

CONCEPTS AND DYNAMICS: A THEORETICAL ISSUE OF OLEB

When I was asked by Alan Schwartz whether I felt willing to edit a thematic issue centred on theoretical issues for this journal, it did not take me much time to say yes. I think that the general readership of OLEB ought to be informed about the vigorous development of theoretical approaches towards cracking one of the major outstanding open riddles of contemporary science, as we see it.

For biology, chemistry is much more than just a method: biology is rooted in, and is firmly based on, the laws of chemistry. If somebody comes along with an idea in biology that violates these laws that person is likely to face the harshest criticism, and justifiably so. The triumph of biochemistry and molecular biology in the 20th century clearly marks the enormous debt of biology to chemistry. In an average curriculum, biology students are expected to learn quite a bit of chemistry, but the situation is by no means symmetric. This may change in the future, however.

Biology seems to be paying back its debt to chemistry, and the field of the origin of life is a prime scientific territory where this is happening in 'real time'. There are a number of reasons for this. First, the origin of life cannot be readily explained without some idea (definition) of what 'life' actually means. This exercise cannot be successful without a profound contribution coming from biology. Otherwise, the result is likely to be a cop-out, or at least moving the goalpost, as it were. I am bound to agree with those (see a recent volume edited by Pályi *et al.*, 2002) who cannot accept definitions defining life in relation to RNA, for example. Attempts at synthesizing or selecting for an autonomously replicating RNA molecule are more than welcome, but tying the definition of life to a population of such molecules is putting the cart before the horse. I predict that as soon as this goal is achieved by somebody, chemists and biologists will immediately ask the question: 'But how did 'real' life originate?' – whatever the successful achievers may or may not claim about their results. And the reason for this is that life, as we know it, even in its simplest manifestations, comes in a form of some kind of cell. Thus, if we follow the traditional route of science by abstraction and idealisation, we are almost forced to accept that a minimum model of life should be that of a minimal cell. Indeed, the important but unjustifiably neglected work of Tibor Gánti, to be published by Oxford University Press soon (2003) is a good case in point. He convincingly shows that life is about the organization of qualitatively different chemical systems, of which only one combination: the so-called chemoton, comprising metabolism,



template polycondensation and a membrane boundary satisfies all criteria of life established with some rigor.

Secondly, ultimate explanation in biology always comes from evolution by natural selection. Manfred Eigen with his seminal work in 1971 called the attention of biologists and chemists alike to the fact that the Darwinian dynamic is relevant for chemists when they want to understand the origin of life. Evolutionary units, capable of multiplication, heredity and heritable variation (cf. Maynard Smith, 1986) in the realm of chemistry logically as well as historically precede life. Survival of the fittest rests on a basically Malthusian type of growth, with an exponential tendency if food is plentiful. Ever since the pioneering work of von Kiedrowski (1986) students of the field know that exponential growth of replicators, leading to selection, can by no means be taken for granted: it must itself have evolved somehow. We do not yet know exactly how.

Thirdly, it may not be obsolete to point out that the very concept of 'replicator' has been conceived by an evolutionary zoologist (Dawkins, 1976), although the term may now be more frequently cited in chemistry than in biology. Undoubtedly, Dawkins' conceptualisation has fertilized evolutionary thinking, including its applications to the origin of life.

Fourthly, it does seem that insight gained from the study of natural selection under the assumption of 'population structure' is playing a central role in the understanding of how primitive replicators could have evolved, aided by dynamical coexistence, into a primordial genome. The need for some kind of resolution comes from Eigen's discovery (1971) of the error threshold problem, although his then favoured alternative: the hypercycle, is losing its central place in contemporary accounts. It is striking that (mineral) surfaces do not seem to be important only because they have favourable thermodynamic and kinetic effects within the chemical realm (see Wächtershäuser, 1988 for a recent advocacy of why surfaces were indispensable), but natural selection also takes a favourable course when acting in structured populations.

Contributions to this thematic issue make an advance in several of the mentioned problematic fields. Let me present a brief survey then. Several authors deal with the questions of issues of the dynamical coexistence of replicators. From what I said about the importance of population structure it could be inferred that the 'soup' is a hopeless scenario, at least from the point of view of dynamical coexistence of unlinked replicators in a primordial genome. A very surprising counterexample is clearly described by Scheuring *et al.*: they show that incomplete mixing in open chaotic flows, rather prevalent in natural waters, can guarantee such coexistence even without surfaces. The chaotic flows around sea hydrothermal vents could be the natural choice for such a scenario. Otherwise the papers deal with replicator populations on surfaces (Rosas and Fontanari, Scheuring *et al.*, Hogeweg and Takeuchi) or in reproducing compartments (Hogeweg and Takeuchi, Santos *et al.*). Studies of surface populations echo the effects known from population biology: the fact that one interacts only with one's neighbours promotes

competitive and mutualistic coexistence. A very important condition is spelled out by Scheuring *et al.*: the results, frequently demonstrated by the application of the cellular automaton technique, must be sufficiently robust. Imagine, for example, that the mineral surface on which replicator dynamics unfolds is 'patchy' in some important respect, such as the strength of adsorption. It can be shown that under such a simple assumption the hypercycle, producing nicely spiralling arms without a parasite, is killed off in its presence.

Although the various contributors make a strong case for the importance of surfaces in promoting dynamical coexistence and functional evolution (see e.g. Szabó *et al.* 2002 for a recent, related result), it goes without saying that at some stage compartments must have replaced surface dynamics. Compartments are, by clonal selection, not only the best countermeasures against molecular parasites (a problem recognized by Maynard Smith, 1979), but the best vehicles for the selection of molecular function, such as catalytic aid in metabolism (Zintzaras *et al.* 2002). Two papers (Hogeweg and Takeuchi, Santos *et al.*) deal with compartmentalized systems. Hogeweg and Takeuchi perform an in-depth study of the effect of compartmentation on the error threshold. They show that reproducing compartments can raise the error threshold (and thus can maintain longer genomes) provided compartment dynamics is not blind to molecular functionality. Indeed, this assumption was already present in the first formulation of compartment dynamics as applied to dynamical coexistence of genome pieces during the origin of life (the stochastic corrector model: Szathmáry and Demeter, 1987). Santos *et al.*, taking the stochastic corrector model (a reproducing bag of functional genes) as a starting point enquire about the origin of sex, first walking in, but then diverging from, the footsteps of Bernstein *et al.* (1984). This seems relevant when compared with ideas about some form of molecular mixis before the last universal common ancestor (LUCA; Woese, 1998). It is shown that the sex habit, understood as fusion and genic reassortment between protocells, can spread by the action of selfish agents, but that it also entails occasional recovery from parasite attack.

The present genetic mechanism, with its 4-digit genetic and 20-digit catalytic alphabet, is too complex to have arisen in one major step. Enquiry about some piecemeal origin scenario is thus highly justified. Mac Dónaill presents an intriguing re-analysis of the problem of why we have basically four digits in the genetic alphabet, although from a purely chemical point of view one could have fewer or more. By the application of coding theory he cogently argues that the present situation is favoured if two aspects, error minimisation and functional density, are both taken into account. Three authors go beyond the RNA world and enquire about the structure of the genetic code. Freeland presents a nice overview and fleshes out a new idea about the structure of the genetic code; namely, that it favours evolvability of protein function. It is somewhat difficult to disentangle cause and effect at the present stage, however. Even the fact that the canonical genetic code excels at error minimisation could be a side effect of the condition that related amino acids have once been recognized by related RNA aptamers in

the RNA world. Di Giulio elaborates on the idea (Wong, 1991; Szathmáry, 1990) that the only plausible driving force for the evolution of protein synthesis could have been selection for increased catalytic potential. He tries to explain the origin of coding and translation starting from a stage where tRNA-like molecules and pre-rRNA molecules participated in diverse metabolic functions and catalytic actions: the present stage is the result of an evolutionary narrowing down, as it were. I have favoured a 'cleaner' scenario with tRNA-like 'handles' charged with amino acid cofactors (Szathmáry, 1999). This and several other contrasting views about the code (such as the relative role of error minimisation and amino acid biosynthetic kinship) are open to further theoretical and experimental tests. Weberndorfer *et al.* simulate code evolution by resorting to a cunning shortcut. Once again, they are dealing with compartments, where a primitive genetic code and translation are already in place (perhaps cleverly, they thus avoid the problem itself). The only functional protein they allow to evolve, accompanied by code evolution, is an RNA polymerase. For this didactic simulation they assume that it must converge on a presently known example. They successfully demonstrate that code evolution does proceed under these assumptions. More investigations are needed in order to have a statistical pattern, however.

Finally, after all these delicious courses, a paper intended for desert. Horváth *et al.* argue for a case of life currently existing on Mars. They claim that the so-called dark dune spots of the polar regions of Mars could be excellent habitats for some photosynthetic organisms, and that they indeed are. Astrobiology is fashionable today, despite the relative paucity of testable *bona fide* hypotheses. Although the paper presented here may be shocking, it does present a testable idea. If life is found on Mars someday, it will be interesting to learn about its basic features, including the genetic material and the catalytic molecules it applies. Even if the two biota turn out to be related (due to past frequent meteorite exchange between the two planets), they are likely to have undergone a few billion years of decoupled evolution. Given the fact that there are deviations from the canonical genetic code even on earth today, it would be fascinating to find out about related traits of a Martian living world.

If readers of this issue will realize that advance in the field cannot happen without theoretical insights, the authors will be overjoyed.

EÖRS SZATHMÁRY

References

- Bernstein, H., Byerly, H. C., Hopf, F. A. and Michod, R. E.: 1984, Origin of Sex, *J. Theor. Biol.* **110**, 323–351.
- Dawkins, R.: 1976, *The Selfish Gene*, Oxford University Press.
- Eigen, M.: 1971, Self-organization of Matter and the Evolution of Biological Macromolecules, *Naturwiss.* **58**, 465–523.

- Gánti, T.: 2003, *Principles of Life*, Oxford University Press.
- Maynard Smith, J.: 1979, Hypercycles and the Origin of Life, *Nature* **280**, 445–446.
- Maynard Smith, J.: 1986, *The Problems of Biology*, Oxford University Press.
- Pályi, G., Zucchi and Caglioti, L. (eds): 2002, *Fundamentals of Life*, Elsevier, Paris.
- Szabó, P., Scheuring, I., Czárán, T. and Szathmáry, E.: 2002, *In Silico* Simulations Reveal that Replicators with Limited Dispersal Evolve Towards Higher Efficiency and Fidelity, *Nature* **420**, 360–363.
- Szathmáry, E.: 1990, ‘Useful Coding before Translation: The Coding Coenzymes Handle Hypothesis for the Origin of the Genetic Code’, in B. Lukács *et al.* (eds), *Evolution: From Cosmogenesis to Biogenesis*, KFKI-1990-50/C, Budapest, pp. 77–83.
- Szathmáry, E.: 1999, The Origin of the Genetic Code: Amino Acids as Cofactors in an RNA World, *Trends Genet.* **15**, 223–229.
- Szathmáry, E. and Demeter, L.: 1987, Group Selection of Early Replicators and the Origin of Life, *J. Theor. Biol.* **128**, 463–486.
- Von Kiedrowski, G.: 1986, A Self-replicating Hexadeoxy Nucleotide, *Angew. Chem. Int. Ed. Engl.* **25**, 932–935.
- Wächtershäuser, G.: 1988, Before Enzymes and Templates: Theory of Surface Metabolism, *Microbiol. Rev.* **52**, 452–484.
- Woese, C.: 1998, The Universal Ancestor, *Proc. Natl. Acad. Sci. USA* **95**, 6854–6859.
- Wong, J. T.-F.: 1991, Origin of Genetically Encoded Protein Synthesis: A Model Based on Selection for RNA Peptidation, *Orig. Life Evol. Biosphere* **21**, 165–176.
- Zintzaras, E., Mauro, S. and Szathmáry, E.: 2002, ‘Living’ under the Challenge of Information Decay: The Stochastic Corrector Model *versus* Hypercycles, *J. Theor. Biol.* **217**, 167–181.