



**European Cooperation
in the field of Scientific
and Technical Research
- COST -**

Brussels, 24 May 2013

COST 009/13

MEMORANDUM OF UNDERSTANDING

Subject : Memorandum of Understanding for the implementation of a European Concerted Research Action designated as COST Action CM1304: Emergence and Evolution of Complex Chemical Systems

Delegations will find attached the Memorandum of Understanding for COST Action CM1304 as approved by the COST Committee of Senior Officials (CSO) at its 187th meeting on 15-16 May 2013.

MEMORANDUM OF UNDERSTANDING
For the implementation of a European Concerted Research Action designated as
COST Action CM1304
EMERGENCE AND EVOLUTION OF COMPLEX CHEMICAL SYSTEMS

The Parties to this Memorandum of Understanding, declaring their common intention to participate in the concerted Action referred to above and described in the technical Annex to the Memorandum, have reached the following understanding:

1. The Action will be carried out in accordance with the provisions of document COST 4154/11 “Rules and Procedures for Implementing COST Actions”, or in any new document amending or replacing it, the contents of which the Parties are fully aware of.
2. The main objective of the Action is to unite researchers from different disciplines and focus them on the study of complex chemical systems, thereby establishing Europe as world leader in this area.
3. The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 44 million in 2013 prices.
4. The Memorandum of Understanding will take effect on being accepted by at least five Parties.
5. The Memorandum of Understanding will remain in force for a period of 4 years, calculated from the date of the first meeting of the Management Committee, unless the duration of the Action is modified according to the provisions of Chapter IV of the document referred to in Point 1 above.

A. ABSTRACT

Complex chemical systems have a huge potential for delivering new applications in areas ranging from materials science (in the short term) to medicine (in the long term). Complex systems are also highly relevant to fundamental questions such as the origin of life. Research on complex chemical systems has developed in parallel in three poorly connected communities working on supramolecular chemistry, far-from-equilibrium systems and the origin of life, respectively. This Action aims to establish Europe as a world-leader in the emerging area of complex chemical systems, by bringing together these research fields. Main objectives are to develop far-from-equilibrium self-assembly and self-replicating systems, self-assembling and reproducing compartments, and the use of information-rich molecules in these contexts. The approach to these subjects is inherently multidisciplinary and will only be possible by combining the expertise of different theoretical and experimental research groups around Europe.

Keywords: Molecular networks, dissipative systems, autocatalysis, self-assembly, origin of life.

B. BACKGROUND**B.1 General background**

Complex systems are all around us, ranging from ecosystems, to computational grids, and social networks. Complexity science is well developed in many disciplines, including sociology, physics and biology, *but has remained underdeveloped in chemistry*. Yet, of all disciplines, chemistry probably harbours the richest diversity of all complex systems, since it deals with the smallest entities that can still be readily manipulated: molecules. A stunning example of what may emerge from chemical complexity is life. Yet life is only one example, and with the creativity that comes natural to chemists many other systems may be created.

Until recently the development of complex chemical systems has been next to impossible, due to a lack of tools for analysing complex mixtures. However, with the recent advances in instrumentation, complex mixtures are now tractable, opening up a huge, exciting and fundamentally new research field. This field is the chemical counterpart to two topical areas in biology: systems biology and synthetic biology. Where the latter fields take a top-down approach, developing complex chemical systems takes place from the bottom up. The advantages of a bottom-up approach are in the ability to control every component and in the unlimited structural variety that is at the synthetic chemist's disposal. The momentum in this field of complex chemical systems is gathering rapidly, but it remains fragmented. Researchers from unconnected fields are now

independently converging on the central topic of complex chemical systems. This applies in particular to scientists from the supramolecular chemistry-, origins of life- and far-from-equilibrium systems communities.

Two of these communities were recently involved in successful separate COST Actions: D31 (Supramolecular Chemistry) and CM0703 (Systems Chemistry). The latter Action followed from Action D27 (Prebiotic Chemistry and Early Evolution). The confluence of these fields is starting to become a reality, yet large barriers between them remain. For example, there is no conference in which all three communities are adequately represented. Given that progress in the subject of this Action relies on efficient transfer of information and people between the communities, there is an acute need for bringing the communities together. The COST scheme is uniquely suited for this purpose.

B.2 Current state of knowledge

Researchers from different communities mentioned above are now converging on the central theme of complex chemical systems. However, progress is slow, due to the fact that research in the various communities is poorly connected. Below, a brief summary of the state-of-the-art in each of the separate communities is given, with emphasis on aspects that have recently started to connect the different fields.

1. Supramolecular chemists are proficient at making molecules and self-assembling systems of increasing structural and organizational complexity. The vast majority of such systems are at thermodynamic equilibrium. Assembly of molecules under equilibrium conditions is relatively easy to control, yet limited in scope in terms of structure and function that may be achieved, since only one inherently stable thermodynamic product can be obtained. Research is now advancing in the direction of performing self-assembly under kinetic control (i.e. out of equilibrium), where several different products may be accessed by controlling the assembly pathway. The resulting assemblies are not thermodynamically stable, but kinetically stable; i.e. large activation energy barriers separate the kinetic assemblies from the thermodynamic one. The presence of these activation barriers means that such kinetic assemblies are not dynamic, but tend to be stationary. By looking at biological systems as inspiration, chemists realize that the next step up in complexity would be to develop self-assembling systems which are far-from-equilibrium. These include dissipative systems, featuring stable states in which self-assembled structures are continuously being formed and degraded through chemically different pathways. When formation and degradation take place at similar rates, a seemingly stable homeostatic state is reached. Energy is required to drive the

continuous formation and degradation processes; i.e. such assemblies are dissipative. As shown in the famous work by Prigogine (Nobel Prize 1977) the presence of a continuous input of energy enables dissipative systems to *show phenomena that cannot exist under equilibrium conditions* or in kinetically controlled assemblies. Supramolecular chemists are now slowly starting to explore far-from-equilibrium systems, and the first publications on this topic (including papers in top journals – *Nature, Science* etc.) have appeared in the last three years. Progress here would accelerate dramatically by teaming up with scientists from the far-from-equilibrium community.

2. The field of far-from-equilibrium systems has developed mostly in isolation from supramolecular chemistry. Research in this area has progressed from discovery of chemical oscillators to methodologies for their design through the exploitation of open (flow) reactors. Following the discovery of propagating chemical waves and spirals, flow reactors including gels were also designed for reaction-diffusion processes, leading to the first experimental examples of stationary concentration patterns (length scale $\sim \mu\text{m}$) predicted in simulations in the 1950s. There have been great advances in the external control of pattern formation on catalytic surfaces (ruthenium gels and CO oxidation on platinum). More recently, research has focused on collective behaviours, such as synchronization of oscillations, in systems involving coupled electrodes, catalytic particles or even reversed micelles. There has also been a move towards coupling oscillators with gels for the design of novel chemo-mechanical devices that might be used in for example, drug delivery. Despite being often inspired by biology, the research in this area is still focused on a relatively small number of established chemical reaction networks that feature quite aggressive inorganic reactants (bromate, iodate and chlorine dioxide). The poor chemical compatibility of these systems with the molecules studied by supramolecular chemists and origin-of-life researchers has kept the field of far-from-equilibrium chemistry relatively isolated. The more broadly compatible organic systems developed by supramolecular and origins-of-life communities hold great potential as new workhorses with which to engineer far-from-equilibrium behavior. Success here would allow all the unique knowledge accumulated in the far-from-equilibrium community to become integrated into mainstream chemistry.

3. The origin-of-life community has a long history with COST, through consecutive Actions on Chembiogenesis and Systems Chemistry. These activities have created a strong nucleus of interdisciplinary origin-of-life research in Europe. The research in this area has focused on three main aspects of life: replication, compartmentalization and metabolism. Research on replication has focused on synthesizing and studying molecules (or networks thereof) that can make copies of themselves, giving rise to autocatalysis. Research on compartmentalization has focused on ways of creating membranes that may have formed the first boundary separating an early life form from its

environment. Finally, research on metabolism has focused on creating networks of molecules and reactions that may have led to the formation of the molecules that were eventually utilized by life. In the very recent years, several research groups, in Europe as well as elsewhere, were able to push this research forward by developing synthetic systems that combine two of the three characteristics mentioned above, and even all of them. One aspect of origin-of-life research has received surprisingly little attention, even though it is well-recognized: life's far-from-equilibrium nature. Almost every aspect of contemporary life is far from equilibrium and subject to continuous synthesis and degradation processes. This applies at the level of an organism; the level of a cell and at the level of individual biomolecules. Yet, somehow chemical systems that operate under a similar regime of synthesis and degradation have received very little attention in the origin-of-life community. Thus, there is an obvious gain for origin-of-life researchers to team up with the far-from-equilibrium community.

B.3 Reasons for the Action

The central idea of this Action is that cross-fertilization between the communities working on supramolecular chemistry, the origin-of-life and far-from-equilibrium systems will boost the scientific development at the interfaces between these areas that is required for advancing any of these areas. As outlined in Section B.2 the three disciplines are approaching the limits of what they can achieve in isolation. Bringing the communities together opens new horizons for each of the disciplines, while at the same time making a ground-breaking contribution to the research on complex chemical systems. This Action should *place Europe in a world-leading position in this emerging discipline* that is likely to become very prominent in the near future.

A convincing indication of the importance of this field comes from the fact that the Dutch Organization for Scientific Research (NWO) has recently awarded a 27 million euro grant from its Gravity Program to a consortium of Dutch research groups that aim to develop far-from-equilibrium supramolecular systems. Furthermore, Euro-Chemistry, an international, worldwide consortium of chemistry research funding and performing agencies, has also singled out Complex Chemical Systems at its first strategy meeting as an important research area for the coming years. The consortium will take actions to promote the further development of this research area by strengthening and combining (inter)national strategies, cross cutting the grand challenges of Horizon 2020. Since Euro-Chemistry aims at enabling cross-border collaborations, it fully supports this COST Action.

B.4 Complementarity with other research programmes

While the subject area of the Action is not covered by any other European activity there are promising interfaces with other programs, including:

- CMST COST Action CM1005: Supramolecular chemistry in water
- CMST COST Action TD 1003: Bio-inspired nanotechnologies: from concepts to applications
- European Science Foundation EUROCORES programme on "Synthetic biology: engineering complex biological systems"
- FP7 Marie Curie Initial Training Network on "Replication and Adaptation in Dynamic Molecular Networks"
- FP7 Marie Curie Initial Training Network on "Dynamic molecular nanostructures"
- The European Space Agency (ESA) Topical Team on "Chemo-Hydrodynamic Patterns and Instabilities"

Forms of exchange and integration with these activities include keeping close contact with the responsible Chairs/Coordinators and inviting leading participants of these Actions or Networks to give lectures, or the organization of special sessions of mutual interest or even joint workshops.

The Action will work in close association with Euro-Chemistry (an international consortium of chemistry funding and performing agencies) in achieving a common goal: fostering research in chemical complexity.

The Action will also liaise with the Complex Systems Society, which is an interdisciplinary organization in which the entire spectrum of complex systems research is united. Chemistry is currently underrepresented in this Society and the Action will redress this.

C. OBJECTIVES AND BENEFITS

C.1 Aim

The aim of the Action is to unite researchers from different disciplines and focus them on the study of complex chemical systems, thereby establishing Europe as world leader in this area.

C.2 Objectives

The Action will pursue the following main goals, which are at the interfaces between the three disciplines:

1. Establish the methodology for self-assembly far from equilibrium (Working Group

1). Traditionally, self-assembly is about obtaining the thermodynamic product of a given system.

However, by operating self-assembly in far-from-equilibrium systems it should be possible to create new properties that are not achievable under thermodynamic control, such as new self-assembled states that do not correspond to the thermodynamic product and stable spatial and temporal inhomogeneity. Attaining this goal will require a joint effort from the supramolecular and far-from-equilibrium communities.

2. Develop a new class of materials that are self-synthesizing, responsive and potentially self-repairing (Working Group 2). This should be achievable by combining the autocatalytic systems explored by the origin-of-life community with the self-assembly principles of supramolecular chemistry. This may lead to, for example, new self-assembled materials for molecular electronics and self-assembled gels for tissue culture.

3. Develop synthetic self-replicating systems capable of undergoing Darwinian evolution (Working Group 2). The approach to such systems relies on operating the replicating molecules created by the origin-of-life researchers under far-from-equilibrium conditions. Success here constitutes an important step towards the development of synthetic life. Approach to this goal will require the input from researchers from the origin-of-life and the far-from-equilibrium communities.

4. Develop methodology for compartmentalization of chemical systems and achieve a direct coupling between chemical reactions, energy harvesting and transport and membrane dynamics (Working Group 3). The development of chemical systems of ever increasing complexity brings with it the need to confine these in space, which protects the systems from the environment and keeps the components together. Yet, in order to be able to interface several different confined systems they need to be separated by semi-permeable barriers with controllable size, stability and permeability. This research requires the involvement of the origin-of-life and supramolecular chemistry communities.

5. Develop synthetic, information-rich molecules or assemblies that have the potential of being replicated in a purely chemical system (Working Group 4). The incorporation of information-rich molecules is particularly relevant, since advanced functional behavior of complex chemical systems will require increasingly elaborate chemical instructions that need to be carried in the constituent molecules.

C.3 How networking within the Action will yield the objectives?

The above objectives all require a combination of skills and expertise that is rarely encountered within a single university department, let alone a single research group. The COST framework is very powerful in bringing together scientists from the different disciplines and facilitate cutting-

edge science. From a practical point of view, the complex chemical systems that are at the heart of most of the Action's objectives are challenging to prepare, handle, study and understand. The preparation requires skills in synthetic chemistry; the handling may require special equipment, ranging from syringe pumps to microfluidics devices; the study of complex mixtures requires advanced analytical equipment and a complete understanding of the systems will only be possible with the help of computational modelling. Here again, the tools provided by COST will be essential for fostering collaborative research, by establishing training schools for early-stage researchers to acquire new techniques and skills, and via sponsoring the Short Term Scientific Missions (STSMs) that facilitate early-stage researchers exchanges between laboratories. Furthermore, theoretical work is essential in guiding experimental design. Collaborating with theoreticians will allow exploring the complex parameter space within a time span of weeks to hours, where experimental approaches tend to be prohibitively time consuming. Thus, achieving the objectives is only possible by bringing the necessary expertise that exists in different labs scattered over Europe together in this COST Action. The Action will also specifically cater for young researchers who will play a key role in building lasting links between the participating research groups.

C.4 Potential impact of the Action

The activities by the COST network will make it possible to engineer molecular systems that exhibit properties that were until now exclusive to living systems. This fundamental research will have profound impacts in a range of very different scientific and technological areas:

1. Medicine: The activities of the Action represent a first step in the direction of a fundamentally new approach to medicine. To date, the pharmaceutical industry is largely focused on developing individual drug molecules for specific diseases. A fundamental mismatch exists between this approach and the way (human) biology works: biological systems are hugely complex molecular networks characterized by redundancies in which (mal)function is controlled by many different factors. Attempting to interact with such systems through a single drug is unlikely to be effective and bound to cause undesirable side-effects. A much more logical approach would be to address diseases at systems level, not with a single drug, but with "intelligent" functional pharmaceutical systems based on the principles of complex molecular networks explored in this Action.

2. De-novo life: Efforts by the Action aimed at generating replicating systems that operate far from equilibrium are starting to close the gap between chemistry and biology, and the idea of generating de-novo life from fully non-biological starting materials becomes increasingly realistic. Efforts in this direction will reveal the essence of life, captured in a chemical system.

3. *Materials chemistry*: The Action will develop the new concept of self-synthesizing materials; i.e. materials that, upon exposure to a stimulus, can induce the formation of their respective building blocks or even of the entire assemblies. Such materials may find applications in fields ranging from tissue engineering to (potentially self-configurable) molecular electronics.

C.5 Target groups/end users

The Action targets theoretical and experimental scientists from a range of different disciplines: Supramolecular chemistry; Far-from-equilibrium research (Chemistry and Physics); Origin-of-life research (Chemistry and Evolutionary Biology); Theoretical physical chemistry and biology; Prebiotic chemistry and astrobiology; Researchers active in complexity science.

End users of the disseminated results may include small and medium-size enterprise and start-up and spin-off companies and, in the long term, the pharmaceutical industry. Many aspects of the work by the Action will also appeal to the general audience and the Action will actively engage with the press to reach this audience.

D. SCIENTIFIC PROGRAMME

D.1 Scientific focus

In brief, the work plan of the Action takes as a starting point the existing expertise contained in the three fields targeted by the Action. It then brings the relevant parts of these expertises together in the pursuit of the individual research objectives.

Relevant expertise from Supramolecular Chemistry includes:

- a basic molecular-level understanding of how non-covalent interactions may lead to self-assembly
- the ability to design and synthesize self-assembling molecules
- the ability to characterize the resulting assemblies using techniques such as electron microscopy, rheology, light scattering, atomic force microscopy, NMR etc.
- the ability to quantify the strength of noncovalent interactions in supramolecular systems
- the ability to design and analyse dynamic combinatorial libraries

Relevant expertise from the far-from-equilibrium community includes:

- skills to simulate and fit the kinetics of complex reaction networks
- knowledge of non-equilibrium thermodynamics and dynamic instabilities
- methodologies for designing emergent functional behaviour in molecular networks (oscillations, Turing patterns, traveling waves, collective behaviour etc.)

- skills in the development of reactors for non-equilibrium studies – continuous flow stirred reactors, flow unstirred (gel) reactors, electrochemistry and optical microscopy

Relevant expertise from the origin-of-life community includes:

- skills to develop autocatalytic reactions and self-replicating systems based on organic molecules
- skills in analysing and simulating the kinetics of autocatalytic processes, including replicator dynamics and evolutionary biology
- synthesis of information-rich molecules (peptides, natural and unnatural nucleic acids such as peptide-nucleic acids)
- skills in the preparation and analysis of compartments, such as bilayer vesicles

Below the specific research methods corresponding to the objectives outlined in Section C.2 are described. These include (but are not limited to):

1. Achieving self-assembly far from equilibrium requires gaining understanding and control over the kinetics of self-assembly, directing the process to specific product states. Progress here will rely strongly on detailed kinetic studies monitoring self-assembly by, for example, circular dichroism, fluorescence and UV/vis spectroscopy, light scattering and diffusion NMR techniques. Furthermore the Action aims to establish new chemical platforms in which the assembling molecules are continuously formed and turned over. This will require the development of clean chemical reactions that activate precursor molecules to assemble as well as the development of a second compatible process that converts the self-assembling molecules back to the precursors with minimum production of waste. Protocols will be developed (experimentally and theoretically) to combine elementary chemical modules into networks with more complex interactions, regulatory loops and global dynamic behaviour.

2. Developing replicating systems that self-assemble into nano- or mesoscale structures will require equipping replicators with functional groups that enable their assembly through specific noncovalent interactions. Compatibility is required between the chemistry of replication and the functional groups that drive the assembly of the replicators into materials. The assembly and replication processes will be monitored in real-time using advanced characterization techniques (electron microscopy, LC-MS). Combining the resulting data with modelling approaches will uncover the assembly and replication mechanisms. The properties of the resulting materials will be studied in detail (including conductivity measurements, rheological properties, potential for self-healing etc). Based on a detailed understanding of the assembly mechanisms it should be possible to control the physical properties of the resulting materials by adjusting specific experimental parameters. Properties that may be targeted include, but are not limited to, the formation of (hydro)gels, and electrical conductivity. Concepts and models in theoretical embryology and pattern

formation, where the joint action of self-assembly and dissipative structures (such as Turing systems resting on coupled reactions and diffusion), will be applied (in appropriately modified form) for the description of self-assembling replicator systems.

3. Achieving Darwinian evolution with replicators will require self-replicating systems to be operated far from equilibrium. Replicators need to be continuously produced from precursors, while being “killed” at the same time through a chemical reaction or by physical removal. Thus, separate but mutually compatible chemical processes for replication and destruction need to be developed. Darwinian evolution requires mutation and selection. The latter can be achieved through the action of the destruction reaction. What remains is to introduce mutation into the replicating systems. Methods will be developed to achieve this through chemical changes introduced by allowing replicators to replicate from a mixture of different building blocks, analogous to how RNA and DNA molecules mutate by incorporating different nucleotides. The recent series reports (all by EU scientists involved in the Action) on replicators emerging from dynamic combinatorial libraries are particularly relevant in this context. The theory of replicator dynamics will be developed further to accommodate the distinguishing features of these self-replicating systems.

4. Developing compartments that self-assemble from simple components (i.e. amphiphilic molecules), or from components that are the products of local chemical reactions. The permeability to relevant molecules will be investigated and the ability of the compartments to grow and divide will be explored. This may be achieved by monitoring the structures at single-compartment level by, for example, confocal fluorescence microscopy. Also theoretical aspects of compartmentalized replicators will be studied with focus on the limits in complexity that may be reached in metabolically coupled replicator systems. Theoretical models to describe the permeability and spatial division of these compartments will be refined. Computational scenarios to describe the possible routes of the coevolution of membranes, templates and metabolism will be worked out in detail.

5. Developing information-rich molecules that have the potential of being replicated or serve as instructions to a complex functional molecular system. New synthetic routes will be developed and various micro-heterogeneous reaction conditions will be explored that may give rise to condensation products that are difficult to obtain otherwise. The integration of the thus formed molecules into the systems described above will be investigated. This will be achieved by the combined input from chemists from the origin-of-life community specialized in prebiotic synthesis and supramolecular chemistry, who will work on routes of information transfer between different molecules through noncovalent interactions. The evolvability properties of these structures will be analysed utilizing concepts and models of population genetics and replicator dynamics.

All of these research tasks involve theoretical analyses and numerical simulations. Thus, the approach to all objectives relies strongly on contributions from both theoretical and experimental groups from across a wide range of disciplines.

D.2 Scientific work plan - methods and means

The scientific approach outlined in Section D.1 features a number of strongly interconnected activities that will require focused efforts by groups of scientists with complementary skills. Thus, the Action will form four Working Groups. Each Working Group will focus on one of the five objectives outlined in Section C.2, with the exception of Working Group 2, which will target both objectives 2 and 3, which are closely connected in practice and feature a central role for replicator chemistry. Given that the approach to each of these objectives is inherently multidisciplinary this will be reflected in the composition of the Working Groups, each of which will consist of researchers from different communities: thus supramolecular chemists, far-from-equilibrium systems researchers and origin-of-life researchers will interact within the individual Working Groups. Moreover, each Working Group will have experimentalist as well as theoreticians.

Working Group 1: Far-from-equilibrium self-assembly

This Working Group will combine expertise from the supramolecular chemistry and far-from-equilibrium communities. Its main aim is to develop new methodology to design, prepare and analyze new systems that feature self-assembly far from equilibrium.

Scientific milestones:

- year 2: new methodology for dissipative self-assembly
- year 3: self-assembled systems showing simple emergent behaviour (such as traveling waves)
- year 4: self-assembled systems that show advanced emergent behaviour (such as oscillations)

Working Group 2: Self-synthesizing materials and evolving replicators

This Working Group will combine expertise in replication from the origin-of-life community and expertise in self-assembly from the supramolecular community and aims at establishing a new class of materials that are not only self-assembling but also self-synthesizing. By combining the supramolecular expertise on dynamic combinatorial chemistry with replicator chemistry and far-from-equilibrium conditions this Working Group will also study the molecular-level evolution of replicators.

Scientific milestones:

- year 2: new methodology for self-synthesizing materials
- year 3: application of self-synthesizing materials (for example as gels for 3D cell culture or in

molecular electronics)

- year 3: new methodology for achieving replication far from equilibrium; adaptation of models from the theory of pattern formation for the description of this dynamic behaviour
- year 4: Darwinian evolution at the molecular level, coupled pattern formation-replicator models.

Working Group 3: Compartmentalization

This Working Group will combine expertise from the origin-of-life community with supramolecular chemistry with the aim of making compartments that may be used to confine complex molecular systems in space.

Scientific milestones:

- year 2: development of compartments with functional properties in terms of the permeability, fluidity or stability, if possible made of prebiotic amphiphiles; theoretical and computational analysis of how these properties have an effect on the whole system dynamics
- year 3: development of compartments that get coupled with simple chemical transformations, within or around them; in particular, explore how this can lead to growth and reproduction dynamics of the compartments; elaboration of refined models of spatial compartment division
- year 4: incorporation of complex functional molecular systems inside compartments; models of coexistence and possible coevolution of such chemical supersystems

Working Group 4: Information-rich molecules

This Working Group combines prebiotic chemists from the origin-of-life community with supramolecular chemists in order to create synthetic information-rich molecules that can interact with complex chemical systems.

Scientific milestones:

- year 2: development of new synthetic routes to information-rich molecules (RNA, DNA, peptides and synthetic analogs)
- year 3: development of methods for transmission of information between molecules and the system into which they may be integrated; replicator dynamic models to account for the special features of these systems
- year 4: integration of information-rich molecules into functional complex chemical systems; modelling the joint pattern formation processes and informational operations

E. ORGANISATION

E.1 Coordination and organisation

Action initiation phase (first 12 months)

This COST Action provides a flexible framework focused on a timely subject: complexity in chemistry. The initial nucleus of the Action will be strengthened by further research groups that will join following a call to European researchers. This call will be advertised through personal contacts, mailing lists, at conferences and on additional relevant websites.

The Action will be governed by the Management Committee (MC) according to the "Rules and Procedures for Implementing COST Actions". At the first MC meeting the Action Chair, Vice Chair, Grant Holder and Working Group Leaders will be elected. Also a Short-Term-Scientific-Mission (STSM) Coordinator will be appointed, who will oversee and process the exchange between researchers of the different groups. Finally, a Dissemination Manager will be elected who will maintain the Action's website and coordinate the public relations of the Action and supply relevant information to potential stakeholders and the press. During the first MC meeting also a venue and organizer for the first annual meeting will be chosen, which will be held within 6 months of the start of the Action.

A Steering Group will be elected, which consist of Chair, Vice-Chair, STMS Coordinator, Dissemination Manager and the Working Group Leaders. The Management Committee will decide about the participation of researchers in the various Working Groups, ensuring a good overall balance and match of expertise. Important other factors that will be considered are scientific merit, gender balance and participation of early-stage researchers.

All Working Groups will have their first meeting in the first year of the Action.

Action operation phase (months 13-48)

The Action will organize one Action-wide workshop every year. MC meetings will be held immediately following this event, while the Steering Group will meet prior to the workshop. Additional MC meetings, online votes, or Steering Group meetings may be held, if necessary. In order to maximize the proportion of the Action's budget that goes to its core activities (networking of scientists and STSMs), additional MC and Steering Group meetings will be held as much as possible in conjunction with Workshops or Working Group meetings. The MC will direct the activities of the Action and will need to approve (changes in) budget allocations. A fixed item on the agenda of MC meetings will be the monitoring of progress and evaluating the achievements of the Action based on reports from the Steering Committee. Attention will be paid to the number and quality of STSMs, gender balance, progress towards the scientific objectives and milestones defined in the Memorandum of Understanding (MoU), progress of the Working Groups, and dissemination activities. Training schools and workshops will be arranged for early-stage researchers (see E4). Another important task of the Steering Group is to identify any new scientific directions and facilitate the development of promising new lines of research within the general scientific

framework of the Action (for example, by arranging talks by external experts). The content of the Action's website will be expanded and updated by the Dissemination Manager, featuring contact details and links to all participating researchers; an overview of equipment that is available within the labs of the Action; a discussion forum; a list of publications; updated highlights of activities of the Action; a list of PhD and postdoc vacancies.

General milestones (for scientific milestones, see D2) of the Action are:

- top-level (*Science or Nature*) research papers published by members of the Action (every year)
- establishing wide-spread awareness of complex chemical systems as a new frontier in chemistry (end year 2)
- launch of research funding programmes seeded by the present Action (by the end of the Action)

E.2 Working Groups

The Action will have 4 Working Groups as outlined in Section D.2. Working Group Leaders will be elected whose responsibilities will include: shaping activities within the Working Group so that it remains well aligned with the overall objectives of the Action; coordinating the COST related activities of the research teams; monitoring the progress and evaluating the achievements of the Working Group, providing the Chair and MC with brief annual reports; maintaining direct lines of communication with the other Working Group Leaders; providing material to the Chair for the written reports. Since the objectives of the Working Groups are highly interconnected there is much to be gained from establishing good connections not only within Working Groups but also between Working Groups. In the first year all Working Groups meet separately to ensure good ties within the Working Groups. In subsequent years, paired Working Group meetings will be encouraged. These meetings will feature plenary lectures by selected Working Group members or external experts, together with parallel breakout sessions of the individual Working Groups. This arrangement will maximize cross-fertilization and the integration between the different disciplines and subjects brought together through the Action.

E.3 Liaison and interaction with other research programmes

The interactions with other research programs are outlined in detail in Section B4.

E.4 Gender balance and involvement of early-stage researchers

This COST Action will respect an appropriate gender balance in all its activities and the Management Committee will place this as a standard item on all its MC agendas. The Action will also be committed to considerably involve early-stage researchers. This item will also be placed as a standard item on all MC agendas.

Involvement of early-stage researchers will be promoted during Working Group meetings by reserving an extra day for oral presentation given exclusively by early-stage researchers. In addition the Action will organize specialized training schools on selected topics that could include, for example, simulations of molecular networks, or analytical chemistry of complex mixtures. Such training schools will be organized in year 1 and year 2 of the Action.

The Action will strive to address the gender balance. While the majority of the field consists of male researchers, the Action will try to include as many female scientists as possible while maintaining the criteria for acceptance into Working Groups outlined in Section E.1. The Action will also try to promote female researchers as role models by encouraging their participation in activities with high visibility, such as roles in the Steering Group or as Session Chairs of Workshops.

F. TIMETABLE

The duration of the Action will be 4 years.

Year 1

- month 1 First MC meeting
- month 3 Website active
- month 6 First Action-wide Workshop (tentative title: "Chemical Systems Far from Equilibrium")
- months 7-12 Meetings of the individual Working Groups
STSMs
- month 9 First training school. Tentative title: "Modern tools for analyzing dynamic chemical networks"

Year 2

- month 1-12 STSMs
- month 5 Second Action-wide Workshop (tentative title: "Systems Chemistry: from Origin of Life to Nanomaterials") + Steering Group + MC meeting
- month 12 Second training school. Tentative title: "Theory and simulations of chemical networks"

month 6-12 Combined Working Group meetings

Working Groups 1 + 2. Tentative title: “Self-assembly and self-replication far from equilibrium”

Working Groups 3 + 4. Tentative title: “Interactions and encapsulation of information-rich molecules within artificial membranes”

Year 3

month 1-12 STSMs

month 3 Third Action-wide Workshop (tentative title: “Functional complexity in chemical systems”) + Steering Group + MC meeting + mid-term evaluation

month 7-12 Combined Working Group meetings

Year 4

month 1-12 STSMs

month 5 Final Action-wide Workshop (tentative title: “Emergence and Evolution in Complex Chemical Systems” + Steering Group + MC meeting + preparation for final report

month 6-12 Combined Working Group meetings

G. ECONOMIC DIMENSION

The following COST countries have actively participated in the preparation of the Action or otherwise indicated their interest: AT, BE, CH, DE, DK, ES, FR, HU, IL, NL, UK. On the basis of national estimates, the economic dimension of the activities to be carried out under the Action has been estimated at 44 Million € for the total duration of the Action. This estimate is valid under the assumption that all the countries mentioned above but no other countries will participate in the Action. Any departure from this will change the total cost accordingly.

H. DISSEMINATION PLAN

H.1 Who?

This Action aims to establish Europe as world leader in the area of complex chemical systems. With this comes the responsibility to actively promote this new area of Science and showcase the achievements of the Action to the world through an intensive dissemination and outreach programme. The audience targeted by this program can be divided in three communities: Target group 1 consists of the researchers within the Action, including all members of the participating research groups or early-stage researchers looking to join the field (i.e. prospective

Action members).

Target group 2 consists of research scientists in academia, research institutes and industry in the following areas:

- supramolecular chemistry
- origin-of-life and prebiotic chemistry
- far-from-equilibrium chemistry
- pharmaceutical chemistry
- synthetic biology
- systems biology and chemical biology
- astrobiology
- materials science
- nanotechnology
- complex systems physics

Target group 3 consists of national and European policy makers in charge of planning:

- future research directions
- new research programmes and funding schemes
- calls for new FP7 projects, national thematic calls, collaborative calls etc.

Target group 4 consists of the general public and in particular the younger generations

H.2 What?

The material that will be disseminated to all target groups and that will be placed on the Action's website includes:

- A description of the scientific focus and objectives of the Action presented such that it will appeal to the general public, with links to more specialized information for researchers in the field
- An open discussion forum
- Recent highlights/news items, including videos of visually appealing experiments
- Calendar announcing the Action's meetings and other activities
- Contact details and links to the homepages of all participating researchers

For Target group 1 material that will be placed on the Action's website includes

- Photos and brief descriptions of the research expertise of the researchers participating in the Action.
- A list of PhD and postdoc vacancies associated with groups participating in the Action
- An overview of relevant specialized equipment that is available within the labs of the researchers

participating in the Action

- An internal discussion forum (access limited to Action members)
- Links to relevant documents on the COST website
- Reports of Working Group meetings, STSMs etc. (access limited to Action members)
- Minutes of meeting (access limited to Action members)

More extensive exchange of scientific expertise will take place through STSMs

Target group 2 will be reached through the established means of dissemination of scientific results, including:

- Perspectives and review articles
- Peer-reviewed publications in top-ranking international journals
- Books and book chapters
- Updated highlights of the scientific achievements of the Action on the Action's website
- Lectures at national and international conferences and workshops
- Talks given at institute seminars

In addition, the Action will organize training schools that will be open to other researchers in the field. The Action will also be the nucleus from which a Society for Complex Chemical Systems will be set up which serves to unite the researchers in this field.

Target group 3 will be addressed through grant applications and proposals from individual researchers or as collective activities by groups of researchers from the Action.

Target group 4 will be reached through articles in the popular science journals, articles in newspapers, appearances on radio and television shows, science open days, and public lectures to general audiences.

H.3 How?

- A logo will be designed for the Action
- All Action participants will be obliged to acknowledge the Action in all their published work derived from the Action's activities, during lectures and on posters, making use of the logos of COST and of the Action.
- Scientists from (pharmaceutical) industry will be invited to participate in the Action's meetings.
- The visibility of the Action will be enhanced by inviting leading scientists from Europe and from outside Europe from academia and industry to take part in the Action's activities.
- Scientists of target group 2 will be made aware of the Workshops and Working Group meetings organized by the Action through mailing lists, flyers and announcements through learned societies.

- The Dissemination Manager of the Action will actively engage with the press to report breakthroughs or particularly appealing results from the Action.
- The participants of the Action will aim to publish their work in the most prestigious journals (*Science* or *Nature*). This is a realistic aim, given the novelty and potential of the research area and will increase the visibility of the Action.