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RESEARCH CONFERENCES

ESF-COST High-Level Research Conference

Systems Chemistry II: Evolution and Systems

Anna Grand Hotel • Balatonfüred, Lake Balaton • Hungary

18 - 23 October 2009

Chair: **Eörs Szathmáry,** Collegium Budapest, HU
Vice-Chair: **Dieter Schinzer**, University of Magdeburg, DE

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Highlights & Scientific Report

Conference Highlights

Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)

The conference was focusing on the unifying organisational and dynamic principles that link systems chemistry with other fields of science. Presentations went beyond chemistry that allowed participants to learn new ways of thinking about chemistry. The conference has served a twofold purpose: to strengthen the field of systems chemistry (as a sequel to the Maratea conference in 2008) and to commemorate the double anniversary of Charles Darwin (his birth and the publication of the Origin of Species), not forgetting that one of the two legs of systems chemistry in theoretical (especially evolutionary) biology. The conference presented a state-of-the-art overview of the attempts to analyze and identify different autocatalytic systems. The relationship to the origin of life has received special attention, in that the origin of membranes, templates and metabolic networks was considered by several speakers. The keynote speakers gave an overview of three different, very important topics: (1) the importance of the quantum world in our basic understanding, and the limitations of the brain set by evolution to deal with quantum phenomena, (2) the possible role of large, reflexively autocatalytic networks (in which the individual chemical species are not replicators by themselves), and (3) agent-based approaches to understanding economic equilibrium and some unifying principles for the social sciences. Darwin's now celebrated theory of evolution by natural selection was universally accepted thanks to the modern synthesis, which unites Darwinian reasoning with classical and population genetics. We are now experiencing a phase of extended evolutionary synthesis deepening and expanding the modern synthesis. The theory of niche construction (whereby organisms modify their environment with long-lasting positive effects on fitness) contributes to this advance. Systems chemistry, evolutionary economics, possible evolutionary approaches to brain dynamics are all part of this extended synthesis, discussed by various contributors at the meeting. The criteria of evolvability have been discussed at length at the meeting, as applied to alternative suggestion of early evolving systems. The same idea has been discussed in the context of experimental evolution of proteins, evolving from one function to another. The view of the RNA world (that there was an era more than 3.5 billion years ago, when RNA served as genes as well as enzymes) has received strong support in the form of two experimental approaches, the first demonstrating the possibility of a purely RNA-based oscillator (there is some evidence for a cyclically coupled template-replicating system with three RNA species), and second, short RNA molecules produced by in vitro selection are specifically binding amino acids and one of them catalyzes peptide bond formation.

☒ I hereby authorize ESF – and the conference partners to use the information contained in the above section on 'Conference Highlights' in their communication on the scheme.

Scientific Report

Executive Summary

(2 pages max)

One of the main goals of systems chemistry is the enquiry into the molecular-chemical roots of evolvable, organized complexity. The second COST-ESF meeting enjoyed the special occasion that the lecturers also celebrated the double anniversary of Charles Darwin, the main founding father of theory of evolution by natural selection. In recognition of this fact the scope of the meeting has been much broader than that of the preceding one (in Maratea, organized by COST Action chair Günter von Kiedrowski): participants also had the task to inform each other, and debate about, the general questions of evolution, from molecules to social evolution. Therefore, the fields of invitees ranged from theoretical physics to anthropology, while a good representation of chemists and molecular biologists was ensured.

The diversity and depth of topics is amply illustrated by the keynote speakers: Károlyházy spoke about the message of the spooky quantum world, and its relation to chemistry and the evolutionary limitations on cognition that render this world invariably weird; Stuart Kauffman investigated open and deep questions about the nature and plausibility of reflexively autocatalytic sets and the concept of agency (how a molecular system can utilize information to drive a thermodynamic work cycle); Herb Gintis discussed the foundations of social sciences and the agent-based models of economic behavior. The associated thinking styles and methodologies have penetrated practically all discussions of the meeting.

Traditionally, in systems chemistry scientists are concerned with three types of autocatalytic system: template replication, metabolic cycles and membrane growth and division. Several examples of these systems have been discussed, also in relation to the origin of biomolecular chirality. Coupling of these systems to yield system doublets (such as coupling of template replication with container growth) is a non-trivial problem, since the conditions must allow for the functioning of both systems and they must work together efficiently so that the unwanted side reactions do not tax the system to such a degree that coupled growth becomes impossible. In the meantime, analytic tools for systems chemistry are being developed.

There has been good exchange of theoretical and experimental investigators throughout the meeting; approaches to issues in the RNA world (where RNA molecules were enzymes and genes at the same time) are a good case in point. New experiments tackle, in a very promising way, the questions of the origin of the genetic code (allowing for translation of information in nucleic acids into proteins) and the possibility of oscillators made of replicationally coupled RNA molecules. These results are complemented by excellent insights about the nature of genotype to phenotype mapping in RNA structures.

Evolvability (the ability of a population of replicators to respond efficiently to directional selection) is a key issue of systems chemistry as well as evolution theory in general. In vitro selection of RNA molecules have shown how powerful artificial evolution can be. Scientists are interested in the question whether molecular systems without template replication can be evolvable in a Darwinian sense at all. This issue has been hotly debated during the meeting. Analysis of a particular model (picturing reproduction of lipid assemblies and proposing the importance of compositional genomes) will, it is hoped, set the standards for the theoretical investigation of the relevant claims.

The meeting also looked at two neighbouring areas; one being industrial/applied systems chemistry (complex organic syntheses and high-pressure, high-temperature microfluidic chemistry) and systems biology (such as the analysis of interactions between genes in yeast).

In conclusion, the participants were satisfied that all the discussed subfields are very much alive and that they yield valuable insights for the others. Theory and experiment are likely to come closer than ever before, thanks to development in experimental methods and deeper theoretical

understanding of the issues.
The infrastructure of the meeting was very pleasant and conducive to creative thought and discussions. Grand Hotel Anna in Balatonfüred proved to be an excellent venue, worthy of attention to similar meetings in the future. The feeling that a third meeting of systems chemistry should be held, preferably already next year, has been widely shared by the participants.

Scientific Content of the Conference

(1 page min.)

- *Summary of the conference sessions focusing on the scientific highlights*
- *Assessment of the results and their potential impact on future research or applications*

1. Overview of three approaches: metabolism,.template replication, and compartmentation. Three talks presented by key players in the field (Martin, von Kiedrowski, Luisi). Of course these boundaries are not sharp: von Kiedrowski presented some propects for a new metabolic autocatalytic system, and Luisi informed about experiments on never-born proteins.
2. Questions of the origin of molecular symmetry breaking was addressed by various speakers (Otto, Ribo).
3. Crucial results for the RNA worls have been presented by Yarus, who reported on selected aptamers that had high over-representation of codonic/anticodonic triplets in their binding sites. Schuster presented a nice overview of the modelling approaches to RNA structures, function, and evolution. Lehman presented an RNA-based system that could turn out to be a 3-membered hypercycle. Kampis preseted an agent-based ecosystem coevolution model in which the genotype-phenotype mapping was borrowed from the RNA algorithms presented by Schuster.
4. Karolyhazy presented the hard-to-digest but crucially important facts and principles of the quantum world, especially that of entanglement. He argued that the reason why quantum mechanics is so intuitively unobvious is due to the fact that animals have been selected to to adopt a certain concept of space during evolution. Goranovic illustrated later how detailed quantum considerations can be indispensable in a chemical systems.
5. Issues of evolvability are very important for evolution. This has been addressed in the context of protein evolution by Tawfik, who argued for the importance of plastic (moderately specific) intermediates. Another approach investigated the evolvability potential of the GARD model to see whether the composome population can respond to directional selection in a Darwinian manner (Santos, Lancet). Epigenetics and evolution, with the example of CpGs and homeobox genes has been Rodin.
6. Papp opened the meeting towards systems biology, by presenting evidence for the nature of genetic interactions in yeast by using modern bioinformatics methods.
7. Kauffman overviewed the theory and implications of hypothetical, reflexively autocatalytic protein networks. In the emerging debate is has become clear that there are two burning issues to investigate: the problem of side reactions and the question of Darwinian evolvability. The importance of agency has been dicussed as a combination of replication with a thermodynamic work cycle. Ashkenazy contributed the special example of the kinetics and mechanism of beta-sheet peptide replication
8. The industrial dimension has been addressed by Darvas (the high potential of high-pressure, high-temperature microfluidics), and Schinzer (complex organic syntheses with pharmaceutical applications).
9. Gintis presented an exciting approach towards the unification of the social sciences, and he dicussed an agent-based model of the market. Odling-Smee has given a detailed account of the concepts and examples of niche construction and ecological inheritance. Fernando argued that a bona fide replication-selection system could work at least in the human brain during complex thinking and language acquisition.
10. Aunger presented the broadest view of evolution by focusing on major transitions, not only in biology but also in material and cultural/technological evolution, and their energetic correlates.

IN SUM, the meeting presented an excellent overview of the state of the art in various fields of evolutionary studies, with a special emphasis on the overlap between systems chemistry and evolution theory. More efforts will be needed to experimentally realize some of the infrabiological chemical superystems (composed of autocatalytic doublets, such as template replication with membrane growth and division, for example), let alone a minimal living chemical system (such as the chemoton where membrane, template and boundary are united). The origin of evolvablity in such system is a burning issue in need of further clarification and experimental realization. Concepts from the now extended evolutionary synthesis (such as niche construction, evolvability, replicator dynamics in various fields) should be more widely known, thought about and possibly implemented in various branches of science, including systems chemistry.

Forward Look

(1 page min.)

- *Assessment of the results*
- *Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe*
- *Identification of emerging topics*

The ESF-COST Meeting at Balatonfüred was quite unique in the sense that it gathered a substantial number of top researches with quite diverse areas of expertise. This is the key to foster cross-disciplinary discussions and fresh approaches to hot topics in science. There were several clear signs from the lively debates during and after the different scientific sessions that the main objectives of the meeting were fulfilled. Thus, big questions such as what are the best theoretical and experimental approaches to understand the origin of life and the emergence of evolvability; how to better comprehend the major transitions in evolutionary history; how to integrate currently incompatible paradigms in the behavioural sciences; or the possibility that natural selection in the brain is a key player in cognition, were hotly debated. As expected, there was no general consensus in all topics but it was clear that new approaches and ‘ways of thinking’ are needed. These hot topics will obviously continue in the scientific agenda for the next years.
Many kinds of origin studies are making progress, but the most successful of these by far is the RNA world hypothesis. It now seems almost certain that an RNA era existed, and that that time hosted the appearance of modern translation. Thus we now have a new scientific outpost about 4 gigayears ago, in which we know some of the truth. The importance of this is that from the RNA world, we have to extrapolate over about 20-fold less time to reach the origin of Darwinian life on Earth, the time of the first replicator. Therefore, success and expansion of the RNA world hypothesis will bring further insights into the dawn of the genetic era, which most of us think of as the origin of Terran life.
In the best case, research in systems chemistry could lead to new paradigms for industrial production. The vision of production plants, which are chemically reprogrammable to synthesize a given set of target compounds by harvesting second-order autocatalytic networks look remote today indeed. The vision will become closer however once chemistry begins to understand that selection means iterated selectivity, Darwinian chemistry builds upon exponential dynamics, while frozen accidents building up from second or higher order autocatalytic dynamics enables to synthesize homochiral compounds from prochiral precursors and more generally "programmable" targets from a network that has the targets in its repertoire, even if there is no difference between the free energy of alternatives at the kinetic or thermodynamic level. Autocatalytic reaction systems are slow explosions in solution. Learning to tame, to control, and finally to design such supersystems will enable a similar transition in chemistry as physics underwent in the process of converting the nuclear bomb into a nuclear power plant. Unlike physics in the latter process, systems chemistry will deal with a subject that is much more innocent and harmless than nuclear energy. Nevertheless, ethical considerations should not be excluded here.
There were still a number of active options for explanation of the origin of life, ranging from

replicator first to compartment first to metabolism first and some different theories of how these various components were put together into the kinds of cells we see today. The meeting was successful in gathering prominent proponents for each of these positions to present their best case, but we are not sure what criteria will be used to further whittle down the 'live' options in this field in future. On the last day, the meeting swicthed to other types of 'origins': of memetic replicators and indeed technological ones. A proper understanding of the most complex contemporary manifestation of the evolutionary processes which began with the origin of life (human cultural evolution) requires an understanding of the tripartite inheritance processes outlined by Odling-Smee at the conference: ecological, genetic and cultural inheritance, working in parallel, and through coevolutionary interactions, to produce the incredibly complex way of life we currently enjoy as a species. How niche construction and technological evolution feed into more standard biological processes are the topics one could nominate as 'emerging'.

- Is there a need for a foresight-type initiative?

No, but there was universal agreement among the participants that we should have a Systems Chemistry III conference, possibly already in the year 2010.

Atmosphere and Infrastructure

- *The reaction of the participants to the location and the organization, including networking, and any other relevant comments*

The atmosphere was very conducive to open an constructive discussions. The wide scope of the meeting turned out to be a useful decision. The venue and the organization have been widely praised: several participants expressed their wish to return to Grand Hotel Anna in the future.