COST

Domain Committee "CMST"

COST Action CM0703

Systems Chemistry

MONITORING PROGRESS REPORT

Period: *from April 3, 2008 to December 31, 2010*

This Report is presented to the relevant Domain Committee and contains two parts:

I. Management Report *prepared by the COST Office/Grant Holder*
II. Scientific Report *prepared by the Chair of the Management Committee of the Action*
III. Previous versions of the Scientific Report*; i.e., part II of past reporting periods*

The report is a "cumulative" report, i.e. it is updated annually and covers the entire period of the Action.

Confidentiality: the documents will be made available to the public via the COST Action web page except for chapter *II.C. Self evaluation*.

Based on the monitoring results, the COST Office will decide on the following year's budget allocation.

I. Management Report *prepared by the COST Office/Grant Holder*

I.A. COST Action Fact Sheet

Title

Systems Chemistry

Contacts

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Details

Draft Mou:		Mou:	248/07
Start of Action:	03/04/2008	Entry into force:	24/01/2008
End of Action:	02/04/2012	CSO approval date:	16/11/2007

Objectives

The main objective of the Action is to investigate autocatalytic reaction sytems within supramolecular, prebiotic, and other fields of chemistry and to develop methods for their integration into dynamic supersystems.Systems chemistry is the joint effort of prebiotic and supramolecular chemistry assisted by computer science from theoretical chemistry, biology, and complex systems research to tackle dynamic supersystem integration including at least one autocatalytic subsystem. It is the bottom-up pendant of systems biology towards synthetic biology. The origin of life is seen as a major stimulus to organize research but the field is open for chemistries of limited prebiotic plausibility. Subsystems may be classified as genetic, metabolic, or compartiment-building. Pairwise integration into higher organized supersystems is expected to yield the knowledge enabling later the triple integration into minimal chemical cells. The integration approach will necessarily link to the question of asymmetric autocatalysis and chiral symmetry breaking, while the key challenge is to find the roots of Darwinian evolvability in chemical systems. 5 workgroups will define a trigonal bipyramid, where the axis theory to asymmetry is surrounded by 3 areas of integration.Keywords: Autocatalysis, self-replication, self-reproduction, supramolecular chemistry, prebiotic chemistry

Parties

Country	Date	Country	Date	Country	Date	Country	Date
Austria	08/05/2008	Belgium	24/01/2008	Denmark	07/02/2008	France	24/01/2008
Germany	24/01/2008	Greece	25/11/2009	Hungary	24/01/2008	Israel	07/02/2008
Italy	12/03/2008	Lithuania	25/11/2009	Netherlands	03/09/2008	Poland	29/01/2008
Spain	24/01/2008	Switzerland	15/02/2008	United Kingdom	24/01/2008		

Total: 15

Intentions to accept the MoU							
Country	Date	Country	Date	Country	Date	Country	Date
Sweden	N/A						

Total: 1

Working Groups
None

Website
None

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I.C. Overview activities and expenditure

Action CM0703 - budget from 03-Apr-2008 to 30-Sep-2010

Meetings

Meeting Type	Date	Place	Paid part	Cost	Status	Total
Management Committe	03-Apr-2008	Brussels (BE)	16	9504.14	Paid	
In conjunction with Wo	08-Oct-2008	Maratea (IT)	28	27763.31	Paid	
Working Group	17-Apr-2009	Zurich (CH)	7	5028.72	Paid	
Working Group	27-Apr-2009	Groningen (NL)	15	11471.31	Paid	
Working Group	16-May-200	Brunnen (CH)	11	6965.74	Paid	
Working Group	06-Oct-2009	Frankfurt (DE)	4	1194.25	Paid	
Joint Management Com	24-Oct-2009	Balaton (HU)	28	27510.26	Paid	
Working Group	24-Apr-2010	Taormina (IT)	10	8199.22	Paid	
Working Group	24-May-201	Dead Sea (IL)	13	17342.09	Paid	
						114979

STSM

Beneficiary	Date	From	To	Cost	Status	Total
Mr Wim Noorduin	17-Oct-2009	Nijmegen (NL)	Madrid (ES)	2200	Paid	
Pr Meir Lahav	26-Jan-2010	Rehovot (IL)	Madrid (ES)	1390	Paid	
Mr Omer Markovitch	14-Mar-201	Rehovot (IL)	Budapest (HU)	1500	Paid	
Dr Alexandra Le Cheval	07-Mar-201	Villeurbanne (FR)	Roma (IT)	3500	Paid	
Ms Vera Vasas	10-May-201	Budapest (HU)	Rehovot (IL)	1500	Paid	
Dr Jerome Peyralans	02-May-201	Groningen (NL)	Beer Sheva (IL)	2100	Paid	
Dr Alexandra Le Cheval	04-Jul-2010	Villeurbanne (FR)	Roma (IT)	2100	Paid	
						14,290

Workshops

Title	Date	Place		Cost	Status	Total
Working Group 1 meeti	17-Apr-2009	Zürich (CH)		191	Paid	
Action CM0703 WG 01 r	27-Apr-2009	Groningen (NL)		1,500	Paid	
Action CM0703 WG 04 r	16-May-200	Brunnen (CH)		2,000	Paid	
Working group 2 meeti	06-Oct-2009	Frankfurt (DE)		300	Paid	
SYSTEMS CHEMISTRY II:	24-Oct-2009	Balaton (HU)		2,434	Paid	
WG4 meeting: Chirality	23-Apr-2010	Taormina (IT)		1,189	Paid	
						7,614

Action Total	**136883**

II. Scientific Report *prepared by the Chair of the Management Committee of the Action*

II.A. Innovative networking

Innovative knowledge, significant scientific breakthroughs and expected socio-economic impacts through the Action and its Working Groups.

COST Action CM0703 "Systems Chemistry" started with its constitutional MC meeting on April 3, 2008 in Brussels. The meeting saw the election of:

Action chair: Günter von Kiedrowski, Ruhr-University Bochum, Germany
Action vice chair: Eörs Szathmary, Collegium Budapest, Hungary
Coordinator of Working Group 1: Sijbren Otto, University of Groningen, Netherlands
Coordinator of Working Group 2: Peter Eigil Nielsen, University of Copenhagen, Denmark
Coordinator of Working Group 3: Peter Walde, ETH Zurich, Switzerland
Coordinator of Working Group 4: Jay Siegel, University of Zurich, Switzerland
Coordinator of Working Group 5: Eörs Szathmary, Collegium Budapest, Hungary

WG coordinators started to contact Action members immediately after the 1st MC meeting to define the implementation of the WG scope and and to refine the scientific content as foreseen in the Memorandum of Understanding (MoU). The following implementation emerged in the course of the Action:

WG1: Supramolecular Systems Chemistry. Component systems are based on organic replicators, peptide replicator networks, synthetic molecular machinery, and dynamic combinatorial libraries (DCL). WG1 has been developing a new generation of DCLs which links the principle of amplification by self-replication with the principle of adaptation explored close to equilibrium in conventional DCLs.

- A significant scientific breakthrough was the finding that a disulfide-exchange based DCL can be "harvested" by a coupled autocatalytic process, in which DCL members form different types of supramolecular fibers (Otto group: *Science* 2010, **327:**1502-1506).
- The work was stimulated by the the successful construction of a template replicator growing from a DCL (Philp group: Angew. Chem. Int. Ed. 2008)
- Innovative knowledge leading to a more detailed understanding of small organic replicator networks came in by linking kinetic studies with ab initio molecular dynamics, also applied to NMR shift prediction. This was the result of a mini-networking project organized by the Action's ESR speaker Arne Dieckmann (von Kiedrowski group, Doltsinis group, Lorentz group: J. Syst. Chem.)
- Medium term socio economic impact is expected from the launch of the open access Journal of Systems Chemistry, in which members of WG1 and WG2 serve as Editors in Chief.

Participants: Sijbren Otto, NL, coordinator; Gonen Ashkenasy, IL; Ben Feringa, NL; Guenter von Kiedrowski, DE; Douglas Philp, UK;Kay Severin, CH; Giuseppone Nicolas, FR; Leonard Prins, IT

WG2: Informational Systems Chemistry. Components are natural nucleic acids such as RNA as well as and artificial nucleic acids mimics such as PNA, HNA, and others. Work aims at the copying and replication of such NAs, both enzymatically and non-enzymatically, its directed molecular evolution, as well as pathways leading to the autogeneration of NAs from primitive precursor units. The role of artificial and mineral surfaces as compartiment of such processes involving charged NAs as well as of organic solvents and micelles for lipophilic NA mimics be studied.

- Using 64 sequences, it is shown that any of the four nucleobases, in combination with any neighboring residue, support enzyme-free primer extension when primer and mononucleotide are sufficiently reactive. These results help to clarify the substrate contribution to copying, as found in polymerase-catalyzed replication, and show an important feature of DNA as genetic material.
- The crystal structure of a xylose-DNA double helix has been solved, and the results demonstrate the chiral orthogonality of the ribose and xylose based episomes, and also shows that in terms of stability and compactness of information storage, the ribose based natural DNA is unsurpassed

Participants: Peter E. Nielsen, DK , coordinator; Piet Herdewijn, BE; Marie-Christine Maurel, FR; Clemens Richert, DE; Raffaele Saladino, IT, Ernesto di Mauro, IT.

WG3: Metabolic and Vesicle Systems Chemistry. Component systems are based on metabolic, as well as intra- and intervesicular reactions.

- A significant scientific breakthough in metabolic systems chemistry was the successful prebiotic synthesis of cytidine 3'-phosphate from components of the formose cycle, cyanamide and cyanoacetylen and phosphate (Sutherland group: *Nature* **2009**, *459*, 239-242). This work was highlighted by Jack Szostak under the title "Systems Chemistry on the Early Earth" (*Nature* **2009**, 459, 171-172)
- Several advancements have been reported on the construction of minimal cell-like entities based on vesicle compartmentation and coupled transcription-translation reactions, mainly from the group of Luisi, here represented by Stano. In particular, it has been shown that active membrane-enzymes can be synthesized inside lipid vesicles, and that these enzymes can in turn synthesize lipids so that a route to vesicle growth and self-reproduction can be implemented. Moreover, the detailed analysis of functional protein synthesis inside small vesicles led to the discovery that solute can indeed spontaneously self-concentrate inside vesicles thanks to the interplay between vesicle closure and solute interaction.
- From the viewpoint of organocatalysis, the report on the peptide bond formation catalyzed by a simple dipeptide (seryl-histidine) paves the way to future advancements in the field of peptide-based self-catalytic networks.

Vesicle systems chemistry has been targeting reactions leading to the formation of amphiphiles inside vesicular and micellar containment as well as intravesicular or compartment-bound reactions coupled to the uptake of photons. Vesicle-vesicle interactions could be developed involving molecular recognition expressed by RNA/DNA or supramolecular equivalents for molecular recognition. Such studies also involve electronically addressable microfluidics for vesicle manipulation.

Participants: Peter Walde, CH, coordinator; Robert Pascal, FR; Steen Rasmussen, DK; Bart-Jan Ravoo, DE; Pasquale Stano, IT; Peter Strazewski, FR; John Sutherland, UK

WG4: Asymmetric Systems Chemistry. Component systems are based on reactions and processes enabling the spontaneous generation of optical activity starting from a racemic or prochiral state. Work has focussed on pericyclic reactions, organo autocata lytic reactions, as well as processes involving supramolecular aggregates, crystals, and interfaces. Experimental approaches towards chiral symmetry breaking have been conjuncted with theoretical approaches based on dynamic modelling and structural aspects of the former.

Participants: Jay Siegel, CH, coordinator; Donna Blackmond, UK (till her move to the Scripps Institute in La Jolla, USA); Axel Brandenburg, SE (Sweden has not yet accepted the MoU); Meir Lahav, IL; Josep Ribo, SP; Svetlana Tsogoeva, DE; Elias Vlieg, NL (sending Wim Noorduin); Guenter von Kiedrowski, DE; Ben Feringa, NL; David Hochberg, ES; Karl-Heinz Ernst, CH; Roberto Purello, IT; Cristóbal Viedma, ES.

WG5:Theoretical Systems Chemistry. Components are the theory of evolution, network theory, bifurcation theory, information theory, protocell theories as well as theoretical chemistry based on quantum mechanics and dynamics. The aim of this Working Group is to provide a platform for the theoretical analysis, modelling and quantitative description of processes investigated experimentally in the various Working groups of the Action. By the conjunction of theoretical chemistry and biology we aim to arrive at a new level of theory for dynamic phenomena relevant to the origin of life.
Up to the present the heaviest research line are: (i) the analysis of evolvability of various molecular systems, and (ii) formal chemistry simulations of an emerging metabolism. A main goal for the next two years is the linking of these two approaches.

- The analysis of the evolvability of non-templated inhertitance system has received special attention. More specifically, this concerns the debate whether the assemblies in the Lipid World model of Doron Lancet are real units of evolution as they seem to be at firs analysis. It turns out that the compositional mutation rates are so high that they do not allow natural selection to be effective (Vasas, V. *et al.* (2010) *Proc. Natl. Acad. Sci. USA*. **107,** 1470-1475). This type of analysis is now being applied to other systems, including reflexively autocatalytic protein networks).
- A simulation environment was developed to allow the detailed analysis of very early evolution of metabolism using a self-consistent toy universe that comprises a genetic subsystem, gene expression, catalysis, and metabolic subsystem based on an explicit representation of the underlying chemistry, as well as fitness function measuring metabolic efficiency (Flamm C, *et al. (2010)* J. Syst. Chem **1**, 4*)* .

Participants: Eors Szathmary, HU, coordinator; Hugues Bersini, BE; Christof Flamm, AT; Adam Kun, HU; Doron Lancet, IL ; Dominik Marx, DE ; Peter Stadler, DE; John McCaskill, DE; Mauro Santos, ES; Kepa Ruiz Mirazo, ES.

Synergies and Spin Offs

(1) ***COST & ESF:***
The kickoff workshop of CM0703 ("Chembiogenesis 2008", October 8-9, Maratea, IT; ANNEX B.1.1) was coupled to the 1st ESF-COST High Level Research Conference on "Systems Chemistry" (October 4-7, Maratea, IT). For a joint meeting report see ANNEX G.1.1. The direct succession of events proved extremely fruitful from a scientific point of view, although difficult to organize due to different rules in ESF and COST. Nevertheless, whenever possible, event coupling between a COST workshop and a COST-ESF HLRC should become a favorable model in the future, because specific rule-based issues, such as the limitation of external experts in the COST model and the limitation of speaker reimbursement funds at the ESF side can be overcome more easily. ChemBioGenesis 2009 (Anna Grand Hotel, Lake Balaton, October ...) was again coupled to the 2nd ESF-COST HLRC on "Systems Chemistry II" (October ...) and again resulted in a formidable scientific success (ANNEX B1.1 and G.1.1). This time the organizational aspects involved in the interaction between COST and ESF worked out to become much smoother, obviously as a result of learning by doing. Unfortunately, a coupled meeting could not be planned for 2010 due to an unclear financial situation for a joint event – but 2011 will again see this coupling, this time at the Dead Sea in Israel. An "ESF-COST frontier of science event" on "Complex Systems & Changes: Water & Life" took place in Taormina, October 29-31, 2008". The chair of CM0703 introduced the COST Action on Systems Chemistry outlining its major objectives by examples.

(2) ***COST & FP7***:
The launch of CM0703 was observed by FP7 policy makers and contributed to the awareness that Systems Chemistry is an emergent field which creates a strong link between chemistry and information science. As a result of a fruitful interaction the programme CHEM-IT by ICT/FET was

launched in 2009 (ANNEX F). Today, several Action members collaborate in the ECCell, eFLUX, and MATCHIT projects (ANNEX D1.1 - D1.3). Action members were invited to express their interest in a preproposal for a FET flagship ("Sustainable Personal LIving Technology/SPLIT, ANNEX D1.4). FET Flagships are ambitious large-scale, science-driven, visionary research initiatives that aim to achieve a scientific breakthrough. The scientific advance should provide a strong and broad basis for future technological innovation and economic exploitation in a variety of areas, as well as novel benefits for society. The Commission has decided to launch two FET flagships in 2013. Each will have a EU-contribution of 1000-2000 Mio€ and will operate for 10 years. As a means to prepare these flagships the Commission will select six Coordinative Actions based on proposals submitted till December 8, 2010.

(3) ***COST & National Activities***:
German Max Planck Society organized an International Workshop on Systems Chemistry in Berlin, January 7-8, 2008. The Action proposer was invited to introduce the field from a European point of view. He gave an overview of the work from individual labs involved in the Action. The University of Groningen, NL, founded a Center for Systems Chemistry directed by Action member Ben Feringa. The center is supported by 5 Mio € over the next 5 years. Its inauguration took place coupled to the kickoff meeting of Working Group 1 of CM0703. Ruhr-University of Bochum, DE, decided to organize a Research Department in Interfacial Systems Chemistry (IFSC) which was started in early 2009. The Italian National PRIN project on compartmentalized reactions (minimal cell models, the subject covered in the WG3), started in 2010 and will end in 2012. It brought about new interests and collaborations in WG3.

II.C. New Networking

New members up to Dec. 31, 2010

WG1:
WG2:Ernesto di Mauro, UniRoma, IT.
WG3: Giovanna Mancini, CNR-IMC Roma, IT; Fabio Mavelli, University of Bari, IT
WG4:
WG5: István Zachár, Eötvös University, HU; Vera Vasas, Autonomous University of Balcelona, ES; Chrisantha Fernando, University of Sussex, UK

Early Stage Researcher and STSMs

As a means to represent the voice of ESRs in future STSMs, and other ESR-related issues, Arne Dieckmann, Ruhr-University of Bochum, DE was elected for inclusion as ESR-speaker in the Action's steering board. STSMs took place from 2010 on, following the 1st annual meetings of the WGs in 2009.

- COST-STSM-CM0703-5645: Meir Lahav, Weizmann Institute of Science, Israel, to David Hochberg, Centro de Astrobiologia, Madrid, Spain (from 26.01.2010 to 04.02.2010)
- COST-STSM-CM0703-05718: Omer Markovitch, Weizmann Institute of Science, Rehovot, Israel to Eörs Szathmary, Collegium Budapest (from 14.03.2010 to 25.03.2010)
- STSM-STSM-CM0703-5849: Alexandra Le Chevalier Isaad, U. Lyon, France, to Pier Luigi Luisi, U. Roma III, Rome, Italy (from 07.03.2010-01.04.2010)
- COST-STSM-CM0703-6054: Vera Vasas, Eötvös University, Budapest, Hungary to Doron Lancet, Weizmann Institute of Science, Rehovot, Israel (from 10.05.2010-23.05.2010)

- COST-STSM-CM0703-6071: J. Peyralans, University of Groningen, The Netherlands, to Gonen Ashkenasy, Ben Gurion University of the Negev, Beer Sheva, Israel (from 02.05.2010-27.05.2010)

Involvement of researchers from outside of COST Countries

The Action implements ENP by means of a very active involvement of scientists from Israel in WG1, WG4, and WG5. 4 of the 5 STSMs were exchanges with Israel. The annual conference "ChemBioGenesis 2011" is scheduled to take place in Israel.

Advancement and promotion of scientific knowledge

The Action published papers and reports acknowledging COST CM0703 funding (ANNEX A). Promotion of scientific knowledge was also achieved by conferences and workshops (ANNEX B). Google finds 150 original (non similar) links when searching for "COST CM0703 'Systems Chemistry'" (see ANNEX C for major links). Action members were invited to give talks on systems chemistry on conferences outside of the COST CM0703 context. COST CM0703 funding was further mentioned by posters and contributed lectures on international conferences and seminars by Action members took place on different locations (ANNEX E).

Fundraising activities and collaborative projects of COST CM0703 members

Three EU-wide projects involving at least 3 CM0703 members each are coordinated by Action members John McCaskill, Steen Rasmussen and Eörs Szathmary, all between systems chemistry and information science (ANNEX D.1.1 - D.1.3). The three projects together have a volume of > 7 Mio€. Groningen's Center for Systems Chemistry (coordinated by Action member Ben Feringa) adds further 5 Mio€. at the National funding level. Action members Ben Feringa, Axel Brandenburg, Gonen Ashkenasy, and Leonard Prins won ERC-grants for individual research.
WG1 members are currently applying for a Marie-Curie RTN coordinated by Sijbren Otto. A German collaborative focus project (DFG SPP) in which three CM0703 members are involved has been organized by Action member Clemens Richert and is currently under evaluation. Action members Steen Rasmussen, John McCaskill and the Chair of CM0703 have been involved in the preparation of a proposal for the Coordinating Action towards a FET flagship. Two WG3 members are also currently involved in the National Italian project PRIN.

Material for this section has been organized in the following annexes:

ANNEX A: Publications and list of reports
ANNEX B: Conferences, Workshops and Training Schools
ANNEX C: Web links to events/pages based on this Action
ANNEX D: Scientific and Technical Cooperation
ANNEX E: Outreach by lectures and seminars
ANNEX F: Contacts in the ERA
ANNEX G: Action Participation
ANNEX H: Documents/Reports

Summary of ANNEX Structure:

ANNEX A: Publications and Reports (list)

A.1 Publications of Working Group 1
A.2 Publications of Working Group 2
A.3 Publications of Working Group 3
A.4 Publications of Working Group 4
A.5 Publications of Working Group 5
A.6 Publications relating to the whole Action

ANNEX B: Conferences, Workshops, Training Schools (list and programme)

B.1 ChemBioGenesis Meetings
B.2 Workshops of the Action's Working Groups
B.3 Other Meetings

ANNEX C: Web site (description)

ANNEX D: Scientific and Technical Cooperation

D.1 EU-Funded Collaborative Research Projects
D.2 Nationally Funded Collaborative Research Projects

ANNEX E: Outreach

E.1 Outreach by lectures and talks at meetings and seminars
E.2 Outreach by media response

ANNEX F: Contacts in the ERA

F.1 FP7 Programmes established relating to Systems Chemistry
F.2 COST/ESF/EUREKA based collaboration

ANNEX G: Action Participation

ANNEX H: Documents

H.1 ChemBioGenesis Meetings
H.2 Meetings of Working Groups
H.3 Other Meetings
H.4 STSMs
H.5 Reports from members of the Management Comitee of CM0703 not participating in Working Groups

ANNEX A: Publications and Reports (list)

A.1 Publications of Working Group 1

- Carnall JMA, Waudby CA, Belenguer AM, Stuart MCA, Peyralans JJP, Otto S: **Mechanosensitive self-replication driven by self-organization.** *Science* 2010, **327:**1502-1506.
- Z. Dadon, M. Samiappan, E. Yishay, G. Ashkenasy **Light-induced peptide replication controls logic operations in small networks** *Chem. Eur. J.* 2010 ***16***, 12096 – 12099.
- Dieckmann A, Beniken S, Lorenz C, Doltsinis NL, von Kiedrowski G: **Unravelling a fulvene based Replicator: Experiment and Theory in Interplay**. *Journal of Systems Chemistry* 2010, **1**:10
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A.5 Publications of Working Group 5

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A.6 Publications relating to the whole Action

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- Luisi, P. L. and Stano, P. (Eds.) **The Minimal Cell**. Springer, Dordrecht 2011.
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- Zagorski ZP: **Ranking of sites on early Earth as cradles for Life**, *Origins of Life and Evolution of Biospheres* (2010) 40: 490.
- Zagorski ZP: **Possible role of radon in prebiotic chemistry and in early evolution of life on Earth**, *Nukleonika* (2010) 55: 555.

A.7 Reports relating to the whole Action

- Joint meeting report on the COST-ESF HLRC on "Systems Chemistry", Hotel Villa del Mare, Aquafredda di Maratea, October 3-7, 2008 and "Chembiogenesis 2008", Kickoff meeting of COST Action CM0703 ("Systems Chemistry"), Hotel Villa del Mare, Aquafredda di Maratea, October 8-10, 2008 (cf. ANNEX H.1.1)
  Meeting report EST-COST High-Level Reseach Conference. Systems Chemistry II: Evolution and Systems. Balatonfüred, 18-23 October 2009
- Meeting report on "Chembiogenesis 2009", COST Action CM0703 Annual meeting, Balatonfüred, 23-27 October 2009

A.9 Reports from STSMs

ANNEX B: Conferences, Workshops, Training Schools (list and programme)

B.1 ChemBioGenesis Meetings

B.1.1 ChemBioGenesis 2008, October 7-11, Maratea, Italy

CHEMBIOGENESIS 2008
KICKOFF MEETING OF COST ACTION CM0703
"SYSTEMS CHEMISTRY"
Programme

TUESDAY, OCTOBER 7
Arrival of Action members not participating at the preceeding ESF COST HLRC on "Systems Chemistry". Option to join with participants of "Systems Chemistry" at the conference dinner – prebooking required.

WEDNESDAY, OCTOBER 8
09:00 – 09:30 Opening of the kickoff meeting

Javier Caldentey, COST office, Brussels
Welcome and organizational remarks
Dieter Schinzer, University of Magdeburg, chair of the CMST domain committee
COST Chemistry: Introduction and Domain overview
Günter von Kiedrowski, Ruhr University of Bochum, chairman of CM0703.
Systems Chemistry: Introduction and Action overview

Session I: ***"Supramolecular Systems Chemistry"***
chaired by **Sijbren Otto**, University of Groningen, coordinator of WG CM0703-1

09:30 – 10:00 **Sijbren Otto**, University of Groningen, NL:
Self-Replication of Peptides Driven by Nanostructure Formation

10:00 – 10:30 **Kay Severin**, EPFL Lausanne, CH:
Adaptive molecular networks

10:30 – 11:00 Coffee break

11:00 – 11:30 **Gonen Ashkenasy**, Ben Gurion University of the Negev, Beer Sheva, IL:
Functional Modules in Small Networks of Replicating Molecules

11:30 – 12:00 **Douglas Philp**, University of St. Andrews, UK:
Manipulating replication processes within a dynamic covalent framework

12:00 – 12:30 **Meir Lahav**, Weizmann Institute of Science, Rehovot, IL:
"Mirror symmetry-breaking" of peptides and amino-acids

12:30 – 13:00 Discussion

13:00 – 15:00 Lunch

"Inter-Action Lecture"

15.00 - 15.30 **Dieter Schinzer**, University of Magdeburg, DE
From a natural product synthesis to a powerful antitumor drug: The success-story of the epothilones

Session II: ***"Prebiotic Systems Chemistry"***
chaired by **Raffaele Saladino**, University of Viterbo

15:30 – 16:00 **Raffaele Saladino**, University of Viterbo, IT:
Advances in the prebiotic chemistry of nucleic acid components

16:00 – 16:30 **Clemens Richert**, University of Stuttgart, DE:
Sequence dependence of primer extension: Individual steps of non-enzymatic replication

16:30 – 17:00 Coffee break

17:00 – 17:30 **Piet Herdewijn**, Leuven Catholic University, BE:
Towards an orthogonal episome

17:30 – 18:00 **Marie-Christine Maurel**, Pierre and Marie Curie University of Paris, FR:
RNA in extreme conditions

18:00 – 18:30 **Dominik Marx**, Ruhr University of Bochum, DE:
Ab initio peptide synthesis in water at extreme conditions

18:30 – 19:00 Discussion

19:00 Dinner

THURSDAY, OCTOBER 9

Session III: ***"Complex Systems Chemistry"***
chaired by **Peter Strazewski**, University of Lyon

09:00 – 09:30 **Peter Strazewski**, University of Lyon, FR:
Deciphering the nature of ribosomal catalysis: (How) did it work before the emergence of translation?

09:30 – 10:00 **Robert Pascal**, University of Montpellier, FR:
Energy carriers, coupled reactions and the driving force towards the emergence of translation

10:00 – 10:30 **Hugues Bersini**, Free University of Brussels, BE:
Decomposition of Complex Chemical Reaction Networks into Reaction Subnetworks

10:30 – 11:00 Coffee break

11:00 – 11:30 **Zbigniew Zagorski**, Institute for Nuclear Chemistry, Warsaw, PL:
Software and hardware in the origins of life chemistry

11:30 – 12:00 **Ludo Diels**, Flemish Institute of Technology, Vito, Mol, BE:
Brainstorm about sustainable chemical processes by the integration of reaction and separation processes

12:00 – 12:30 Discussion

13:00 – 15:00 Lunch

Session IV: **"*Asymmetric Systems Chemistry*"**
chaired by **Jay Siegel**, University of Zurich, coordinator of WG CM0703-4

15:00 – 15:30 **Jay Siegel**, University of Zurich, CH:
Could 3-letters and one hand suffice?

15:30 – 16:00 **Ben Feringa**, University of Groningen, NL:
Controlling dynamics in molecular systems

16:00 – 16:30 **Donna Blackmond**, Imperial College London, UK:
The role of autocatalytic systems in the origin of life

16:30 – 17:00 Coffee break

17:00 – 17:30 **Günter von Kiedrowski**, Ruhr University of Bochum, DE:
Replicator systems chemistry: Tools and examples

17:30 – 18:00 **Josep M. Ribo**, University of Barcelona, SP:
Mechanical induction of molecular chirality

18:00 – 18:30 **Wim Noorduin**, University of Nijmegen, NL:
The emergence of a single chiral solid phase under near-equilibrium conditions: Survival of the fittest

18:30 – 19:00 Discussion

19:00 Dinner

FRIDAY, OCTOBER 10

Session V: ***"Theoretical Aspects of Systems Chemistry"***
chaired by **Eörs Szathmáry**, Collegium Budapest, coordinator of WG CM0703-5

09:00 – 09:30 **Eörs Szathmáry**, Collegium Budapest, HU:
Open questions in early genome dynamics

09:30 – 10:00 **Adam Kun**, Eötvös Loránd University Budapest, HU:
How common are RNAs that the Qb replicase connot replicate –

What does it tell us about the replicability of ribozymes?

10:00 – 10:30 **Christoph Flamm**, University of Vienna, AU:
Evolving catalysed metabolisms within the toy chemistry universe

10:30 – 11:00 Coffee break

11:00 – 11:30 **John McCaskill**, Ruhr University of Bochum, DE:
Integrated mesoscale simulation of physical self-assembly and chemical reaction: a tool for System Chemistry.

11:30 – 12:00 **Goran Goranovich**, University of Odense, DK:
A system exhibiting Darwinian evolution

12:00 – 12:30 **Raphael Plasson**, Nordic Institute for Theoretical Physics, Stockholm, SW:
Emergence of protometabolisms and the self-organiziation of non-equilibrium reaction networks

12:30 – 13:00 Discussion

13:00 – 15:00 Lunch and Meeting closure

B.1.2 Chembiogenesis 2009, 23-27 October, Balatonfüred, Hungary

Chair: Eörs Szathmáry, HU, Collegium Budapest
Scientific secretary: Ádám Kun
Secretary: Szilvia Zimber

23 October, Friday

Registration
Welcome Reception

24 October, Saturday

WG1 Supramolecular Chemistry (Sijbren Otto)
Sijbren Otto: Mechanically induced emergence of replicators from dynamic molecular networks
Gonen Ashkenazy: Light-induced replication governs network behavior
Günter von Kiedrowski: Replication vs. metabolic autocatalysis in asymmetric Mannich reactions
Douglas Philp (or Jürgen Huck): Designing instructable networks using synthetic replicators

Guest lecture
Stuart Kauffman: Autocatalytic sets and recent results on peptide catalysis

WG2 Informational Systems Chemistry (Peter Nielsen)
Raffale Saladino: Overview of work in the WG (provisional)

Marie-Christine Maurel: RNAs as starters of life? Insights into structural, catalytic and robustness properties

MC meeting

25 October, Sunday

WG4 Asymmetric Systems Chemistry (Jay Siegel)

Jay Siegel: Systems Stereochemistry
Elias Vlieg: Chiral purification: grinding backwards
Josep Ribo: The role of the primary nucleation process in the homochiral shift in the crystalization of systems as NaClO3

Guest lecture

Michael Yarus: Aminoacylation and peptide synthesis by a 5 nucleotide ribozyme

WG3 Metabolic and Vesicle Systems Chemistry (Peter Walde)

Peter Walde: Vesicles as reaction compartments and templates
Pascale Stano: Vesicles-based systems: recent developments
Robert Pascal: Epimerization of the N-terminal residue in peptides - The APED model subjected to experimentation
Jens Voskuhl (for Ravoo): Molecular recognition of vesicles
Steen Rasmussen - Pierre-Alain Monnard: Coupling of a minimal protocellular information, metabolic and container system: Status report I-II
Constantinos Paleos: Guanidinium Group: A Group Inducing Membrane Transport and Multicompartment Systems Formation

Contributed lecture

Zbigniew Zagorski: Summary of relations of radiation chemistry to origin of life and early evolution of the biosphere (in connection to recent chapter on that topic in an astrobiology monograph)

26 October, Monday

Guest lecture

Sergei Rodin: Frozen Complementarity of the Genetic Code: Relics of Primordial Mirror Symmetry in tRNAs and Aminoacyl-tRNA Synthetases

WG5 Theoretical Systems Chemistry (Eörs Szathmáry)

Eörs Szathmáry: A comprehensive approach to the origin of the genetic code
Christoph Flamm: RNA folding dynamics on changing energy landscapes
Kun Ádám: TBA
Doron Lancet: Prebiotic GARD simulation with realisitc lipids
Tamás Czárán (local invitee): Evolutionary dynamics of replicators on surfaces
Mauro Santos: TBA
Raphaël Plasson (for Axel Brandenburg) Analysis of Stoichiometric Matrices: Towards Automatic Detection of Autocatalysis?

General Discussion

Small excursion

Working dinner

27 October, Monday

Departure (to Budapest airport)

POSTERS
Ewa Maria Kornacka: Radiation chemistry of the DNA, as origins of life connection

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
www.esf.org/conferences/09332

Final Programme
Sunday 18 October
Late afternoon/early evening
Registration at the COST-ESF desk
19:00-19:30 Eörs Szathmáry, Collegium Budapest, HU
Dieter Schinzer, University of Magdeburg, DE
Welcome Note from Chair and Vice-Chair
19:30-21:00 Dinner
21:00 Welcome Drinks

Monday 19 October
Session 1
Chair: Mauro Santos, Autonomous University of Barcelona, ES
09:00-9:50 **William Martin,** Heinrich-Heine University Düsseldorf, DE
Hydrothermal Vents and the Origin of Life
09:50-10:40 **Günter von Kiedrowski,** Ruhr University Bochum, DE
TBD (Replicator and Systems Chemistry)
10:40-11:10 Coffee break
11:10-12:00 **Pier Luigi Luisi,** University of Rome, IT
Chemical Aspects of Synthetic Biology
Short Talks
12:00-12:15 **James Cleaves,** Carnegie Institution of Washington, US
What Were the Building Blocks Available for Proto-Life? The Prebiotic Small Molecule Inventory
12:15-12:30 **Sijbren Otto,** University of Cambridge, UK
Shaken, not Stirred: Spontaneous Emergence of Competing Synthetic Self-

Replicators from Dynamic Molecular Networks determined by Mechanical Energy.
12:30-14:30 Lunch
Session 2
Chair: Chrisantha Fernando, University of Sussex, UK
14:30-15:20 **Michael Yarus,** University of Colorado, US
Empirical Study of Inaccessibly Ancient Events: The Genetic Code
15:20-16:**10 Sergei Rodin, The** Beckman Research Institute, US
Frozen Complementarity of the Genetic Code: Relics of Primordial Mirror Symmetry in tRNAs and Aminoacyl-tRNA Synthetases
16.10-16:30 Coffee break
Short Talks
16:30-16:45 **Josep Ribo,** University of Barcelona, ES
Frank Model and Spontaneous Emergence of Chirality in Closed Systems
16:45-17:00 **Addy Pross,** Ben Gurion University, IL
Seeking the Chemical Roots of Darwinism: Bridging between Chemistry and Biology
17:00-17:15 **Christoph Kuhn,** University Hospital Zürich, CH
On an Early Theory of Life's Emergence in the Light of Future Artificial Chemical Life
17:15-17:30 **Kepa Ruiz-Mirazo,** University of the Basque Country, ES
On the 'Lipid-peptide Minimal Cell' Scenario.
17:30-17:45 **Peter Strazewski,** Université Claude Bernard Lyon 1, FR
Of the Darwinian Advantage to be Neither too Soluble, nor too Insoluble, Neither too Solid, nor Completely Liquid

Evening Lecture
18:00-19:00 **Frigyes Károlyházy,** Eötvös University, HU
The Spell of the Quantum World
19.00 Dinner

Tuesday 20 October
Session 3
Chair: Kepa Ruiz Mirazo, University of San Sebastian, ES
09.00-9:50 **Mauro Santos,** Autonomous University of Barcelona, ES
TBD (Evolvability and Network Models)
09:50-10:40 **Doron Lancet,** Weizmann Institute of Science, IL
Evolving Simulated Chemical Networks
10:40-11:10 Coffee break
11:10-12:00 **Niles Lehman,** Portland State University, US
A Self-constructing and Autocatalytic Set of RNAs
Short Talks
12:00-12:15 **Leroy Cronin,** University of Glasgow, UK
TBA (Nanostructures)
12:15-12:30 **Alina Ion,** Politehnica of Bucharest, RO
Carbon Nanostructures as Sorbents for Contaminants from the Environment
12:30-14:30 Lunch
Session 4
Pier Luisi Luigi, University of Rome, IT
14:30-15:20 **Peter Schuster,** University of Vienna, AT
Evolution at the Molecular Level – 150 Years after Darwin's Origin of Species
15:20-16:10 **Dan Tawfik,** Weizmann Institute of Science, IL

The Evolution of New Protein Functions and Structures - a Reconstructive Approach
16.10-16:30 Coffee break
16:30-18:00 Poster session
Evening Lecture
18:00-19:00 **Stuart Kauffman,** University of Calgary, CA
Collectively Autocatalytic Sets Plus Agency
19.00 Dinner

Wednesday 21 October

Session 5
Chair: Luc Steels, SONY Lab, Paris
09.00-9:50 **Ferenc Darvas**, ThalesNano, HU
TBD
09:50-10:40 **Balázs Papp,** Biological Research Center Szeged, HU
Systems biology of genetic interactions in yeast metabolism
10:40-11:10 Coffee break
11:10-12:00 **Günter Wagner,** Yale University, US
TBD (Evolvability)
Short Talks
12:00-12:15 **Gonen Ashkenasy,** Ben Gurion University of the Negev, IL
Kinetics and Mechanism of b-Sheet Peptide Replication
12:15-12:30 **Pierre-Alain Monnard,** University of Southern Denmark, DK
Biopolymerization in self-assembled, structured media
12:30 Lunch
Afternoon Half-day excursion
19.00 Dinner

Thursday 22 October

Session 6
Chair: John Odling-Smee, University of Oxford, UK
09.00-9:50 **Robert Aunger,** London School of Hygiene and Tropical Medicine, UK
TBD
09:50-10:40 **Chrisantha Fernando,** University of Sussex, UK
The Neuronal Replicator Hypothesis
10:40-11:10 Coffee break
11:10-12:00 **Luc Steels,** Free University of Brussels, BE
TBD
Short Talks
12:00-12:15 **Bjørn Østman,** Keck Graduate Institute, US
Impact of Epistasis on Evolutionary Adaptation
12:15-12:30 **Goran Goranovic,** University of Southern Denmark, DK
Systems Chemistry: Coupled Electron Transfer from a Nucleobase to a Lipid via a Photocatalyst
12:30-14:30 Lunch
Session 7
Chair: Bob Aunger, London School of Hygiene and Tropical Medicine, UK
14:30-15:20 **John Odling-Smee**
University of Oxford, UK
Niche Construction
15:20-16:10 **György Kampis,** Eötvös University, HU
TBD (Self-modifying systems?)

16.10-16:40 Coffee break

Evening Lecture
16:40-17:40 **Herbert Gintis,** Central European University Budapest, HU
Five Principles for the Unification of the Behavioral Sciences

Forward Look Plenary Discussion
Chair: György Kampis, Eötvös University Budapest, HU
17.40-17.43 Günter von Kiedrowski, Ruhr University Bochum, DE
17.43-17.46 Mauro Santos, University Autonoma di Barcelona, ES
17.46-17.49 Bob Aunger, London School of Hygiene and Tropical Medicine, UK
17.49-17.52 Luc Steels, Free University of Brussels, BE
17.52-18.10 Audience Discussion
20.00 Get-together & Conference Dinner

Friday 23 October
Breakfast & Departure

B.2 Workshops of the Action's Working Groups

B.2.1.1. Working Group 1, Meeting 2009

Opening Symposium Centre for Systems Chemistry
and
COST CM0703 Working Group 1 Kickoff Meeting
University of Groningen,
Bernoulliborg, Nijenborgh 9, 9747 AG Groningen
Room 5161.0105

Tuesday 28 April
08:30 – 09:00 **Coffee**

09:00 – 09:05 Welcome by **Serge Daan** (Dean Faculty of Natural Science, University of Groningen)

09:05 – 09:15 Opening Address by **Ben Feringa** (University of Groningen)

09:15 – 09:30 Intoduction to the COST action on Systems Chemistry by **Günter von Kiedrowski** (Ruhr University of Bochum, Germany)

Session Chair: Sijbren Otto

09:30 – 10:10 **Douglas Philp**, University of St. Andrews, UK
Selecting one reagent from a mixture: Exploiting replication networks in dynamic covalent chemistry

10:10 – 10:50 **Leonard Prins,** University of Padova, Italy

Dynamic covalent capture

10:50 – 11:05 **Coffee**

11:05 – 11:35 **Wesley Browne,** University of Groningen
Catalytic systems - the systems approach to homogenous catalysis

11:35 – 12:35 **Bert Meijer,** Technical University Eindhoven, the Netherlands
Plenary Lecture: *How to control supramolecular polymerization processes*

12:35 – 13:40 **Lunch**

Session Chair: Sabeth Verpoorte

13:45 – 14:00 European Launch of the *Journal of Systems Chemistry*

14:00 – 14:40 **Kay Severin,** EPFL Lausanne, Switzerland
Functional nanostructures and sensors by self-assembly

14:40 – 15:20 **Nicolas Giuseppone,** University of Strasbourg, France
Selection processes in dynamic combinatorial chemistry:
Toward the development of responsive systems

15:20 – 15:40 **Tea**

15:40 – 16:10 **Gerard Roelfes,** University of Groningen
DNA based catalytic systems

16:10 – 17:10 **Stefan Matile,** University of Geneva, Switzerland
Plenary Lecture: *Synthetic photosystems, soft and smart*

19:00 **Conference Dinner**

Wednesday 29 April

08:30 – 09:00 **Coffee**

Session Chair: Wesley Browne

09:00 – 10:00 **Günter von Kiedrowski**, Ruhr University of Bochum (Germany)
Plenary lecture: *Systems chemistry:*
Chemical self-replication and multicomponent assembly

10:00 – 10:40 **Ludovic Jullien,** Ecole Normale Superieure, Paris, France
Caging groups and photochromes for free energy transduction

10:40 – 11:00 **Coffee**

11:00 – 11:30 **Sijbren Otto,** University of Groningen
Mechanosensitive self replication

11:30 – 12:00 **Sabeth Verpoorte,** University of Groningen

The potential of microfluidics for systems chemistry:
Fluid and particle handling on the nL scale

12:00 – 12:40 **Gonen Ashkenasy,** Ben Gurion University of the Negev, Beer Sheva, Israel
New peptidic platforms for systems chemistry

12:40 – 13:45 **Lunch**

Session Chair: Gerard Roelfes

13:50 – 14:30 **Piet Herdewijn,** University of Leuven, Belgium
Towards an orthogonal episome through the chemical diversification of nucleic acids

14:30 – 15:00 **Ben Feringa,** University of Groningen
In control of dynamics of complex molecular systems

15:00 – 15:20 **Tea**

15:20 – 16:20 **Alan Rowan,** Radboud University Nijmegen, The Netherlands
Plenary Lecture: *Catalysis: Dynamics and Motion*

18:30 **Dinner (COST working group only)**

B.2.1.2. Working Group 1, Meeting 2010

Recent Topics in Systems Chemistry: Molecular Replication and Computation

Lemeridien hotel, Dead Sea, May 24-26, 2010
all lectures will take place in the Business Lounge at floor 16

Sunday, May 23, 2010

15:00 Students Arrival

18:30 Dinner **please go to the "Systems Chemistry" tables**

Monday, May 24, 2010

8:30 Registration (all day)

9:00-12:30 Young Scientists Session 1

Chairperson Gonen Ashkenasy, Ben Gurion University of the Negev, Israel

9:00	Light-Dependent Networks

	Zehavit Dadon
	Ben Gurion University, Israel
9:30	Peptide Self-Replication Driven by Self-Assembly
	Mathieu Colomb-Delsuc
	University of Groningen, The Netherlands
10:00	Controlling Electron Transfer through Coiled Coil Proteins
	Inbal Berkovich
	Ben Gurion University, Israel
10:30	***Coffee Break***
11:00	Exploiting Non Covalent Interactions for the Discovery of New Catalysts: Dynamic Covalent Capture Approach
	Marta Dal Molin
	University of Padova, Italy
11:30	Analysis of a Fulvene Based Replicator: Experiment and Theory in Interplay
	Arne Dieckmann
	Ruhr University of Bochum, Germany
12:00	2-Hydroxy-Azobenzenes to Tailor pH Pulses and Oscillations with Light
	Matthieu Emond
	Ecole Normale Superieure, France
12:30	Lunch

14:00-15:30 Young Scientists Session 2
Chairperson Gonen Ashkenasy, Ben Gurion University of the Negev, Israel

14:00	Combining Supramolecular Chemistry with Dynamic Covalent Chemistry: Synthesis of Large Molecular Cages
	Anton Granzhan
	EPFL Lausanne, Switzerland
14:30	Development of Extended Replicating Networks
	Jurgen Huck
	University of St. Andrews, UK
15:00	Peptide Self-Replication Driven Self Assembly
	Jerome Peyralans
	University of Groningen, The Netherlands
16:00	***Coffee Break***

16:30-18:30 Opening Session
Chairperson Addy Pross, Ben Gurion University of the Negev, Israel

16:30	Opening Remarks
17:00	Nanosystems Chemistry: Procedural replication and programmable multimodular assembly
	Gunter von Kiedrowski

	Ruhr University of Bochum, Germany
17:45	2010: A Small Space Odyssey with Luminescent Molecules
	A. Prasanna de Silva
	Queen's University, Northern Ireland
18:30	Dinner
20:00	GUEST LECTURE - Will the Dead Sea Die? Prof. Jiwchar Ganor

Tuesday, May 25, 2010

8:30-12:30

Chairperson Rivka Choen-Luria, Ben Gurion University of the Negev, Israel

8:30	Reconstructing Synthetic Cellular Compartments on a Surface
	Roy Bar Ziv
	Weizmann Institute, Israel
9:15	Novel Molecular Computing Systems
	Ehud Keinan
	Technion, Israel
10:00	***Coffee Break***
10:30	Lanthanoid Clusters: Unique Luminescent Probes and MRI Contrast Agents
	Abraham Shanzer
	Weizmann Institute, Israel
11:15	Multi-Scale Sequence Correlations are Evolutionary Selected to Increase Protein Promiscuity
	David (Dima) Lukatsky
	Ben-Gurion University, Israel
11:45	Minimal Model of Chemical Self-Replication and its Dynamic Consequences
	Enrique Peacock-Lopez
	Williams College, Massachusetts, USA
13:00	Lunch

14:00-16:00

Chairperson Nathaniel Wagner, Ben Gurion University of the Negev, Israel

14:00	Information Processing in Solution Using Common Luminescent Molecules
	David Margulies
	Weizmann Institute, Israel
14:45	Light and Heat for Systems Chemistry
	Ludovic Jullien
	Ecole Normale Superieure, France
15:30	Diploidy and the Selective Advantage for Sexual Reproduction in Unicellular Organisms
	Emmanuel Tannenbaum
	Ben-Gurion University, Israel

20:00 Dinner - Taj Mahal Restaurant Cost Business Meeting.

Wednesday, May 26, 2010

8:30-12:30

Chairperson N. Gabriel Lemcoff, Ben Gurion University of the Negev, Israel

8:30	Mechanosensitive Self-Replication Driven by Self-Organisation
	Sijbren Otto
	University of Groningen, The Netherlands
9:15	Stochastic Scenarios on "Mirror Symmetry Breaking" May Remove the Mist of Biochirogenesis
	Meir Lahav
	Weizmann Institute, Israel
10:00	Light Induced Reactivity in Systems Chemistry
	Gonen Ashkenasy
	Ben-Gurion University, Israel
10:30	***Coffee Break***
11:00	Molecular Interactions of Fluorinated Amino Acids within Native Protein-Like Environments
	Mario Salwiczek
	Free University, Germany
11:30	Amphiphilic β-Sheet Peptides as Building Blocks in Synthetic Biology
	Hanna Rapaport
	Ben-Gurion University, Israel
12:00	Simulation Tools for Probing Logic, Symmetry and Order in Systems Chemistry
	Nathaniel Wagner
	Ben-Gurion University, Israel
12:30	Lunch

Wednesday, May 26, 2010 - Continued
14:00-17:00
Chairperson Gonen Ashkenasy, Ben Gurion University of the Negev, Israel

14:00	Molecular Assemblies on Solid-Support
	Milko E. van der Boom
	Weizmann Institute, Israel
14:45	New Reactions with Thiols. An Original Entry to Dynamic Combinatorial Chemistry?
	N. Gabriel Lemcoff
	Ben-Gurion University, Israel
15:15	***Coffee Break***
15:35	Toward a General Theory of Evolution. A Goal for Systems Chemistry
	Addy Pross
	Ben-Gurion University, Israel
16:05	Chemistry at a Higher Level of Abstraction
	Milan N. Stojanovic
	Columbia University, New York, USA

16:50	Closing Remarks

B2.2.1 Working Group 2, Meeting 2009

Scientific Meeting for Work Group 2 of Cost Action CMO703 "Systems Chemistry"
Conference Center, Frankfurt Airport, October 6, 2009

Agenda

12.00 Project presentations of work group members:
R. Saladino
C. Richter
G.v. Kiedrowski
P. Nielsen

14.00 Discussion and selection of material for presentations at the "CHEMBIOGENESIS 2009" meeting at Lake Balaton, Hungary, 23-27 October, 2009 by Raffale Saladino

15.00 Discussions and planning of the future activities and meetings in work Group 2

B2.3.1 Working Group 3, Meeting 2009

COST CM0703 "Systems Chemistry"
Workgroup 3: "Integration of metabolic and compartimentalization subsystems"

1st workgroup meeting of the Workgroup 3

Place
Zürich, Switzerland, ETH Hönggerberg campus, room HCI J 498

Dates
April 16-18, 2009

Local organizer
Prof. Peter Walde, Department of Materials, ETH, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich, Switzerland

Program

Thursday, April 16, 2009
Evening Arrival of the participants and gathering in the Hotel Sternen in Oerlikon for those staying at Hotel Sternen

Friday, April 17, 2009
09:00 – 09:10 Opening
Prof. Peter Walde, ETH Zürich, CH

09:10 – 09:40 Short presentation 1: *Our plan to make peptidyl-RNA visible on lipid vesicles*
Prof. Peter Strazewski, Université Claude Bernard Lyon 1, F
09:40 – 10:10 Short presentation 2: *Molecular recognition of vesicles*
Prof. Bart-Jan Ravoo, Universität Münster, DE
10:10 – 10:30 Short presentation 4: *New prebiotic activation pathways for amino acids – toward the emergence of metabolism*
Dr. Laurent Boiteau, Université de Montpellier, FR

10:30 – 11:00 Coffee and Tea Break

11:00 – 11:30 Short presentation 5: *Lipid-producing minimal cells as a route to synthetic self-reproduction*
Dr. Pasquale Stano, Università degli Studi di Roma Tre, IT
11:30 – 12:00 Short presentation 7: *Recent progress towards self-assembly of a minimal protocell*
Sarah Maurer, University of Southern Denmark, DK
12:00 – 12:20 Short presentation 8: *Towards polymer-enzyme conjugates for compartimentalized reactions*
Prof. Peter Walde, ETH Zürich, CH

12:20 – 13:30 Lunch

13:30 – 14:30 Invited lecture 1: *Coenzyme autocatalytic network on the surface of oil microspheres as a model for the origin of life*
Dr. Alexei A. Sharov, National Institute on Aging, Baltimore, MD, US:

14:30 – 15:30 Invited lecture 2: *Shape behavior of growing vesicles and vesicle self-reproduction*
Prof. Sasa Svetina, University of Ljubljana, SI

15:30 – 16:00 Coffee and Tea Break

16:00 – 18:30 Discussions (coordinated by Prof. Peter Strazewski)
Exchange of information concerning possible collaborations

19:00 Diner

Saturday, April 18, 2009
10:00 -13:00 Discussions (coordinated by Prof. Peter Walde)

B2.5.1 Working Group 5, Meeting 2009

WG5 Meeting 2009. October 7-8, Collegium Budapest
October 7th Wednesday
10.00 – 10:30 Welcome and Agenda discussion
10.30 – 12.00 **Eörs Szathmáry:** Open questions in systems chemistry and systems biology
12.00 – 13.00 **Tamás Czárán:** Prebiotic replicase evolution in a surface-bound metabolic system
13:00 – 15:00 Lunch

15.00 – 16.00 **Chrisantha Fernando:** Evolvability in chemical and biological systems
16.00 – 17.00 **Mauro Santos:** The trade-off model of +/- strand replication
17.00 – 18.00 Free discussion among the working group participants

October 8th Thursday
10:00 – 12:00 **Christoph Flamm:** Evolution of Metabolic Networks: A Computational Framework
12.00 – 13.00 **Ádám Kun:** Strand separation via molecular wedges
13:00 – 15:00 Lunch
15.00 – 16.00 **Vera Vasas:** Lack of evolvability in self-sustaining autocatalytic networks
16.00 – 18.00 Free discussion among the working group participants

B2.5.2 Working Group 5, Meeting 2009

Evolvablity of molecular systems
7-8 May, 2010 Visegrád, Hotel Silvanus, Hungary

7 May
10:00 **Stuart Kauffman:** The nature of preadaptations and the non-algorithmic nature of evolution
11:30 **Eörs Szathmáry:** Evolvability issues in the GARD model, as desciibed by the Vasas et al. PNAS paper

15:00 General discussion of open-endedness, including quantum-mechanical considerations of facticity, of various systesm

8 May
10:00 **Chrisantha Fernando:** Analysis of evolvability of reflexively autocatalytic protein networks

14:00 General discussion: comparative aspects of GARD, protein networks, and templat-based evolution
16:00 Condlusions and plan for future research and publications

ANNEX C: Web site (description)

http://www.ruhr-uni-bochum.de/oc1/syschem/index.html

ANNEX D: Scientific and Technical Cooperation

D.1 EU-Funded Collaborative Research Projects

D.1.1 ECCell

Three CM0703 members launched a FP7-ICT/FET STREP on the systems chemistry of chemical cells in September 2008 (2.1 Mio, 3 years). The aim of the project is to establish a novel basis for future adaptive embedded information technology at the molecular level by constructing the first electronically programmable chemical cells (ECCell). This is naturally a high-risk, embryonic research project, but aimed at a breakthrough which will lay the foundation for immersed micro- and nanoscale molecular information processing with a paradigm shift to digitally programmable chemical systems. Chemical cells must combine self-replication, self-containment and self-regulation of resources (metabolism) enabling evolution to qualify as alive. ECCell will employ novel families of fully synthetic hybrid informational polyelectrolyte copolymers (not simply DNA), which simultaneously support all three cell functionalities. Their microscopic multiphase self-assembly under electric field control is the primary information processing mode of this technology. Realtime digital electric field control sequences, regulating the semi-autonomous self-assembly and reactive molecular processing, will both provide an online programming methodology for these complex systems and potentially serve as electronic genomes for the chemical cells. Programming methodologies (beyond optimal control theory) will be explored and evaluated which deal effectively with the remote real time distributed regulation of these novel semi-autonomous combinatorially complex chemical systems. The research will establish an effective IT interface between microelectronic and molecular information processing, by demonstrating its use to achieve a hard chemical synthetic systems objective (an artificial cell) opening a platform for programming a novel chemical living technology at the microscale. *Participants:* J.S. McCaskill (coordinator) & G. von Kiedrowski, Ruhr-U. Bochum, DE; A. Herrmann, U.Groningen, NL; I. Willmer, Hebrew U. Jerusalem, IL; S. Rasmussen, U. Southern Denmark, Odense, DK, K. Lindgren, Chalmers U., SE.
More info:
http://www.istpace.org/Web_Final_Report/the_pace_report/summary_and_conclusions/impact_on_ongoing_activitie/electronic_chemical_cell_-_.html

D.1.2 eFLUX

Three CM0703 members launched a FP7-ICT/FET STREP project on evolutionary microfluidics in February 2009 (2.3 Mio, 3 years). e-Flux will develop droplet-based digital microfluidic systems for the manipulation of reproducing artificial compartments and natural cells (including the analysis of adaptive pathways and molecular cooperation). e-Flux will distil insights from the comparative investigation of results on cooperation, adaptation, robustness and evolvability that could be utilized by future biomimetic and biology-inspired, reproducible and mutable fluid automata, and analyze the non-symbolic computations and the evolving representations from the perspective of selfreproducing automata. e-Flux will validate its progress by designing better artificial genetic representations for use in evolutionary computing applied to hard search problems. The e-Flux team will produce and test designs for implementations of associative learning networks in various biochemical systems and synthesise a version of the network. Experiments will demonstrate how bio-complexity can increase by evolutionary modification. The team will build an evolution machine by the development of a (semi-)automated serial-transfer protocol using micro- or mini-fluidics, which will be able to automatically cycle a population of few hundred thousand individual molecules or cells, evolving in parallel over a long time period. In contrast to the mass selection conditions in a macroscopic chemostat, this device allows the detailed monitoring of unique and repeatable evolutionary pathways taken by an unprecedented number of very small populations under identical conditions. This instrument will be a new and powerful tool for drug discovery and for biotechnology. *Participants:* E. Szathmary (coordinator), Parmenides Foundation, Munich, DE;

A. Kun, Collegium Budapest, HU; A. Griffith, ISIS, U. Louis Pasteur, Strassbourg, FR; J. Bibette, U. Pierre et Marie Curie, Paris IV, Fr; P. Husbands & C. Fernando, U. Sussex, UK; M. Santos, U. Autónoma di Barcelona, ES; A de Visser, Wageningen U., NL.
More Info: http://www.parmenides-foundation.org/research/projects/e-flux

D.1.3 MATCHIT

Four CM0703 members launched a FP7-ICT/FET/CHEM-IT project on the systems chemistry of chemical containers in April 2009 (2.7 Mio, 3 years). MATCHIT (MATrix for CHemical IT) will develop programmable information chemistry by introducing an addressable chemical container (chemtainer) production system and interfacing it with electronic computers via MEMS technology with regulatory feedback loops. As in the biological subcellular matrix, the chemical containers at the micro and nanoscales will be self-assembling, replicable and self-repairing. At the nanoscale, DNA containers will provide a programmable and replicable chemistry in which positional information can be harnessed for a range of nanoscale utilities. At the microscale containers based on DNAlabelled heterophase droplets and vesicles, will form microscopic labelled reaction vessels, which can themselves determine their next processing steps. Their DNA based addresses will be computable, enabling parallel chemical programming in a new multilevel architecture through autonomous address modification and resolution at the containercontainer, containersurface, and container molecule levels, providing a concrete embedded application for DNA computing. This generic programmable information chemistry will not only be an enabling technology for "immersed systems" IT applications in the life sciences, chemistry, and nanotechnology, but also promote a deeper understanding of the computational power of coupled production and information processes, as in biology, and provide a platform for building the more organic computers of the future. MATCHIT will investigate the general use of self-assembling chemtainers for informationintensive ChemIT. The project will develop and apply multiscale physical simulation tools and novel embedded IT architectures to process and integrates modular chemical and digital information. It will integrate and disseminate multidisciplinary European activities in ChemIT, supported by the European Center for Living Technology and provide an assessment of the likely longterm sociotechnical impact of this powerful technology. *Participants:* S. Rasmussen (coordinator) & M.M. Hanczyc, P.A. Monnard, Mærsk-McKinney Møller Institute, U. Southern Denmark, Odense, DK; J.S. McCaskill & G. Von Kiedrowski, Ruhr U. Bochum, DE; D. Lancet & E. Shapiro, Weizmann Institute of Science, Rehovot, IL.
More Info: http://fp7-matchit.eu/

D.1.4 Synthcells

Three CM0703 members (P. L. Luisi/P. Stano and P. Strazewski of WG3, and P. Nielsen of WG2) were involved in the EU FP6 Synthcells project, recently terminated. The Synthcells project deals with the construction of minimal cell models by bottom-up and top-down strategies. In particular, joint research was carried out on decoration of giant as well as small lipid vesicles by peptidyl-RNAs species and glycolipids. Giant vesicles were characterized by confocal microscopy, revealing several details of peptides/lipids interaction; small vesicles were studied by classical methods such as fluorescence spectroscopy and by using water-soluble and membrane probes. Further studies were carried out on Ser-His catalysis on peptide-nucleic acids (PNAs).

D.2 Nationally Funded Collaborative Research Projects

AYA2009-13920-C02 (124025 € + 136000 €). **Experimental and theoretical models for the abiotic emergence of chirality and its detection as the signature for evolutive systems in extraterrestrial materials.** ***David Hochberg Newman (Group at CAB-CSIC Madrid; MC and WG4), Josep M. Ribo (Group at the UB, Barcelona; MC and WG4)***
Biological homochirality Study of:

a) Chemical processes that adapt to the model of polarized bifurcations with nonlinear dynamics.
b) The possible generation in the laboratory of homochiral biases through processes of mirror symmetry breaking and chiral polarizations in chemical systems currently accepted as being significant prebiotic sources of bioorganic compounds.
c) Polarimetric and ellipsometric techniques as the only possible methodology for the direct detection of chirality.
d) The proposal for a generalist sensor system for the detection of homochirality based on the repetition of a reference process of mirror symmetry breaking that is very sensitive to the selection of chirality exerted by the sample.

The Italian PRIN Project “Experimental and theoretical approaches to synthetic cells” #2008FY7RJ4_001 involves two WG3 members (Stano and Mavelli) who investigate the course of compartmentalized reaction by combining experimental determination of reaction rate and yield as well as stochastic simulation of compartment formation, encapsulation, and internal (bio)chemical reaction, by giving much emphasis on stochastic phenomena as well as to a “population” approach that is quite innovative in the field.

ANNEX E: Outreach

E.1 Outreach by lectures, posters, seminars

E.1.1 Plenary and invited lectures on international conferences

Outside COST CM0703, the Action's mission was communicated during invited and/or plenary lectures on the following conferences/symposia/meetings:

- International Symposium on "Systems Chemistry-From Visions to Reality" organized by the Max-Planck Society, Berlin, Jan. 7-8, 2008.
- NRSC Catalysis Conference "Vision on Catalysis 2020", Amsterdam, Jan. 7-9, 2008.
- Gordon Research Conference "On the Origin of Life", Ventura, Jan. 20-25, 2008.
- Nordita Conference "On the Origin of Homochirality", Stockholm, Feb. 25-29, 2008.
- ECLT Summer School „Blueprint for an Artificial Cell", European Center for Living Technology, Venice, 4.-17.5.08.
- Beilstein Bozen Symposium "Systems Chemistry", Bozen, May 26.-31, 2008.
- Annual meeting of the the Society of Molecular Biology and Evolution, Barcelona, Spain, 5-8 June, 2008
- TECT-INCORE Summer School, Tools of the trade in cooperation research, Obernai, France, 1-5 September, 2008
- ESF-COST High Level Research Conference "Systems Chemistry", Hotel Villa del Mare, Maratea, 3.-7.10.08.
- ESF-COST LESC Frontier of Science Event „Water and Life – Complex Systems and Changes", Taormina, Sicily, 29.-31.10.08.
- EuroTides 2008, Düsseldorf, Dec. 4, 2008.
- Northrine-Westphalian Academy of Sciences, Apr. 26, 2009.
- Symposium "Physics of DNA Assembly and Applications", École de Physique, Les Houches, 3.-8.5.09.
- 44th Bürgenstock Conference, Brunnen, 17.-20.05.09.
- Agricultural University of Wageningen, Netherlands, 3 June 2009
- Centre for Ecological and Evolutionary Synthesis, Oslo, Norway, 5 June 2009
- Regio-Symposium on Organic and Bioorganic Chemistry, Castle Beuggen, Rheinfelden, 23.-25.09.09.
- Universitat de les Illes Balears, Darwin a l'era genòmica, Palma de Mallorca, Spain, 25 May, 2009
- ESF-COST High-Level Research Conference "Systems Chemistry II – Evolution and Systems", Anna Grand Hotel, Lake Balaton, 18.-23.10.09.
- Lindhard Lecture, Evolution today Symposium, Aarhus University, Denmark, 12 November 2009
- 5th German Chemoinformatics Conference, Goslar, 8.-10.11.2009.
- Dechema Symposium "Synthetic Bio(techno)logy", Frankfurt, 9.-10.11.2009.
- Gordon Research Conference "On the Origin of Life", Galveston, TX, USA, January, 10-15, 2010.
- "Konstanz Symposium Chemical Biology", Steigenberger Inselhotel, Konstanz, 16.-18.06.2010.
- Gordon Research Conference "Oscillations and Dynamic Instabilities in Chemical Systems", Lucca, 4.-9.7.2010.
- Annaul SMBE meeting, Lyon, France, 4-8 July, 2010
- IRT on Nucleosides, Nucleotides and Nucleic Acids 2010, Lyon, 29.08.-03.09.2010
- Symposium "From Molecular Structure to Systems Biology", Societá Chimica Italiana, San Vito di Cadore, 9.-11.9.2010.

- SupraBio, Bordeaux, 14-15.10.2010
- TNA 2010 "Therapeutic Nucleic Acids", Łódź, 14.-16.10.2010
- Gordon Research Conference "Radiation Chemistry, Radiation driven processes in physics, chemistry and biology", 18-23 July, 2010
- SynbioNT Kickoff meeting, Nottingham, 12-13.03.2009
- ESF Conference "ECSB II: Design, programming and optimisation of biological systems", San Feliu de Guixols (Spain), 29.03-3.04-2009

The resonance on the Action on "Systems Chemistry" was generally positive and even lead to the adoptation of the fields name by several prominent collegues worldwide.

E.1.2 Contributed lectures and posters on international conferences

- IRT on Nucleosides, Nucleotides and Nucleic Acids 2009, Kyoto, 8.-12.09.2008
- "Systems Chemistry I", Acquafredda di Maratea, 3-7.10.2008
- "Chembiogenesis 2008", Acquafredda di Maratea, 8-10.10.2008
- "Systems Chemistry II", Balatonfüred, 18-23.10.2009
- Fifth Meeting of the Spanish Network of Systems Biology "Fostering Systems and Synthetic Biology in Southern Europe", Madrid, 13-15.12.2009
- Challenges in top-down, bottom-up and computational approaches in synthetic biology, Nottingham, 18-22.03.2010
- XII International Artificial Life Conference,Odense (Denmark), 20-23.08.2010
- International conference on synthetic biology, Evry (France), 15-16.12.2010

E.1.2 Seminars

- Astrobiology Seminar, Alba Nova University, Stockholm, 15.02.08.
- ISIS Seminar, Université Louis Pasteur, Strasbourg, 14.03.08.
- Colloqium on Origins of life, ENS Paris, 0.10.08.
- Astrobiology Seminar, Alba Nova University, Stockholm, 05.12.08.
- Colloquium of the German Chemical Society (GDCh), University of Dortmund, 12.01.09.
- Colloquium in Organic Chemistry, LMU Munich, 26.01.09.
- 1384th Colloquium of the Chemical Society of Heidelberg. 07.04.09.
- Colloquium of the German Chemical Society (GDCh), University of Constance, 04.06.09.
- CENS Seminar, LMU Munich, 23.07.09.
- Seminar at the COST DC-Meeting, La Sapienza University of Rome, 18.9.09.
- Colloquium of the German Chemical Society (GDCh), University of Bochum, 15.7.10
- Colloquium of the German Chemical Society (GDCh), University of Kiel, 26.11.09
- Colloquium of the Israelian Chemical Society, Ben Gurion University of the Negev, 25.05.10.
- 3rd. Worshop of the Spanish Network on Asymetric Catalysis, University of the Balearic Islands, 07-08/10/2010.
- 8th symposium on Chemical Approaches to Chirality, Tokyo University of Science, 01/12/2010
- Theoretical Biology Seminars, CREA, Paris, 06.10.2010
- Colloquium of the German Chemical Society (GDCh), University of Tübingen, 26.11.10
- Introductory Lectures on Aspects of Complexity, Manchester, 6-8.07.2009.

- Erasmus Summer Schools “Evolution of The Biosphere”, Banyuls sur Mer (France), 17-28.08.2009 and 23.08-3.09.2010
- Techische Universiteit Eindhoven, 8.02.2010

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E.2 Outreach by media

- RUB press release 109 (14.05.08): http://www.pm.ruhr-uni-bochum.de/pm2008/msg00109.htm
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ANNEX F: Contacts in the ERA

F.1 FP7 Programmes established relating to Systems Chemistry

F.1.1 CHEM-IT

FET proactive initiative: Bio-chemistry-based Information Technology
(Extract from Work programme 2009-2010- Objective 2009.8.3 - Call 4)

The research will aim at realising programmable information chemistry by revolutionising the means to very precisely direct, control and analyse the chemical processes in sophisticated bio-inspired chemical systems in order to exploit the information processing capabilities of such systems. In addition, the research should aim at implementing evolution and self-organisation into these systems. This could imply the need to control, synthesise, analyse, adapt and/or proliferate chemical (sub-)systems.

Target outcome:

Foundations for a radically new kind of information processing technology inspired by chemical processes in living systems. This technology will exploit the information handling capabilities of such systems, as well as their ability to rapidly adapt/evolve and flexibly reconfigure in response to changing conditions by avoiding the constraints separating information handling from processes that create or reconfigure the physical system. Projects are expected to experimentally demonstrate in a physical impleÂ¬mentation major steps towards the realisation of such advanced information processing systems. In addition, proposals should express a clear vision on the potential implementation and impact of the proposed concept in the field of information processing. Expected impact:

* Enable the development of ICT systems and devices that utilize interactions between components to assemble complex functional information processing materials
* Enable a new generation of systems capable of interfacing with conventional IT systems that are self-replicating, self-repairing and/or capable of rapid adaptation/evolution as well as flexible reconfiguration in response to changing conditions

F.2 COST/ESF/EUREKA based collaboration

F.2.1 High-Level Research Conferences in Systems Chemistry

Stimulated by the approval of COST Action CM0703, COST and ESF jointly decided to support the emergent field of systems chemistry by a new series of research conferences which have a similar structure as the Gordon Research Conferences in the US. After the success of *Systems Chemistry* in Italy 2008, *Systems Chemistry II* in Hungary 2009, *Systems Chemistry III* is scheduled to take place in Israel 2011.

ANNEX G: Action Participation

- ASHKENASY Gonen gonenash@bgu.ac.il WG1
  Zehavit Dadon: Network behavior induced by light
  Boris Rubinov: Beta-sheet self replicating systems
  Nathaniel Wagner: Simulating molecular networks dynamics
- BERSINI Hugues bersini@ulb.ac.be WG5
- BLACKMOND Donna d.blackmond@imperial.ac.uk EXT
- BOITEAU Laurent laurent.boiteau@univ-montp2.fr ?
- BRANDENBURG Axel brandenb@nordita.org WG4?MC?
- DIECKMANN Arne arne.dieckmann@rub.de ESR speaker
- DIELS Ludo ludo.diels@vito.be ? MC
- FERINGA Ben feringa@chem.rug.nl WG1 MC
- FLAMM Christoph xtof@tbi.univie.ac.at WG5 MC
- GIUSEPPONE Nicolas giuseppone@ics.u-strasbg.fr WG1
- HERDEWIJN Piet piet.herdewijn@rega.kuleuven.be WG2
- HOCHBERG David hochbergd@cab.inta-csic.es WG4 MC
  Celia Blanco: Chiral polymerization models and mirror symmetry breaking
- JULLIEN Ludovic Ludovic.Jullien@ens.fr WG1
  Mathieu Emond: 2-Hydroxy-Azobenzenes to Tailor pH Pulses and Oscillations with Light
- KUN Adam kunadam@ludens.elte.hu WG5 MC
- LAHAV Meir meir.lahav@weizmann.ac.il WG4 MC
- LANCET Doron doron.lancet@weizmann.ac.il WG5 MC
- LEE Bo Ram boram.lee@epfl.ch WG1
- LUISI Pier-Luigi luisi@mat.ethz.ch WG3
- MARX Dominik dominik.marx@theochem.rub.de ?
- MANCINI Giovanna giovanna.mancini@uniroma1.it WG3
- MAUREL Marie-Christine marie-christine.maurel@upmc.fr
  Clementine Delan-Forino:replication of viroid in aspecific host
  Hussein Kaddour: studies of viroids and ribozymes in extreme conditions
  Claire Torchet: Autocatalytic ribosomal RNA maturation studies by SELEX. WG2
- MCCASKILL John john.mccaskill@rub.de WG5 MC
- MERCADER Juan-Perez delicadomd@inta.es MC
- NIELSEN Peter pen@imbg.ku.dk WG2 coord
- OTTO Sijbren so230@cam.ac.uk WG1 coord
- PASCAL Robert rpascal@univ-montp2.fr WG3 MC
- PHILP Douglas dp12@st-andrews.ac.uk WG1
- PRINS Leonard leonard.prins@unipd.it WG1
  Marta Dal Molin: Dynamic Covalent Capture for Catalyst Discovery
- PURELLO Roberto rpurrello@dipchi.unict.it WG4
- RASMUSSEN Steen steen@ifk.sdu.dk WG3 MC
- RAVOO Bart Jan b.j.ravoo@uni-muenster.de WG3
- RIBO Josep jmribo@ub.edu WG4 MC
  Arteaga, Oriol; Determination of polarization optical properties by Mueller matrix determination
  Crusats, Joaquim: Self-Assembly and Supramolecular

Chirality El-Hachemi, Zoubir: Emergence of chirality in crystallizations of racemic conglomerates Sorrenti, Alessandro: Self-assembly and auto-organization of amphihilic porphyrins

- RICHERT Clemens cr@rrg.uka.de WG2
- RUIZ-MIRAZO Kepa kruizmirazo@hotmail.com WG5
- SALADINO Raffaele saladino@unitus.it WG3 MC
- SANTOS Mauro mauro.santos@uab.es WG5 MC

Vera Vasas: Evolvability of non-templated molecular networks

- SEVERIN Kay kay.severin@epfl.ch WG1
- SIEGEL Jay jss@oci.unizh.ch WG4 coord
- STADLER Peter studla@bioinf.uni-leipzig.de WG5
- ULLRICH Alexander alexander@bioinf.uni-leipzig.de WG5
- KLEMM Konstantin klemm@bioinf.uni-leipzig.de WG5
- STANO Pasquale stano@uniroma3.it WG3 MC

Allegretti, Matteo: entrapment of solutes inside vesicles
Souza, Tereza: vesicle self-reproduction Martini, Chiara: protein synthesis inside vesicles
D'Aguanno, Erica: enzymatic reactions inside vesicles
Carrara, Paolo: formation and reactivity of giant vesicles

- STRAZEWSKI Peter peter.strazewski@unibas.ch WG3 MC

Michel, Benoît Y.: Multistep synthesis of puromycin analogues, ribosome kinetics
Krishnakumar, K. S.: Synthesis of puromycin analogues and amphiphilic peptidyl-RNA (minimal cell project SynthCells)
Le Chevalier Isaad, Alexandra: Synthesis of amphiphilic peptidyl-RNA and anchoring into liposomes (minimal cell project SynthCells)

- SUTHERLAND John john.sutherland@man.ac.uk WG3 MC
- SZATHMARY Eors szathmary@colbud.hu WG5 vice

István Zachár: General characterization of replicators
Chrisantha Fernando: Evolvability of different molceular systems

- TSOGOEVA Svetlana Svetlana.Tsogoeva@chemie.uni-erlangen.de WG4
- VIEDMA Cristobal viedma@geo.ucm.es WG4
- VLIEG Elias vlieg@sci.kun.nl WG4
- VON KIEDROWSKI Günter kiedro@rub.de WGX chair

Dieckmann, Arne: Experimental and theoretical studies on small replicators
Grzeschik, Daniela: Dissymetrisation based organo-autocatalysis Kramer, Daniel: Mechanistic studies on the Tsogoeva-reaction
Patzke, Volker Dr: Oligonucleotide replicators with 3',5'-disulfide links Plöger, Tobias: Fluorinated PNA for self-replicating studies using NMR

- WALDE Peter peter.walde@mat.ethz.ch WG3
- ZAGORSKI Zbigniew P. zagorski@ichtj.waw.pl MC

ANNEX H: Documents

H.1 Reports on ChemBioGenesis Meetings

H.1.1 Joint meeting report on the COST-ESF HLRC on "Systems Chemistry", Hotel Villa del Mare, Aquafredda di Maratea, October 3-7, 2008 and "Chembiogenesis 2008", Kickoff meeting of COST Action CM0703 ("Systems Chemistry"), Hotel Villa del Mare, Aquafredda di Maratea, October 8-10, 2008

By Günter von Kiedrowski

Background: October 2005 saw two events in Venice: "Chembiogenesis 2005" - the midterm evaluation conference of COST Action D27 "Prebiotic chemistry and Early Evolution" - laid the ground for a post-conference workshop in "Systems Chemistry" convening internationally renowned speakers from Europe, USA, and Japan to discuss the future of research connected to the Origin of Life problem. What came out from these discussions was the tentative scope and vision of an emergent field in chemistry: Systems chemistry was recognized as the offspring of supramolecular and prebiotic chemistry brought into existence by the influence of theoretical biology and complex systems physics as midwifes. The origin of life was seen as a key problem for systems chemistry – but also as a key and a problem at the same time: The problem is that chemistry is an ahistoric science. Chemistry cannot travel back in time to find out exactly the framework of conditions that existed on the early Earth enabling the startup of the origin of life as a process. It shares this problem with physics: The big bang and the Origin and Evolution of the Universe is out of scope of physics when it comes to the history of what happened in detail. On the other hand – the origin of the Universe is as much a source of inspiration to physics as it is the origin of life to chemistry. The key to the origin of the Universe in physics is to expand the range of energies at which particles can be studied by orders of magnitude, a direction which has resulted in the Large Hadron Collider at CERN by now. The key to the origin of life for chemistry might be to expand the degree of complexity of chemical reactions to be studied by orders of magnitude. This way systems chemistry may be viewed as the bottom-up pendant of systems biology heading for synthetic biology. Consequently, challenges for systems chemistry include (a) the search for a deeper understanding of structural and dynamic prerequisites leading to self-replication and self-reproduction in chemistry, (b) the quest for the coupling of autocatalytic systems, the integration of metabolic, genetic, and membrane-forming subsystems into protocellular entities, (c) the quest for the roots of Darwinian evolvability in chemical systems, and (d) the quest for chiral-symmetry breaking and asymmetric autocatalysis in such systems. Recently, the common denominator of these challenges were condensed to describe the mission of the new COST Action CM0703 ("Systems Chemistry") whose main objective "is to investigate autocatalytic reaction sytems within supramolecular, prebiotic, and other fields of chemistry and to develop methods for their integration into dynamic supersystems."

Almost exactly 3 years later the kickoff of this Action ("Chembiogenesis 2008") took place in Maratea, 200 km south of Naples. It was preceeded by the 1st ESF COST High Level Research Conference on "Systems Chemistry". The conference convened 25 internatio nally leading experts from various relevant areas to elucidate where we stand in 2008. Facets from this intriguing and truly interdisciplinary endeavour came from fields as diverse as geochemistry and organocatalysis, biomolecular chemistry and liposome technology, metal-organic chemistry and the theory of networks and evolution. Joining these facets by the unifying principle of autocatalysis lead to a new view which may be especially attractive for the next generation of chemists.

"ESF COST High Level Research Conference "Systems Chemistry": After the conference opening by Ken Dawson, IR, the field of Systems Chemistry was introduced by the conference chair, Günter von Kiedrowski, Germany, who pointed to its roots in nonlinear physics and chemistry, as well as in prebiotic chemistry. 22 years after the first demonstration of a chemical self-replicating system, replicator systems chemistry – the issue of the Saturday morning session (chaired by Peter Strazewski) - has arrived in a remarkably growing stage. Douglas Philp, UK, reported on the supramolecular origins of organic replicators and showed that the concepts of self-replication can be linked to the concept of dynamic combinatorial libraries, central to today's supramolecular research. His demonstration of the "harvesting" of a dynamic library by means of a "greedy" replicator is one of the first examples pointing to supersystem construction. Reza Ghadiri, USA, intro-duced an elegant and promising new concept for the replication of a peptide hybrid whose backbone was modified by nucleobases. Instead of making bonds between the building blocks bound to the template, Ghadiri demonstrated bond-making between a preformed oligomeric backbone and the template-bound nucleobases employing a fast thioester exchange chemistry. Gonen Ashkenasy, IL, expanded his earlier work with Reza Ghadiri on peptide replicator networks into the domain of molecular information processing. Literally all logic gates employed in today's digital computers can be "dynamically wired" inside such replicator networks. Whether this could lead to a change of today's IT com puting paradigm remains to be answered in the future, for today it at least shows a fruitful crosstalk of chemistry and information science.

A link between systems chemistry and the chemistry of the Early Earth was highlighted by two US speakers in the evening session, chaired by Zbig Zagorski, Poland. George Cody's approach to study high-pressure chemistry aims at reconstructing processes relevant to the chemolithoautotrophic scenario of Günter Wächtershäuser. While a remarkable num ber of key intermediates have been identified so far indeed, the hunt for the autocatalytic closure inside a "metabolic" geochemical cycle remains a challenge for the future. Jim Cleaves gave an overview of what mineral surfaces can do for the selective adsorbtion of biomolecules and their precursors, also with respect to the enantioselectivities involved.

Metabolic Systems Chemistry was the theme of the Sunday morning session chaired by Dieter Schinzer, Germany. Steven Benner, USA, gave an overview of his highly successful approach to expand the genetic alphabet by the utilisation of nucleobase mimics which express an alternative pattern of hydrogen bonds – not being used by nature – but being compatible with today's genuine or reengineered polymerases. He then focussed on his recent work on the formose reaction in the presence of borate. Individual steps of the network have been analyzed in detail and from Benner's results it looks that in the future one may be able to harvest the formose network, a goal that has been forseen for the COST Action mentioned above. Another goal of this Action is to couple the formose reaction with other "external" catalytic or autocatalytic cycles. Pioneering research into this direction was presented by Arthur Weber, USA, who showed that sugars and the intermediates of the formose network react with ammonia and primary amines to yield organocatalysts feeding back into their own synthesis – at least in an autoinductive fashion. Many of these reactions proceed with the growth of so-called microspherules, mesoscale structures that look like budding liposomes under the microscope and may be indicative for a successful coupling metabolic and containment subsystems. Much further work is needed however to decipher the detailed mechanistic pathways inside such coupled networks. Carlos Barbas III, USA, one of the founding fathers of organocatalysis, reported on the history of the field and the remarkable success story starting around the change in the millenium. Today, organocatalysis is one of the fastest growing fields in organic chemistry. Interestingly, one of the text-book examples from the Barbas lab, namely the proline-catalyzed Mannich reaction between acetone and the imine from ethyl glyoxylate and p-anisidine became the subject of the question adressed by Svetlana Tsogoeva, Germany: Do such reactions also proceed in the absence of an external catalyst? Her finding, that the enantiopure Mannich

product (prepared following the Barbas route) is an catalyst for its own formation received wide recognition. Even more remar kable was her finding that asymmetric autocatalysis can occur with spontaneous mirror-symmetry breaking. In a brief statement following Tsogoeva's lecture, von Kiedrowski reported that the finding could be reproduced by independent kinetic studies based on NMR and polarimetry. Much work is however need to decipher the mechanism of the reaction which is far away from a "simple" Mannich reaction.

Sunday evening saw a session on the link between Systems Chemistry and Synthetic Biology. Piet Herdewijn, Belgium, reported the remarkable finding that many polymerases accept deoxynucleoside 5'-phoshoramidates from various amino acids instead of dNTPs as substrates in primer elongation reactions. Pierre-Alain Monnard showed a case of light-driven formation of micelle-forming fatty acids from benzylic esters. The "metabolic" ingredient consists of a Ru-bipyridine complex tethered to 8-oxoguanosin, a light-sensitve system which on irradiation induces cleavage of the benzylic ester. Pasquale Stano gave a review on the work in the Luisi lab, starting with the self-reproduction for fatty acid micelles and vesicles from suitable precursors, but also mentioning later work on Luisi's statistical protein synthesis using filamenteous phages (never born proteins) and recent achieve ment of performing in vitro translation inside liposomes. Ludovic Jullien outlined a possible influence of periodic distortions of coupled reactions and a classification scheme for work done or better to be done in Systems Chemistry. Sunday evening also saw a forward look discussion adressing the goals of Systems Chemistry. It was pointed out that systems chemistry may play the same role for biology today as quantum physics played in the past for chemistry. Quantum physics transformed chemistry from a mainly descriptive science into the chemistry we know today. Life's roots have to be discovered in chemistry. Ken Dawson, IR, raised the question on the issue of fundraising for an international endeavor in Systems Chemistry, at least beween USA and Europe – and perhaps within a new EU-instrument called Topcores.

The Monday morning session, chaired by Josep M. Ribo, was devoted to Asymmetric Systems Chemistry. Kenso Soai, Japan, gave an impressive lecture about what his reaction can do for the detection of minute energy differences in certain classes of enantiomers. Cryptoenantiomers, viz. hydrocarbons having an asymmetric carbon and 4 alkyl chains of different lenghts, showing no optical rotation for the enantiopure form and being indistinguashable by any physical or chemical means, belong to such cases as well as "isotope enantiomers" such as symmetric glycerol derivatives, in which one of the peripheral carbons is replaced by 13C. So far, only their induction role within the Soai system can reveal whether there is R or S. Recent kinetic studies from Soai's lab reveals a second-order autocatalysis, such as it was proposed by Blackmond based on calorimetric data earlier, but the structure of the dimeric autocatalyst may deviate from earlier pictures. Latest X-ray studies show that the autocatalyst aggregates into linear non-helical polymeric forms which may be shorter in solution. Donna Blackmond presented a brilliant lecture on the fundamentals of chiral symmetry breaking. Her point that dynamic modelling should not be based on a "If pigs could fly chemistry" but on serious investigations on the underlaying mechanism – as well as on the proper consideration of Tolman's microscopic reversibility principle – has to be taken more seriously in the future, especially as the field is open for interpretation by researchers with little or no background in chemistry. Ben Feringa, Netherlands, gave an overview of his lab's broad and visionary work on pro grammed organogelation, the utilization of photochemical switching undergoing with visible photochromaticy, DNA/metal mediated catalysis of cycloaddition reactions, as well as the development of purely organic molecular motors. The session was finished by Meir Lahav, Israel, who introduced racemic ß-sheets as templates in the biochirogenesis of peptides. Although the self-sorting of activated amino-acids into strands of different handedness becomes understandable by the structural model of templating proposed, it remains open for future investigations, how this mechanism could lead to chiral symmetry breaking.

A session on theoretical aspects of systems chemistry, chaired by John McCaskill, took place on Tuesday morning. Peter Schuster, Austria, presented a very well compiled step-by-step introduction into the line of thinking that needs to be adopted once Systems Chemistry is ready to settle the quest for the roots of Darwinian evolvability, one of the field's central challenges. Although the issue of molecular evolution based on autonomous or directed schemes involving RNA molecules is currently limited to enzymatic "help", many general insights explained by Schuster may also apply to Darwinian chemistry. Eörs Szathmary focussed on one of the most difficult problems in the origin of life, viz. the origin of the genetic code. Building up on his cofactor handle hypothesis according to which amino acids bound or charged to RNA enriched the latter's catalytic repertoire, the code might have emerged from pairs of interacting tRNA-prototypes partly complementary to each other. Vladik Avetisov expressed his interest in the latter question but pointed out that the emergence of life deeply rests in chiral symmetry breaking within complex reaction networks of high dimensionality/complexity. Indeed, future experimental investigations of "messy" chemical networks may in fact benefit when looking for chiral symmetry breaking on the base of a "systemic signature". Addy Pros raised the provocative question "How can a chemical system act purposefully?". The answer is found in the insight that living systems constitute a kinetic state of matter (as opposed to the thermodynamic states that dominate the inanimate). Although this line of thinking may be an (intended) oversimplifi cation it may guide to the point where emergence meets the roots of Darwinian evolvabi lity. Christoph Kuhn gave an overwiew on his father's pioneerering contributions to the field of systems chemistry, beginning with the utilisation of Langmuir to organize functional modules such as FRET dye pairs into defined distances and ending in a logical sequence of events that marked the transition from self-replication to the evolution of the translation apparatus. We all enjoyed Hans Kuhn in the audience, who in turn enjoyed witnessing that many of his early ideas on the origin of life became a platform of active experimental research today.

The final session, chaired by Eörs Szathmary on Tuesday evening, saw the lectures of Peter Nielsen and John S. McCaskill, both participants of a European project on minimal artificial cells. Peter Nielsen introduced his peptide nucleic acids (PNAs) and presented data on the ligative copying of PNA in the presence of water-soluble carbodiimides. Interestingly, the PNA duplex structure does not collapse if water is replaced by mixtures of water and organic solvents mimicking the environment PNA may experience when bound to micelles. In any case, PNA being an achiral molecule adopting a helical double-stranded conformation, looks to very promising molecule for studies within systems chemistry. John McCaskill concluded the meeting with an overview on field-controlled oligonucleotide reactions inside microfluidic electrochemical cells, while setting a focus on novel dynamic simulation techniques which can explain the demixing and domain forma tion experimentally observed on the surface of liposomes.

Two poster sessions, many informal discussions, a Monday afternoon excursion, a beach accessable from the meeting venue only as well as an excellent treatment by the chief of the couisine were as important to the success of the event as the scientific menu composed by the lectureres. Thanks to the European Science Foundation and the COST support, the meeting was high-level indeed.

"Chembiogenesis 2008" started on Wednesday morning, October 8, with a welcome, an overview of the COST programme and its chemistry domain, and organizational remarks given by Javier Caldentey, Brussels. Dieter Schinzer, Magdeburg, outlined the success of several COST Actions and pointed to the need of continuation of COST under its current administrative setting. An overview of the Action on "Systems Chemistry", its main objec tive, mission and structuring was presented by the Action Chair Günter von Kiedrowski, Bochum.

The sessions were organized along the themes of the Action's Working Groups. Each working group leader (or deputy) had been appointed as session chairman. This scheme proved to be efficient to keep the meeting's timetable, giving each speaker a slot of 30 min. The following report will highlight presentations from speakers who did not talk at the preceeding meeting.

Session I, chaired by Sijbren Otto, Groningen was devoted to Supramolecular Systems Chemistry. Otto presented a very interesting example of a stochastic nucleation process leading to the nonlinear growth of either one or another class of supramolecular fibers. In the first class the subunits consisted of macrocycles containing six disulfide bonds, while seven in the second. The macrocycles were formed from a dynamic library of peptide-derived disulfide-linked cyclo/oligomers. The whole process reminded to somewhat between symmetry breaking (6 versus 7), the formation of peptide fibrils in the Alzheimer desease, and the principle of Ostwald ripening in crystals. Stochasticity is presumably the result of a criticality issue in nucleation. Nuclei of either class I and II compete for their formation from common precursor. Once a single nucleus reaches a critical size it continues to grow into longer fibers which occasionally may (or may not) break and create 4 instead of 2 ends for elongation (Orgel's "sorcerers apprentice" model). Kay Severin, Lausanne, presented his elegant inorganic approach towards dynamic combinatorial libraries based on metal-dye exchange reactions. The combination of "templating" by a given biomolecular analyte (AA's, peptides, nucleotides) and the concomitant color changes in a variety of such libraries is especially promising for the rapid identification and quantification of analytes by pattern recognition and multivariate analysis. Also, his construction of macrocycles and cages from the pool of commercially available boronic acids shows that the potential of classical supramolecular approaches can be elegantly expanded when choosing a set of molecules with the pragmatic sense of market availability. Lectures given by Douglas Philp, St. Andrews, Gonen Ashkenasy, Beer Sheva, and Meir Lahav, Rehovot completed the session.

Wednesday afternoon started with an exciting Inter-Action lecture by Dieter Schinzer, Magdeburg, on the Epothilone story. The hunt for novel highly potent anti-cancer drugs is inherently linked to the need for top-notch synthetic approaches. Once a new lead is found, only well chosen synthetic chemistry can create variants with better bioavailibility, lower toxicity, and more effective suppression of unwanted side reactions in the patient. One result, Ixabelipone, now on the US market, reflects the success of the race for the molecular summit undertaken by Danishewski, Nicolaou, and Schinzer a decade ago.

The afternoon continued with Session II on prebiotic systems chemistry chaired by Raffaele Saladino, Viterbo, who also gave the first lecture. Formamide was introduced as a prebiotic storage molecule, because high temperature allows both, its dehydration to hydrogen cyanide and its hydrolysis to formic acid and ammonia, all well documented members of a prebiotic repertoire. High temperature chemistry in the presence of titanium dioxide yields a variety of N9-formylpurines, but also a disproportionation of formate to give carbon dioxide and formaldehyde. The latter is important because the same chemistry which gives formyl-purines also causes formose-type conditions allowing the synthesis of acyclonucleosides. Clemens Richert, Karlsruhe, convincingly demonstated that the potential of Orgel's template directed reactions has not come to an end but can be even pushed into the direction of rapid biomedical applications (SNP detection) when choosing the proper leaving group at phosphorous and providing the proper supramolecular constraints, such as the "clamping" of an activated nucleotide between a primer and a downstream helper strand. Preorganizations of that kind can have a tremendeous effect on the rate of phosphordiester formation which can be even improved by exchanging the 3'-hydroxy group by a more nucleophilic amino group. The effect of extreme conditions caused by high-pressure on prebiotic reactions was the subject of the lectures given by Marie-Christine Maurel, Paris, and Dominik Marx, Bochum. While Maurel presented a solid physicochemical study on the mechanism

of the hairpin ribozyme showing that the activation volume is in line with data from proteinogenic enzymes and reflecting that the compactation of the transition state comes from a release of water molecules, Marx pointed out that water itself under high pressure is a completely different solvent than regular water. “Wächtershäuser” water is less polar than regular water, causing a change of the whole energy profile for prebiotic reactions. Using high-level computational methods based on Car-Parinello molecular dynamics the Marx group studied the activation of amino-acids by COS, and the concomittant formation of peptides at the surface of pyrite, an extremely demanding theoretical study which was only possible by ample access to supercomputer power. The session also included a lecture by Piet Herdewijn, Leuven.

Session III on Thursday morning was about complex systems chemistry. The session chair, Peter Strazewski, Lyon, addressed the stunning question how ribosomal catalysis could have worked before the emergence of translation. The question is linked to the acid/base properties and structures of aminoacyl nucleotide analogues, such as puromycin analogues whose conformations were studied by ab initio approaches and whose amino-basicities were measured by pH dependant 1H NMR experiments. These data will help to clarify the rate determining step in the ribosomal peptidyl transfer process. Robert Pascal, Montpellier, outlined a research programme his group will carry out in the COST Action. Central is the question which abiotic processed could have lead to the emergence of protobiochemical pathways. To answer this question work is heading to identify an inventory of energy sources, energy carriers and coupled reactions that may contribute to a plausible scenario. Hugues Bersini, Brussels, presented his algorithm to decouple complex reaction networks into simpler subsystems. The approach aims to automatize the detection of feedbacks and network autocatalysis that are constitutively present in any arbitrary reaction network. Zbigniew Zagorski, Warsaw, made a plea to set a systems chemistry direction into the realm of slow processes, such as to be expected when exposing organic matter to low concentrated sources of ionizing radiation.

The afternoon session chaired by Jay Siegel, Zurich, focussed on asymmetric systems chemistry. It included lectures by Jay Siegel, Zurich, Ben Feringa, Groningen, Donna Blackmond, London, Günter von Kiedrowski, Bochum, and Josep M. Ribo, Barcelona. Wim Norduin reported on the emergence of a single chiral solid phase under near equilibrium conditions presenting the stunning finding that simple grinding of an almost racemic amino acid derivative yielded a homochiral product. He showed for a conglemorate derivative of phenylalanine, that attrition enhanced total resolution is possible for a system exhibiting the complication of enantiomeric epitaxial growth.

The Friday morning session was devoted to theoretical aspects of systems chemistry. Chaired by Eörs Szathmary, Budapest, it included his talk as well as lectures by Adam Kun, Budapest, and John McCaskill, Bochum. Christoph Flamm reported on his approach towards the evolution of metabolism in silico. The approach utilizes a RNA based structure-to-function map which classifies functional motives with respect to their involvement in catalytic transformations of small molecules. Molecules and their reactions are first randomly generated by graph-based methods. Each transition in the reaction graph is then “rated” for chemical feasibility by quantum chemical computation of the respective ground and transition states. Goran Goranovich presented a concept for the exponential amplification and evolution of PNA molecules in a microfluidic apparatus. Copies of noncovalently immobilized PNA molecules are formed by chemical ligation and then transported to another site where they become immobilized as new templates. The scheme can be viewed as a combination of the SPREAD and SELEX technique and should be implementable in the laboratory. Raphael Plasson, Stockholm, reported on the emergence of protometabolism and the self-organization of non-equilibrium reaction networks. His view is based on his APED model for spontaneous symmetry breaking by polymerisation, depolymerisation, and racemisation but extends the latter into the realm of metabolism. According to Plasson evolution of the first replicators did

not work on templating mechanism and sequence encoded variation but on network replicators of similar reaction cycles, competing with each other. The view calls for experimental systems chemistry to find such cases.

Overall, the impression that emerged and was shared by many participants was that Systems Chemistry, while currently standing in its infant shoes, might have a bright future.

H.1.3 ESF-COST High-level Research Conference LAKE BALATON, HUNGARY 23-27 OCTOBER, 2009 SYSTEMS CHEMISTRY, COST ACTION CM0703, GRAND HOTEL ANNA, BALATONFÜRED, Chair: Eörs Szathmáry, Vice-Chair: Dieter Schinzer, University of Magdeburg, DE

Highlights:
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.

Executive summary
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. 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

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'.

Atmosphere and structure

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.

H.1.3 Meeting report on CHEMBIOGENESIS 2009 LAKE BALATON, HUNGARY 18-23 OCTOBER, 2009 SYSTEMS CHEMISTRY, COST ACTION CM0703, GRAND HOTEL ANNA, BALATONFÜRED, Organizer and chair: Eörs Szathmáry, Scientific secretary: Ádám Kun

Highlights

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 criteria of evolvability have been discussed at length at the meeting, as applied to alternative suggestion of early evolving systems. 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 experimental approaches, one of them showing that short RNA molecules produced by *in vitro* selection are specifically binding amino acids and one of them catalyzes peptide bond formation.

One of the main goals of systems chemistry is the enquiry into the molecular-chemical roots of evolvable, organized complexity. 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. For example, experiments tackle the stability and enzymatic potential of ribozymes under extreme conditions, and novel computational methods allow for fast kinetic folding of RNAs. The possibility of autocatalytic reaction networks producing target molecules was discussed and methods for analyzing such large and complex reaction networks were presented.

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 has 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.

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.

Topics

WG1 Supramolecular Systems Chemistry: The main topic of the section was molecular networks capable of producing complex behaviour and / or complex structure. Otto reported the formation of complex nano-structures. Ashkenazy showed that complex behaviour, even computation, can be achieved by small chemical networks. Huck discussed the possibility of dynamic covalent reaction networks that are programmable to produce a target molecule.

WG2 Informational Systems Chemistry: The RNA world hypothesis gained strong support in the presentations of the WG members. Saladino presented advances on convergent prebiotic synthesis

of key intermediates of the metabolic and genetic apparatus. Maurel discussed the stability of RNA molecules in extreme temperature and pressure that might be prevalent is some places on the primitive Earth, and also presented strong support for the idea that RNA could have been a catalyst even under these conditions. Yarus (guest speaker) reported on a 5 nucleotid long ribozyme capable of aminoacylation in *trans*. It is suggested that minuscule RNA enzymes could have participated in early forms of translation.

WG3 Metabolism and Vesicle Systems Chemistry: There are two main lines of research in this WG, one dealing with catalytic peptide networks, the other with reaction in and between vesicles (Pascal). Kauffmann (guest lecturer) reviewed recent advances in reflectively autocatalytic sets of peptides. Theory and supporting experimental results has been discussed. 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.

Reactions within vesicles and their application was discussed by Walde; advances in synthetic cell design were also reported (Stano, Monnard, Rasmussen). Study of interaction (recognition) and aggregation between vesicles were presented by Voskuhl and Paleos.

WG4 Asymmetric Systems Chemistry: There is accumulating evidence that spontaneous symmetry breaking in chemical reactions is much more common than previously thought (von Kiedrowski). Several methods for spontaneous asymmetric synthesis, enantioselective supramolecular aggregation, symmetry breaking during polymerization, and enantioselective processes at surfaces were reviewed (Siegel). Advances in controllable, efficient deracemization of chiral crystals have been presented (Vlieg, Ribo).

WG5 Theoretical Systems Chemistry: The genetics first (RNA world) and the compartmentalization first theories were discussed in a broad sense. Evolvability potential of the GARD model was investigated to see whether the assembly population can respond to directional selection in a Darwinian manner (Santos, Lancet). Advances in the simulation of the dynamics of surface-bound genetic replicators were presented by Czárán, and Flamm presented a novel and efficient method for the analysis of kinetic folding landscapes for RNAs. New insights into the transition from the RNA world to the peptide enzymes era, i.e. the origin of the genetic code, were shown by Rodin (guest lecturer).

IN SUM, the meeting presented an excellent overview of the state of the art in systems chemistry. Novel ways of generating asymmetry in chemical systems opened up a new and rapidly expanding research field. More effort will be needed to experimentally realize some of the infrabiological chemical supersystems (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 evolvability in such system is a burning issue in need of further clarification and experimental realization.

Prospects

The COST Annual Meeting Chembiogenesis 2009 at Balatonfüred gathered a substantial number of top researches from system chemistry in the broad sense. 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, have been addressed. 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 chemically reprogrammable production plants 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 enable the synthesis of 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 are 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.

Atmosphere and venue
The atmosphere was very conducive to open and 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.

H.2 Reports from Meetings of Working Groups

H.2.1.1 Working Group 1, 2009

H.2.1.2 Working Group 1, 2010
Brief report of the meeting by Gonen Ashkenasy:

Annual meeting of working group 1 of COST CM0703

The annual meeting of working group 1 of COST CM0703 was held in conjunction with the Israel Science foundation workshop entitled**:** "Recent Topics in Systems Chemistry: Molecular Replication and Computation". The meeting was held at Lemeridien hotel, Dead Sea, Israel - during 3 full days on May 24-26, 2010.

On the first morning and afternoon (24-5) students and postdocs from WG1 gathered to discuss their research projects with one another. The meeting was chaired by Dr. Ashkenasy, and was kept informal to stimulate discussion and interaction between the young researchers. Every research group participating in WG1 (with the exception of the Giuseppone group) was represented by at least one student or postdoc, while several groups sent larger delegations.

The evening sessions of the 1st day and the 2nd and 3rd days, featured talks by group leaders of the working groups. In addition, talks were given by other senior scientists from Israel, Europe and the

US (please refer to the attached program). Several local research groups from Ben Gurion University also presented short talks.

Topics that were discussed by the various speakers reflect the spread of subjects that is encompassed by Systems Chemistry, as well as topics in the adjacent field of Supramolecular Chemistry, such as molecular computation. After a short opening address by Gonen Ashkenasy and **Addy Pross** from Ben Gurion University, **Günter von Kiedrowski**, and then the guest lecturer from the UK, **AP de Silva**, presented plenary talks on nano-structures in Systems Chemistry, and molecular computation with metal complexes.

The second and third days of the meeting were devoted to scientific talks. **Ludovic Jullien** described the role of light and heat for Systems Chemistry application. A novel molecular system was described, in which light-induced structure isomerism can dramatically affect the properties of the molecule, such as its pKa. It was shown that the new system can be used to control dynamic processes in Systems Chemistry, as well as to track chemical changes within biological medium in cells. **Sijbren Otto** summarized the progress in the field of dynamic combinatorial chemistry, which lies at the very centre of Systems Chemistry. He then discussed in more details the new mechanosensitive self-replication system, recently developed in his lab. Intriguing information was given, showing how shaking or steering can lead to totally different dynamic behavior, and formation of different supramolecular structures. **Gonen Ashkenasy** described the newly developed peptide-based systems for studying light induced reactivity in Systems Chemistry. Thus, the design and synthesis of protein conformational switches were described, together with their potential use for controlling molecular replication, molecular electronics devices and drug delivery.

As mentioned, scientific lectures were given by other scientists that study System Chemistry or closely related topics. A short list of selected relevant talks is given in the following. **Roy Bar Ziv** (Weizmann Institute, Israel) described the reconstruction of synthetic cellular compartments on surfaces, using the newly developed 'DNA brushes'. **Enrique Peacock-Lopez** (Williams College, Massachusetts, USA*)* discussed theoretical models of chemical self-replication and their dynamic consequences. **Mario Salwiczek** (Free University of Berlin, Germany) presented the role of fluorinated amino acids within native protein-like environments. **Meir Lahav** (Weizmann Institute, Israel) introduced several Scenarios on “Mirror Symmetry Breaking” that may shine light Biochirogenesis. **Milan Stojanovic** (Columbia University, New York, USA) presented a plenary lecture on the current and future progress in the development of DNA molecular machinery and robotics.

On the first evening of the meeting (24-5), Prof. Jiwchar Ganor, the chairman of the Geology Department at Ben Gurion Univesity, presented a guest lecture on the geology and ecology of the area neighbouring the meeting site, entitled "Will the Dead Sea Die?". On the second evening (25-5), all participant had dinner together in a near-by local restaurant. During this dinner more informal discussion and exchange of ideas could take place. On the same evening, the WG1 business meeting took place, where we discussed potential locations for next year meeting, plans for exchanging students using the STSM COST funding, and plans to attract more funding for the group from other resources.

The meeting attracted the total number of 45 participants; students, postdocs and PIs attended the lectures during all three days. Non-lecturer participants came from Ben Gurion University as well as from other Universities inside Israel - all came to learn more about Systems Chemistry. Feedback received from numerous participants was that people enjoyed and appreciated the variety of subjects featured in the talks.

H.2.3.1 Working Group 3, 2009

Minutes of the COST CM0703 „Systems Chemistry“ WG03 meeting Zürich from 17/04/2009 to 18/04/2009

The meeting was the first meeting of the workgroup 3 of the COST action CM0703 “Systems Chemistry”. The meeting was held on the Hönggerberg campus of the ETH in Zürich, organized by Peter Walde. It was a useful and stimulating gathering with short presentations of six representers of the workgroup members, followed by two invited lectures given by Alexei Sharov (National Institute on Aging, Baltimore, MD, USA) and Sasa Svetina (University of Ljubljana, SI). The workgroups were represented by Peter Strazewski (Université Claude Bernard Lyon 1, F), Bart-Jan Ravoo (Universität Münster, DE), Pasquale Stano (Università degli Studi di Roma Tre, IT), Laurent Boiteau (Université de Montpellier, FR , replacing Robert Pascal), Sarah Maurer (University of Southern Denmark, DK, replacing Steen Rasmussen), and Peter Walde (ETH Zürich, CH). There were extensive discussions about possible collaboration and various aspects of the different research presented.

The local participants were interested in the different presentations and contributed with their questions and comments.

Unfortunately, Giovanna Mancini (Università Roma La Sapienza, IT) and John Sutherland (The University of Manchester, UK) could not participate due to health problems.

Thanks to the ETH infrastructure the meeting could be run very efficiently with low costs. Lunch and diner were taken on the ETH campus to save time and to have more time for discussions, Overall, the meeting was successful without any problems.

H.2.3.2 Working Group 3, 2010

No WG3 meeting

H.2.4.2 Working Group 4, 2010

Brief report of the meeting by Roberto Purello

SCIENTIFIC REPORT

2nd meeting of the Working Group 4 (Chirality in Systems Chemistry)
COST action CM0703 “Systems Chemistry”.
Taormina, April 23 to April 25

The scientific theme mainly discussed during the meeting was the mechanisms underlying the “Viedma Ripening”: that is, the resolution of racemic conglomerates by simply grinding slurries of the (racemate) crystalline forms in the presence of a racemizing catalyst in solution. The main discussion was centered on the differences between Ostwald (which is not catalytic) and Viedma experimental conditions which cause the former method not to be catalytic. Different mechanism has been discussed and the final, convergent (even if non final) view is that cluster-cluster interaction is central to the catalytic mechanism in which the changes of the distribution of the cluster size play a big

role. Other relevant topics have been discussed deeply during the meeting. Here follows a more detailed presentation of the talks.

The first two talks presented from Prof. Michael McBride and Prof. Elias Vlieg have shown a possible thermodynamic/kinetic mechanism concerning the "Viedma Ripening". Prof. Mehir Lahav has presented clear evidences of the role of thioesters of □-amino acids in the generation of prieval peptides, being them able to act both as initiators and multimer species. Dr. Karl-Heinz Ernst has discussed various example of amplification of chirality in 2D. This finding can be explained on the basis of the "Sergeant and Soldiers" principle, yet the role of the metallic surface needs to be clarified. Prof. Svetlana Tsogoeva has described very recent results, inspired from Prof. Cristobal Viedma results, concerning a complete deracemization of the conglomerate products by a Mannich reaction. Prof. Cristobal Viedma has presented new results concerning sublimation of racemate to give only one enatiomer. Dr. David Hochberg has illustrated a theoretical model to describe the role of external "noises" vs. "noises" intrinsic to chemical systems. The ultimate goal is the understanding of the role of possible environmental changes in prebiotic scenarios in driving a chiral symmetry break. Prof. Josep Ribó has shown very recent results concerning the role of the shape of the vessel on the transfer of chirality from clock-wise (CW) or counter-clock-wise (CCW) eddies to supramolecolar J aggregates of the tetraanionic meso-tetrakis-5, 10, 15, 20 - (4-phenylsulphonato) porphine. Prof. Roberto Purrello has discussed some possible applications of chirality tranfer. The talk presented from Prof. Joaquim Crusats has catalyzed a long, collegial discussion leading to one unified (but not definitive) proposal of the mechanism underlying "Viedma ripening".

H.2.5.1 Working Group 5, 2010??

No WG5 meeting in this year.

H.3 Other Meetings

H.4 Reports from STSMs

- H.4.1: COST-STSM-CM0703-5645: Meir Lahav, Weizmann Institute of Science, Israel, to David Hochberg, Centro de Astrobiologia, Madrid, Spain (from 26.01.2010 to 04.02.2010)
- H.4.2: COST-STSM-CM0703-05718: Omer Markovitch, Weizmann Institute of Science, Rehovot, Israel to Eörs Szathmary, Collegium Budapest (from 14.03.2010 to 25.03.2010)
- H.4.3: COST-STSM-CM0703-5849: Alexandra Le Chevalier Isaad, U. Lyon, France, to Pier Luigi Luisi, U. Roma III, Rome, Italy (from 07.03.2010-01.04.2010)
- H.4.4: COST-STSM-CM0703-6054: Vera Vasas, Eötvös University, Budapest, Hungary to Doron Lancet, Weizmann Institute of Science, Rehovot, Israel (from 10.05.2010-23.05.2010)
- H.4.5: COST-STSM-CM0703-06030: Alexandra Le Chevalier Isaad, U. Lyon, France, to Pier Luigi Luisi, U. Roma III, Rome, Italy (from 04.07.2010-24.07.2010)
- H.4.6: COST-STSM-CM0703-6071: J. Peyralans, University of Groningen, The Netherlands, to Gonen Ashkenasy, Ben Gurion University of the Negev, Beer Sheva, Israel (from 02.05.2010-27.05.2010)

H.5 Reports from members of the Management Comitee of CM0703 not participating in Working Groups

Z.P. Zagorski: Decades long investigations on ionizing radiation induced phenomena in objects important to prebiotic chemistry resulted in publications listed above, in particular in the monographical chapter on the role of radiation chemistry in the field. Our Laboratory offers irradiation of any sample by ionizing radiation of low (e.g. gamma and high energy electrons) or high LET (linear energy transfer). Irradiations for members of the COST action CM0703 are free, because our participation is supported by Polish Ministry of Science. Conditions of irradiations are adjusted to those occuring in the near Earth space or in outer space, as assumed, e.g. in testing panspermia hypothesis. Early Earth atmosphere can be simulated as well.

III. Previous versions of the Scientific Report

II.A. Results achieved during 2008

COST Action CM0703 "Systems Chemistry" started with its constitutional MC meeting on April 3, 2008 in Brussels. The meeting saw the election of:
Action chair: Günter von Kiedrowski, Ruhr-University Bochum, Germany
Action vice chair: Eörs Szathmary, Collegium Budapest, Hungary
Coordinator of Working Group 1: Sijbren Otto, University of Groningen, Netherlands
Coordinator of Working Group 2: Peter Eigil Nielsen, University of Copenhagen, Denmark
Coordinator of Working Group 3: Peter Walde, ETH Zurich, Switzerland
Coordinator of Working Group 4: Jay Siegel, University of Zurich, Switzerland
Coordinator of Working Group 5: Eörs Szathmary, Collegium Budapest, Hungary
WG coordinators started to contact Action members immediately after the 1st MC meeting to define the implementation of the WG scope and and to refine the scientific content as foreseen in the Memorandum of Understanding (MoU). The following implementation structure emerged during summer 2008:
WG1 will focus on **Supramolecular Systems Chemistry**. Component systems will be based on organic replicators, peptide replicator networks, synthetic molecular machinery, and dynamic combinatorial libraries (DCL). WG1 aims at a new generation of DCLs which links the principle of amplification by self-replication with the principle of adaptation explored close to equilibrium in conventional DCLs and to be explored far from equilibrium in this WG.
Participants: Sijbren Otto (currently UK, NL after April 2009), coordinator;
Gonen Ashkenazy, IL; Ben Feringa, NL; Guenter von Kiedrowski, DE; Douglas Philp, UK; Kay Severin, CH; Giuseppone Nicola, FR.
WG2 will focus on **Informational Systems Chemistry**. Components are natural nucleic acids such as RNA as well as and artificial nucleic acids mimics such as PNA, HNA, and others. Work will address the copying and replication of such NAs, both enzymatically and non-enzymatically, its directed molecular evolution, as well as pathways leading to the autogeneration of NAs from primitive precursor units. The role of artificial and mineral surfaces as compartiment of such processes involving charged NAs as well as of organic solvents and micelles for lipophilic NA mimics will be studied.
Participants: Peter E. Nielsen, DK , coordinator; Piet Herdewijn, BE;
Marie-Christine Maurel, FR ; Clemens Richert, DE; Raffaele Saladino, IT
WG3 will will focus on **Metabolic and Vesicle Systems Chemistry**. Component systems will be based on intra- and intervesicular reactions. The former will study reactions leading to the formation of amphiphiles inside vesicular and micellar containment as well as reactions in which small energy-rich and diffusable species such als photons, NOx and COS trigger the formation of peptides or PNAs inside. The latter will address vesiclevesicle interactions involving molecular recognition expressed by RNA or supramolecular equivalents for molecular recognition. Such studies will involve electronically addressable microfluidics for vesicle manipulation.

Participants: Peter Walde, CH, coordinator; Robert Pascal, FR; Steen Rasmussen, DK; Bart-Jan Ravoo, DE; Pasquale Stano, IT; Peter Strazewski, FR; John Sutherland, UK
WG4 will focus on **Asymmetric Systems Chemistry**. Component systems will be based on reactions and processes enabling the spontaneous generation of optical activity starting from a racemic or prochiral state. Work will focus on pericyclic reactions, organoautocatalytic reactions, as well as processes involving supramolecular aggregates, crystals, and interfaces. Experimental approaches towards chiral symmetry breaking will be conjuncted with theoretical approaches based on dynamic modelling and structural aspects of the former.
Participants: Jay Siegel, CH, coordinator; Donna Blackmond, UK; Axel Brandenburg, SE (Sweden has not yet accepted the MoU); Meir Lahav, IL; Josep Ribo, SP;
Svetlana Tsogoeva, DE; Elias Vlieg, NL (sending Wim Noorduin);
Guenter von Kiedrowski, DE; Ben Feringa, NL; David Hochberg, ES; Karl-Heinz Ernst, CH; Roberto Purello, IT; Cristóbal Biedma, ES.
WG5 will focus on **Theoretical Systems Chemistry**. Components are the theory of evolution, network theory, bifurcation theory, information theory, protocell theories as well as theoretical chemistry based on quantum mechanics and dynamics. The aim of this Working Group is to provide a platform for the theoretical analysis, modelling and quantitative description of processes investigated experimentally in the various Working groups of the Action. By the conjunction of theoretical chemistry and biology we aim to arrive at a new level of theory for dynamic phenomena relevant to the origin of life.
Participants: Eors Szathmary, HU, coordinator; Hugues Bersini, BE; Christof Flamm, AT; Adam Kun, HU; Doron Lancet, IL ; Dominik Marx, DE ; Peter Stadler, DE;
John McCaskill, DE; Mauro Santos, ES; Kepa Ruiz Mirazo, ES.
The MC agreed on the refined implementation structure on October 10, 2008. As a means to represent the voice of ESRs in future STSMs, and other ESR-related issues, Arne Dieckmann, Ruhr-University of Bochum, DE was elected for inclusion as ESR-speaker in the Action's steering board. STSMs were forseen from the 2nd year on, following the constitutional meetings of the WGs.
The following synergetic activities of the Action CM0703 were achieved in the first year:
(1) ***COST & ESF:*** (a) The kickoff workshop of CM0703 ("Chembiogenesis 2008", October 8-9, Maratea, IT; see section IIB) was coupled to the 1st ESF-COST High Level Research Conference on "Systems Chemistry" (October 4-7, Maratea, IT). The direct succession of events proved extremely fruitful from a scientific point of view, although difficult to organize due to different rules in ESF and COST. Nevertheless, whenever possible, event coupling between a COST workshop and a COST-ESF HLRC should become a favorable model in the future, because specific rule-based issues, such as the limitation of external experts in the COST model and the limitation of speaker reimbursement funds at the ESF side can be overcome more easily. (b) An "ESF-COST frontier of science event" on "Complex Systems & Changes: Water & Life" took place in Taormina, October 29-31". The chair of CM0703 introduced the COST Action on Systems Chemistry outlining its major objectives by examples.
(2) ***COST & FP7***: The launch of CM0703 was observed by FP7 policy makers and contributed to the awareness that Systems Chemistry is an emergent field which creates a strong link between *chemistry and information science*.
(3) ***COST & National Activities***: (a) The German Max Planck Society organized an International Workshop on Systems Chemistry in Berlin, January 7-8. The Action proposer was invited to introduce the field from a European point of view. He gave an overview of the work from individual labs involved in the Action. The Max-Planck Society decided to dedicate one of its institutes to the field of systems chemistry in the near future. (b) On February 19, the University of Groningen, NL, announced the start of a Center for Systems Chemistry directed by Action member Ben Feringa. The center will be supported by 5 Mio € over the next 5 years. (c) Ruhr-University of Bochum, DE, decided to organize a Research Department in Interfacial Systems Chemistry to be started in early 2009.

II.B. Dissemination of results

Conference:

CHEMBIOGENESIS 2008
KICKOFF MEETING OF COST ACTION CM0703
"SYSTEMS CHEMISTRY"

Programme

TUESDAY, OCTOBER 7

Arrival of Action members not participating at the preceeding ESF COST HLRC on "Systems Chemistry". Option to join with participants of "Systems Chemistry" at the conference dinner – prebooking required.

WEDNESDAY, OCTOBER 8

09:00 – 09:30 Opening of the kickoff meeting
Javier Caldentey, COST office, Brussels
Welcome and organizational remarks
Dieter Schinzer, University of Magdeburg, chair of the CMST domain committee
COST Chemistry: Introduction and Domain overview
Günter von Kiedrowski, Ruhr University of Bochum, chairman of CM0703.
Systems Chemistry: Introduction and Action overview
Session I: *"Supramolecular Systems Chemistry"*
chaired by **Sijbren Otto**, University of Groningen, coordinator of WG CM0703-1
09:30 – 10:00 **Sijbren Otto**, University of Groningen, NL:
Self-Replication of Peptides Driven by Nanostructure Formation
10:00 – 10:30 **Kay Severin**, EPFL Lausanne, CH:
Adaptive molecular networks
10:30 – 11:00 Coffee break
11:00 – 11:30 **Gonen Ashkenasy**, Ben Gurion University of the Negev, Beer Sheva, IL:
Functional Modules in Small Networks of Replicating Molecules
11:30 – 12:00 **Douglas Philp**, University of St. Andrews, UK:
Manipulating replication processes within a dynamic covalent framework
12:00 – 12:30 **Meir Lahav**, Weizmann Institute of Science, Rehovot, IL:
"Mirror symmetry-breaking" of peptides and amino-acids
12:30 – 13:00 Discussion
13:00 – 15:00 Lunch
"Inter-Action Lecture"
15.00 - 15.30 **Dieter Schinzer**, University of Magdeburg, DE
From a natural product synthesis to a powerful antitumor drug:
The success-story of the epothilones
Session II: *"Prebiotic Systems Chemistry"*
chaired by **Raffaele Saladino**, University of Viterbo
15:30 – 16:00 **Raffaele Saladino**, University of Viterbo, IT:
Advances in the prebiotic chemistry of nucleic acid components
16:00 – 16:30 **Clemens Richert**, University of Stuttgart, DE:
Sequence dependence of primer extension: Individual steps of non-enzymatic replication
16:30 – 17:00 Coffee break
17:00 – 17:30 **Piet Herdewijn**, Leuven Catholic University, BE:
Towards an orthogonal episome
17:30 – 18:00 **Marie-Christine Maurel**, Pierre and Marie Curie University of Paris, FR:
RNA in extreme conditions
18:00 – 18:30 **Dominik Marx**, Ruhr University of Bochum, DE:
Ab initio peptide synthesis in water at extreme conditions
18:30 – 19:00 Discussion
19:00 Dinner

THURSDAY, OCTOBER 9

Session III: *"Complex Systems Chemistry*"

chaired by **Peter Strazewski**, University of Lyon
09:00 – 09:30 **Peter Strazewski**, University of Lyon, FR:
Deciphering the nature of ribosomal catalysis: (How) did it work before the emergence of translation?
09:30 – 10:00 **Robert Pascal**, University of Montpellier, FR:
Energy carriers, coupled reactions and the driving force towards the emergence of translation
10:00 – 10:30 **Hugues Bersini**, Free University of Brussels, BE:
Decomposition of Complex Chemical Reaction Networks into Reaction Subnetworks
10:30 – 11:00 Coffee break
11:00 – 11:30 **Zbigniew Zagorski**, Institute for Nuclear Chemistry, Warsaw, PL:
Software and hardware in the origins of life chemistry
11:30 – 12:00 **Ludo Diels**, Flemish Institute of Technology, Vito, Mol, BE:
Brainstorm about sustainable chemical processes by the integration of reaction and separation processes
12:00 – 12:30 Discussion
13:00 – 15:00 Lunch
Session IV: "*Asymmetric Systems Chemistry*"
chaired by **Jay Siegel**, University of Zurich, coordinator of WG CM0703-4
15:00 – 15:30 **Jay Siegel**, University of Zurich, CH:
Could 3-letters and one hand suffice?
15:30 – 16:00 **Ben Feringa**, University of Groningen, NL:
Controlling dynamics in molecular systems
16:00 – 16:30 **Donna Blackmond**, Imperial College London, UK:
The role of autocatalytic systems in the origin of life
16:30 – 17:00 Coffee break
17:00 – 17:30 **Günter von Kiedrowski**, Ruhr University of Bochum, DE:
Replicator systems chemistry: Tools and examples
17:30 – 18:00 **Josep M. Ribo**, University of Barcelona, SP:
Mechanical induction of molecular chirality
18:00 – 18:30 **Wim Noorduin**, University of Nijmegen, NL:
The emergence of a single chiral solid phase under near-equilibrium conditions: Survival of the fittest
18:30 – 19:00 Discussion
19:00 Dinner
FRIDAY, OCTOBER 10
Session V: *"Theoretical Aspects of Systems Chemistry"*
chaired by **Eörs Szathmáry**, Collegium Budapest, coordinator of WG CM0703-5
09:00 – 09:30 **Eörs Szathmáry**, Collegium Budapest, HU:
Open questions in early genome dynamics
09:30 – 10:00 **Adam Kun**, Eötvös Loránd University Budapest, HU:
How common are RNAs that the Qb replicase connot replicate – What does it tell us about the replicability of ribozymes?
10:00 – 10:30 **Christof Flamm**, University of Vienna, AU:
Evolving catalysed metabolisms within the toy chemistry universe
10:30 – 11:00 Coffee break
11:00 – 11:30 **John McCaskill**, Ruhr University of Bochum, DE:
Integrated mesoscale simulation of physical self-assembly and chemical reaction: a tool for System Chemistry.
11:30 – 12:00 **Goran Goranovich**, University of Odense, DK:
A system exhibiting Darwinian evolution
12:00 – 12:30 **Raphael Plasson**, Nordic Institute for Theoretical Physics, Stockholm, SW:
Emergence of protometabolisms and the self-organiziation of non-equilibrium reaction networks
12:30 – 13:00 Discussion
13:00 – 15:00 Lunch and Meeting closure
Note that ChemBioGenesis 2008 was event-coupled to the ESF-COST High Level Research Conference on "Systems Chemistry". A report on both meetings is given in

Appendix A. Additional information is listed on the web site of the conference:
http://www.ruhr-uni-bochum.de/oc1/syschem/index.html

Scientific and Technical Cooperation

CM0703 members launched an EU-IST/FET STREP on the systems chemistry of chemical cells in September 2008 (2.1 Mio, 3 years). The aim of the project is to establish a novel basis for future adaptive embedded information technology at the molecular level by constructing the first electronically programmable chemical cells (ECCell). These ECCells will function through an interplay of chemical microprocessors and information molecule chemistry. Chemical microprocessors act as coprocessors coupled to chemical information systems through a digital electronically programmable microelectrode MEMS interface, taking advantage of inte-grated electronics and microfluidics. Participants: J.S. McCaskill (coordinator) & G. von Kiedrowski, Ruhr-U. Bochum, DE; A. Herrmann, U.Groningen, NL; I. Willmer, Hebrew U. Jerusalem, IL; S. Rasmussen, U. Southern Denmark, Odense, DK, K. Lindgren, Chalmers U., SE.

Appendix A:

Joint meeting report on the COST-ESF HLRC on "Systems Chemistry",
Hotel Villa del Mare, Aquafredda di Maratea, October 3-7, 2008
and

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"Chembiogenesis 2008",
Kickoff meeting of COST Action CM0703 ("Systems Chemistry"),
Hotel Villa del Mare, Aquafredda di Maratea, October 8-10, 2008

October 2005 saw two events in Venice: "Chembiogenesis 2005" - the midterm evaluation conference of COST Action D27 "Prebiotic chemistry and Early Evolution" - laid the ground for a post-conference workshop in "Systems Chemistry" convening internationally renowned speakers from Europe, USA, and Japan to discuss the future of research connected to the Origin of Life problem. What came out from these discussions was the tentative scope and vision of an emergent field in chemistry: Systems chemistry was recognized as the offspring of supramolecular and prebiotic chemistry brought into existence by the influence of theoretical biology and complex systems physics as midwifes. The origin of life was seen as a key problem for systems chemistry – but also as a key and a problem at the same time: The problem is that chemistry is an ahistoric science. Chemistry cannot travel back in time to find out exactly the framework of conditions that existed on the early Earth enabling the startup of the origin of life as a process. It shares this problem with physics: The big bang and the Origin and Evolution of the Universe is out of scope of physics when it comes to the history of what happened in detail. On the other hand – the origin of the Universe is as much a source of inspiration to physics as it is the origin of life to chemistry. The key to the origin of the Universe in physics is to expand the range of energies at which particles can be studied by orders of magnitude, a direction which has resulted in the Large Hadron Collider at CERN by now. The key to the origin of life for chemistry might be to expand the degree of complexity of chemical reactions to be studied by orders of magnitude. This way systems chemistry may be viewed as the bottom-up pendant of systems biology heading for synthetic biology. Consequently, challenges for systems chemistry include (a) the search for a deeper understanding of structural and dynamic prerequisites leading to self-replication and selfreproduction in chemistry, (b) the quest for the coupling of autocatalytic systems, the integration of metabolic, genetic, and membrane-forming subsystems into protocellular entities, (c) the quest for the roots of Darwinian evolvability in chemical systems, and (d) the quest for chiral-symmetry breaking and asymmetric autocatalysis in such systems. Recently, the common denominator of these challenges were condensed to describe the mission of the new COST Action CM0703 ("Systems Chemistry") whose main objective "is to investigate autocatalytic reaction sytems within supramolecular, prebiotic, and other fields of chemistry and to develop methods for their integration into dynamic supersystems."

Almost exactly 3 years later the kickoff of this Action ("Chembiogenesis 2008") took place in Maratea, 200 km south of Naples. It was preceeded by the 1st ESF COST High Level

Research Conference on “Systems Chemistry”. The conference convened 25 internationally leading experts from various relevant areas to elucidate where we stand in 2008.
Facets from this intriguing and truly interdisciplinary endeavour came from fields as diverse as geochemistry and organocatalysis, biomolecular chemistry and liposome technology, metal-organic chemistry and the theory of networks and evolution. Joining these facets by the unifying principle of autocatalysis lead to a new view which may be especially attractive for the next generation of chemists.
After the conference opening by Ken Dawson, IR, the field of Systems Chemistry was introduced by the conference chair, Günter von Kiedrowski, Germany, who pointed to its roots in nonlinear physics and chemistry, as well as in prebiotic chemistry. 22 years after the first demonstration of a chemical self-replicating system, replicator systems chemistry – the issue of the Saturday morning session (chaired by Peter Strazewski) - has arrived in a remarkably growing stage. Douglas Philp, UK, reported on the supramolecular origins of organic replicators and showed that the concepts of self-replication can be linked to the concept of dynamic combinatorial libraries, central to today’s supramolecular research. His demonstration of the “harvesting” of a dynamic library by means of a “greedy” replicator is one of the first examples pointing to supersystem construction. Reza Ghadiri, USA, introduced an elegant and promising new concept for the replication of a peptide hybrid whose backbone was modified by nucleobases. Instead of making bonds between the building blocks bound to the template, Ghadiri demonstrated bond-making between a preformed oligomeric backbone and the template-bound nucleobases employing a fast thioester exchange chemistry. Gonen Ashkenasy, IL, expanded his earlier work with Reza Ghadiri on peptide replicator networks into the domain of molecular information processing. Literally all logic gates employed in today’s digital computers can be “dynamically wired” inside such replicator networks. Whether this could lead to a change of today’s IT computing paradigm remains to be answered in the future, for today it at least shows a fruitful crosstalk of chemistry and information science.
A link between systems chemistry and the chemistry of the Early Earth was highlighted by two US speakers in the evening session, chaired by Zbig Zagorski, Poland. George Cody’s approach to study high-pressure chemistry aims at reconstructing processes relevant to the chemolithoautotrophic scenario of Günter Wächtershäuser. While a remarkable number of key intermediates have been identified so far indeed, the hunt for the autocatalytic closure inside a “metabolic” geochemical cycle remains a challenge for the future. Jim Cleaves gave an overview of what mineral surfaces can do for the selective adsorbtion of biomolecules and their precursors, also with respect to the enantioselectivities involved.
Metabolic Systems Chemistry was the theme of the Sunday morning session chaired by Dieter Schinzer, Germany. Steven Benner, USA, gave an overview of his highly successful approach to expand the genetic alphabet by the utilisation of nucleobase mimics which express an alternative pattern of hydrogen bonds – not being used by nature – but being compatible with today’s genuine or reengineered polymerases. He then focussed on his recent work on the formose reaction in the presence of borate. Individual steps of the network have been analyzed in detail and from Benner’s results it looks that in the future one may be able to harvest the formose network, a goal that has been forseen for the COST Action mentioned above. Another goal of this Action is to couple the formose reaction with other “external” catalytic or autocatalytic cycles. Pioneering research into this direction was presented by Arthur Weber, USA, who showed that sugars and the intermediates of the formose network react with ammonia and primary amines to yield organocatalysts feeding back into their own synthesis – at least in an autoinductive fashion. Many of these reactions proceed with the growth of so-called microspherules, mesoscale structures that look like budding liposomes under the microscope and may be indicative for a successful coupling metabolic and containment subsystems. Much further work is needed however to decipher the detailed mechanistic pathways inside such coupled networks. Carlos Barbas III, USA, one of the founding fathers of organocatalysis, reported on the history of the field and the remarkable success story starting around the change in the millenium. Today, organocatalysis is one of the fastest growing fields in organic chemistry. Interestingly, one of the text-book examples from the Barbas lab, namely the proline-catalyzed Mannich reaction between acetone and the imine from ethyl glyoxylate and p-anisidine became the subject of the question adressed by Svetlana Tsogoeva, Germany: Do such reactions also proceed in the absence of an external

catalyst? Her finding, that the enantiopure Mannich product (prepared following the Barbas route) is an catalyst for its own formation received wide recognition. Even more remarkable was her finding that asymmetric autocatalysis can occur with spontaneous mirrorsymmetry breaking. In a brief statement following Tsogoeva's lecture, von Kiedrowski reported that the finding could be reproduced by independent kinetic studies based on NMR and polarimetry. Much work is however need to decipher the mechanism of the reaction which is far away from a "simple" Mannich reaction.

Sunday evening saw a session on the link between Systems Chemistry and Synthetic Biology. Piet Herdewijn, Belgium, reported the remarkable finding that many polymerases accept deoxynucleoside 5'-phoshoramidates from various amino acids instead of dNTPs as substrates in primer elongation reactions. Pierre-Alain Monnard showed a case of lightdriven formation of micelle-forming fatty acids from benzylic esters. The "metabolic" ingredient consists of a Ru-bipyridine complex tethered to 8-oxoguanosin, a light-sensitve system which on irradiation induces cleavage of the benzylic ester. Pasquale Stano gave a review on the work in the Luisi lab, starting with the self-reproduction for fatty acid micelles and vesicles from suitable precursors, but also mentioning later work on Luisi's statistical protein synthesis using filamenteous phages (never born proteins) and recent achievement of performing in vitro translation inside liposomes. Ludovic Jullien outlined a possible influence of periodic distortions of coupled reactions and a classification scheme for work done or better to be done in Systems Chemistry. Sunday evening also saw a forward look discussion adressing the goals of Systems Chemistry. It was pointed out that systems chemistry may play the same role for biology today as quantum physics played in the past for chemistry. Quantum physics transformed chemistry from a mainly descriptive science into the chemistry we know today. Life's roots have to be discovered in chemistry. Ken Dawson, IR, raised the question on the issue of fundraising for an international endeavor in Systems Chemistry, at least beween USA and Europe – and perhaps within a new EUinstrument called Topcores.

The Monday morning session, chaired by Josep M. Ribo, was devoted to Asymmetric Systems Chemistry. Kenso Soai, Japan, gave an impressive lecture about what his reaction can do for the detection of minute energy differences in certain classes of enantiomers. Cryptoenantiomers, viz. hydrocarbons having an asymmetric carbon and 4 alkyl chains of different lenghts, showing no optical rotation for the enantiopure form and being indistinguashable by any physical or chemical means, belong to such cases as well as "isotope enantiomers" such as symmetric glycerol derivatives, in which one of the peripheral carbons is replaced by 13C. So far, only their induction role within the Soai system can reveal whether there is R or S. Recent kinetic studies from Soai's lab reveals a second-order autocatalysis, such as it was proposed by Blackmond based on calorimetric data earlier, but the structure of the dimeric autocatalyst may deviate from earlier pictures. Latest X-ray studies show that the autocatalyst aggregates into linear non-helical polymeric forms which may be shorter in solution. Donna Blackmond presented a brilliant lecture on the fundamentals of chiral symmetry breaking. Her point that dynamic modelling should not be based on a "If pigs could fly chemistry" but on serious investigations on the underlaying mechanism – as well as on the proper consideration of Tolman's microscopic reversibility principle – has to be taken more seriously in the future, especially as the field is open for interpretation by researchers with little or no background in chemistry. Ben Feringa, Netherlands, gave an overview of his lab's broad and visionary work on programmed organogelation, the utilization of photochemical switching undergoing with visible photochromaticy, DNA/metal mediated catalysis of cycloaddition reactions, as well as the development of purely organic molecular motors. The session was finished by Meir Lahav, Israel, who introduced racemic ß-sheets as templates in the biochirogenesis of peptides. Although the self-sorting of activated amino-acids into strands of different handedness becomes understandable by the structural model of templating proposed, it remains open for future investigations, how this mechanism could lead to chiral symmetry breaking.

A session on theoretical aspects of systems chemistry, chaired by John McCaskill, took place on Tuesday morning. Peter Schuster, Austria, presented a very well compiled stepby-step introduction into the line of thinking that needs to be adopted once Systems Chemistry is ready to settle the quest for the roots of Darwinian evolvability, one of the field's central challenges. Although the issue of molecular evolution based on autonomous or directed schemes involving RNA molecules is currently limited to enzymatic "help",

many general insights explained by Schuster may also apply to Darwinian chemistry. Eörs Szathmary focussed on one of the most difficult problems in the origin of life, viz. the origin of the genetic code. Building up on his cofactor handle hypothesis according to which amino acids bound or charged to RNA enriched the latter's catalytic repertoire, the code might have emerged from pairs of interacting tRNA-prototypes partly complementary to each other. Vladik Avetisov expressed his interest in the latter question but pointed out that the emergence of life deeply rests in chiral symmetry breaking within complex reaction networks of high dimensionality/complexity. Indeed, future experimental investigations of "messy" chemical networks may in fact benefit when looking for chiral symmetry breaking on the base of a "systemic signature". Addy Pros raised the provocative question "How can a chemical system act purposefully?". The answer is found in the insight that living systems constitute a kinetic state of matter (as opposed to the thermodynamic states that dominate the inanimate). Although this line of thinking may be an (intended) oversimplification it may guide to the point where emergence meets the roots of Darwinian evolvability. Christoph Kuhn gave an overwiew on his father's pioneerering contributions to the field of systems chemistry, beginning with the utilisation of Langmuir to organize functional modules such as FRET dye pairs into defined distances and ending in a logical sequence of events that marked the transition from self-replication to the evolution of the translation apparatus. We all enjoyed Hans Kuhn in the audience, who in turn enjoyed witnessing that many of his early ideas on the origin of life became a platform of active experimental research today.

The final session, chaired by Eörs Szathmary on Tuesday evening, saw the lectures of Peter Nielsen and John S. McCaskill, both participants of a European project on minimal artificial cells. Peter Nielsen introduced his peptide nucleic acids (PNAs) and presented data on the ligative copying of PNA in the presence of water-soluble carbodiimides. Interestingly, the PNA duplex structure does not collapse if water is replaced by mixtures of water and organic solvents mimicking the environment PNA may experience when bound to micelles. In any case, PNA being an achiral molecule adopting a helical doublestranded conformation, looks to very promising molecule for studies within systems chemistry. John McCaskill concluded the meeting with an overview on field-controlled oligonucleotide reactions inside microfluidic electrochemical cells, while setting a focus on novel dynamic simulation techniques which can explain the demixing and domain formation experimentally observed on the surface of liposomes.

Two poster sessions, many informal discussions, a Monday afternoon excursion, a beach accessable from the meeting venue only as well as an excellent treatment by the chief of the couisine were as important to the success of the event as the scientific menu composed by the lectureres. Thanks to the European Science Foundation and the COST support, the meeting was high-level indeed.

"Chembiogenesis 2008" started on Wednesday morning, October 8, with a welcome, an overview of the COST programme and its chemistry domain, and organizational remarks given by Javier Caldentey, Brussels. Dieter Schinzer, Magdeburg, outlined the success of several COST Actions and pointed to the need of continuation of COST under its current administrative setting. An overview of the Action on "Systems Chemistry", its main objective, mission and structuring was presented by the Action Chair Günter von Kiedrowski, Bochum.

The sessions were organized along the themes of the Action's Working Groups. Each working group leader (or deputy) had been appointed as session chairman. This scheme proved to be efficient to keep the meeting's timetable, giving each speaker a slot of 30 min. The following report will highlight presentations from speakers who did not talk at the preceeding meeting.

Session I, chaired by Sijbren Otto, Groningen was devoted to Supramolecular Systems Chemistry. Otto presented a very interesting example of a stochastic nucleation process leading to the nonlinear growth of either one or another class of supramolecular fibers. In the first class the subunits consisted of macrocycles containing six disulfide bonds, while seven in the second. The macrocycles were formed from a dynamic library of peptidederived disulfide-linked cyclo/oligomers. The whole process reminded to somewhat between symmetry breaking (6 versus 7), the formation of peptide fibrils in the Alzheimer desease, and the principle of Ostwald ripening in crystals. Stochasticity is presumably the result of a criticality issue in nucleation. Nuclei of either class I and II compete for their

formation from common precursor. Once a single nucleus reaches a critical size it continues to grow into longer fibers which occasionally may (or may not) break and create 4 instead of 2 ends for elongation (Orgel's "sorcerers apprentice" model). Kay Severin, Lausanne, presented his elegant inorganic approach towards dynamic combinatorial libraries based on metal-dye exchange reactions. The combination of "templating" by a given biomolecular analyte (AA's, peptides, nucleotides) and the concomitant color changes in a variety of such libraries is especially promising for the rapid identification and quantification of analytes by pattern recognition and multivariate analysis. Also, his construction of macrocycles and cages from the pool of commercially available boronic acids shows that the potential of classical supramolecular approaches can be elegantly expanded when choosing a set of molecules with the pragmatic sense of market availability. Lectures given by Douglas Philp, St. Andrews, Gonen Ashkenasy, Beer Sheva, and Meir Lahav, Rehovot completed the session.

Wednesday afternoon started with an exciting Inter-Action lecture by Dieter Schinzer, Magdeburg, on the Epothilone story. The hunt for novel highly potent anti-cancer drugs is inherently linked to the need for top-notch synthetic approaches. Once a new lead is found, only well chosen synthetic chemistry can create variants with better bioavailibility, lower toxicity, and more effective suppression of unwanted side reactions in the patient. One result, Ixabelipone, now on the US market, reflects the success of the race for the molecular summit undertaken by Danishewski, Nicolaou, and Schinzer a decade ago.

The afternoon continued with Session II on prebiotic systems chemistry chaired by Raffaele Saladino, Viterbo, who also gave the first lecture. Formamide was introduced as a prebiotic storage molecule, because high temperature allows both, its dehydration to hydrogen cyanide and its hydrolysis to formic acid and ammonia, all well documented members of a prebiotic repertoire. High temperature chemistry in the presence of titanium dioxide yields a variety of N9-formylpurines, but also a disproportionation of formate to give carbon dioxide and formaldehyde. The latter is important because the same chemistry which gives formyl-purines also causes formose-type conditions allowing the synthesis of acyclonucleosides. Clemens Richert, Karlsruhe, convincingly demonstated that the potential of Orgel's template directed reactions has not come to an end but can be even pushed into the direction of rapid biomedical applications (SNP detection) when choosing the proper leaving group at phosphorous and providing the proper supramolecular constraints, such as the "clamping" of an activated nucleotide between a primer and a downstream helper strand. Preorganizations of that kind can have a tremendeous effect on the rate of phosphordiester formation which can be even improved by exchanging the 3'-hydroxy group by a more nucleophilic amino group. The effect of extreme conditions caused by high-pressure on prebiotic reactions was the subject of the lectures given by Marie-Christine Maurel, Paris, and Dominik Marx, Bochum. While Maurel presented a solid physicochemical study on the mechanism of the hairpin ribozyme showing that the activation volume is in line with data from proteinogenic enzymes and reflecting that the compactation of the transition state comes from a release of water molecules, Marx pointed out that water itself under high pressure is a completely different solvent than regular water. "Wächtershäuser" water is less polar than regular water, causing a change of the whole energy profile for prebiotic reactions. Using high-level computational methods based on Car-Parinello molecular dynamics the Marx group studied the activation of amino-acids by COS, and the concomittant formation of peptides at the surface of pyrite, an extremely demanding theoretical study which was only possible by ample access to supercomputer power. The session also included a lecture by Piet Herdewijn, Leuven.

Session III on Thursday morning was about complex systems chemistry. The session chair, Peter Strazewski, Lyon, addressed the stunning question how ribosomal catalysis could have worked before the emergence of translation. The question is linked to the acid/base properties and structures of aminoacyl nucleotide analogues, such as puromycin analogues whose conformations were studied by ab initio approaches and whose aminobasicities were measured by pH dependant 1H NMR experiments. These data will help to clarify the rate determining step in the ribosomal peptidyl transfer process. Robert Pascal, Montpellier, outlined a research programme his group will carry out in the COST Action. Central is the question which abiotic processed could have lead to the emergence of protobiochemical pathways. To answer this question work is heading to identify an inventory of energy sources, energy carriers and coupled reactions that may contribute to

a plausible scenario. Hugues Bersini, Brussels, presented his algorithm to decouple complex reaction networks into simpler subsystems. The approach aims to automatize the detection of feedbacks and network autocatalysis that are constitutively present in any arbitrary reaction network. Zbigniew Zagorski, Warsaw, made a plea to set a systems chemistry direction into the realm of slow processes, such as to be expected when exposing organic matter to low concentrated sources of ionizing radiation.

The afternoon session chaired by Jay Siegel, Zurich, focussed on asymmetric systems chemistry. It included lectures by Jay Siegel, Zurich, Ben Feringa, Groningen, Donna Blackmond, London, Günter von Kiedrowski, Bochum, and Josep M. Ribo, Barcelona. Wim Norduin reported on the emergence of a single chiral solid phase under near equilibrium conditions presenting the stunning finding that simple grinding of an almost racemic amino acid derivative yielded a homochiral product. He showed for a conglemorate derivative of phenylalanine, that attrition enhanced total resolution is possible for a system exhibiting the complication of enantiomeric epitaxial growth.

The Friday morning session was devoted to theoretical aspects of systems chemistry. Chaired by Eörs Szathmary, Budapest, it included his talk as well as lectures by Adam Kun, Budapest, and John McCaskill, Bochum. Christof Flamm reported on his approach towards the evolution of metabolism in silico. The approach utilizes a RNA based structure-to-function map which classifies functional motives with respect to their involvement in catalytic transformations of small molecules. Molecules and their reactions are first randomly generated by graph-based methods. Each transition in the reaction graph is then “rated” for chemical feasibility by quantum chemical computation of the respective ground and transition states. Goran Goranovich presented a concept for the exponential amplification and evolution of PNA molecules in a microfluidic apparatus. Copies of noncovalently immobilized PNA molecules are formed by chemical ligation and then transported to another site where they become immobilized as new templates. The scheme can be viewed as a combination of the SPREAD and SELEX technique and should be implementable in the laboratory. Raphael Plasson, Stockholm, reported on the emergence of protometabolism and the self-organization of non-equilibrium reaction networks. His view is based on his APED model for spontaneous symmetry breaking by polymerisation, depolymerisation, and racemisation but extends the latter into the realm of metabolism. According to Plasson evolution of the first replicators did not work on templating mechanism and sequence encoded variation but on network replicators of similar reaction cycles, competing with each other. The view calls for experimental systems chemistry to find such cases.

Overall, the impression that emerged and was shared by many participants was that Systems Chemistry, while currently standing in its infant shoes, might have a bright future