Energetics of the First Life

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Chapter 1
Energetics of the First Life

Armen Y. Mulkidjanian

Abstract Life can exist only when supported by energy flow(s). Here, the tentative mechanisms of coupling between the natural energy fluxes and the first life forms are discussed. It is argued that the evolutionarily relevant, continuous fluxes of reducing equivalents, which were needed for the syntheses of the first biomolecules, may have been provided by the inorganic photosynthesis and by the redox reactions within hot, iron-containing rocks. The only primordial environments where these fluxes could meet were the continental geothermal systems. The ejections from the hot, continental springs could contain, on the one hand, hydrogen and carbonaceous compounds and, on other hand, transition metals as Zn and Mn, which precipitated around the springs as photosynthetically active ZnS and MnS particles capable of reducing carbon dioxide to diverse organic compounds. At high pressure of the primordial CO_2 atmosphere, both the inorganic photosynthesis and the abiotic reduction of carbon dioxide within hot rocks should have proceeded with high yield. Among a plethora of abiotically produced carbonaceous molecules, the natural nucleotides could accumulate as the most photostable structures; their polymerization and folding into double-stranded segments should have been favored by the further increase in the photostability. It is hypothesized that after some aggregates of photo-selected RNA-like polymers could attain the ability for self-replication, the consortia of such replicating entities may have dwelled in honeycomb-like ZnS-enriched mineral compartments which provided shelter and nourishment. The energetics of the first life forms could be driven by their ability to cleave the abiogenically formed organic molecules and by reactions of the phosphate group transfer. The next stage of evolution may be envisaged as a selection for increasingly tighter envelopes of the first organisms; this selection may have

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eventually yielded ion-tight lipid membranes able to support the sodium-dependent membrane bioenergetics. Lastly, the proton-tight, elaborate membranes independently emerged in *Bacteria* and *Archaea*, and enabled the transition to the modern-type proton-dependent bioenergetics.

> The first primeval step would appear to be indicated by the union of single crystalloidal inorganic molecules to form inorganic colloids, and that these meta-stable colloids acting on inorganic carbon compounds, such as carbon dioxide, in presence of water and sunlight, and taking energy from the sunlight, built up at first simple organic bodies, and now these in turn reacting with one another formed more and more complex organic compounds. In any such transformation external energy is necessary, because the reacting bodies, carbon dioxide and water, are fully oxidised, and must be reduced with . . . uptake of energy in what is called an endothermic reaction. To this reaction, the inorganic colloid plays the part of an activator or catalyst, the solar energy being converted into chemical energy of the organic compound, so serving as a reservoir of the energy necessary for the coming living organic world.
>
>   B. Moore and T.A. Webster (1913)

1.1 Introduction

Living organisms can exist only when supported by energy (Bauer 1935; Schrödinger 1945; Glansdorff and Prigogine 1971; Williams and Frausto da Silva 2006; Danchin 2009). Therefore, from the very beginning, the life forms should have exploited the natural energy fluxes. Here, I focus on the tentative mechanisms of coupling between the first life forms and the natural energy fluxes at different stages of the early evolution.

Because of the energetic continuity requirement – which follows from the Darwinian evolutionary continuity principle (see Lahav (1999); Wolf and Koonin (2007) and references therein) – the energy flows that deserve attention in evolutionary context are those that remain constant on the evolutionary relevant, geological timescale. This consideration essentially discounts the evolutionary importance of occasional energy inputs from impact bombardment, atmospheric electric discharges, shock waves, volcanic explosions, and so on. It is also unlikely that life could notably depend on the chemical compounds that were produced or delivered during such occasional events. It seems implausible that the first life forms could wait from one occasional event (e.g., volcanic explosion) to another to get energy and nourishment. There are no known organisms that obligatorily depend on such irregular sources of energy and matter.

Mauzerall has insightfully noted that the energy requirements of the first living beings had to be compatible with those of modern organisms (Mauzerall 1992). He argued that "*the ur-cell would be simpler, but it would also be less efficient*". More rigorously speaking, the intensity of the energy flux(es) that supported the emergence of life should be either comparable with the intensity of modern life-supporting energy flows or stronger.

As will be shown below, there are only few energy fluxes in nature that fulfil these criteria and, hence, may have been used by the first organisms. Therefore, the energetic constraints are very useful upon testing different hypotheses on the early evolution of life.

1.2 Reducing Power for the First Syntheses

The geochemical and cosmochemical data indicate that the primordial atmosphere on Earth was dominated by carbon dioxide (Nisbet 1991; Nisbet and Sleep 2001; Kasting and Howard 2006; Zahnle et al. 2007). Therefore, energy was initially needed for reducing CO_2 to compounds that could further participate in pre-biological syntheses (see Lazcano and Miller (1996); Bada (2004); Miller and Cleaves (2006); Lazcano (2010)) and references therein). More specifically, the reduction of CO_2 should have required electrons with high reducing potential. The first step of the reduction of CO_2 can be described by an equation:

$$CO_2 + 2H^+ + 2e^- \rightarrow HCOOH$$
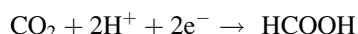
where $2e^-$ are the two required electrons. The standard redox potential of this reaction is as low as ~ -0.6 eV (at room temperature, neutral pH, and atmospheric pressure of 1 bar), therefore the task of CO_2 reduction is far from being trivial.

Currently, the reduction of CO_2 by living organisms is supported by the two fluxes of reducing power, at least. The communities at the Earth's surface depend, via photosynthesis and its products, on the solar light. Upon photosynthesis, the energy of light quanta is used to produce electrons with high reductive potency within sophisticated, membrane-embedded, (bacterio)chlorophyll-carrying proteins, called photochemical reaction centers (see Mulkidjanian et al. (2006) and references therein). The biotopes at the sea floor, besides consuming the organic fall-out from the upper, inhabited photic zone (where photosynthesis takes place), can also exploit the redox potential difference between reduced hydrothermal fluids and oxygenated ocean waters by coupling the downhill transfer of electrons to oxygen with an uphill electron transfer to CO_2 (Kelley et al. 2002). This mechanism, however, could not be used by the first life forms, since the redox energy span of >1 eV between the reduced compounds of hydrothermal fluids and the sea water-dissolved oxygen became exploitable only after the ocean waters – some 2–2.5 Ga ago – became saturated by molecular oxygen, a waste product of cyanobacterial photosynthesis (Bekker et al. 2004; Mulkidjanian et al. 2006). Some prokaryotes can use other electron acceptors instead of oxygen, then however, the yield of CO_2 reduction is much lower (Thauer et al. 1977, 2008).

It is noteworthy that the hydrothermal fluids may already contain organic molecules; they are believed to stem, at least partly, from the so-called serpentinization reactions within the rocks of the oceanic crust (Russell and Arndt 2005).

These reactions occur when iron-containing rocks interact with water at temperatures of 200–500°C. Under these conditions, part of the Fe^{2+} ions in the rock get oxidized to Fe^{3+} yielding magnetite (Fe_3O_4). The electrons that are released upon this reaction are taken either by protons of water or by the available carbon (usually present as water-dissolved CO_2), so that H_2 and diverse hydrocarbons are produced according roughly to the following equation (Martin et al. 2008):

$$(Mg, Fe)_2SiO_4 + H_2O + C \rightarrow Mg_3SiO_5(OH)_4 + Mg(OH)_2 + Fe_3O_4 + H_2 \\ + CH_4 + C_2 - C_5 \qquad (1.1)$$
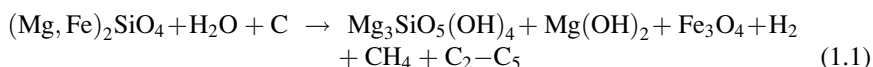
Thus it has been argued that the organic compounds, as produced upon the serpentinization reactions, contribute to the energy budget of the marine organisms (see Martin et al. (2008) and references therein).

Not surprisingly, the aforementioned sources of reducing power have been suggested also as promoters of the primeval synthetic reactions, which ultimately could lead to the origin of life. Some scholars, starting from Moore – a quote from his paper (Moore and Webster 1913) serves as epigraph to this chapter – have suggested that solar radiation served as the driving force upon the emergence of life (Haldane 1929; Granick 1957; Skulachev 1969; Hartman 1975; Halmann et al. 1980; Mauzerall 1992; Skulachev 1994; Hartman 1998; Mulkidjanian et al. 2003; Mulkidjanian and Galperin 2007; Guzman and Martin 2009). Indeed, the very lack of oxygen in the primordial atmosphere should have favoured light-driven chemical syntheses. Without the ozone shield, the solar light reaching Earth contained a UV component that was by orders of magnitude stronger than it is today (Sagan 1973; Vazquez and Hanslmeier 2006) and could drive diverse chemical reactions, in particular, the carbon fixation. No other known energy source could compete with solar irradiation in terms of strength and access to the whole of the Earth's surface (Miller and Orgel 1973).

At least two UV-driven abiogenic processes of CO_2 reduction are known to proceed with efficiency comparable to that of modern photosynthesis. One is the photo-oxidation of Fe^{2+} ions in solution, which may lead to the reduction of CO_2 to formaldehyde with a quantum yield of up to 2–3% (Getoff 1962; Borowska and Mauzerall 1988). Next, several naturally occurring minerals, in particular TiO_2 (anatase/rutile), WO_3 (wolframite), MnS (alabandite), and ZnS (wurtzite, sphalerite), possess the properties of broad-band semiconductors and can photoreduce CO_2 at their surfaces (Inoue et al. 1979; Reiche and Bard 1979; Halmann et al. 1980, 1981; Henglein 1984; Henglein et al. 1984; Kisch and Künneth 1991; Eggins et al. 1993; Fox and Dulay 1993; Hagfeldt and Gratzel 1995; Inoue et al. 1995; Yoneyama 1997; Schoonen et al. 1998; Xu and Schoonen 2000; Schoonen et al. 2004; Zhang et al. 2004, 2007; Guzman and Martin 2009; see also Chap. 4 for details). The highest quantum yield of 80% has so far been reported for the reduction of CO_2 to formate at the surface of colloidal ZnS particles (Henglein 1984; Henglein et al. 1984). The crystals of ZnS, which is commonly known as "phosphor" (from

"phosphorescence"), can trap the energy of light and store it on a time scale of minutes. In addition, these crystals are the most powerful photocatalysts known in nature. Particles of ZnS and other semiconducting minerals can produce diverse organic compounds from CO_2 (Fox and Dulay 1993; Eggins et al. 1998), including the intermediates of the Krebs cycle (Zhang et al. 2007; Guzman and Martin 2009), can catalyze photocondensation of HCN or formamide (Senanayake and Idriss 2006; Liu et al. 2008), and, generally, can drive various transformations of carbon- and nitrogen-containing substrates (see (Henglein 1984; Yanagida et al. 1985; Kisch and Twardzik 1991; Hagfeldt and Gratzel 1995; Kisch and Lindner 2001; Marinkovic and Hoffmann 2001; Ohtani et al. 2003) and Chap. 4). The Fe^{2+}-mediated CO_2 reduction and the ZnS/MnS-mediated photosynthesis are not mutually exclusive; the addition of Fe^{2+} ions was shown to enhance the ZnS-mediated reduction of CO_2 (M. Schoonen, personal communication).

The possibility of the ZnS/MnS-mediated inorganic photosynthesis is particularly remarkable since the evolutionarily oldest proteins, which could be traced to the Last Universal Common Ancestor (LUCA), showed particular enrichment in the atoms of Zn and, to lesser extent, Mn as cofactors and structural elements (Mulkidjanian and Galperin 2009, 2010b), which implies availability of these metals for the primordial life forms. Where could these metals be found on the primordial Earth? The levels of transition metals in the aqueous systems are determined by the solubility constants of the respective salts and oxides. Specifically, the primordial anoxic ocean, as compared to the modern ocean, should have been enriched in well-soluble Fe^{2+} ions but depleted of Zn^{2+} ions (with estimated Zn concentration of $<10^{-13}$ M (Williams and Frausto da Silva 2006; Anbar 2008)). As argued elsewhere (Mulkidjanian et al. 2008b; Mulkidjanian and Galperin 2009, 2010a, b), the LUCA could hardly possess ion-tight membranes and the membrane pumps needed to maintain large gradients of Zn^{2+} ions between the Zn-rich cell interior and the Zn-depleted primeval anoxic waters. Thus, the high content of Zn and Mn in the "oldest" proteins could be explained by thriving of the first life forms not in the water column of the primordial ocean, but in some habitats that were enriched in these transition metals (Mulkidjanian and Galperin 2009, 2010a, b). On the modern Earth, the enrichment in transition metals, such as Zn and Mn, is routinely reported for the sites of geothermal activity, e.g., at the deep-sea hydrothermal vents. Here, the extremely hot hydrothermal fluids reach metal ions from the crust and bring them to the sea floor (Kelley et al. 2002; Tivey 2007). Because of high pressure at the sea bed, the ejected fluids with temperatures reaching 400°C remain liquid and can carry transition metal ions. Since hydrothermal fluids are rich in H_2S, their interaction with cold ocean water leads to the precipitation of metal sulfide particles that form "smoke" over the "chimneys" of hydrothermal vents (Kelley et al. 2002; Tivey 2007). These particles eventually aggregate, settle down, and, ultimately, form sponge-like structures around the vent orifices. The sulfides of Fe and Cu precipitate promptly (Seewald and Seyfried 1990; Metz and Trefry 2000) even inside the orifices of hydrothermal vents (Kormas et al. 2006). The sulfides of Zn and Mn precipitate more slowly (Seewald and Seyfried 1990; Metz and Trefry 2000) and can spread over, forming halos around the iron-sulfur apexes of hydrothermal vents (Tivey 2007).

The ZnS precipitates that cover the deep-sea vents cannot catalyze photosynthesis. Therefore, in relation to the problem of plausible energy sources for the earliest life forms, it was suggested that, at high CO_2 pressure of the primordial atmosphere, very hot springs, similar to the deep-sea vents, could deliver metalliferous fluids within reach of solar light, namely at shallow hydrothermal vents or at geothermal systems on land (Mulkidjanian 2009). Accordingly, it was speculated that the illuminated ZnS/MnS precipitates (hereafter, for simplicity, denoted as ZnS precipitates) may have catalyzed the photosynthesis of different organic compounds from CO_2, as well as the formation of first polymers, and may have served as feeding grounds for the first life forms (Mulkidjanian 2009; Mulkidjanian and Galperin 2009; see also Chap. 4). The feasibility of the ZnS precipitation within the reach of solar light is supported by the data from the modern Kamchatka volcanic system where the level of Zn^{2+} ions in the acidic, thermal waters can reach 0.2 mM (Karpov et al. 2009) yielding Zn-enriched precipitates around the hot springs (Kardanova 2009; Karpov et al. 2009).

In relation to the aforementioned abundance of Zn^{2+} ions in the evolutionarily old proteins (Mulkidjanian and Galperin 2009, 2010b), it is noteworthy that the ZnS-mediated photosynthesis is accompanied by the release of Zn^{2+} ions (Henglein 1984; Kisch and Künneth 1991), yielding steadily Zn-enriched milieu at the ZnS surfaces according to the following equation:

$$ZnS^* + CO_2 + 2H^+ \rightarrow HCOOH + Zn^{2+} + S$$
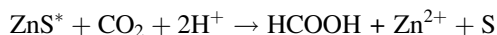
Hence, the prevalence of Zn in the "oldest" proteins can be tentatively explained by the thriving of the first cells in illuminated, ZnS-enriched habitats where photo-released Zn^{2+} ions could be preferably recruited as metal cofactors by the proteins and RNA molecules of the first cells (Mulkidjanian and Galperin 2009, 2010b).

Alternatively to the inorganic photosynthesis, some authors have focused on the sources of reductive power at the floor of the primordial ocean. Specifically, Wächtershäuser has proposed a detailed chemical mechanism where oxidation of FeS to FeS_2 was suggested to drive the reduction of CO_2 (Wächtershäuser 1988, 1990, 1992; Huber and Wächtershäuser 1997; Wächtershäuser 2006, 2007). Indeed, the free energy of the redox transition of FeS to FeS_2, at least under some conditions, seems to be sufficient to drive the reduction of CO_2. However, as argued by Schoonen and co-workers (Schoonen et al. 1999), the favorable thermodynamics alone is not sufficient in the case of redox reactions. In addition, the redox potential of the electron donor has to be lower than that of the electron acceptor. To drive CO_2 reduction at an appreciable rate, one needs a reducing agent with a redox potential that is lower than the redox potential of the CO_2/formate redox pair (-0.6 V), whereas the reducing potential of the FeS/FeS_2 redox pair is higher than that, at least, under conditions that are compatible with life.

The reducing power of the iron-containing minerals, however, depends on temperature, pressure, and the exact chemical composition of the minerals. While below $100°C$, the oxidation of Fe^{2+} cannot drive the reduction of CO_2, at

temperatures of 200–500°C and high pressures, the interaction of iron-containing rocks with water could, as discussed above, lead to the production of hydrogen, hydrocarbons, and organic compounds. Building on this phenomenon of serpentinization, Russell and coworkers have suggested that life could emerge at the deep-sea hydrothermal vents being supported by the delivery of organic compounds and hydrogen, as produced within hot rocks (see (Russell 2007; Martin et al. 2008)). Hence, while the model of Wächtershauser implies a direct coupling between the redox reactions of mineral iron and the syntheses of biological molecules, the model of Russell of coworkers suggests that the reductive formation of organic molecules may have taken place within hot rocks, at temperatures which were incompatible with life; the subsequent interactions of these organic molecules and the eventual condensation reactions could then take place at the sea floor or at hydrothermal vents, after the ejection and cooling of hydrothermal fluids.

Besides the reduced carbon, biological macromolecules contain large amounts of nitrogen. The atmospheric dinitrogen is chemically inert; therefore, nitrogen could participate in the primeval syntheses as chemically reactive ammonia. Since hydrothermal fluids contain ammonia (Kelley et al. 2002; Karpov et al. 2009), it has been argued that dinitrogen could be reduced to ammonia within hot hydrothermal systems (Brandes et al. 1998; Wander et al. 2008; Wander and Schoonen 2008). Experimentally, it was shown that dinitrogen (at partial pressure 50 bar) was reduced in dilute hydrogen sulfide (H_2S) solutions to ammonium at 120°C; the ammonia yield increased in the presence of iron monosulfide (Wander et al. 2008; Wander and Schoonen 2008). Nitrogen could also enter the primeval syntheses as formamide. Since formamide is, in fact, a stand-alone peptide bond, its reactions can yield amino acids (Miller and Cleaves 2006). In addition, the synthesis of nucleotides can be also relatively easy achieved at elevated temperatures either by starting from formamide (Saladino et al. 2009, 2010) or in formamide solutions (Powner et al. 2009).

One more key element of life is phosphor. The reactions of phosphate group transfer make the essential part of cellular chemical reactions, and the concentration of phosphate within the cells is on the order of 10 mM. Large part of the ubiquitous, evolutionarily oldest proteins are involved in the phosphate group transfer, mostly as ATPases and GTPases (Koonin 2003; Mulkidjanian and Galperin 2009). Hence, the importance of phosphate and its high level within modern cells indicates the abundance of phosphorus compounds in the habitats of the first life forms (Cairns-Smith et al. 1992; Schwartz 2006; Mulkidjanian and Galperin 2007; Danchin 2009). Still, the concentration of PO_4^{3-} in sea water is low (the phosphates of Ca and Mg are hardly soluble in water). Here we have a conundrum: On the one hand, the concentration of free phosphate in natural aqueous systems could never be high enough to satisfy the cellular needs. On other hand, the first life forms could not accumulate sufficient amounts of phosphate since they had neither tight membranes nor phosphate-scavenging pumps. This conundrum has first been noted by Gulick (1955); in the following decades, several tentative solutions were put forward (see Schwartz (2006) for a review). Specifically, several authors have speculated that more reduced phosphorus-containing compounds such as hypophosphite

(phosphinate, $PO_2{}^{3-}$) and/or phosphite (phosphonate, $PO_3{}^{3-}$), which have better solubility in water, could have been abundant under primordial reduced conditions (Gulick 1955; Glindemann et al. 1999; Buckel 2001; Bryant and Kee 2006; Schwartz 2006; Pasek 2008; see also Chap. 3). It is important that (hypo)phosphite ions can exergonically interact with diverse organic molecules in exergonic reactions yielding their phosphorylated derivates (Hagan 1996; Schwartz 2006; Bryant et al. 2010). Obviously, de-phosphorylation of such derivates could provide living organisms with energy. The idea of (hypo)phosphite-utilizing biochemistry is highly attractive; its plausibility, however, depends on finding a continuous primordial source of inorganic (hypo)phosphite. One suggestion is that the reduced oxidation state phosphorus originated from extraterrestrial material that fell from space and persisted in the mildly reducing atmosphere long enough to support the emergence of life (Pasek 2008). An alternative source of (hypo)phosphite is suggested by the recent finding of compatible amounts of phosphate and phosphite in the pristine geothermal pool at Hot Creek Gorge near Mammoth Lakes, California, which is fed by hot, bicarbonate-rich geothermal waters (Pech et al. 2009). The finding of phosphite in nature, on the one hand, explains why diverse prokaryotes possess systems of hypophosphite and phosphite oxidation (see (White and Metcalf 2007) for a review). On other hand, the presence of (hypo)phosphite in the geothermal waters of modern Earth strongly supports the possibility of its abundance in the geothermal fluids of the more reduced primordial Earth.

Where may the phosphite of the Hot Creek Gorge have come from? The serpentinization-type reactions are not limited to the sea bed, but proceed within any ultramafic rock in the presence of water and at $\sim 300°C$ (see (Sleep et al. 2004)), for a review of the continental reactions of hydrothermal alteration. There are many reports of hydrocarbon production by terrestrial rocks; in the case of the rocks of the Canadian Shield, at least, the abiogenic origin of these hydrocarbons was demonstrated (Sherwood Lollar et al. 2002). The standard redox potentials of CO_2 reduction to formate and of phosphate reduction to phosphite have similar standard redox potentials of about -0.6 V. It is tempting to speculate that the hydrothermal rock alteration may account for the reduction of insoluble mineral phosphate to soluble (hypo)phosphite in geothermal fluids (Pech et al. 2009). Analogously, the high ammonia content in the hot springs of Kamchatka (that reach 130 mg/L in the mud pot solutions (Bortnikova et al. 2009)) might be due to the abiogenic reduction of dinitrogen to ammonia within the hot volcanic rocks.

Hence, continuous fluxes of reducing equivalents, which were needed for the first syntheses, may have been provided by: (1) The inorganic photosynthesis; and (2) The redox reactions within hot iron-containing rocks. The only primordial environments where these fluxes could meet were the continental geothermal systems. On the one hand, the hot springs should have ejected transition metals that precipitated as photosynthetically active ZnS and MnS particles. On the other hand, the same hydrothermal fluids could be enriched in hydrogen and carbonaceous compounds. At high pressure of the primordial CO_2 atmosphere, both the inorganic photosynthesis and the abiotic reduction of CO_2 within hot rocks should have proceeded with higher yield than nowadays. The content of (hypo)phosphite and ammonia in the

H_2S-enriched hydrothermal fluids should have been also higher on the anoxic primeval Earth, not to mention sulfur, which is also essential for life. It is noteworthy that the formamide molecules, which could serve as building blocks for amino acids and nucleotides, can build from formate and ammonia after the elimination of water; hence, formamide could concentrate in continental locations upon evaporation, thanks to its high boiling temperature (210°C).

In sum, only at continental geothermal springs, the formation of organic nitrogen-, phosphor-, and sulfur-containing compounds could be supported by two different fluxes of reducing equivalents resulting from the abiotic photosynthesis and the hydrothermal alteration of the iron-containing rocks. In addition, only continental environments could be characterized by wet/dry cycles, favorable for condensation reactions (Bernal 1951; Miller and Orgel 1973; Lahav and Chang 1976; Lahav 1999; Bada 2004; Miller and Cleaves 2006), see also Chap. 12.

1.3 Energetics of Natural Selection

The countdown of life, as argued by many authors (Eigen 1971; Orgel 1986; Lazcano and Miller 1996; Bada 2004; Orgel 2004; Wolf and Koonin 2007; Orgel 2008; Koonin 2009; Lazcano 2010), started to run with the emergence of the first replicating systems. Since the modern replicating systems are based on nucleic acids, the earliest steps of evolution are usually considered in the framework of the "RNA World" scenario, according to which RNA-like molecules capable of both self-reproduction and simple metabolism were the first inhabitants of Earth (see (Belozersky 1959; Woese 1967; Crick 1968; Orgel 1968; Eigen 1971; Gilbert 1986; Benner et al. 1989; Ellington 1993; Spirin 2005; Koonin et al. 2006; Ellington et al. 2009; Lincoln and Joyce 2009; Powner et al. 2009) and Chaps. 9–11). This scenario is supported by the discovery of RNA enzymes (ribozymes) with different catalytic activities (see (Curtis and Bartel 2005; Chen et al. 2007; Joyce 2007; Scott 2007; Lincoln and Joyce 2009) and references therein), by the ability of RNA colonies to grow and propagate on gels or other solid media (Chetverin and Chetverina 2007), by the documented interactions of RNA molecules with metabolites (Shu and Guo 2003; Roth and Breaker 2009), in particular in the case of riboswitches (Gelfand et al. 1999; Cochrane and Strobel 2008), and by the demonstration of a RNA enzyme complex capable of self-replicating (Lincoln and Joyce 2009).

The RNA world model implies a step-by-step emergence of increasingly complex RNA-like molecules. Some scholars have considered such a scenario to be implausible. The problem of increasing complexity, however, is not limited to the transition from simple organic molecules to the first replicating biopolymers. The evolutionary development from the simplest prokaryotes to mammals is accompanied by a comparable increase in complexity. This complexity increase, however, is not considered as improbable, but is taken for granted; it is routinely explained by the Darwin's principle of natural selection (Darwin 1859; Smith and Szathmáry 1995; Danchin 2009).

The role of selection in the abiotic generation of increasingly complex macromolecules has been addressed by several authors who suggested that the higher stability of complex macromolecules, as compared to the simpler ones, could favour the relative accumulation of the former. It was speculated that the lower susceptibility of more complex polymer molecules to the lysis or hydrolysis might drive accumulation of increasingly complex polymers (Quastler 1964; de Duve 1987). This speculation might, with certain reservations, be applicable to proteins (see below), but not to the RNA-like oligomers. In the RNA oligomers, the binding of new monomers can proceed only at the two terminal positions, while hydrolysis can implicate any bond. Hence, the probability of hydrolysis should increase with the length and prevent the formation of long polymers (D. Cherepanov, personal communication, (see also (Mulkidjanian et al. 2003; Mulkidjanian 2009)). Therefore, it is unlikely that the first RNA-like polymers were selected as particularly resistant to hydrolysis.

Why then have they been selected? In biology, it is often possible to identify the major selective factor(s) just by inspecting particular organisms. For example, the long ears, large eyes, and strong legs of hares indicate that the survival of their ancestors depended on their ability to catch sight of hunting predators and to run away as fast as possible. Elsewhere (Mulkidjanian et al. 2003), we applied the same naïve rationale to polynucleotides and attempted to reconstruct the circumstances of their emergence from their specific traits. The exclusive feature of natural nucleobases is their unique photostability (Cadet and Vigny 1990). Since this trait is not related to the storage of genetic information, several authors (Skulachev 1969; Sagan 1973; Cadet and Vigny 1990) have noted that this property could have been of some use when the UV flux at the surface of primordial Earth – owing to the absence of the ozone layer – was much stronger than it is now. Nucleobases apparently can absorb excess energy quanta from sugar-phosphate moieties and protect them from photo-dissociation (Goossen and Kloosterboer 1978). This feature explains why the UV damage to the backbones even of modern RNA and DNA molecules is 10^3–10^4 times less frequent than the destruction of nucleobases proper (Cadet and Vigny 1990). Under the assumption that the unique photostability of nucleobases could hardly be incidental, we have argued that natural nucleotides should have been selected within the reach of solar light and that nucleobases may have protected the first RNA-like polymers from photo-dissociation (Mulkidjanian et al. 2003).

More recently, the reason for the particularly high photostability of nucleotides and nucleobases has been clarified (Sobolewski and Domcke 1999; Marian 2005; Perun et al. 2005a, b; Merchan et al. 2006; Sobolewski and Domcke 2006; Frutos et al. 2007; Serrano-Andres and Merchan 2009). Two types of photochemical reaction paths, which lead to an extremely fast transition from the excited state into the ground state, have been identified, namely: (1) The torsion of certain C-N bonds of rings and (2) The de-protonation of azine or amino groups (Perun et al. 2005a; Sobolewski and Domcke 2006). It has been argued that the high photostability is not affected by the alkylation of nucleobases; such alkylated, mostly methylated, derivates (minor bases) are found in the structures of tRNA

and rRNA (Nagaswamy et al. 2000). Together, major and minor nucleobases could represent the initial pool of primeval photostable compounds from which the major nucleobases were gradually selected by evolution.

Important experimental evidence of the particular photostability of natural nucleotides has recently been provided by Sutherland and co-workers, who have obtained activated pyrimidine ribonucleotides from cyanamide, cyanoacetylene, glycolaldehyde, glyceraldehyde, and inorganic phosphate in a reaction that bypassed free ribose. The synthesis yielded activated ribonucleotide β-ribocytidine-2′,3′-cyclic phosphate (natural cytidine) as a major product as well as several co-products (Powner et al. 2009). Prolonged irradiation of this mixture by 254 nm light caused the destruction of various co-products and the partial conversion of ribonucleotide β-ribocytidine-2′,3′-cyclic phosphate into ribonucleotide β-ribouridine-2′,3′-cyclic phosphate (natural uridine). The authors concluded that there must be some (photo) protective mechanism functioning with natural nucleotides but not with other pyrimidine nucleosides and nucleotides (Powner et al. 2009).

Admittedly, the least physically plausible step in the hypothetical RNA World scenario is the polymerization of the abiogenically produced nucleotides into oligomers, followed by their joining into complex systems capable of self-replication, with each oligomer involved being composed of 50–100 nucleotides, or more (Eigen 1971; Bada 2004; Lincoln and Joyce 2009). In modern organisms, the enzymes that synthesize RNA molecules are driven by hydrolysis of nucleoside triphosphates. In the RNA world, where these NTP-driven enzymes were absent, the polymerization could be catalyzed by mineral surfaces, as demonstrated in several systems, (see (Ferris 2006) and references therein). The polymerization may also have been promoted by the UV quanta, specifically in the presence of photoactive ZnS crystals (Senanayake and Idriss 2006; Liu et al. 2008). In addition, the aforementioned thermodynamically favourable oxidation of phosphite to phosphate could potentially provide free energy for polymerization reactions. And still, it is unclear whether these factors alone could have been sufficient for maintaining a notable steady-state population of RNA-like polymers – needed as a starting material for further evolutionary transformations. The results of our earlier Monte-Carlo simulations of primordial photochemistry (Mulkidjanian et al. 2003) suggest one more, rather paradoxical, way to channel external energy into the syntheses of increasingly complex compounds.

The aim of the simulations was to quantify the significance of the UV-protection mechanism for the evolution of primordial RNA-like polymers by modelling the polymerization of sugar-phosphate monomers in the presence of nucleobases under varying conditions (Mulkidjanian et al. 2003; Mulkidjanian 2009). The simulation has shown that the ability of nucleobases to protect the adjoining sugar-phosphate units from UV-dissociation could alone result in a dramatic increase both in the length of formed polymers and in the fraction of nucleobase-carrying sugar-phosphate units, as compared to the simulations where no UV-protection was "switched on" (Mulkidjanian et al. 2003).

This finding is not trivial since in both types of simulations, with the UV protection switched on and switched off respectively, the utilization of radiation

energy for any kind of synthesis was not "permitted". The fraction of complex polymers grew only owing to the breakage of less photostable molecules by the UV quanta. The broken pieces steadily re-arranged anew into more photostable and, accordingly, more complex polymers. Therefore – and this is the key point – the enrichment in more complex RNA-like polymers was driven by the photo-dissociation of their less stable counterparts, in the absence of any direct coupling between the energy flow and the synthetic reactions.

From the experimental viewpoint, the results of this modelling might be related to the aforementioned enrichment of photostable natural nucleotides on account of non-natural nucleotides after prolonged UV illumination (Powner et al. 2009). From the theoretical viewpoint, the described mechanism of "indirect" energy utilization might be related to the so-called Landauer principle (Landauer 1961; Bennett and Landauer 1985; Bennett 2003). According to this principle, the creation of information requires energy in any case, but the energy can be utilized in two different ways: (1) For creating the information itself, and/or (2) For erasing the "garbage" from the system. More recently, Danchin has applied this principle to biological systems (Danchin 2009). Danchin describes a selection process that has to "*actively discriminate between entities that are in some degree functional and those that cannot function. This is because the process needs to avoid destroying the elements that carry increased information and this is where energy comes in. Energy has to be consumed to make innovations stand out in a discriminant process; energy is used to prevent degradation of functional entities, permitting destruction of the non-functional ones*" (quoted from (Danchin 2009)). This approach seems to be applicable to the primordial RNA-like polymers in illuminated environments, provided that we consider the more photostable constructs as "functional" ones and the solar UV radiation as the selecting and erasing energy input.[1]

Earlier, we have hypothesized that the excitonic interaction between the stacked nucleotides as well as their Watson-Crick pairing may have been favoured by higher photostability of the resulting structures in a UV-irradiated environment (Mulkidjanian et al. 2003; Mulkidjanian and Galperin 2007). This suggestion is built on the empirical evidence of the higher UV stability of double-stranded RNA samples as compared to single-stranded molecules (Bishop et al. 1967; Jagger

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[1]Incidentally, the interplay between supporting and erasing energy fluxes, which was disclosed during the aforementioned simulations (Mulkidjanian et al. 2003; Mulkidjanian 2009), should also persist on a higher, organismic level. Indeed, let us take a hare as an example. Via consumed plants, the hare is supported by solar energy. How can the "erasing" flux of solar energy affect the hare? The hare, of course, has a chance to dye of sunstroke. The probability of such indiscriminative elimination is, however, negligibly small. Much larger is the probability of encoutering a fox that (i) exploits a different flow of solar energy than the hare and (ii) can catch the hare, but only if the latter is not smart enough. Hence, one energy flow sustains the population of hares, while the other energy flux, which supports the foxes, cares for the fitness of hares. It is tempting to speculate that the interplay between supporting and erasing energy fluxes might represent the physical essence of biological evolution (see Lotka (1922); Darlington (1972); Danchin (2009) for related discussions).

1976; Koonin et al. 1980). Recently, the physical background of the higher photostability of paired nucleotides has been clarified. For the nucleotides that form a Watson–Crick pair, the lifetime of the excited state has been estimated to be as low as a few femtoseconds (Abo-Riziq et al. 2005), i.e., ca. one hundred times shorter than that of single bases (Cadet and Vigny 1990; Cohen et al. 2004; Crespo-Hernandez et al. 2004, 2005; Satzger et al. 2006). This extremely short lifetime has been attributed to excited-state deactivation via electron-driven proton shuttling between the bases (Sobolewski et al. 2005; Perun et al. 2006; Frutos et al. 2007). It is noteworthy that other possible (non Watson–Crick) conformers of paired nucleobases have not shown these unique photochemical properties (Abo-Riziq et al. 2005). It has been suggested "*that the biologically relevant Watson-Crick structures of GC and AT are distinguished by uniquely efficient excited-state deactivation mechanisms which maximize their photostability*" (quoted from (Sobolewski and Domcke 2006)). Hence, the flux of solar energy may have supported the formation of RNA-like polymers in two complementary ways, namely (1) by driving fortuitous photopolymerization events, and (2) by supporting the relative enrichment of the photostable RNA-like polymers via the systematic photo-dissociation of more labile molecules.

The minerals of the aforementioned ZnS-enriched precipitates around continental hot springs, besides catalyzing abiogenic photosynthesis of useful metabolites and serving as templates for the synthesis of longer biopolymers from simpler building blocks, could protect the first biopolymers from photo-dissociation by absorbing the excess radiation (Biondi et al. 2007; Mulkidjanian 2009). In addition, Zn^{2+} ions are known for their exclusive ability to catalyze the formation of the naturally occurring $3'–5'$ linkages upon abiogenic polymerization of nucleotides (Bridson and Orgel 1980; van Roode and Orgel 1980).

The selection of first proteins may have differed from the selection of nucleotides. Proteins are synthesized by the RNA molecules of ribosomes (Steitz and Moore 2003). Recently, the ancient active center, supposedly capable of catalyzing peptide bond formation, have been identified within the large ribosomal subunit (see (Bokov and Steinberg 2009; Davidovich et al. 2009) and the chapter by Lankenau). Therefore, polypeptides could begin evolving only after the emergence of the first pro-ribosomes[2]. The exclusive property, which is common for proteins and distinguishes them from other random polymers, is the large energy gap between the energy of the most stable, native protein structure and the energy spectrum of other possible structures, e.g., misfolded or denatured states (Finkelstein and Ptitsyn 2002). In other words, proteins, unlike random polymers, can endure large thermal quanta without changing their conformation. Because the large part of their peptide bonds is tightly packed within the hydrophobic protein

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[2]These considerations do not rule out the possibility of abiotic peptide formation (see Chaps. 5–8 and 12). Abiogenically formed peptides may have paved the way to the biogenic protein synthesis by serving as nourishment for the first RNA-based organisms and by protecting them from different hazards (Mulkidjanian 2009).

core, the folded proteins are more resistant to hydrolysis, *cf.* (de Duve 1987). Hydrolysis is driven by thermal energy, via the Brownian motion of water molecules. Hence, while the energy of light may have served as a selection force for the first abiogenically synthesized (poly)nucleotides, the proteins, after being produced by pro-ribosomes, may have been selected by thermal energy; this selection process could favour the accumulation of folded proteins on account of simpler, but unfolded polypeptides. It is tempting to speculate that one of the initial functions of proteins could be the protection of RNA-like polymers from overheating and denaturation (Mulkidjanian 2009).

In summary, the unique photochemical properties of nucleotides and their natural polymers suggest the involvement of UV light as a selecting factor during the initial stages of evolution and point to illuminated habitats as the tentative cradles of life.

1.4 Compartmentalization and the Emergence of Membrane Bioenergetics

In modern prokaryotes, the energetics is intimately coupled with compartmentalization since the main energy-converting machinery is embedded in the cell membrane. This machinery consists of diverse enzyme complexes that can pump protons and/or sodium ions out of the cell yielding an electrochemical ion gradient across the membrane. This gradient can be used by the rotary membrane ATP synthases for synthesis of ATP (see (Cramer and Knaff 1990; Mulkidjanian et al. 2009) for reviews). In the vast majority of cases, including the animal mitochondria and the plant chloroplasts, the ATP synthases are driven by proton gradients; only in some prokaryotic organisms, the ATP synthases translocate sodium ions. Not surprisingly, several authors suggested that the very first organisms could utilize pH gradient for synthetic reactions, (see e.g., (Russell 2007; Lane et al. 2010)). This beguiling scheme, however, is not supported by phylogenomic analysis of the membrane rotary ATPases (Mulkidjanian et al. 2007, 2008a, 2008b; Mulkidjanian et al. 2009; Dibrova et al. 2010). This analysis is instrumental since the rotary ATPase was operative already in the LUCA (Gogarten et al. 1989; Mulkidjanian et al. 2007, 2008b) and is the only ubiquitous enzyme that is involved in membrane bioenergetics.

The membrane ATP synthases are complex rotary machines that couple ATP synthesis and hydrolysis with the translocation of protons or sodium ions across the membrane, (see (Mulkidjanian et al. 2009) for a review). The direction of rotation depends on whether enzyme synthesizes ATP by using the ion gradient or, the other way around, translocates ions by hydrolyzing ATP. These ATP synthases/ATPases are present in all organisms and exist in distinct archaeal (A/V-type) and bacterial (F/N-type) versions (Hilario and Gogarten 1998; Dibrova et al. 2010). Both archaeal and bacterial ATPases can be proton- or sodium-translocators, respectively. Comparative analyses of the crystal structures of the ion-binding membrane

subunits of Na^+-translocating archaeal and bacterial ATPases (Meier et al. 2005; Murata et al. 2005) have shown that nearly identical sets of amino acid residues were involved in Na^+ binding; these sets almost perfectly superimpose in space (Mulkidjanian et al. 2008b). Since a convergent emergence of the same set of Na^+ ligands in several lineages looked extremely unlikely, the similarity of the Na^+-binding sites in the two prokaryotic domains led to the suggestion that the last common ancestor of the extant rotary ATPases possessed a Na^+-binding site (Mulkidjanian et al. 2008b).

The ion specificity of the rotary ATPases is decisive for the nature of the bioenergetic cycle in any organism. Although membrane ion gradients can be generated by a plethora of primary sodium or proton pumps, the rotary ATPases are unique in their ability to use these gradients for producing ATP (Cramer and Knaff 1990). Therefore, evolutionary primacy of the sodium-binding ATPase indicates the evolutionary primacy of the sodium-based bioenergetics. This evolutionary primacy could be explained by the higher resistance of lipid membranes to sodium ions as compared to protons (Deamer 1987; Nagle 1987; Konings 2006). As argued in more detail elsewhere (Mulkidjanian et al. 2008b, 2009), creating a non-leaky membrane that can hold a large proton potential, needed to drive the synthesis of ATP, is a harder task than making a sodium-tight membrane. The representatives of the three domains of life employ distinct solutions to make their membranes tighter to protons, (see (Haines 2001; Konings 2006; Mulkidjanian et al. 2008b) for details). This fact supports the suggestion on the independent transition from the sodium to proton bioenergetics in different lineages. This transition was accompanied by losses of different Na^+-ligands in different lineages and happened after the separation of *Bacteria* from *Archaea* (Mulkidjanian et al. 2008b, 2009). Hence, the phylogenomic analysis (Mulkidjanian et al. 2007; Mulkidjanian and Galperin 2010a, b; Mulkidjanian et al. 2009; Dibrova et al. 2010) rules out the possibility that the first cells could rely on proton-dependent bioenergetics.

The membrane proteins show a non-random distribution of hydrophobic and hydrophilic amino acid residues; hence, they should have emerged after the water-soluble proteins in which this distribution is quasi-random (Finkelstein and Ptitsyn 2002). Arguably, the emergence of modern, ion-tight membranes should have taken place relatively late, after the separation of *Bacteria* from *Archaea* (Mulkidjanian et al. 2008b, 2009), since the membranes of *Archaea* and *Bacteria* are fundamentally different (Pereto et al. 2004; Koonin and Martin 2005; Koga and Morii 2007). These and some other considerations have prompted the "lipids late" evolutionary scenarios (Koonin and Martin 2005; Koonin 2006; Mulkidjanian et al. 2009; Mulkidjanian and Galperin 2010a) where the advent and evolution of simple, virus-like, RNA/protein life forms preceded the emergence of lipid membranes[3].

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[3]This suggestion does not contradict the possibility of abiotic formation of amphiphilic molecules, see the chapters by Egel and Sturgis in this volume. Such abiotically formed molecules, by serving as food for the first organisms, may have paved the way to the biogenic syntheses of lipids via reversion of the respective catabolic chains (Mulkidjanian 2009).

The suggested late emergence of lipid membranes then posits the question of the compartmentalization of the first life forms. The separation of replicating entities, which nowadays is achieved by lipid membranes, is a condition of the biological evolution and should have taken place from its very beginning. The separation of the first life forms into discrete units could, however, proceed even without lipids. Russell and co-workers have hypothesized that the early stages of evolution may have taken place inside the "FeS bubbles" – the pores of the iron-sulfide precipitates at the aforementioned deep-sea hydrothermal vents (Russell and Hall 1997; Martin and Russell 2003; Russell and Hall 2006). This "inorganic" solution of the compartmentalization problem could be applied also to the precipitates at the sites of continental geothermal activities (Mulkidjanian 2009; Mulkidjanian and Galperin 2009). Compartmentalized structures should have formed around terrestrial hot springs as well; they form around hot springs and fumaroles even in the modern volcanic systems (Kardanova 2009; Morgan et al. 2009). Such habitats could accommodate the first life forms; the affinity of the evolutionary old proteins to the Zn^{2+} ions (Mulkidjanian and Galperin 2010b, 2009) indicate that the first replicators may have been shaped within mineral compartments that were Zn-enriched. The replicating entities in each compartment could share a common pool of metabolites and genes, so that each interacting consortium would comprise a distinct evolutionary unit. Such a scheme, with an extensive (gene) exchange between the members of one consortium but not between different, mechanistically separated consortia solves a major conundrum between the notion of extensive gene mixing that is considered a major feature of early evolution (Woese 1998) and the requirement of separately evolving units as subjects of Darwinian selection (Koonin and Martin 2005; Mulkidjanian et al. 2009). The advantage of the sub-aerial ZnS-enriched porous precipitates, as compared to the FeS bubbles at the sea floor (Russell et al. 1988; Martin and Russell 2003; Russell 2007), is that the Zn ions are redox inert while the redox active Fe^{2+} ions and FeS clusters can generate harmful hydroxyl radicals and are therefore detrimental for the "naked" RNA molecules (Meares et al. 2003; Cohn et al. 2004; Luther and Rickard 2005; Cohn et al. 2006). In addition, the suggested scenarios of the emergence of life at the deep-sea hydrothermal vents (Russell et al. 1988; Martin and Russell 2003; Russell 2007; Martin et al. 2008) do not account for the exceptional photostability of natural nucleotides and their polymers.

Generally, the central theme in the evolution of compartmentalization should have been the increasing tightness of cell envelopes. Szathmáry and co-workers have recently developed and modeled a set of evolutionary scenarios that exemplified the crucial importance of the interaction and exchange between the primeval replicating entities for the stability of their populations (Szathmáry 2006; Szathmáry 2007; Könnyű et al. 2008; Branciamore et al. 2009). According to Szathmary and co-workers, an increase in the complexity of pro-cells should have been accompanied by their progressive sequestering from the environment, so that the gradual build up of enzymatic pathways inside the pro-cells would be

accompanied by decrease in membrane permeability, ultimately paving the way to the membrane bioenergetics that required ion-tight membranes.

In sum, the intimate coupling between the membrane bioenergetics and the cellular compartmentalization, which is observed in modern prokaryotes, should have been absent during the first evolutionary steps. The first compartments inhabited by consortia of replicating entities may have been inorganic, they may have been built of ZnS-enriched sediments around continental hot springs. The membrane bioenergetics should have appeared much later, only after the emergence of ion-tight lipid membranes, with the sodium-dependent energetics appearing first and the proton-dependent energetics emerging last.

1.5 Evolution of the Early Energy-Converting Mechanisms

Figure 1.1 suggests how the early energy-converting mechanisms may have evolved. The scheme places the emergence of the first replicating entities within the ZnS-enriched, photosynthesizing precipitates around continental hot springs. As in the case of modern continental volcanic systems (Karpov and Naboko 1990; Kardanova 2009; Karpov et al. 2009), the Zn^{2+} ions of metalliferous fluids, being carried by geothermal waters, should ultimately precipitate as ZnS particles. Since ZnS is the slowest precipitating transition metal sulfide (Seewald and Seyfried 1990; Metz and Trefry 2000), the ZnS-enriched precipitates should fall out further off the geothermal springs and form interwoven "haloes" around them (Mulkidjanian and Galperin 2009). While carried by geothermal fluids, the precipitating ZnS particles should have mixed with the clay particles, the products of rock-weathering; in this case, compartmentalized clay-ZnS sediments may have formed. ZnS crystals, as powerful photocatalysts, may have photosynthesized diverse organic compounds from CO_2 under the solar UV light. In addition, the hydrothemal fluids should have brought organic molecules synthesized within the hot rocks (Sleep et al. 2004). The organic compounds could become phosphorylated in the presence of hydrothermally derived (hypo)phosphite, yielding diverse phospho-derivates that could condensate into larger molecules, in particular, during occasional dry periods. Among a plethora of different carbonaceous molecules (see Chap. 2), the natural nucleotides could accumulate as the most photostable structures, their polymerization and folding into double-stranded segments should be favored by further increases in the photostability (Mulkidjanian et al. 2003; Sobolewski and Domcke 2006; Mulkidjanian 2009; Powner et al. 2009; Serrano-Andres and Merchan 2009).

Occasionally, some aggregates of photoselected RNA-like polymers may have shown the ability of self-replication. The multiplication of such replicators should have led to the depletion of the abiotically synthesized nucleotides. The competition for "building blocks" may have favoured the emergence of catalytic activities enabling the synthesis of nucleotides from the available simpler organic molecules by ribozymes. Ultimately, the broadening of the catalytic repertoire of ribozymes
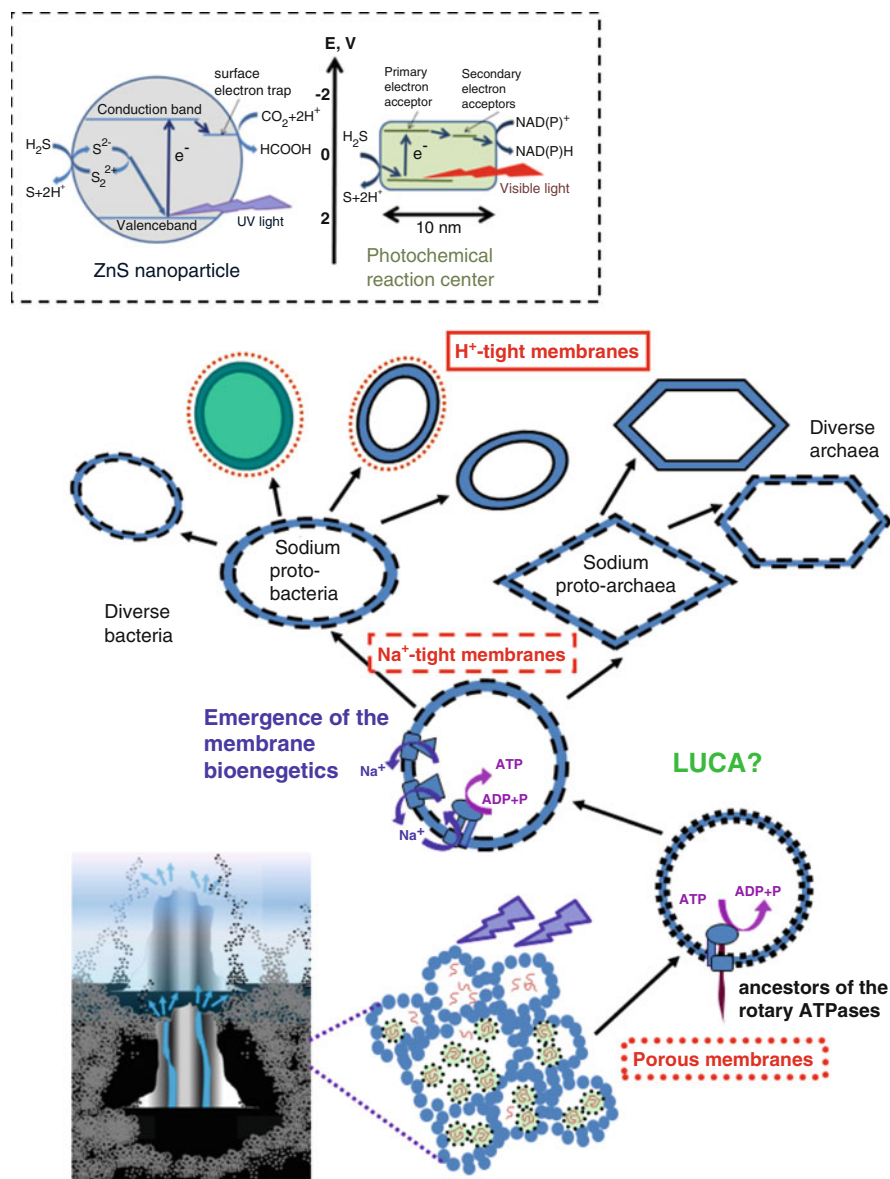
Fig. 1.1 The proposed scenario for the evolution of the early energy-converting mechanisms. The scheme suggests the emergence of the first replicating entities within ZnS-enriched precipitates around continental hot springs. Note that the ZnS particles (*grey dots*) precipitate farther than other transition metal sulfides (The picture is modified from Mulkidjanian and Galperin (2010a) and is based on data from Metz and Trefry (2000); Kelley et al. (2002); Russell (2006)). The evolution of membranes is shown as a transition from primitive, porous membranes that were leaky both to Na^+ and H^+ (*dotted lines*), via membranes that were Na^+-tight but H^+-leaky (*dashed lines*) to the modern-type membranes that are impermeable to both H^+ and Na^+ (*solid lines*). As the common

could result in the synthesis of polymers other than ribozymes, proteins in the first line. As argued elsewhere (Mulkidjanian and Galperin 2007; Danchin 2009; Mulkidjanian 2009; Mulkidjanian and Galperin 2009), the enzymatic repertoire of the evolutionary oldest proteins indicates that the energetics of the first organisms was based on the reactions of phosphate group transfer. As argued by Watson and Milner-White (Watson and Milner-White 2002), the phosphate-binding "nests" are formed by the protein backbone and therefore could be present already in the very first polypeptides (see also Chap. 7). In the described system, ATP could be recycled not only chemically, via substrate level phosphorylation (i.e., by phosphate group transfer from the abiogenically produced phosphorylated compounds), but also photochemically, via the light-driven phosphorylation of ATP at mineral surfaces (see (Kritsky et al. 2007)). The honeycomb-like, ZnS-enriched mineral compartments could provide, besides shelter and nourishment, an ample supply of reducing equivalents for biosyntheses.

The ZnS precipitates would have attenuated the UV component of solar light, thus providing shade for the inhabitants of the deeper-lying compartments. Hence, a stratified system could be established with the illuminated external layers being involved in the "harvesting" of reduced organic compounds and the deeper, less productive, but more protected layers providing shelter for the first replicating entities in their pores (see Fig. 1.1). As argued elsewhere (Mulkidjanian 2009; Mulkidjanian and Galperin 2009), the ZnS-enriched precipitates should have formed large topologically connected fields around the hot springs. The displacement of life forms within these fields by water flows could ensure the exchange the spreading of the genetic material. The precipitation, proper, should have led to a continuous formation of new, empty compartments at the surface. The life forms should have thrived to propagate into these new compartments; otherwise, they could become buried and isolated from the sources of organic molecules. The porosity of the ZnS-enriched precipitates (Takai et al. 2001; Petersen et al. 2005) would have enabled some metabolite transport between the surface layers. Both the gradient of light and the interlayer metabolite exchange are typical of

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Fig. 1.1 (continued) ancestor of the rotary membrane ATPases possessed a Na^+-binding site (Mulkidjanian et al. 2008a, 2009), the LUCA, most likely, could possess sodium energetic (see Mulkidjanian et al. (2007, 2008b, 2009) for details). The emergence of the membrane energetic is shown as a reversion of the Na^+-translocating ATPase in a sodium-rich sea water. The emergence of elaborated proton-tight membranes is shown to be followed by the rise of the (bacterio) chlorophyll-based photosynthesis among bacteria; the phototropic bacteria are shown in green (see main text, and Mulkidjanian et al. (2006); Mulkidjanian and Galperin (2009) for details). *Insert*: A comparison of energy diagrams for a photosynthesizing ZnS nanoparticle (*left panel*, see also Chap. 4 where the mechanism of semiconductor-mediated photosynthesis is discussed) and a Bacterial photochemical reaction center (*right panel*, a primitive, sulfide-oxidizing reaction center complex of green sulfur Bacteria is shown schematically as an example, see Frigaard and Bryant (2004); Jagannathan and Golbeck (2008) for reviews on this type of reaction centers) (The diagram is taken from Mulkidjanian and Galperin (2009))

modern stratified, phototrophic communities (e.g., stromatolites (Nisbet 1991; Nisbet and Sleep 2001; Westall et al. 2006)).

The next stage of evolution is envisaged as selection for increasingly tighter cellular envelopes, perhaps initially protein-made. Such envelopes may have prevented the uncontrolled escape of polymers, but still enabled the sharing of small molecules (Mulkidjanian et al. 2009). At this stage, the energetics consisted in the interplay between the delivery of abiogenically produced organic molecules (metabolites) at the sites of geothermal activity and the increasingly complex heterotrophy of the first organisms (see also (Lazcano and Miller 1999)). This heterotrophy may have been based on coupling the exergonic breakdown of (phosphorylated) metabolites with endergonic (bio)synthetic reactions. The same interplay of autotrophy (phototrophy and chemotrophy), on the one hand, and heterotrophy, on other hand, drives the majority of terrestrial communities today.

The emergence of the first lipid membranes may have been coupled with the spreading of the life forms into the Fe-enriched habitats. Generally, the environments of the primordial Earth should have been enriched in well-soluble ions of Fe^{2+}, the dominating transition metal ion of the primordial aqueous systems (with an estimated content of $10^{-6}-10^{-5}$ M (Williams and Frausto da Silva 2006; Anbar 2008)). Since lipids can prevent the damaging action of iron-containing minerals on RNA (Cohn et al. 2004), the need to protect polynucleotides from the Fe^{2+} ions may have driven the transition towards lipid-encased life forms. The isolation by lipid membranes should have prompted the emergence of enzymes that could extract reducing equivalents, needed for synthetic reactions, from inorganic electron donors such as H_2 and H_2S, and for the transportation of these reducing equivalents into the cells. First such enzymes, most likely, could use the FeS clusters, which are least structurally demanding (Watson and Milner-White 2002; Russell et al. 2007), as redox cofactors. Still, unless the lipid membranes became electrically tight, no coupling between the redox reactions and the synthesis of ATP via the membrane potential was possible.

The very difference between the ionic compositions of cellular cytoplasm and of the seawater (Williams and Frausto da Silva 2006) implies that the cellular organisms could colonize the seawater only after attaining ion-tight membranes. Indeed, according to the principle of chemistry conservation (see e.g. (Macallum 1926; Mulkidjanian and Galperin 2007)), primordial cells would strive to keep their internal chemistry similar to the chemical compositions of the brine in which the first life forms had emerged. Since the cytoplasm of all cells contains more potassium than sodium, and the translation systems specifically require K^+ ions for functioning (Bayley and Kushner 1964; Conway 1964; Spirin et al. 1988), the first life forms were likely to emerge in K^+ -rich environments (Macallum 1926; Natochin 2007; Mulkidjanian 2009; Mulkidjanian and Galperin 2010a). Hence, besides striving to maintain a high internal Zn level, the first cells should also have been challenged by the high sodium content in the ocean. Therefore, the propagation of cells in sea water should have specifically required ion-tight membranes and ion pumps capable of ejecting Na^+ ions out of the cell. As argued elsewhere (Mulkidjanian et al. 2009; Dibrova et al. 2010), the common ancestor of the rotary

ATPases may have acted as an ATP-driven, outward Na^+-pump. This enzyme complex, owing to its rotating scaffold, would be potentially able to translocate Na^+ ions in both directions. At high ocean salinity, a reversal of the rotation would result in Na^+-driven synthesis of ATP by this primordial rotary machine (see Fig. 1.1). Already in the Archean eon, the concentration of Na^+ in the ocean water was approximately 1 M (DeRonde et al. 1997; Foriel et al. 2004; Pinti 2005), i.e., it was high enough for the rotary machine to switch from ATP hydrolysis to the ATP synthesis mode. This event marked the birth of membrane bioenergetics; together with the ancient outward Na^+ pumps, the ancestral rotary ATP synthases would complete the first, sodium-dependent bioenergetic cycle in a cell membrane. Only after this stage, further membrane-embedded energy-converting systems, such as methanogenesis or anoxic respiration (Thauer et al. 1977; Thauer et al. 2008), could start to emerge.

The final evolutionary step in the present scenario is envisaged as a transition(s) to the proton-tight, elaborate membranes that provided better protection to the cells. These membranes, in addition, were more lucrative from the point of view of energetics, since the proton transfer events could be chemically coupled to redox reactions, especially those of water and diverse quinones, thus enabling the advent of efficient redox-and light-driven generators of membrane potential (Mulkidjanian et al. 2008b, 2009; Mulkidjanian and Galperin 2010a). Since the membranes are fundamentally different in Archaea and Bacteria (Pereto et al. 2004; Koonin and Martin 2005; Koga and Morii 2007), it is tempting to speculate that the separation of the two domains might have been coupled with spreading of the two branches of the LUCA's descendants, perhaps, differing in their habitats and metabolic strategies, away from the ZnS-enriched habitats (Mulkidjanian and Galperin 2009).

The decreased dependence on the ZnS-mediated photosynthesis may also have paved the way to the emergence of the (bacterio)chlorophyll-based photosynthesis. Figure 1.1 (insert) illustrates the similarity between physical mechanisms of the (bacterio)-chlorophyll-based and ZnS-based photosyntheses, which both include light-induced charge separation followed by energy loss needed for stabilization of reduced states (see also (Halmann et al. 1980; Mulkidjanian 2009; Mulkidjanian and Galperin 2009) and Chap. 4). This figure also shows that the same reaction of sulfide oxidation could be used to re-fill the photo-generated electron vacancies (holes). Hence, the emergence of biogenic photosynthesis might represent a clearcut case of a functional takeover – with the primeval photochemical reaction centers and primordial Calvin cycle together accomplishing the function that the ZnS-enriched precipitates could perform alone, namely the utilization of solar energy for fixation of CO_2.

After the ancestors of cyanobacteria attained the ability to use the solar light for extracting electrons from water (Mulkidjanian et al. 2006), oxygen, the byproduct of this reaction, shifted the redox balance of the biosphere. This development led to the emergence of increasingly complex organisms, striving to decrease the oxidative damage to their cells (Broda 1975; Shnol 1981; Skulachev 1998; Williams and Frausto da Silva 2006). The consideration of these relatively recent evolutionary events is outside the scope of this volume.

1.6　Outlook

Here, I have considered the natural energy fluxes that could be involved in sustaining the first life forms. Apparently, solar light should have played the major role. Rather counter-intuitively, the gradients of thermal energy could also be supportive. They may have been involved in the formation of hydrogen and carbonaceous compounds within the hot, iron-containing rocks, as well as in the selection of the folded, thermostable proteins.

The evolution of biological energy conversion may have started from the selection of RNA-like polymers that could promptly get rid of the UV quanta or, in other words, "process" these quanta without undergoing photodamage. The ability to discard the energy of light is less structurally demanding than the ability to store and exploit energy; so, this ability may have been inherent already in simple organic molecules. The energy requirements of the first replicators could have been covered by the breakdown of "nutrients" that were produced in abiogenic reactions. Only the emergence of biogenic dielectrics, namely proteins and lipid membranes, enabled the storage of the energy of light in the form of charge-separated states, physically analogous to those involved in the abiotic, ZnS-mediated photosynthesis. As the accessible assets of reducing power ran out with the oxygenation of the atmosphere, living organisms had to increase their complexity, if they wanted to access and exploit new energy sources.

The common energetic denominator of living organisms – throughout the whole evolutionary time span – may have been not the ability to exploit high-energy quanta, which could not be inherent in the simplest life forms, but the ability to "deal" with such quanta – in a general sense. From this viewpoint, one can follow a continuous evolutionary thread from the emergence of life to the modern struggle of mankind for energy.

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