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

**Secretariat**
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**Brussels, 4 September 2001**

**COST 280/01**

**DRAFT MEMORANDUM OF UNDERSTANDING**

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| Subject : | Draft Memorandum of Understanding for the implementation of a European Concerted Research Action designated as COST Action D27 "Prebiotic Chemistry and Early Evolution" |

Please find attached the abovementioned draft Memorandum of Understanding.

DRAFT

Memorandum of Understanding

For the implementation of a European Concerted Research Action

Designated as COST ACTION D27

"Prebiotic Chemistry and Early Evolution"

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

1. The Action will be carried out in accordance with the provisions of document COST 400/01 “Rules and Procedures for Implementing COST Actions”, the contents of which are fully known to the Signatories.

2. The main objective of the Action is to develop the chemistry connected with the origin of life and early evolution of life on Earth, with special emphasis on self-replicating systems, prebiotic synthesis of nucleic acids and polypeptides, as well as simple protocells as early models of biological cells.

3. The overall cost of the activities carried out under the Action, or under very related fields of inquiry, has been evaluated in the year 2000 at over Euro 80 million.

4. The memorandum of Understanding will take effect on being signed by at least five Signatories.

5. The Memorandum of Understanding will remain in force for a period of 5 years, unless the duration of the Action is modified according to the provisions of Chapter 6 of the document to in Point 1 above.

# COST ACTION D27
# "PREBIOTIC CHEMISTRY AND EARLY EVOLUTION"

## A. GENERAL BACKGROUND

### *A.1. Why a COST action on this topic/defining the topic*

Our scientific view today is that life originated on Earth by a prebiotic molecular evolution, whereby simple endogenous molecules, by continuously increasing their molecular complexity, have given rise to more and more complex structures and specifities, up to the onset of the first protocells and living organisms. **Prebiotic chemistry** is the chemistry that describes the chemical processes associated with this transition to life from the inanimate matter. It is a classic field within the chemical world. It was initiated in the early 1920s with the seminal book by Alexander Ivanovich Oparin, but it was not until the famous experiments by Stanley Miller in 1953 that it became an independent and respected area of research. Miller could show in fact that simple electrical discharges in a prebiotic-like gaseous mixture could produce amino acids and other important biomolecules. Since then, prebiotic chemistry has expanded greatly, and thanks to researchers like J. Orò, S. Fox, A. Eschenmoser, A. Brack, J. Ferris, L. Orgel, G. Wächsterhäuser, G. Ourisson and many others, conditions could be described, under which several biomolecules could be fabricated under alleged prebiotic conditions.

This does not mean that the questions related to the origin of life on Earth have been solved. Actually, most of the main questions are still open-which is one of the reasons why a coordinated scientific action is needed.  For example, we do not know how specific sequences of proteins (enzymes and transport proteins) could be formed, nor how nucleotides could be stereospecifically polymerised in specific sequences which were able of self-replication. The questions of the onset of the genetic code, as well as the origin of the first metabolic cells, are still unanswered. The elucidation of all these unknown processes is the great challenge in this field of prebiotic chemistry.

Some of these studies are carried out in different laboratories in Europe, however up to now there has been no coordination and not mutual reinforcement.
All this makes clear **why the new COST action** under the headline of prebiotic chemistry and early evolution is necessary: i) to coordinate the activities of the various European laboratories, so that a situation of complementarity and integration arises instead of the present fragmentation; ii) this constitution of working groups across different European laboratories will favour the focussing of a selected number of basic questions, which can be then more efficiently elaborated and investigated. In particular, the groups specialised in the organic chemistry of low molecular weight compounds should be encouraged to work together with researchers specialised in polymerisation reactions; researchers specialised in the RNA-world should be encouraged to work with people specialised with membranes and compartmentalisation; and researchers in the field of experimental chemistry should be encouraged to join efforts with theoretical chemists well experienced in modelling and computer science.

In addition to these very important scientific aspects, the COST action would also fulfil a more political aim. To this point, one should consider that the field of origin of life is nowadays mostly an American monopoly. This is due in large part to the powerful support of NASA, that has also led to a considerable increase of research activities in prebiotic chemistry and all areas related to the origin of life in the United States; in this country, prebiotic chemistry has recently witnessed a remarkable increase of interest also in the public opinion, due to the dispute around the alleged forms of life discovered on a Martian meteorite. It must be said at this regard that the research NASA programs in the USA have been able to co-opt most of the more active European scientists in the American research projects. A strong, unifying European coordination in this field is lacking, and one of the aims of the present COST action is to catalyse an autonomous European design in the field.

### *A.2. In what respect is Prebiotic Chemistry and Early Evolution different from the other fields of chemistry?*

This part of chemistry is the only one dealing with the relation between molecular structures and minimal life, and as such is the only branch of chemical sciences which attempts to interpret the key mechanism of life in chemical terms. The chemical understanding of these key living processes of life is based on characteristic notions, such as:

- *autocatalysis* : the processes which leads to an amplification of the concentration of a given structure or system, due to the fact that the reaction product is able to accelerate its own rate of production.

- *self-replication*: the process by which a given chemical structure or system is able to make copies of itself, thus multiplying the number of particles, generally due to one or more autocatalytic steps.

- *molecular evolution*: the process by which chemical systems can increase their complexity due to thermodynamically controlled processes.

- the whole question of *complexity* : although this notion is present in other field of chemistry and physics, it acquires in the field of prebiotic chemistry a particular importance, as in this case it is linked to the simultaneous increase of structural order.

- *emergence*: this notion, very important in the epistemology of science, is related to the fact that at each level of higher hierarchic structure (higher complexity) new qualities arise, which are not present in the lower components.

It appears from the above that work in this field links together classic preparative and analytical chemistry with notions which go beyond the usual framework of chemical work. Actually, there is already a good tradition of philosophical questions related to the field, such as the question of determinism and reductionism in prebiotic molecular evolution, the question of whether life consists of only molecules and their dynamical interactions, the question of whether minimal life can be reproduced in the laboratory.

The field of prebiotic chemistry is also unique because it is related to bio-astronomy (actually bio-astronomy is part of the prebiotic program), namely to the chemistry occurring in the interstellar space or in other planets; is related to space ship programs and the exploration of other planets; to the definition of life on this Earth and elsewhere.

Finally, on a quite different line of thinking, the field of prebiotic chemistry and early evolution is related to the question, of whether the simplest forms of life (models of prokaryotic cells for example) can be reconstituted in the chemical laboratory. There are several research groups involved with such a program. The realisation of this program would permit one to solve or at least clarify the question: what are the minimal and sufficient conditions for a chemical system to be defined as living? And this, in addition of being a great achievement from the point of view of basic science, would also open the way of new forms of biotechnology (the construction of simple artificial living cells).

### *A.3. Relation with other European programs, as well to other COST-chemistry actions.*

COST-chemistry: the present action does not overlap with any other COST-chemistry actions. However, there are links with Supramolecular Chemistry (D-11), limited to those cases in which supramolecular systems are used as models for biologically relevant systems. It is also blandly linked to those COST-chemistry actions related to biochemical problems, such as D-22 (protein-lipid interactions) and in even less degree to those actions dealing with polymerisations (such as D-17 or D-16). However it can safely be said that this COST-action covers grounds which are not yet covered by the previous actions.

As far as other European agencies are concerned, the one that comes to mind is the ESA, the European Space Agency. This agency, in analogy to the American NASA, coordinates the activities in space research, and therefore also in bioastronomy, which at some extent can be considered part of prebiotic chemistry.

At the best of our knowledge, there are no European associations or programs dealing directly with prebiotic chemistry, origin of life and early evolution. As already mentioned, the present action will also aim at filling this gap.

## B. SCIENTIFIC PART: OBJECTIVES OF THE ACTION AND SCIENTIFIC CONTENT

### B.1. Main objectives

The main objective of the Action is to develop the chemistry connected with the origin of life and early evolution of life on Earth, with special emphasis on self-replicating systems, prebiotic synthesis of nucleic acids and polypeptides, as well as simple protocells as early models of biological cells.

To accomplish the objectives of the action is necessary: 1. to coordinate the scientific activities of the very many European research laboratories working in the field of prebiotic chemistry and early evolution; 2. to focus these activities into a few more important research directions so that a greater efficiency may result; 3. to constitute for the first time an organised European research network on prebiotic chemistry, origin of life and early evolution, which is capable of interacting at an international level and in particular be competitive with the American counterpart.

Whereas all these objectives are important, we believe that the coordination and the possibility of mutual interaction among the different European laboratories are a general prerequisite. In fact, as already mentioned, and now it is clear from a survey associated with the preparation of the action, a surprisingly large number of European laboratories are active in the field (more than 60!). However, until now none or a very modest collaborative effort has been present, and the

COST action should be very helpful in this respect. The work on prebiotic chemisty and early evolution involves different areas of expertise, for example organic chemistry of small prebiotic compounds, macromolecular chemistry, computational chemistry, metabolic pathway chemistry, biophysics. These different specialists have not been working with each other, and the new COST action should promote their interaction and mutual understanding.

This interaction among different laboratories will be particularly fruitful for young researchers, like Ph.D students or post Docs, who will then work in such interdisciplinary projects.

**B.2. Sub-Topics**

The action should emphasise the following sub-topics:

1. **Prebiotic chemistry of small molecules.** Novel aspects of prebiotic chemistry, particularly in connection with bio-monomers and membrane-forming molecules; due emphasis should be given on surface chemistry (such as clay or minerals or crystals). This chapter also includes nucleotide and nucleotide-analogs chemistry as well as carbohydrate chemistry.

2. **Origin and evolution of biopolymers.** Polymerisation processes leading to polypeptides, polynucleotides, polysaccharides: In particular the question of the selection processes leading to specific sequences of polypeptides and polynucleotides. This chapter includes the macromolecular chemistry of RNA and DNA in relation to the origin of life; template chemistry, models for RNA and DNA self-replication (see also entry 6); the RNA-world and the pre-RNA world.

3. **Origin of homochirality.** Theoretical and experimental work to explain the prevalence of one enantiomer in the molecules of life, e.g., L-amino acids or D-sugars. Methods of spontaneous separation of racemates, amplification of enantiomeric excess, enantioselective autocatalysis.

4. **Bio-astronomy and Cosmochemistry.** The extra-atmospheric chemistry and the chemistry in meteorites, comets, and other planets. Spectroscopic bioastronomy. Models of panspermia.

5. **Self-assembly, Self-organisation.** Origin of the first self-assembling molecules. Micelles, vesicles, other self-assembling systems. Transition from vesicles to protocellular structures; theoretical aspects of self-organisation. This chapter includes the **chemistry of compartimentation**: chemical reactions in closed structures (lipidic or not); compartmentalised reaction networks; models for homeostasis, primitive metabolism and autopoiesis. Origin of bio-membranes, Permeability studies on bilayers; entrapment of biomolecules in vesicles and other bio-mimetic structures.

6. **Self-replication and Self-reproduction.** New theoretical and experimental systems capable of autocatalytic self-replication. Template chemistry with nucleotides and analogs (see entry 2). This includes **information and theoretical chemistry**; non-linear chemistry; Information in relation to origin of life, experimental and theoretical models. Theoretical models, molecular modelling; definition and criteria of minimal life.

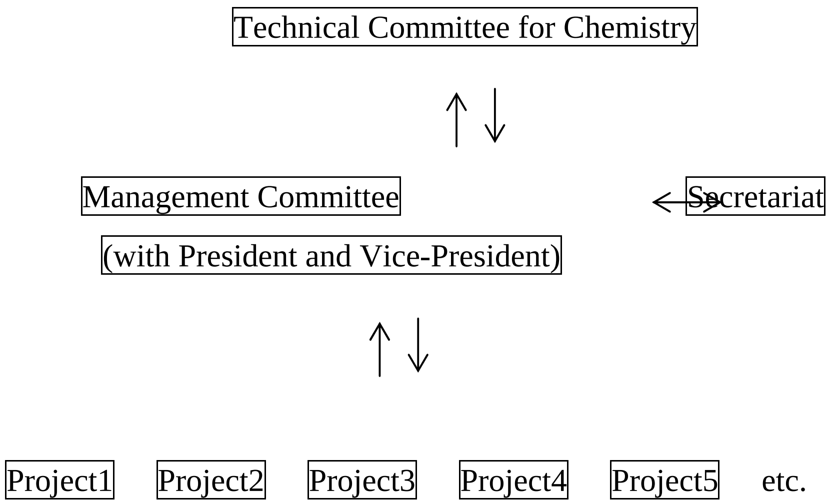
7. **Directed chemical evolution.** In vitro directed mutagenesis and amplification of nucleic acids; chemical evolution of RNA libraries; RNA and protein selection models.

8. **Origin of genetic code.** Interactions peptides-nucleotides; elementary forms of polypeptide expression; experimental and theoretical models for the formation of the primitive genetic code. The prebiotic forms of ribosomes and the translation machinery.

## C. ORGANISATION, MANAGEMENT AND RESPONSIBILITIES

### C.1. Management and Organisation

The Action will be structured as the previous COST-Chemistry Actions: there will be a Management Committee, which is under the general direction of the Technical Committee, as shown below:




with a president and a vice-president elected by the Management Committee for a period of a year. Projects fitting in the 8 topics listed above will be presented by researchers of the European countries, under the regulations of COST Chemistry (e.g. scientific cooperation between at least three European countries etc.) to the Management Committee.

**C.1. Responsibilities**

The Management Committee is responsible for:

i. Start of the activity, which includes advertisement of the new Action in the different European countries;
ii. Selection of working groups from applications based on projects which fit the criteria described above
iii. Exploration of wider participation and exchange of information with other specific European programs (as we have already mentioned under B);
iv. Organisation of workshops, as well as yearly meetings. Planning of the various reports, including the annual report to be presented to the Technical Committee;
v. Evaluation of the incoming grant applications by a peer Referee system.

vi. Planning the intermediate reports, the final report and the concluding symposium. In particular, the Management Committee will prepare a milestone report after 2 years of joint activities. A final report will be published to inform non-participating scientists about the results obtained in this action.

### C.3. Evaluation of progress

The progress of the programme will be monitored by means of brief annual reports from each of the participating scientists. These will describe the results obtained throughout the concerted actions. The Management Committee will prepare a milestone report after 2 years of joint activities, which will be presented to the TC for chemistry for their review and to the COST Committee of Senior Officials for information. A final report will be published to inform non-participating scientists and interested researchers. A symposium will be held yearly and a larger one at the end of the Action. All these symposia will be accessible to other scientists.

## D. TIMETABLE

### D.1. Scientific programme

Working groups will be established on the basis of applications submitted by European research teams as outlined above. Selection will be performed on the basis of the criteria outlined in the previous pages, giving priority to interdiscliplinarity and high scientific quality.

After approximately one year of working groups activity, the Management Committee will review the results and organise a first Symposium. This will have the goal of looking and criticise the achievements of the Action, and also to promote new activities: in fact this meeting will be publicized and made accessible also to the scientists who do not adhere yet to the Action.

This will be repeated after each year of activity. A larger symposium will be organised at the end of the first cycle of activity. Details of this scientific timetable are given below.

## D.2. Timetable

A 5-year programme is proposed and consists of three stages.

*Stage 1* : The first act will be to establish a Management Committee. In this first phase of the work, the first series of applications will be received and refereed, and the Management Committee will be busy in scrutinising and assessing priority criteria to the incoming project applications. A first meeting accepting the projects will make a first balance of the people really interested.

Stage 2: This will be the "Steady-State" period, in which the action has entered in the equilibrium phase. In this phase, many more project applications are expected. Meetings will be planned yearly, possibly in conjunction with other actions. A report, or a booklet of abstract, will be prepared by the Management Committee after each meeting. An international midterm evaluation workshop will be organised.

Stage 3: The final phase will begin after a ca. 4 year life of the action and will involve the evaluation of the obtained results and the preparation of a (possible) development of future actions. A final evaluation meeting will close the Action.

## E: DURATION OF THE ACTION

The duration of the Action will be 5 years. This estimate is based on previous experience with other COST Actions, like Supramolecular Chemistry. For the first time there has to be established a robust co-ordination network involving very different areas of expertise and as these different specialists have not worked with each other before, some additional time will be required. Also new procedures for their interaction and mutual understanding will have to be developed.

## F. ECONOMIC DIMENSION OF THE ACTION

As it results from the preparatory survey to the Action, European research in the field of prebiotic chemistry is represented well in at least fifteen European countries. Accordingly, the researcher capacity involved, expressed in Full Time Equivalents, can be roughly accounted 700 FTE.

The estimated breakdown of funding to the above research groups based on statistical data is:

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| University | 35% |
| NF (CNR or equiv.) | 45% |
| Non-profit | 15% |
| Industry | 5% |

From these data, one can also estimate the present operational and running costs of this research enterprise. Although these figures must be considered as approximate, they give a fair representation of the large volume of work already involved in the area in Europe.

On the basis of national estimates provided by the representatives of these countries, the overall cost of the activities to be carried out under the Action has been estimated, in 2000 prices at roughly Euro 80 million.

The estimate is valid under the assumption that all the countries expected but no other countries will participate in the Action. Any departure from this will change the total cost accordingly.

## G. DISSEMINATION

The Management Committee will inform the chemistry departments of all the major Universities and research institutions about COST D 27. They will be informed of the time schedule, and in particular about the date for submission of research projects.

The Symposia at the end of each working year will be widely publicized, so that also the scientists not involved directly in the action will be present. In order to achieve this, reputed scientists will be invited to give talks at these symposia, even though they do not belong to working groups of the Action. Also the COST Chemistry web site (http://www.unil.ch/cost/chem) will be exploited for the dissemination.

The Management Committee will ask the working group leaders to credit COST in the publications. The major results of the Action will be reported in the local university press.