hydrogenases. As shown, iron and nickel also dominate in metal meteorites, suggesting that these metals were the most available catalysts, probably initiating biogenesis. Thus, these iron–nickel hydrogenases reflect the most archaic kind of metabolism.
- The functional classification and genomic data on more than a hundred hydrogenases show a consistent picture of the [NiFe] and [Fe]-hydrogenases as phylogenetically distinct groups of proteins, which can be interpreted in terms of the changing abundance of nickel and iron in geological history.
- The fact that [NiFe]-hydrogenases only occur in Archaea, and Bacteria and [Fe]-hydrogenases in Bacteria and Eukaryotes, suggests their antiquity, and that [NiFe]-hydrogenases were primary.
- The metal sites of hydrogenases can be classified into three groups: (1) iron–sulphur clusters [2Fe–2S], [3Fe–4S] and [4Fe–4S] that shuttle electrons between the  $H_2$ -activating site and the redox partners of hydrogenases, (2) [NiFe] and [Fe] sites activating hydrogen, and (3) nickel–iron–selenium (NiFeSe) hydrogenases. Genome sequencing shows that there is a relationship between NiFe and NiFeSe hydrogenases. This is also supported by the fact that the cysteine in NiFe enzymes is homologous to a seleno-cysteine residue in NiFeSe hydrogenases.
- The association of selenium with NiFe clusters rather than with FeFe clusters in active sites of hydrogenases suggests a common evolutionary root of selenium and nickel at an early, reducing biogenetic stage.

### 11.3 The Reduction of Non-Metals

Transition metals can both donate and accept electrons easily. Therefore, after donating an electron to facilitate another reaction, their atomic constitution is easily restored. Similarly, although selenium is a non-metal, it donates and accepts electrons easily; due to its position in Period 4, it has a metallic character. This ease

of electron exchange is also expressed by its photoelectric properties. Hydrogen, on its part, combines the ionic bonding of metals with the covalence of the non-metals. This allows it to accept electrons from a transition metal and then to bind temporarily to selenium in a covalent bond, which stores the energy carried by the electron. Selenium accepts this electron from hydrogen because selenium has a slightly larger electronegativity, 2.4 relative to 2.1. Because these differences are slight, hydrogenation may have alternated with dehydrogenation, the latter with the release of energy into the environment. Under these conditions, the reduction and oxidation of selenium, although relatively easy due to its metallic character, may thus have been catalysed by transition metals, such as nickel and iron in the mineral crust enveloping a tiny cavity.

After selenium was reduced into hydrogen selenide,  $\text{H}_2\text{Se}$ , sulphur into hydrogen sulphide,  $\text{H}_2\text{S}$ , and subsequently oxygen into hydrogen oxide or water,  $\text{H}_2\text{O}$ , carbon and nitrogen followed. The reduction of carbon and nitrogen—in the latter case known as dehydrolysis—resulted in their condensation into macromolecules of the present day, the thioesters, nucleotides, lipids, proteins, and carbohydrates. Modules of covalently binding, non-metal elements combined with each other in an endless variety of ways, leaving the transition metals, that were so prominent in early life, a quantitatively secondary place.

Initially, the condensation and hydrolysis of phosphates, or of compounds of carbon, nitrogen and oxygen, may have required too much energy. The hydrogenation–dehydrogenation redox reactions between hydrogen or transition metals in the middle and non-metals at the right of the table, respectively, may have preceded acid–base, condensation–hydrolysis reactions. Hydrogenation–dehydrogenation possibly preceded condensation–dehydrolysis, because it happened more easily. These two reaction types use different metals as catalysts, the first, for example, transition metals as iron, which is able to change its valence, and the second, metals as magnesium, calcium or zinc that are not able to change (Williams and Fraústo da Silva 2006). From the initial stages onwards, iron could have operated as an electron buffer,  $\text{Fe}^{3+}$  accepting an electron using the energy from UV radiation, and  $\text{Fe}^{2+}$  releasing it again.

The stronger electronegative sulphur (2.5 compared to selenium, 2.4) may have taken over, again forming bonds with transition metals, possibly more with vanadium and tungsten, and also with hydrogen. Thus, a new biochemical system could have been initiated, de Duve's (1991, 2005) thioester world. At this point, the phosphates may have begun their career as electron carriers, which initiated the RNA world during which lipids could have originated (Janas et al. 2006) and be inserted into the mineral crust. Only after this phase, and particularly with the origin of photolytic hydrolysis in photosystem II, which liberates a large amount of energy by splitting water instead of hydrogen sulphide, could the strongest covalent bonders, carbon, nitrogen, and oxygen, have been incorporated as carbohydrates and proteins into the early biochemistries.

These very strongly electron pulling, oxidising elements, carbon with an electronegativity of 2.5, nitrogen (3.0) and oxygen (3.5), followed suit as the energy flow thus became stronger, the metabolic system more intricate, and the environment even more oxidised. This may have happened particularly after

photolytic hydrolysis became feasible, which not only supplied the system with a large amount of energy, but which also made the environment even more strongly oxidising than it had already become before. Because of their strong electronegativity, this third type of biochemistry was highly energetic, soon being able to store large quantities of energy, in phosphates and proteins, and then mainly in carbohydrates. Yet, the first organisms to put photosystems I and II in series, the cyanobacteria, apparently lack an adequate storing apparatus, as they still expel large amounts of unused oligosugars into the environment. Oxygen, though, never formed an active part of the cell metabolism; the cytosol has always remained anaerobic. Under still more oxidising conditions, the even stronger oxidising, more electronegative halogens began to take part. Iodine (2.5) in the lowest, fourth period came first, and finally fluorine (4.0) in the second period of the table. However, they are all active in extracellular communication only; they are not active metabolically. The same evolutionary trend can be seen in the strongly reducing metals at the left of the periodic table with, first, the group 2 and then group 1, which all occur extracellularly, having mechanical (for example, calcium in shells and skeletons on proteins such as collagen, or communication functions as sodium and potassium in the nervous system. Concentrations of potassium ions in the cell are 20 times as high as outside it; they dominate over those of sodium, magnesium and calcium (Williams and Fraústo da Silva 1996). Intracellularly, calcium stabilises proteins such as calmodulin by binding as a positive calcium ion to carbonyl and carboxylate centres (Fraústo da Silva and Williams 1991).

#### 11.4 Origin of Enzymes

The concept of an enzyme such as a ribozyme, an RNA, or a protein, catalysing a biochemical reaction, does not reflect the fact that the apozymatic part of a protein does not take an active part in the reaction. The extraction of the metal ions from the prosthetic group they are part of, results in a reduction of its catalytic function, if not its complete loss. On the other hand, an *in vitro* insertion of the metal ion makes the prosthetic group regain its catalytic function. This suggests that the apozymatic part of a protein is a secondary acquisition, and the metal in the prosthetic part is primary. The role of the proteinaceous part is directing, fine tuning, and facilitating the operation of the metal ion in its interaction with the substrate. This regulation of the catalytic working by shielding off the ion with a protein screen, by optimising its distance relative to the substrate, or by both, are the main functions of the protein. There may also be some chemical protection of an active catalytic centre within a protein.

Biochemical catalysis probably originated with metal ions, in combination with, initially, selenium or sulphur as electron acceptors, and later with phosphorus, carbon, nitrogen and, finally with oxygen; the proteinaceous part may have been included as a third component. The sequence of evolutionary development could have been: metals first, the prosthetic group second, and the proteinaceous part third.

## 12 The Periodic Table

### 12.1 Trends

In the periodic table, the elements roughly decrease in size to the right because of the greater number of positively charged protons in their nucleus, and become larger towards the bottom, in each period one more electron shell being added. This implies that the electronegativity—electron pulling power, or oxidising power—increases towards the right and decreases towards the bottom of the table. Therefore, the electron donating or reducing, metallic elements are at the left-hand side and in the lower periods of the table; the electron accepting, non-metallic and halogenic elements being in the upper part on the right. Elements at the extremes of these trends, as well as the transition metals with an equally balanced pulling power, therefore have ionic bonding, that is an exchange of electrons. Those that are more equal in power, particularly the non-metals, share them in covalent bonds.

Towards the left along each period (row) in the periodic table of elements, elements become increasingly more metallic, and increasingly less metallic and eventually non-metallic to the right. Elements between the non-metals and the noble gases at the extreme right are salt forming or halogenic. Also, going down each group (column) elements become increasingly more metallic and, consequently, less metallic or increasingly non-metallic going up a group. The metallic, electron-donating elements are therefore found towards the left and bottom of the table and the non-metallic electron acceptors towards the top right. In other words, the non-metals and halogens as strongest acceptors at the top right-hand corner have the strongest electronegativity in the highest periods of these groups; they form the inverse triangle immediately to the right of the metalloids in the table. Conversely, the weakest electronegativities are found in elements towards the lower periods at the far left. Moreover, the non-metals bind covalently, sharing electrons, which, among other things, means that they can store energy better than elements that have ionic bonding, exchanging electrons. Combining these two trends in the non-metallic elements, those in the highest periods, carbon, nitrogen and oxygen, with electronegativities of 2.5, 3.0, and 3.5, respectively, are the strongest and least reactive of the covalently bonding elements; they pull electrons the hardest and retain them the longest. Selenium with an electronegativity of 2.4 is the weakest covalent element, with sulphur (2.5) falling in between (Fig. 1). Following the general trends, phosphorus (2.1) has a lower value, being found to the left of sulphur. Selenium in particular, and phosphorus to a lesser extent, is known for its photoelectric properties, which indicates that, of the non-metals, it can exchange electrons most easily, and does so under the influence of light. In this, it is comparable to  $\text{Fe}^{3+}$ , although it is restored by UV radiation, forming  $\text{Fe}^{2+}$ .

In covalent bonds, electron sharing makes them strong, as the nuclei reach a noble gas complement. These stronger bonds, found at the top right of the table, are, because of their great strength, the shortest and most stable, making these elements the least reactive; they have the lowest exchange rates. As a consequence, the time

												H		He			
												<b>2.1</b>					
Li	Be											B	C	N	O	F	Ne
<b>1.0</b>	<b>1.5</b>											<b>2.0</b>	<b>2.5</b>	<b>3.0</b>	<b>3.5</b>	<b>4.0</b>	
Na	Mg											Al	Si	P	S	Cl	Ar
<b>0.9</b>	<b>1.2</b>											<b>1.5</b>	<b>1.8</b>	<b>2.1</b>	<b>2.5</b>	<b>3.0</b>	
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
<b>0.8</b>	<b>1.0</b>	<b>1.3</b>	<b>1.5</b>	<b>1.6</b>	<b>1.6</b>	<b>1.5</b>	<b>1.8</b>	<b>1.9</b>	<b>1.9</b>	<b>1.9</b>	<b>1.6</b>	<b>1.6</b>	<b>1.8</b>	<b>2.0</b>	<b>2.4</b>	<b>2.8</b>	
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
<b>0.8</b>	<b>1.0</b>	<b>1.2</b>	<b>1.4</b>	<b>1.6</b>	<b>1.8</b>	<b>1.9</b>	<b>2.2</b>	<b>2.2</b>	<b>2.2</b>	<b>1.9</b>	<b>1.7</b>	<b>1.7</b>	<b>1.8</b>	<b>1.9</b>	<b>2.1</b>	<b>2.5</b>	
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
<b>0.7</b>	<b>0.9</b>	<b>1.1</b>	<b>1.3</b>	<b>1.5</b>	<b>1.7</b>	<b>1.9</b>	<b>2.2</b>	<b>2.2</b>	<b>2.2</b>	<b>2.4</b>	<b>1.9</b>	<b>1.8</b>	<b>1.9</b>	<b>1.9</b>	<b>2.0</b>	<b>2.2</b>	

**Fig. 1** Electronegativities of the elements of the first 6 periods

the energy is stored in a bond, the retention time, will also be the longest in bonds of these elements, the opposite holding towards the left-hand side and the bottom of the table. In most or all covalent bonds, energy is kinetically stored, meaning that the molecules have a resistance to react, even when oxygen is present. Therefore, there is a barrier preventing them from reacting, which can only be overcome by a catalyst or an enzyme. Biologically, the energy stored in these bonds allows life to occur. Stability of bonds and the storage of energy in them are compulsory for the maintenance of stable reaction systems. The kinetic stability of covalent bonds is pivotal. Conditional to their dynamics is nevertheless that the formation and break up of covalent bonds is cheap in terms of energy, a condition that is met by the way coenzymes and enzymes operate (see above). Typically, the transition metals and metals involved in energy generation, catalysis and communication are, in contrast, ionic bonders and therefore thermodynamically, rather than kinetically stable.

According to the Second Law of thermodynamics, the energy exchange involved in a reaction, often being accompanied by proton and electron exchange, concerns a degradation of energy. This means that during a reaction chain, a few, high-energy quanta are degrading into many low-energy ones. And reducing conditions that express a relatively great abundance of available protons and electrons, are gradually being replaced by oxidising ones that express a shortage because the protons and electrons are bound. The consequence for biological systems is that, over time, they find themselves more and more in energetically impoverished conditions, which causes them to stop operating. The only possibility is that they develop stronger pulling power mechanisms for their energy supply. In fact, biological systems developed two types of adaptations. In terms of the position that biologically selected elements take in the periodic table, they shifted gradually towards the higher periods at the right hand side of the stronger oxidisers. Also, more reducing elements became involved in the reactions. Moreover, the energy source shifted from relatively poor and exhaustible chemical ones in the environment to the rich, inexhaustible source of light. Its material basis, formed by electrons and protons, is unlimited as well because of the ubiquity of water on Earth. The whole historical process of the

early chemical evolution of life seen as a response to changes in energy supply is typically a bootstrapping process, whereby a simple, energetically weak system developed into a complex, strong one.

As to the metals, transition metals came to the fore because they can easily accept and donate electrons, thereby adopting different valences. As mentioned, under the influence of UV radiation,  $\text{Fe}^{3+}$  accepts an electron which results in  $\text{Fe}^{2+}$ . The energy of which is released when it again forms  $\text{Fe}^{3+}$  plus one electron. This electron can be fed into the iron cycle (see de Duve (1991) for its biological relevance). Similarly, it can be imagined that the electron exchange in selenium under the influence of light may have facilitated early reactions with, possibly, hydrogen.

This means that, with regard to biogenesis, we have to look at possible reactions between metals in the centre of the table with some of the non-metals at the right, remembering that hydrogen occupies an intermediate position (electronegativity 2.1) as both an electron donor and electron acceptor (e.g. Williams and Fraústo da Silva 2006). Moreover, this element is capable of bonding both ionically, and covalently. Initially, therefore, the covalent bonding between non-metals with, for example hydrogen, made use of transition metals as catalysts (hydrogenases) for splitting hydrogen into  $2\text{H}^+$  and  $2\text{e}^-$ . Later in evolution, specialised, stronger enzymes came into play. In general, we expect that, as the energy flow through the system went more smoothly and intensified evolutionarily, elements of the fourth and, then third period were probably involved in the more ancient reactions, those in the second period entering last.

These trends thus constitute the chemical expression of the bootstrapping of the physical energy flow. Physical bootstrapping would have gone from an initially weak energy flow to stronger and a stronger one. The latter required systems of energy capture in the membranes, such as photosynthesis, in concert with more and more efficient catalysts, first transition metals, then phosphates in coenzymes and RNAs, and finally, nitrogen in proteins. This also means that storing energy in covalent bonds, and its subsequent functional release from them, became increasingly more important. At present, together with hydrogen and the non-metals carbon, nitrogen, oxygen dominate, and, to a lesser extent, phosphorus and sulphur, the so-called CHONSP elements. These elements are known as macroelements because they make up more than 99% of the biomass. A comparison of their abundances in the Earth's crust with the chemical composition of all living matter shows their chemical segregation related to the origin of life, and the evolution of their involvement in biological systems. These elements are now considered characteristic for living structures, possibly as even having been involved in biogenesis. Furthermore, due to the input of solar energy at later evolutionary stages, broad biospheric nutrient cycles predominate, whereas the initial phases of life only resulted in the exhaustion of the chemical resources of protons and electrons. This exhaustion of reducing elements in the environment resulted in a shift in chemical elements active in the metabolism of living systems. Due to the biospheric nutrient cycling, subsequent metabolisms have remained stable since the rise of oxygen in the biosphere.

## 12.2 Covalence: Chemical Markov Chains

The overall, underlying process of this evolutionary trend may be partly environmental and partly stochastic, as it is based on a temporal Markov chain. This kind of process is defined by stochastic differences in retention time of the units concerned, in this case, the energy stored in bonds of increasing kinetic stability and decreasing reactivity (Hengeveld 2007). However, basic to this system is that one or more enzymes are present which allow the formation of stable molecules, and their subsequent break down for the release of the energy they contain. The shift in retention time and storage capacity thus required a more and more energy-demanding set of interrelated reactions, which led to a shift in importance from non-metal elements with the weakest covalent bonds to those with the strongest. Thus, it may have begun with the metal-assisted hydrogenation of the non-metal selenium, and ended with the complete set of covalently binding CHONSP elements that dominate our present biochemical systems. In this sense, the individual molecules reach an equilibrium state, despite the fact that the system as a whole is in a state that is far-from-equilibrium. This distinction between the two states evolved as a basic property of the biochemistry of biological systems (Williams and Fraústo da Silva 2006).

Gradually, a system of reactions could thus have evolved by the insertion of more and more transition steps, eventually reaching a stable state, in which the energy is retained for some time. Stable molecules could then have released their stored energy for further utilisation on the longer term. Step-by-step, covalent bonds, being more stable, and therefore storing the energy longer than ionic ones, will have gradually begun to dominate the system, assisted by a more and more complex set of reaction chains and cycles, each step being catalysed by a specific enzyme. The whole system is kept in a state of homeostatic balance through a regulated production or destruction by enzymes. Depending on their function, these enzymes have a specific turnover rate as well. Thus, a system of reactions with higher reaction rates—reaction chains and cycles—separated out from those with low rates. When we define, with von Bertalanffy (1968), processes with high rates as functional relative to processes with low rates, we can imagine how a functioning biochemical system can have crystallised out.

## 12.3 Catenation

Apart from their covalent bonding, one of the properties of several non-metals is their ability to form chains or rings with the same or other elements. This property is known as catenation, and is most pronounced in carbon, and to a lesser extent, in sulphur. Other elements with this property are silicon, germanium and tin in the same group (14) as carbon. It also occurs to some extent in nitrogen and phosphorus in group 15, and in oxygen (although only in ozone), sulphur and selenium in group 16. Thus, this property diminishes in strength from carbon to the top right, as well as to the periods downwards in the table.

For example, chain length is unlimited in carbon, is 14 atoms long in silicon, 9 in germanium, and 2–3 in tin. Similarly, sulphur can also form rather long chains, up to 16 atoms, but selenium only up to 10. Moreover, double bonding occurs in carbon, nitrogen and oxygen, and triple bonding only in carbon and nitrogen. Carbon, moreover, not only makes one-dimensional chains, but also two-dimensional rings, networks or lattices (graphite), and three-dimensional bodies (diamond, fullerenes and nanotubes). Networks can also be found in silicon compounds, such as quartz,  $\text{SiO}_2$ . Apart from homocyclic and heterocyclic rings in carbon, ring structures are found in sulphur and selenium. The binding energy between atoms of the same element is strongest in hydrogen (H–H: 435), decreasing from 345 in C–C, 209 in N–N, down to 146 in O–O; between carbon and one of these elements, the bond is stronger, decreasing from hydrogen to oxygen: 426 in C–H, 293 in C–N, and 293 in C–O. Double and triple bonds, however, show the opposite trend of increasing strength, and this at a higher energy level: 610 in C=C, 627 in C=N, and 732 in C=O, while triple bonds are even stronger, 836 in  $\text{C}\equiv\text{C}$  and 900 in  $\text{C}\equiv\text{N}$ . The binding energy between carbon and sulphur (272) is, as expected for an element more to the right and one period down, weaker than that with oxygen, one period higher (293).

When double or triple bonds alternate with single ones, the electrons from the first two kinds of bonds can spread over the single bonds as well. Such delocalised electrons occur especially in carbon and nitrogen, and to a lesser extent in phosphorus and sulphur. They can be found diffused along the backbone of many phosphates, lipids, carbohydrates and proteins, as well as in ring structures, especially in heterocycles found in the purines and pyrimidines of the nucleotides. Electronic delocalisation strengthens the backbone and rings, because resonance energy is added to the single bonds. Pullman (1972) suggested that they occur especially in the more ancient compounds of these elements, such as nucleotides and lipids, since delocalised electrons stabilise particularly in conditions with much UV radiation, that is during the early stages of the history of life.

All this shows a substantial versatility of the CHONSP elements in forming compounds and in their energy-storing capacity, the versatility being greatest in carbon, although also present in neighbouring elements within the periodic table. Apart from this, the reactivity decreases to the right of carbon in the direction of the halogens fluorine, chlorine, bromine, and iodine, and downward in this group. Their binding energies are 451, 349, 293, and 234, respectively, with the lowest reactivity at the top. This suggests that the bootstrapping process could have started with the relatively reactive selenium in period 4, possibly developing via sulphur and phosphorus in period 3 to carbon, nitrogen and oxygen in period 2. Each step formed some kind of biochemistry constituting various, successive living structures. As the elements are bonding covalently, their compounds are kinetically stable, meaning that it costs energy to make and to break a bond. With increasing binding energies, not only the reactivity diminishes, but an ever stronger flow of energy has to be generated and an ever stronger catalytic apparatus has to evolve. Moreover, the elements with the strongest electronegativity are found outside the cytosol, and do not take part in the metabolism. They may have become available only after the basis of the metabolism had been laid, which not only applies to the halogens but

also to oxygen. Furthermore, oxygen, when it occurs as a radical in the cytosol, easily disrupts the processes. Oxygen radicals have to be neutralised by special organelles, such as hydrogenosomes, or by chemical compounds like ascorbic acid. From this perspective, mitochondria and heterotrophic organisms such as animals, can be considered neutralisers, while plants neutralise oxygen internally in this way.

In fact, the H–C–H groups in the hydrocarbons and the H–C–OH groups in carbohydrates are extremely stable and can only be broken enzymatically. The enzymes concerned are exceedingly complex, and constitute series of successive steps of formation and breakdown in metabolic pathways and cycles. The complexity in structure and operation indicates the relatively recent origin of the metabolism based on carbon. Aldolase, for example, one of the enzymes active in the glycolytic breakdown of oligosugars into glucose, a H–C–OH chain, consists of four subunits, and has a molecular weight of 156,000 u. The binding of pyruvate to the nucleotide coenzyme acetyl-CoA happens with the even more complex molecule pyruvate dehydrogenase, which consists of 60 subunits with a molecular weight of ca. 10 million u. Clearly, these carbohydrates, together with their enzymes, could impossibly have formed the early beginning of life; they are occasionally presumed to be prebiotic. In contrast, ribonuclease, an enzyme hydrolysing the supposedly earlier nucleic acids, consists of one single polypeptide chain and has a molecular weight of only 13,700 u, thus fitting our bootstrapping hypothesis for belonging to an early stage.

On the other hand, oligophosphates transfer energy by means of group transfer; individual phosphates are not dismantled into the individual constituent elements but remain as phosphate modules. The same happens to amino acids, being transferred as modules and reutilised as such in new polypeptides. The stronger covalent bonds therefore need not always be broken down. Similarly, the backbone of carbohydrates is often the non-reactive part of the molecule, the active groups being –OH, –COOH, –CH<sub>3</sub>, and so on. Significantly, these active groups are usually found at the ends of the chain or of side branches. Other points of attack are double or triple bonds. Thus, life became modular, as a result of the catenation of molecules held together by covalent bonds in their chain, the modules usually combining by condensation.

### 13 Shifts in the Selection of Elements, and in their Biological Functions

Trends in the periodic table of elements express differences in exchange rates, and therefore in the stability of the compounds they form; this could be of biogenetic relevance. Of the non-metals, for example, selenium in period 4 has higher exchange rates than sulphur in period 3, and sulphur again higher ones than oxygen in period 2. The same holds for phosphorus in period 3 relative to nitrogen in period 2. Differences in stability mean that energy in covalent bonds is retained or stored longer in the less reactive, smaller non-metals of the higher periods than in larger ones, such as selenium. As the system became more complex and its efficiency greater, the smaller non-metal elements in the upper periods became more involved in energy metabolism, whereas the larger ones that started up the process, were

replaced by smaller ones. Moreover, as the environment became more oxidising, stronger electronegative elements in those upper periods may have become compulsory to keep the system dynamics going.

Fitting best into the energy flow or energetics of the evolving system, this shift in the selection of elements forms the heart of the bootstrapping process that constitutes biogenesis. Biogenesis, as we conceive it, was therefore not a momentary event, but one that covered a relatively long time. It comprised the very first reactions up to those unambiguously recognised as constituting a primitive living system. It concerns a hazy period which, as any historical transition period, will be defined differently by various students. However, it is the process within that is of concern, not its delimitation.

### 13.1 Groups at the Left and at the Right

Of all the metals of groups 1 and 2, none has taken an active role in the early reaction mechanisms; in spite of being the most reactive, their ionic bonds are too unstable for storing energy (Fig. 1). This is different in the transition metals iron, cobalt and nickel in groups 8, 9 and 10, respectively, as the earliest metals that may have been involved in biogenesis. Vanadium in group 5 and, first tungsten and then molybdenum in group 6, probably came in under slightly more oxidising conditions. Copper and zinc from groups 11 and 12, respectively, entered the picture only towards the end of the Precambrian; the environment had become strongly oxidising, nickel and cobalt practically unavailable, and iron had largely precipitated out. The same happened in the non-metals where, presumably, first selenium and then sulphur (Anbar and Knoll 2002) precipitated out, being replaced by oxygen. Possibly, phosphorus lost its pivotal catalytic and energy storing role in the coenzymes and enzymatic RNAs, leaving their role as catalysts to nitrogen in proteins, and to carbon in energy-storing macromolecules. It may be significant that the enzymatically active, prosthetic part of proteins, presumably evolved later, are composed of RNA. Yet, both the initial metals and non-metals are still found scattered in hydrogenases, enzymes and coenzymes, and as remnants of a possibly selenium-based biochemistry, of an ancient RNA world (e.g. White 1976, 1982), or a Thioester World (de Duve 1991, 2005). Interestingly, selenium, possibly because of its position in the periodic table between metals and non-metals, both donating and accepting electrons, shifted from a reductive synthetic function in anaerobes to an oxidative, protective one in aerobes (Williams and Fraústo da Silva 2006). In fact, selenoproteins are ideal catalysts for many biological redox transformations.

Contrary to the metals of groups 1 and 2, the transition metals are characterised by variable oxidation states, implying that they can easily donate, as well as accept electrons. They are, therefore, easily restored after having donated their electrons. The transition metals, particularly nickel and iron, as hydrogenases (Cammack et al. 2001) still form the active part, the co-factor, of modern metalloproteins, catalysing reactions by donating electrons. These electrons can either be used directly in redox reactions, or they play a role in nucleophilic attacks, by protons in acid–base reactions by charging molecules. As the latter mechanism is more complex and

usually requires larger molecules with stronger bonds, it may have originated after one that was based on oxidation–reduction.

The non-metals at the right of the table, immediately to the left of the halogens, form a small, yet more intricate group because of their great difference in accepting or donating electrons. The core of this group is formed by the biologically important sulphur, phosphorus, oxygen, nitrogen, and carbon, carbon connecting in the table with hydrogen when this is given a position at its centre. These CHONSP elements form covalent bonds and their compounds are kinetically, rather than thermodynamically stable. Hence the use of these elements in complex biological systems that depend on the stability of their compounds, and the importance of enzymes to overcome the barrier making and decomposing them.

Immediately on their right and directly to the right of oxygen are the halogens, electron acceptors with a very strong electronegativity, varying between 2.5 for iodine in period 5 and 4.0 for fluorine in period 2 (Fig. 1). To the left of the biological core elements are those, such as phosphorus, silicon, and barium, with a smaller electronegativity (2.1, 1.8, and 2.0, respectively), too small in fact to reduce carbon (2.5) in order to form compounds based, for example, on C–P bonds. This makes them also unsuitable for those redox reactions that involve the transfer of electrons, but better for acid–base reactions, involving the transfer and covalent bonding of protons. Phosphorus can donate electrons to oxygen (3.5) to form strong covalent bonds in phosphates, thereby charging oxygen negatively. This charge makes phosphate suitable for acid–base reactions; it can also store energy; both properties come out favourably in ATP, the energy carrier by group transfer central to all condensation reactions in the cell. In contrast, as long as the environment was reducing, none of the halogens could form bonds with the central non-metals, not even iodine with the smallest electronegativity of them all.

This leaves the core elements of the non-metals as the most suitable for both redox and acid–base reactions with the transition metals vanadium (1.6), tungsten (1.7), molybdenum (1.8), manganese (1.5), iron (1.8), cobalt (1.9), and nickel (1.9) with  $H^+$ , respectively, although cobalt was too rare to take an active part in the reactions. Selenium can exchange electrons easily and as  $H_2Se$  taking part as a very early or even as the earliest non-metal in these reactions. It could possibly have been replaced by, respectively, sulphur and oxygen in the same group, and could form bonds such as C–SeH, similar to C–SH or C–OH, or initially have even taken the place of carbon.

From this broad perspective of a shift from a highly reducing environment surrounding a compartment to a less and less reducing, more oxidising environment in which cells with oxidising processes lived, we can attempt to reconstruct the bootstrapping evolution of life. At first, redox reactions dominated, in which protons and electrons that had been produced interstitially in an iron–nickel crust, came into the cavity where selenium hydride could then have been formed. The redox reactions thus generating energy in the crust could have been supplemented by, first, hydrogenating–dehydrogenating processes in the cavity and later by hydrolysis–condensation. The latter processes were catalysed by non-metal components, and based first on phosphorus and later, nitrogen. When the redox balance tipped, hydrogen may have begun to leak out of the cavity, which could have been

counteracted by the insertion of lipids into the crust. Thus, as in present-day systems, phospholipids may have been formed initially by thioesters and phosphates, and would thus date from an early evolutionary stage, although not the earliest. The lack of oxygen in these macromolecules and the abundance of double bonds making them resistant to UV radiation (Pullman 1972) point to their early origin. Special pumping mechanisms for material interchange will have become necessary because bilayers of phospholipids close off any such interchange; such mechanisms, though, could not have originated right at the beginning of life. With further exhaustion of protons and electrons in the environment, even stronger electronegative, less reactive elements came into play, first carbon, then nitrogen and, finally, oxygen.

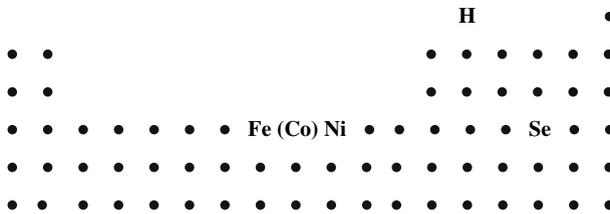
The very electropositive metals of groups 1 and 2 at the far left are not actively taking part in the cell metabolism, and are mostly found extracellularly, as are the very electronegative halogens at the far right of the table. Significantly, even at present, the cell metabolism is still anaerobic, implying that oxygen, being poisonous to the modern biochemistry, was absent during the first stages of biogenetic evolution (Williams and Fraústo da Silva 2006). The primarily extracellular activity of the transition metal copper, metals like sodium, potassium, and calcium, the metalloids and the halogens similarly suggests that they were added relatively late to the chemistry of the environment and the living systems.

### 13.2 Periods at the Top and at the Bottom

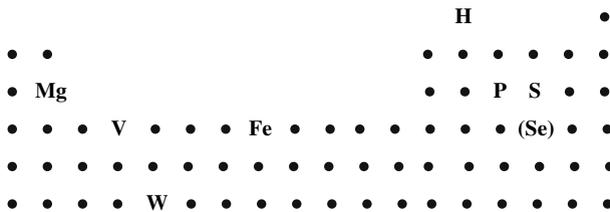
Elements in the upper periods of the periodic table are the least reactive, those in the periods towards the bottom increasing in reactivity; reaction rates of the metallic elements increase towards the left of the table and towards the bottom. Also, these elements are the most reducing, and become acidic. Consequently, the more to the top of the non-metals, that is towards its modern biological core elements carbon, nitrogen, and oxygen in period 2, the stronger the covalence of their bonds; these elements are oxidising. Their bonds are also the strongest; as mentioned, they resemble those of the noble gas in their period: forming or breaking them requires the largest amount of energy, and therefore needs the help of enzymes. Exchange rates within groups are generally higher for the heavier, larger atoms than for the lighter, smaller ones, for example,  $\text{Se} > \text{S}$  (Williams and Fraústo da Silva 2006). This implies that at the initial stages of biogenesis, carbon, nitrogen and oxygen would have been least likely to take part in the formation of living structures, and to a lesser extent sulphur and phosphorus as well: if compounds were formed at all, they would have been deadly sinks for the little energy captured at that stage.

### 13.3 Shifts in the Selection of Elements

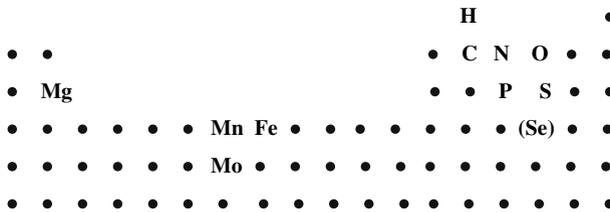
Figure 2 shows the few initial elements that were possibly involved in biogenesis, according to information in Fraústo da Silva and Williams (2001) and Williams and Fraústo da Silva (2006).



**Fig. 2** Elements of the first 6 periods possibly involved in the first stage of biogenesis



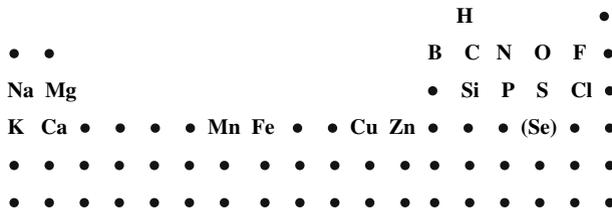
**Fig. 3** Elements of the first six periods possibly involved in the second stage of biogenesis



**Fig. 4** Elements of the first six periods possibly involved in the third stage of biogenesis

Under slightly more oxidising, although still reducing conditions, nickel and cobalt were replaced by vanadium and tungsten, and selenium by sulphur (Fig. 3). Phosphorus too, may also have come in by then, although possibly following sulphur. These two metals superimposed group transfer on the still operating electron and proton transfer in the initial redox reactions of Fig. 2. Phosphorus also introduced Lewis acid reactions and thereby cycles based on condensation–hydrolysis, for example, in the formation and degradation of thioesters. As phosphates came in, magnesium may also have been added, its cation  $\text{Mg}^{2+}$  stabilising the negatively charged oligophosphates.

As conditions grew even more oxidising, manganese and molybdenum were added as redox catalysts, in addition to iron, which has remained prominent as a redox catalyst right from the beginning up to the present time. At this stage, the three smallest non-metal elements, carbon, nitrogen and oxygen, entered the early biochemistry (Fig. 4).



**Fig. 5** Elements of the first six periods possibly involved in the stage of biogenesis before and after the Cambrian

With the advent of photosynthesis, more energy could be processed and stored, first based on the splitting of  $H_2S$ , and then on that of  $H_2O$  in combination with  $H_2S$ . With the release of the highly electronegative, free oxygen into the environment, the tendency towards more oxidising conditions now increased substantially. Because the O-O bond is weaker than the bond of oxygen with other elements, it became part of many biochemical reactions and compounds. At this point, sulphides were replaced by sulphates, and iron precipitated out to a large extent as iron oxide (Anbar and Knoll 2002), and along with it, phosphorus. Copper and manganese, being released from sulphides, became available to the biological systems as metal catalysts, followed by zinc and calcium (Fig. 5). After this, the halogens chlorine and fluorine and the metals sodium and potassium were added to this set of elements that were increasingly used by biological systems. The set was finally completed well after the Cambrian with *bromine* and silicon.

Overall, therefore, we see a broadening in the periodic table of the transition metals being used as catalysts from a narrow core formed by iron and nickel; it moved first to the left and then to the right, eventually including the metals at the far left. The non-metals, in turn, fanned out from selenium at the bottom in period 4, first to include the narrow triangle of six elements, which subsequently broadened to include the halogens at the right and, ultimately, the half-metals at the left. During this process, the redox reactions in the membrane, generating energy, were supplemented by energy-processing, Lewis acid–base reactions of condensation and hydrolysis in the cytosol. Throughout, hydrogen provided the oxidising internal environment with electrons and protons needed for all condensation–hydrolysis cycles. Hydrogen seems to have remained the pivotal element of all life processes right from beginning, driving the processes at the molecular level, as well as determining the overall trend from very reducing conditions in the beginning towards the oxidising ones of the present. Water, apart from being a dipole solvent, is thus essential to life, principally as it ensures a continual supply of hydrogen.

### 13.4 Shifts in Biological Functions

According to our hypothesis of biogenesis by bootstrapping evolution, the first reactions were between the non-metal selenium and protons in a  $FeNiSe_2$  complex, forming  $H_2Se$  and other selenium compounds. This complex is still found in ancient



formose reaction that forms aldehydes and sugars (Gánti 2003). The first aldehydes could have formed ribose and base rings, subsequently to be added to the oligophosphate strings resulting in the first nucleotides. Phosphorus also introduced a new metabolism based on hydrogen exchange, thus initiating condensation–hydrolysis cycles. For their part, the transition metals, vanadium and tungsten, joined iron as metal catalysts.

Figure 8 suggests that, about the time that the transition metals manganese and molybdenum were added as catalysts, carbon, nitrogen and oxygen completed the set of non-metals in the early metabolism. All three were strongly oxidising, stable and weakly reactive elements, with oxygen as main oxidiser. Carbon compounds specialised in the storage of energy, while nitrogen because of many hydroxyl groups on the outside of proteins specialised in non-metal catalysis based on Lewis bases. Oxygen, finally, specialised in accepting electrons during photolytic hydrolysis by photosynthesis, after which it is expelled as a waste product, dioxygen, into the atmosphere. The initial functions of phosphorus had proliferated into a variety of nucleotide coenzymes and RNAs. Eventually, one of the many forms of RNA began to stabilise the number of reactions happening. It thus became a metabolic reaction standard. Eventually, it developed into DNA, a transferable standard, in the reproductive transfer of the system.

Figure 9 shows the addition of halogens, and the metals sodium and potassium, to living systems; all these elements have a communication function. Calcium, boron and silicon developed an extracellular, mechanical reinforcement with carbohydrates, such as lignin and cellulose, and proteins. Calcium precipitated out extracellularly on collagen as calcium carbonate, CaCO<sub>3</sub>, and boron and silicon formed molecular lattices.

### 14 Biogenesis by Bootstrapping, An Hypothesis

Our systems-based, physical theory proposes an initial reducing, aqueous environment into which some fine trickle of alkaline water seeped from the basalt seafloor. This may have resulted in the precipitation of a mineral crust of FeNiSe<sub>2</sub>, containing interstitial hydrogen. Within the interstices, hydrogen molecules split into two protons and two electrons, which could have formed hydrides with elements in the

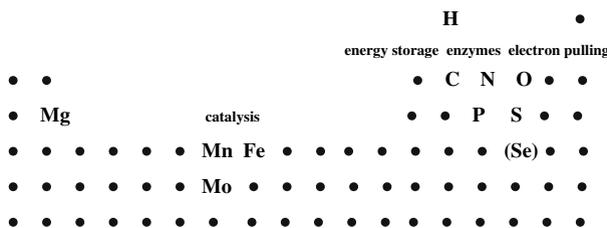
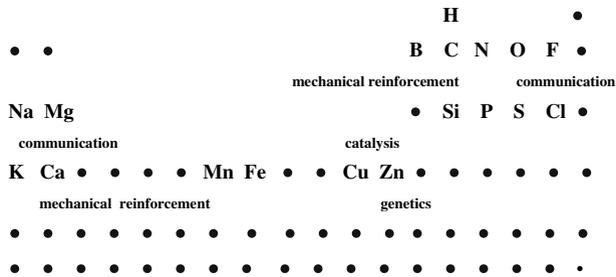


Fig. 8 Functional aspects of elements of the first six periods possibly involved in the third stage of biogenesis



**Fig. 9** Functional aspects of elements of the first six periods possibly involved in the stage of biogenesis before and after the Cambrian

crust itself and, with non-metals in the alkaline cavity. The transduction of these particles through the crust formed an initial, natural proton-motive force. Within the crust, redox reactions generated an electron-based energy flow, and within the cavity, Lewis acid–base reactions formed the initial covalent bonds between alkaline compounds and the protons. Hydrogenase and subsequent hydride formation thus form the two initial chemical processes of life; they have remained basic to it ever since, although partly being replaced by hydrogen exchange in hydrolysis–condensation reactions. All other processes are variations on this theme. These variations involve different elements and molecules as substrates that has resulted in increasingly complex living structures and life processes. This complexity easily obscures from its simple, unifying basis.

Here, we see the two sides of the processes of life, the physical one and the chemical one. The physical one is usually phrased in terms of a reducing flow of electrons by quantum degradation of energy. The chemical processes are phrased in terms of hydride formation or the reduction of other chemicals. At this initial stage, the covalent bonds are relatively weak; selenium may have already formed more complex structures by catenation and ring formation. Sulphur would soon have substituted selenium at many points in the metabolism, thus initiating de Duve's (e.g. 1991) Thioester World. The rates of change in the environment on which this partly depended are unknown and thus it is impossible to say when exactly this would have happened.

Much must have changed when external conditions changed: the initially reducing environment became oxidising, despite the absence of free oxygen at that time. This shift from reducing to oxidising conditions became the driving force of life's evolution. The redox potential was a universal selection criterion for elements operating in living systems. In the cavity, the initially oxidising conditions became more reducing relative to the environment. This could have tipped the balance, stopping the energy flow from outside to inside. These altered conditions led to two changes, (1) in the structure of the system, and (2) in the involvement of elements and in the composition of molecules.

(1) The structural response of the system may have been the reversal of the original, physical proton-motive force in the crust into the biological one in the membrane. Now, protons are pumped out of the system, subsequently to be allowed

in again as happened before. Mechanistically, this means that an artificially reducing environment is created immediately around the system after the initially, natural one became too oxidising. Thus, the proton-motive force, initially bringing protons from the environment into the cavity, acquired its present dual mechanism (e.g. de Duve 2005). We can imagine that part of this mechanism, lipids were inserted in the crust, preventing protons from leaking out freely; thioesters may have been involved in the formation of these lipids. The complex molecule of CoA, which at present is also involved in lipid formation, may have evolved at this stage, rather than at the initial one, as Martin and Russell (2003) surmised.

(2) A shift towards elements with a stronger electronegativity, and thus a greater pulling power for electrons, resulted in a change in elemental composition of the systems as a possible response to these changing environmental conditions. For example, sulphur largely came to substitute selenium in a less reducing environment probably because of its greater electronegativity. It pulled harder than selenium, so to speak, the less protons and electrons were available, and the harder the environment held them back. Similarly, iron may have taken the place of nickel completely. Also, sulphur having atoms smaller than those of selenium, is less reactive: once reduced, it is less likely to oxidise. The larger, more stable molecules could now attach to each other through condensation, acting as stable modules in longer chains than possible in selenium. Thus, thioacids may first have been formed, as Wächtershäuser (1988) envisages, after which de Duve's thioesters may have condensed. According to de Duve (1991, 2005), thiols would have allowed phosphates to be formed. In his Thioester World, phosphates are group carriers, instead of being electron carriers, in that way transferring electrons and protons. At this stage, oxygen could have been transmitted anaerobically by the new, more energy-demanding processes of hydrolysis and dehydrolysis, these processes becoming a part of the new sulphur-based biochemistry. Also, magnesium may have entered the picture, facilitating the hydrolysis and condensation of phosphates. The fact that the operation of RNA require high concentrations of magnesium suggests something about the pertaining environmental conditions at that time. Having stronger electronegativities, sulphur and phosphorus may, in fact, have supplemented (de)hydrogenation by (de)hydrolysis, the latter forming the basis of the new biochemistry. At some point, even stronger electronegative elements were added to the system, carbon in carbohydrates and nitrogen in proteins (de Duve 1991, 2005). The phosphates also shielded off hydrogenation processes by metals that could otherwise have been affected by electric disturbances in the cytosol. The phosphates themselves could have been supplemented by ribose and nucleosides, resulting, first in the formation of ATP and other nucleoside triphosphates or NTPs (White 1976, 1982). These may subsequently have evolved into the nucleotide coenzymes, such as NAD or NADP, and from these into various nucleotide coenzymes and RNAs, and eventually into DNA.

The final stage of this development would have been the independent, biological production of hydrogen from water that happens in photolytic hydrolysis by photosystem II. This process produces oxygen instead of sulphur as a waste product. Other organisms subsequently used oxygen in which the same membrane system operates in reverse, oxidative phosphorylation. Photosystems II and I operate in

series, system II being an evolutionarily improved duplicate of system I, which still splits the weaker H–S bond in H<sub>2</sub>S, while system II splits the strong H–O bond in H<sub>2</sub>O. In a way similar to the earlier replacement of selenium by sulphur from a higher period in the same group of the periodic table, the substitution of sulphur by the even more electronegative oxygen left the metabolic system intact. This is still expressed in the difference in the redox potentials of the two photosystems, the phylogenetically later system II operating at higher, positive potentials than the earlier system I. Thus, the replacement of chemical energy by solar energy even allowed the reduction of carbon dioxide, CO<sub>2</sub>. In this molecule carbon and oxygen have a very high binding energy, O–C: 1077, much higher than that of oxygen with other elements, O–H: 428; O–S: 521; O–P: 599; O–N: 631; O–Si: 810. By generating much energy, photosynthesis allowed alternating reduction and oxidation of carbon and oxygen, with the strongest and most stable bonds in CO<sub>2</sub> and H<sub>2</sub>O.

The shift in elements towards those with higher electronegativities required in the first place the development of an intricate enzymatic apparatus. Secondly, it required the availability of an unlimited energy supply captured by the complex photosynthetic apparatus in the membrane which operates with the help of metals and nitrogen. Thirdly, an energy storing and processing apparatus was needed in the cytosol; carbohydrates fulfilled this need. Finally, the system gets rid of oxygen by the process of respiration that occurs in the membrane. Probably, respiration as the reverse process of photosynthesis is derived from it and uses the oxygen released by photosynthesis. Oxygen has first to be produced before it could be used in respiration, a process that both detoxifies the environment and releases a great deal of energy. Photosynthesis and respiration evolved separately in two different taxa; only later, are they found together in plants.

The full cytosolic apparatus could have been put together by several, successive endosymbiotic events (Kooijman and Hengeveld 2003). When oxygen as a strong electronegative element was expelled from the system as a waste product into the environment, it reacted, first with sulphide and then with iron, both of which largely precipitated out from the environment (Anbar and Knoll 2002). In the Late Precambrian, when this environment became even more oxidising, phosphorus too became even less available (de Duve 2005). Thus, the increase of dioxygen greatly enhanced the existing trend towards a higher oxidation state of the environment.

The material basis of the evolutionary bootstrapping process towards elements in the higher periods in the periodic table was expressed by the shift to elements with a greater electronegativity, and to module formation. The origin and early evolution of life is a continual channelling of the entropic energy degradation, adapting to shifting redox conditions in the environment. The living system thereby maintains the far-from-equilibrium conditions that keep the energy flow going. These far-from-equilibrium conditions were biologically maintained by the proton-motive force in which, even under the extremely oxidising conditions of salt lakes is maintained, Na<sup>+</sup> with a low electronegativity of 0.9, in that case replacing H<sup>+</sup> with a much higher electronegativity, 2.1 (Alberts et al. 2002). Therefore, throughout the evolutionary process, the energetic side continued to be the quantum degradation of energy, and the chemical side the addition or interchange of protons and electrons. Possibly, this was the reason for the symbiosis of bacteria of different taxa that came

to constitute the eukaryotic cell (Martin and Muller 1998). The basis of life remained the reduction of ever more strongly oxidising elements. Only the matrix changed, the electronegativity of the component elements or molecules increasing step by step.

## 15 Discussion

This paper suggests how a physical approach rather than the chemical one currently followed can account for the first biogenetic phases of evolutionary development, thereby putting the energy flow through the system central. The free energy in the environment has been decreasing throughout geological history, whereas the power of living structures to extract and accumulate this energy has been increasing. The resulting entropic degradation and dissipation of energy, however, has become directed and structured. It began at some mineral crust of precipitate, flowing through some tiny cavity in this crust. It may have been the direction given to this flow, that gave rise to a build up of reaction chains within this cavity. Here, we adopted Russell and Hall's (1997) model of the formation of an  $(\text{FeNiS}_2)_n$  crust, although we developed it into one based on hydrogenase in an  $(\text{FeNiSe}_2)_n$  crust, together with the subsequent formation of selenium hydrides.

The formation of a cavity is pivotal to the physical approach to biogenesis. It introduces dynamic, systems-theoretical considerations into the discussion, rather than proposing a development of a static chemical equilibrium with the production of individual compounds. A dynamic structure is compulsory, in order to generate energy. It thus maintains itself, and this without an input of compounds from the environment. Adenine or ribose in ATP, for example, should not have been supplied by external sources, be they terrestrial or extra-terrestrial (e.g. Shapiro 1988, 1995), but they produced the chemical mechanism of the living structure itself; i.e. this structure must itself have had the means and mechanisms for producing adenine and ribose. Thus, as to their basic biochemical components, the new structures had to be self-producing, not consuming entities.

A systems approach dictates that the energy flux and chemical elements and compounds present in the cavity directed the system's chemistry, i.e. the evolution of the processes was internal. It would have been impossible for external forces, such as intense electrical discharges, such as lightning (e.g. Miller 1953; Miller and Orgel 1974), or shockwaves (see Hazen (2005) for a recent example), to have shaped the intricate chemical mechanisms of reaction chains and cycles. Instead, these reaction chains and cycles were formed by the organised entropic decay of matter within the system itself, and thus were given direction and continuity. However, external forces are important, but only when a living structure is a compartment of its environment. It once started in this way and, with all its sophistication, has remained so ever since.

Initially, the flow of energy determined the dynamic order of the system; at this stage, there was no fine-tuning of reaction rates. In fact, mutations would have disrupted any intricate system of mutually dependent rates (Harold 2001). Metabolism depends on the organising energy flow itself, rather than on mutating

genes, that determine which chemical compounds carry the flux. This flux brings about a certain co-ordination and coherence in the reactions taking place, with the stability of the system as its emergent property. Thus, the biochemical pathways and cycles are self-organising, as are homeostatic mechanisms for the processing of energy, and energy-capturing membranes. By their nature, they channel this flux, halting it or facilitating the flow. The process of organised energy decay that constitutes life therefore remains physical at heart, whereas the particular metabolic compounds and enzymes are chemical and subject to the genetic system.

Thus, we need to study biogenesis from another perspective and to reconsider many established ideas. For example, the debate on the problem of metabolism-first or information-first (e.g. Dyson 1999) may prove obsolete with its present arguments. The debate presumes an initial production of either carbohydrates or proteins, and concentrates on the way information carriers could have been formed in an unstructured, primordial environment, independently of some biochemical context. Carbohydrates, as condensed, energy-storing molecules, would have formed and maintained themselves in an aqueous, hydrolysing environment without a highly intricate enzymatic apparatus of proteins evolving independently. Similarly, a genetic system for information transfer between generations would have been formed in the pre-biotic soup (Eigen and Schuster 1982). But how could any of these functions apply out of context? How could they have been maintained, unaltered, when put into the new context of a living cell?

Apart from the obvious Lamarckism inherent to these opinions (Hengeveld 2007), the early formation of CHONSP compounds seems unlikely from a thermodynamic viewpoint. Instead, according to our reasoning, these compounds were preceded by hydrogen, metals and by non-metals farther down in the periodic table. The CHONSP molecules with their strong, covalent bonds are more likely to have been formed only after a long history of molecular-biological evolution rather than before it. In our opinion, the energy flow by the transfer of electrons and protons would have started up slowly, only speeding up and intensifying during subsequent bootstrapping processes at the elemental, molecular and organisational levels. The CHONSP elements of the carbon world, forming carbohydrates, proteins, various RNAs, and DNA, could only have started to play a role after the photolysis of water. Although photolysis frees, stores and transduces large amounts of energy, it requires an elaborate system of standardised and mutually tuned enzymes.

Moreover, considering RNA and DNA as reference molecules that standardise and tune reactions in their hierarchically arranged homeostatic context, rather than as information carriers, fits recent interpretations well (e.g. Keller 2000). The genome is part and parcel of a metabolically interactive, self-generating (Oyama 1985) regulatory system (Davidson 2006); it is no longer seen as a blueprint. Similarly, the role of the apozymatic part of proteins relative to that of their metal and nucleoside cofactors needs to be reconsidered in its historical development (White 1976, 1982; Hengeveld 2007). This has already happened to spliceosomes (Reanny 1979) and ribosomes (Cech 2000). The place of reproduction may need to be reconsidered as well, the first systems being thermodynamically closed, dissipating the incoming energy through a series of internal cycles of, first,

hydrogenation–dehydrogenation and later condensation–hydrolysis. The system could hardly have been able to grow, if at all, the initial energy flow and the bonds would have been weak, and the reactions two-way. The system will not have reproduced; initially, its growth implied intensification rather than extensification.

One aspect of this article concerns elemental trends in the environment that would have been tracked over evolutionary time. Broadly speaking, the molecular evolution of the living structures would have been deterministic rather than stochastic. Yet, stochasticity enters the picture at several points. For example, cobalt could have, in principle, played a larger role, had it been more abundantly available (Williams and Fraústo da Silva 2006). Furthermore, the tiny cavities enveloped by a crust of mineral precipitates, here presumed to have been the cradle of life, contained chemicals of a particular abundance, composition, and availability that depended on chance; they may not have been representative of the conditions that predominated on Earth at that time. Therefore, it is an academic question whether life originated inevitably or purely by chance. Many reactions could have taken place, their interdependencies being largely unpredictable because of their stochasticity and non-linearity. Yet, within a closed space, the interdependence of reaction equilibria may have resulted in a homeostatic systems; the reactions would thus be constrained. Homeostasis will at first have been determined by a diffusion of atoms and molecules within the cavity, but as soon as spatial structuring began, the stochasticity of diffusion would decrease. Furthermore, once enzymatic systems developed, reaction became more specific, reaction rates more finely tuned, and so on, again reducing the chance character of the reactions within the system.

Evolutionary adaptation means that in one form or another, the stochasticity of a process or a dynamic system is reduced. For the initial phase of life, this is expressed by the structuring of the system of chemical processes. Bootstrapping meant that there was a trend from simple to intricate and highly complex.

## 16 Summary

The shift from a reducing to an oxidising, later, aerobic environment, was accompanied in the early living systems by a trend towards using both stronger electron-accepting elements and stronger electron-donating elements, the closing off of the membrane, and by the replacement of physical osmosis of hydrogen by biological chemiosmosis of protons. As the stronger electron-accepting elements are less reactive, forming kinetically stable compounds, a set of proteinaceous enzymes evolved, keeping the metabolic cycles and processes of genetic homeostasis going. As the metabolic waste products, carbon dioxide and water, are very stable, a large amount of external, solar energy was needed to bring their component elements back into circulation. This was achieved along two different lines, photophosphorylation and oxidative phosphorylation. The principal process is hydrogen metabolism, operating right from the beginning up to the present. The whole evolutionary process followed a bootstrapping mechanism.

**Acknowledgments** Fedonkin conducted this study within the Priority Program 18 of the Presidium of the Russian Academy of Sciences (“Problem of the Origin of the Earth’s Biosphere and Its Evolution”) and is also supported by the Russian Foundation for Basic Research. Kees Libbenga and Huub de Groot, with their stimulating and informative discussions with Hengeveld, contributed to this paper. Thomas Reydon, as the Editor of *Acta Biotheoretica*, was extremely patient, allowing the time for these ideas to mature. Claire Hengeveld contributed by giving much time for many essential corrections to be made, thus adding to the paper’s clarity!

## References

- Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P (2002) *The molecular biology of the cell*, 4th ed. Garland, New York
- Alves R, Chaleil RAG, Sternberg MJE (2002) Evolution of enzymes in metabolism: a network perspective. *J Mol Biol* 320:751–770
- Anbar AD, Knoll AH (2002) Proterozoic ocean chemistry and evolution: a bioinorganic bridge? *Science* 297:1137–1142
- Ball P (2004) By chance or by design? *Nature* 431:396–397
- Becker H, Brandon AD, Walker RJ (2004) Origin of tungsten excess in Komatiites. *Eos Trans. AGU, Fall Meet Suppl.* Abstract U41A-0718
- Bowen HJM (1966) *Trace elements in biochemistry*. Academic Press, New York
- Brock TD (1978) *Thermophilic micro-organisms and life at high temperature*. Springer, New York
- Buurman G, Shima S, Thauer RK (2000) The metal-free hydrogenase from methanogenic archaea, evidence for a bound cofactor. *FEBS Lett* 24:200–204
- Cammack R (1988) Nickel in metalloproteins. *Adv Org Chem* 32:297–333
- Cammack R, Frey M, Robson R (eds) (2001) *Hydrogen as a fuel*. Taylor and Francis, New York
- Cech TR (2000) The ribosome is a ribozyme. *Science* 289:878–879
- Cowen JP, Massoth GJ, Baker ET (1986) Bacterial scavenging of Mn and Fe in a mid- to far-field hydrothermal particle plume. *Nature* 322:169–171
- Chapelle FH, O’Neill K, Bradley PM, Methé BA, Ciuffo SA, Knobel LL, Lovley DR (2002) A hydrogen-based subsurface microbial community dominated by methanogens. *Nature* 415:312–314
- Darwin E (1803) *The temple of nature; or, the origin of society*. Johnson, London
- Davidson EH (2006) *The regulatory genome. Gene regulatory networks in development and evolution*. Academic Press, Amsterdam
- de Duve C (1991) *Blueprint for a cell. The nature and origin of life*. Patterson, Burlington
- de Duve C (2005) *Singularities. Landmarks on the pathways of life*. Cambridge University Press, Cambridge
- Di Toro DM, Kavvas CD, Mathew R, Paquin PR, Winfield RP (2001) The persistence and availability of metals in aquatic environments. *International Council on Metals and the Environment, Ottawa*
- Dutton L, Scrutton N, Sutcliffe M, Munro A (eds) (2006) *Quantum catalysis in enzymes—beyond the transition state theory*. *Phil Trans Roy Soc B* 361:1291–1455
- Dyson F (1999) *Origins of life*, 2nd edn. Cambridge University Press, Cambridge
- Eigen M, Schuster P (1982) Stages of emerging life—Five principles of early organisation. *J Mol Evol* 19:47–61
- Elsasser WM (1987) *Reflections on a theory of organisms. Holism in biology*. Johns Hopkins University Press, Baltimore
- Ermakov VV (2004) Biogeochemistry of selenium and its role in prevention of endemic diseases of man. *Vestnik Otdeleniya Naul o Zemle RAN*. URL: [http://www.scgis.ru/russian/cp1251/h\\_dgggms/1-2004/scpub-4.pdf](http://www.scgis.ru/russian/cp1251/h_dgggms/1-2004/scpub-4.pdf)
- Ermiler U, Grabarse W, Shima S, Goubeaud M, Thauer RK (1998) Active sites of transition metal enzymes with a focus on nickel. *Curr Opin Struct Biol* 8:749–758
- Fedonkin MA (2003) Geochemical starvation and origin of the kingdoms. *Chem Life* 6:12–17 (In Russian)
- Fedonkin MA (2005) Metal availability change and eukaryotization of biosphere through the Precambrian. In: Gavrilov YuO, Hutorskoi MD (eds) *Modern problems of geology. Transactions of the Geological Institute, Russian Academy of Sciences* 565:426–447. (In Russian, with extensive English resume)

- Fontecilla-Camps JC (1998) Biological nickel. In: Williams RJP (ed) Bioinorganic chemistry: trace element evolution from anaerobes to aerobes. Struct Bonding 91:1–30
- Fraústo da Silva JJR, Williams RJP (1991) The biological chemistry of the elements. The inorganic chemistry of life. Clarendon Press, Oxford
- Fraústo da Silva JJR, Williams RJP (2001) The biological chemistry of the elements. 2nd edn. Oxford University Press, Oxford
- Galimov EM (1998) Earth's core build-up as a source of its internal energy and factor of evolution of redox state of the mantle. Geochemistry 8:755–758. (In Russian)
- Galimov EM (2005) Redox evolution of the Earth caused by a multi-stage formation of its core. Earth Planet Sci Lett 233:263–276
- Gánti T (2003) The principles of life. Oxford University Press, Oxford
- Hammes-Schiffer S (2006) Hydrogen tunnelling and motion in enzyme reactions. Acc Chem Res 39:93–100
- Hammes-Schiffer S, Benkovic SJ (2006) Relating protein motion to catalysis. Annu Rev Biochem 75:519–541
- Hammes-Schiffer S, Watney JB (2006) Hydride transfer catalysed by *Escherichia coli* and *Bacillus subtilis* dihydrofolate reductase: coupled motions and distal mutations. Phil Trans Roy Soc Lond B 361:1365–1373
- Harold FM (1986) The vital force. A study of bioenergetics. Freeman, New York
- Harold FM (2001) The way of the cell. Oxford University Press, Oxford
- Hausinger RP (1993) Biochemistry of nickel. Plenum, New York
- Hayes KF, Roe AL, Brown GE, Hodgson KO, Leckie JO, Parks GA (1987) In situ X-ray absorption study of surface complexes: selenium oxyanions on  $\alpha$ -FeOOH. Science 238:783–786
- Hazen RM (2005) Genesis: the scientific quest for life's origins. Joseph Henry Press
- Ho M-W (ed) (1995) Living processes. Book 2: bioenergetics. Open University Press, Milton Keynes
- Ho M-W (1998) The rainbow and the worm, 2nd edn. World Scientific, Singapore
- Jaenicke R (1996) Glyceraldehyde-3-phosphate dehydrogenase from *Thermatoga maritima*: strategies of protein stabilisation. FEMS Microbiol Rev 18:215–224
- Janas T, Janas T, Yarus M (2006) RNA, lipids, and membranes. In: Gesteland RF, Cech TR, Atkins JF (eds) The RNA world, 3rd ed. Cold Spring Harbor Laboratories Press, New York, pp 207–225
- Kaufmann S (2000) Investigations. Oxford University Press, Oxford
- Keller EF (2000) The century of the gene. Harvard University Press, Cambridge Mass
- Kletzin A, Adams MW (1996) Tungsten in biological systems. FEMS Microbiol Rev 18:5–63
- Kooijman SALM (2000) Dynamic energy and mass budgets in biological systems, 2nd edn. Cambridge University Press, Cambridge
- Kooijman SALM, Hengeveld R (2003) The symbiotic nature of metabolic evolution. In: Reydon TAC, Hemerik L (eds), Current themes in theoretical biology, Springer, Berlin, pp 159–202
- Kooijman SALM, Hengeveld R (2005) The symbiotic nature of metabolic evolution. In: Reydon TAC, Hemerik L (eds) Current themes in theoretical biology: a Dutch perspective. Springer, Dordrecht, pp 159–202
- Lin L-H et al (2006) Long-term sustainability of a high-energy, low diversity crustal biome. Science 314:479–482
- Lumry R (1994) A new paradigm for protein research. In: Gregory RB (ed) Protein–solvent interactions. Dekker
- Martin W, Muller M (1998) The hydrogen hypothesis for the first eukaryote. Nature 392:37–41
- Martin W, Russell MJ (2003) On the origin of cells: an hypothesis for the evolutionary transitions from abiotic geochemistry to chemoautotrophic prokaryotes, and from prokaryotes to nucleated cells. Phil Trans Roy Soc Lond B 358:59–85
- Miller SL (1953) The production of amino acids under possible primitive earth conditions. Science 117:528–529
- Miller SL, Orgel LE (1974) The origins of life on the earth. Princeton University Press, Princeton
- Morowitz HJ (1968) Energy flow in biology. Academic Press, New York
- Morozov NP (1983) Chemical elements in the hydrobionts and trophic chains. In: Monin AS, Lisitsin AP (eds) Biogeochemistry of the ocean. Nauka, Moscow, pp 127–165 (In Russian)
- Myers CR, Nealon KH (1988) Bacterial manganese reduction and growth with manganese oxide as the sole electron acceptor. Science 240:1319–1321
- Nealon KH (2005) Hydrogen and energy flow as “sensed” by molecular genetics. Proc Natl Acad Sci 102:3889–3890

- Oyama S (1985) The ontogeny of information. Cambridge University Press, Cambridge
- Patching SG, Gardiner PHE (1999) Recent developments in selenium metabolism and chemical speciation: a review. *J Trace Elements Med Biol* 13:193–214
- Presser TS, Swain WC (1990) Geochemical evidence for Se mobilization by the weathering of pyritic shale, San Joaquin Valley, California, USA. *Appl Geochem* 5:703–717
- Pullman B (1972) Electronic factors in biochemical evolution. In: Ponnampertuma C (ed) *Exobiology*. North Holland Publishing Company, Amsterdam, pp 136–169
- Ragsdale SW (1998) Nickel biochemistry. *Curr Opin Chem Biol* 2:208–215
- Reaney D (1979) RNA splicing and polynucleotide evolution. *Nature* 277:598–600
- Rice DW et al (1996) Insights into the molecular basis of thermal stability from the structure determination of *Pyrococcus furiosus* glutamate dehydrogenase. *FEMS Microbiol Rev* 18:105–117
- Robson R (2001) Biodiversity of hydrogenases. In: Cammack R, Frey M, Robson R (eds) *Hydrogen as a fuel*. Taylor and Francis, New York, pp 9–32
- Russell M (2006) First life. *Am Sci* 94:32–39
- Russell MJ, Hall AJ (1997) The emergence of life from iron monosulphide bubbles at a submarine hydrothermal redox and pH front. *J Geol Soc Lond* 154:377–402
- Schrauser HW (2003) Selenium. In: Merian et al (eds) *Elements and their compounds in the environment*, 3. Nonmetals. Wiley, pp 100–106
- Schulte MD, Blake D, Hoehler T, McCollom T (2006) Serpentinization and its implications for life on the early earth and mars. *Astrobiology* 6:364–376
- Shapiro R (1995) The prebiotic role of adenine: a critical analysis. *Orig Life Evol Biosph* 25:83–98
- Shapiro R (1988) Prebiotic ribose syntheses: a critical analysis. *Orig Life Evol Biosph* 18:71–85
- Sorokhtin OG, Ushakov SA (1991) *Global evolution of earth*. Moscow State University Press, Moscow (In Russian)
- Telser J (1998) Nickel in F430. In: Williams RJP (ed) *Bioinorganic chemistry: trace element evolution from anaerobes to aerobes*. *Struct Bonding* 91:31–64
- Vignais PM, Billoud B, Meyer J (2001) Classification and phylogeny of hydrogenases. *FEMS Microbiol Rev* 25:455–501
- Vikre PG (2005) Se-rich precious metal deposits and the significance of Se in sinter, Northern Great Basin. Paper No. 235–8. Geological Society of America Abstracts with Programs 37:517. Salt Lake City Annual Meeting (October 16–19, 2005)
- von Bertalanffy L (1968) *General system theory: foundations, development, applications*. Penguin University Books, 1973, London
- Wackett LP, Dodge AG, Ellis LBM (2004) Microbial genomics and the periodic table. *Appl Environ Microbiol* 70:647–655
- White HB (1976) Coenzymes as fossils of an earlier metabolic phase. *J Mol Evol* 7:101–104
- White HB (1982) Evolution of coenzymes and the origin of pyridine nucleotides. In: Everse J, Anderson B, You K-S (eds) *The pyridine nucleotide coenzymes*. Academic Press, New York, pp 2–17
- Wächtershäuser G (1988) Origin of life and iron sulphides. *Microbiol Rev* 52:482–486
- Williams GE (2000) Geological constraints on the precambrian history of earth's rotation and the moon's orbit. *Rev Geophys* 38:37–59
- Williams RJP, Fraústo da Silva JJR (1996) *The natural selection of the chemical elements*. Clarendon Press, Oxford
- Williams RJP, Fraústo da Silva JJR (1999) *Bringing chemistry to life. From matter to man*. Oxford University Press, Oxford
- Williams RJP, Fraústo da Silva JJR (2003) Evolution was chemically constrained. *J Theor Biol* 220:323–343
- Williams RJP, Fraústo da Silva JJR (2006) *The chemistry of evolution. The development of our ecosystem*. Elsevier, Amsterdam
- Yin Q, Jacobsen SB, Yamashita K, Blichert-Toff J, Telouk P, Albarede F (2002) A short timescale for terrestrial planet formation from Hf–W chronometry of meteorites. *Nature* 418:949–952