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NASA SPECIALIZED CENTER OF RESEARCH AND TRAINING (NSCORT) IN EXOBIOLOGY

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1992-1996 FINAL REPORT (NASA NAGW-2881)
The Chemistry of Early Self-Replicating Systems

NSCORT in Exobiology is a Consortium of:

THE UNIVERSITY OF CALIFORNIA, SAN DIEGO (UCSD)
THE SALK INSTITUTE FOR BIOLOGICAL STUDIES (SALK)
THE SCRIPPS RESEARCH INSTITUTE (TSRI)

LA JOLLA, CALIFORNIA

NASA SPECIALIZED CENTER OF RESEARCH & TRAINING (NSCORT) IN EXOBIOLOGY

NASA NAGW-2881: FINAL REPORT
The Chemistry of Early Self-Replicating Systems
January 1, 1992 through December 31, 1996

Respectfully submitted by:

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I. Executive Summary

The NASA Specialized Center of Research and Training (NSCORT) in Exobiology is a consortium of scientists at the University of California at San Diego (UCSD), The Salk Institute for Biological Studies (Salk) and The Scripps Research Institute (TSRI). All three institutions are located in close geographical proximity in La Jolla, California. The NSCORT/Exobiology is administered through the Scripps Institution of Oceanography.

Since its inception in January 1992, the NSCORT in Exobiology has made major contributions with respect to the question of how life began on Earth. The Principal Investigators (PIs) and their associated Fellows have published numerous articles in peer reviewed journals on topics relevant to Exobiology. They have presented papers and sponsored symposia at several meetings of national and international scientific societies. A total of 30 undergraduate, 12 graduate and 15 postdoctoral Fellows have been supported by the NSCORT. The Fellows have met on their own at least once a month to discuss Exobiology topics and research progress. The NSCORT has arranged seminars and evening discussion meetings, and offered an undergraduate class on "Biochemical Evolution" as well as graduate courses dealing with topics in Exobiology. A visiting scientist program has allowed 11 scientists from the U. S. and 4 foreign countries to conduct cooperative research with the various PIs. An active outreach program has been initiated, which includes an Exobiology high school level teaching module and curriculum guide, and an elementary school level booklet about basic atomic structure and formation of the universe, Sun and Earth. A World Wide Web Homepage (http://www-chem.ucsd.edu/~nscort/NSCORT.html) has been developed, which describes the NSCORT activities, research programs and Fellowship opportunities. The various activities of the NSCORT in Exobiology have received wide-spread coverage in both the scientific and public media [for example, see Appendix II-E-2, *Science* **270**, 1925-1926 (1995), and Appendix II-E-5, New York Times, Tuesday, July 4, 1995, page 19].

The major function of the NSCORT is the training of young scientists in the field of Exobiology. Thus, the bulk of the $1,000,000 annual budget is used to support the research and training of undergraduate, graduate and post-doctoral Fellows who are selected on a competitive basis. About five Fellows at each level are supported each year. Our goal is to train scientists whose major research interest is Exobiology, but whose mastery in the classical fields of chemistry, biology and earth science is so strong that they outstanding candidates for either graduate school or academic tenure-track positions in departments at leading national and international Universities. Applicants for these Fellowships are solicited by advertisements in journals such as *Science* and *Nature* and in organizational newsletters such as the one published by the International Society for the Study of the Origin of Life (ISSOL), by contacting academic and NASA colleagues working in Exobiology or related fields and by recruiting students who have already been admitted into the various academic programs with which the PIs are affiliated. The training program consists, depending on the student level, of a series of core courses relevant to the field of Exobiology, invited specialized seminars, monthly journal club meetings, NSCORT sponsored discussion meetings, basic research in some aspect of Exobiology and presentations at scholarly meetings.

The NSCORT/Exobiology research program concerns the central issue of the origin of life: the nature of the first genetic material. The first appearance of a molecular system that could store information and replicate imperfectly marked the transition from the abiotic chemistry of the primitive Earth to biochemical evolution. The projects of the various PIs are a concerted effort to investigate all aspects of the chemistry that led to the origin and evolution of the first self-replicating systems and how these systems eventually evolved into the biochemistry associated with modern day organisms.

i.) Dr. Bada studies the stability and sources of important prebiotic molecules on the primitive Earth and other solar system bodies.

ii.) Dr. Arrhenius works on the synthesis, concentration and oligomerization processes, with emphasis on geochemical plausibility.

iii.) Dr. Miller investigates which purines and pyrimidines besides adenine, uracil, guanine and cytosine are likely prebiotic compounds and how they may form under drying lagoon conditions rather than in the open ocean.

iv.) Dr. Joyce studies the reaction wherein an oligonucleotide template is used to direct the ligation of a peptide to an oligonucleotide via an amide linkage.

v.) Dr. Orgel explores two approaches to the discovery of novel replicating systems; oligonucleotide analogues with unusual backbones; and prebiotic analogues of solid-phase synthesis involved in the formation and template properties of long polymers adsorbed on mineral surfaces.

Exobiology is central to answering one of "The Big Questions" posed by NASA Administrator Daniel Goldin [*Science* **272**, 800-802 (1996)]: "Is life, carbon-based or other, unique to Earth?". The NSCORT/Exobiology research and training program that we have implemented addresses this question in a comprehensive manner. The research focus is directed at the processes that generated the first self-replicating system on Earth that was capable of undergoing Darwinian evolution. Knowing how life originated on Earth will allow us to predict whether this may have happened elsewhere. Our training program will produce the next generation of young scientists knowledgeable in Exobiology. These scientists will provide an important resource pool for future NASA efforts in understanding the origin, evolution and distribution of life in the universe.

II. THE NSCORT IN EXOBIOLOGY: 1992-1996

PROGRAM SUMMARY

The NASA Specialized Center of Research and Training in Exobiology (NSCORT/Exobiology) is a program within the California Space Institute (University of California Statewide) funded by a 5-year Federal Demonstration Project Grant from NASA. Its specific aims are:

1. The support and training of Postdoctoral, Graduate and Undergraduate Fellows.
2. The support of research by the Principal Investigators and Fellows.
3. The dissemination of information about Exobiology to pre-college and college students, teachers and the public.
4. The sharing of research results in the field of Exobiology with all interested segments of the Scientific Community.

Field of Endeavor

Exobiology is the study of the origin and evolution of life on the Earth and the forms life might take elsewhere in the universe. The only life currently known to exist is on planet Earth. Therefore, the Exobiology program focuses on the conditions, substances and chemical reactions of primitive Earth and its extraterrestrial environment, beginning about 4.6 billion years ago.

A. Administration and Management

Management Summary

The NASA Specialized Center of Research and Training (NSCORT) in Exobiology is a consortium of scientists at three administratively independent institutions in the La Jolla area of San Diego, California.

The administrative recipient of the NASA grant is the California Space Institute, Scripps Institution of Oceanography, University of California, San Diego (UCSD). The program partners—The Salk Institute for Biological Studies (Salk), and The Scripps Research Institute (TSRI)— receive their assigned funds to support research and training in Exobiology through the central NSCORT office at UCSD.

At the inception of the NSCORT grant (January 1992), UCSD had no previous experience with a comparable consortium arrangement involving independent institutions. Consequently no administrative mechanism existed, and the initial responsibility of the Associate Director was to create the administrative processes for organizational cooperation, policy congruence and budgetary transfer/control. These have functioned smoothly during the ensuing years, prompting Dr. Edward Frieman, Director of the Scripps Institution of Oceanography, to report to the third year Site Visit Panel that "...[NSCORT/exobiology] was one of the most efficiently run multi-investigator organizations that he has been associated with."

Academic and administrative policy, as well as competitive selection of Fellowship recipients (see II-D., Training and Education), are determined by an Executive Committee of NSCORT Principal Investigators, chaired by the Director, in cooperation with the Associate Director.

Administration

The NASA Specialized Center of Research and Training (NSCORT) in Exobiology is a consortium of scientists at three institutions in the La Jolla area of San Diego, California. The administrative recipient of the NASA grant is the University of California, San Diego (UCSD), and the Business Office of that institution is responsible for overseeing the expenditure of funds in accordance with NASA Guidelines and UCSD policy and regulations. The California Space Institute—a University-wide Organized Research Unit—is responsible for disbursement of funds, at the request of the NSCORT Associate Director. Funds for Fellows' salaries and research support are transferred directly to the program partners—The Salk Institute for Biological Studies (Salk) and The Scripps Research Institute (TSRI)—and to the involved UCSD departments; Chemistry and The Marine Research Division of Scripps Institution of Oceanography (SIO). Funds for administrative expenses, outreach programs, meetings, visiting scientists and lecturers, etc., are controlled by the NSCORT Central Office, Associate Director, in consultation with the Director. Budget control is exercised through these entities [see Figure II-A-(1)]. The overall NSCORT organization is diagrammed in Figure II-A-(2).

The proportion of each PI's time devoted to NSCORT research, training and administration is: J. L. Bada 30%, G. Arrhenius 30%; S. L. Miller 35%; L. E. Orgel 30% and G. F. Joyce 25%.

NSCORT Administrative Central Office consists of a 1/2 time Associate Director and a full time Administrative Assistant. An equivalent 1/2 time Administrative Assistant is provided by the California Space Institute at no charge to NASA. The duties and responsibilities of the Office of the Associate Director include: Preparation and Control of Budget; Preparation of Annual Report, Interim Reports, Brochures; Collection and Maintenance of Records; Organization of Local, National and International Meetings; Administrative Aspects of NSCORT Fellowship Program; Liaison with Extramural Professional Organizations; Development and Coordination of Outreach Programs and Search for Extramural Funds [see Appendix II-A-(1) for details].

The day to day operation of the NSCORT program is handled by the Associate Director and his Administrative Assistant. Management decisions and operational requirements are transmitted to the PIs, Affiliates, Fellows and other personnel from the Director through the Associate Director's Office. This arrangement has proved both effective and efficient in the preceding 5 years of the NSCORT program and was favorably reviewed by the 3-year Site Visit Panel [see Appendix II-A-(2)].

During the five years of productive operation thus far, the NSCORT/Exobiology program has been incorporated into its parent institutions without negative impact on their infrastructure or policies. Indeed, the NSCORT program has in every case contributed to the reputation for excellence and scientific accomplishment which these institutions have achieved.

With respect to under-represented groups (women, minorities) in science, it is the policy of UCSD, the Salk Institute and the Scripps Research Institute to provide equal employment opportunity to all individuals regardless of race, nationality, religion, sex, marital status, sexual orientation, age, handicap, veteran status, physical or mental disability, and membership or non-membership in any organization. As for the involvement of under-represented groups in science, the respective institutions of the NSCORT members have ongoing active recruitment policies for this purpose. Programs include UC Postdoctoral Fellowships for women, and several graduate and postdoctoral minority fellowships. For example, the Salk Institute has a Postdoctoral Fellowship for Distinguished Minority Scientists. The Dean of Graduate Studies and Research at UCSD has provided one San Diego Fellowship each year to the NSCORT. This Fellowship is designed to support graduate students from under-represented minority groups.

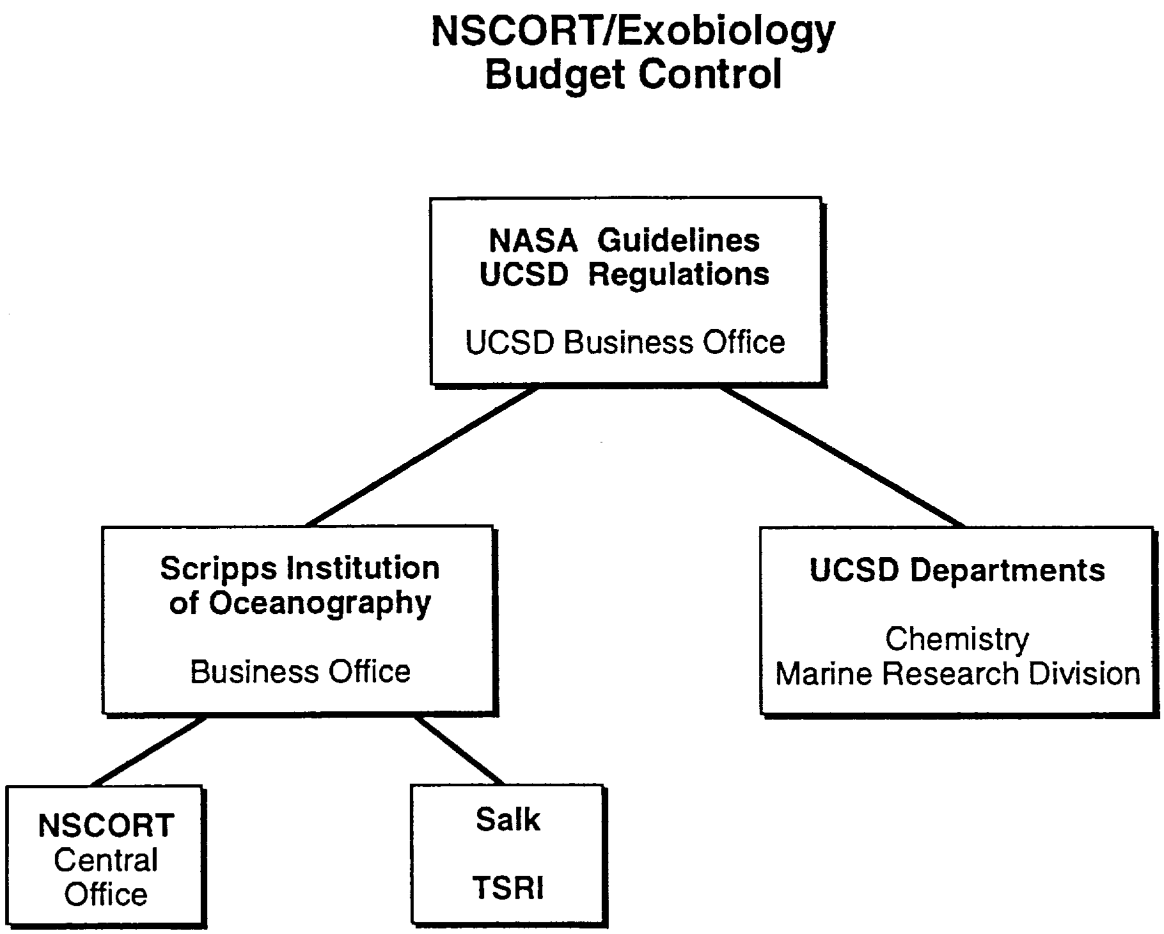
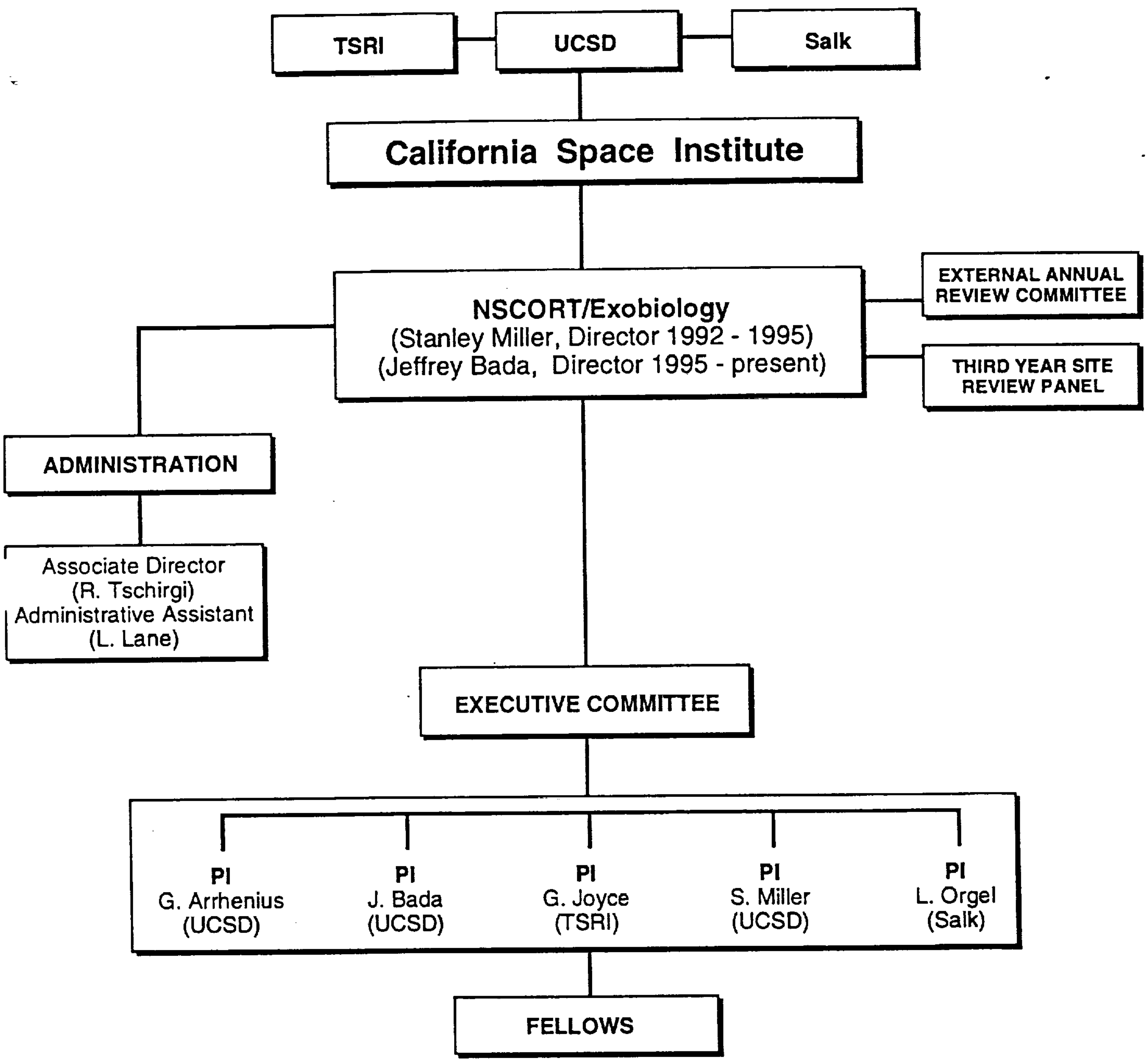

NSCORT/Exobiology
Budget Control
NASA Guidelines
UCSD Regulations
UCSD Business Office
Scripps Institution
of Oceanography
Business Office
UCSD Departments
Chemistry
Marine Research Division
NSCORT
Central
Office
Salk
TSRI

Figure II-A-(1)

NSCORT/Exobiology
Organizational Flow Chart, 1992-1996



Notes:

NSCORT -- NASA Specialized Center of Research and Training
UCSD -- University of California, San Diego
TSRI -- The Scripps Research Institute
Salk -- The Salk Institute for Biological Studies
PI -- Principal Investigator

Figure II-A-(2)

B. Research Accomplishments, 1992-1996

The following research summary is not meant to be comprehensive; rather, it attempts to highlight some of the most significant research accomplishments of the NSCORT laboratories over the past four and one half years. What began as a set of five independent research programs in 1992, soon coalesced into a coordinated effort focused on important unsolved problems in Exobiology. Two of the central themes that emerged were: one, understanding the inventory of organic compounds that would have been available on the prebiotic Earth; and two, ascertaining the chemical nature of the first genetic material. While neither of these two difficult problems has been solved, considerable progress has been made on both fronts and several promising avenues for research have been developed. A complete listing of publications pertaining to NSCORT-sponsored research is provided in Appendix II-B.

1. Inventory of Prebiotic Organic Compounds

a. Exogenous delivery of amino acids

One of the major questions in origins-of-life research concerns the relative contribution of terrestrial syntheses versus extraterrestrial sources (e.g. interplanetary dust particles and impacting meteorites) to the inventory of organic materials on the prebiotic Earth. In a search for evidence of exogenous input on the moon and the modern Earth, the Bada laboratory measured α-amino-isobutyric acid (Aib) in lunar soil samples and polar ice cores. Aib is one of the most abundant amino acids in carbonaceous meteorites and is readily synthesized in abiotic experiments, but does not occur in the proteins of modern organisms. Thus it serves as a good indicator of abiotic organic synthesis. The moon provides a severe test for the survival of exogenous organics because there is no atmosphere to cushion infalling bodies and particles and to shield the solar UV flux. The total amount of amino acids in lunar soil was found to be < 0.1% of that predicted by a simple accumulation model for organics delivered to the lunar surface by interplanetary dust particles and carbonaceous meteoritic debris (*1*). These results support the expectation of poor survival of exogenous organics delivered to planetary bodies that have no atmosphere.

In order to evaluate whether the delivery of exogenous organics can be detected on the Earth today, the Bada laboratory searched for Aib in polar ices, considered to provide a pristine record of the Earth's hydrosphere. No detectable amount of Aib (< 0.001 ppb) was found in over 20 polar ice samples (2). One sample of 4,270 – 4,440 year old Greenland ice did contain 0.1 – 0.3 ppb Aib, but did not contain any of the other common non-protein amino acids, suggesting that the source of the Aib was not a carbonaceous chondrite-like object. Rather, the pattern was similar to what is observed when amino acids are produced abiotically from HCN. Thus the Aib in the Greenland ice sample may have been provided by an isolated event that involved an HCN-containing impactor, such as a comet.

The Bada laboratory also evaluated the delivery of exogenous amino acids to the modern Earth by micrometeorites. Antarctic ice has an excellent repository of micrometeorites that can be recovered by melting large amounts (hundreds of tons!) of ice. Aib was found in only a small fraction of Antarctic micrometeorites, although in those few instances, the Aib content was about ten times greater than that of the Murchison meteorite (*3*). No isovaline was detected, again suggesting that the Aib may have been synthesized from HCN. Whether micrometeorite material would have been sufficient to supply the early Earth with a rich inventory of organic compounds is presently unknown.

b. Cosmogeochemistry of fullerenes

The discovery of fullerenes (the simplest being C_{60}) soon led to the hypothesis that this class of carbon molecules may be abundant in the universe (*4*). Recently, Luann Becker in the Bada laboratory, in collaboration with groups at the Argonne National Laboratory and the NASA Ames Research Center, reported that C_{60} is present in trace amounts (~ 0.1 ppm) in the Allende meteorite (*5*). On Earth, fullerenes have been found in unusual rocks, such as shungite and fulgurite, that were formed under highly energetic conditions and at intense temperatures and pressures. This observation prompted a search for fullerenes in the shock-produced breccias of the 1.85-billion-year-old Sudbury impact structure in Ontario, Canada. Fullerenes were detected at a level of 1 – 10 ppm, the richest natural occurrence that has been reported to date (*6*).

It is not clear whether the fullerenes were already present in the bolide and survived impact or were synthesized within the impact plume from the carbon contained in the bolide. In order to distinguish between these two possibilities, Bada and collaborators investigated the isotopic composition of helium atoms trapped within the Sudbury fullerenes (*7*). If the fullerenes were formed in the impact plume, then the helium isotope composition should reflect the composition of the Earth's atmosphere at the time of impact, but if they were present prior to impact, then the helium would have an extraterrestrial signature. The C_{60} and C_{70} fullerenes from the Sudbury impact structure were found to contain trapped helium with a $^3He/^4He$ ratio of 5.5 – 5.9 x 10^4, about 10-fold greater than the maximum reported mantle value, but similar to that found in meteorites and some interplanetary dust particles. The implication is that the $He@C_{60}$ molecules in the Sudbury rocks are of extraterrestrial origin, suggesting that some organic molecules may survive impact delivery.

c. Concentration of prebiotic starting materials

Hydrogen cyanide and formaldehyde are key starting materials for the prebiotic synthesis of the nucleotide bases and sugars, respectively. The Arrhenius laboratory has studied mechanisms by which each of these compounds could have been concentrated and incorporated into biologically-relevant organic materials. One such mechanism involves the reaction of HCN with Fe^{2+} in the hydrosphere to form hexocyanoferroate ion and insoluble ferrocyanides, such as zinc ferrocyanide, which may then become co-concentrated with ammonium ion (*8*). Hexocyanoferroate also is efficiently sorbed by positively charged minerals, such as ferroferric oxyhydroxides (green rust). Upon UV irradiation, the ferrocyanide ion photo-oxidizes to FeOOH, returning the HCN to the environment.

A second geochemically plausible pathway for concentrating HCN and formaldehyde involves their reaction to produce glycolonitrile, which then oligomerizes to form a dimer, trimer, and higher oligomers (*9*). These oligomers undergo spontaneous hydrolysis, giving rise mainly to glycolamide. However, at concentrations of glycolonitrile >0.05 M, oligomerization dominates over hydrolysis, eventually producing a water insoluble tar. This tar and the intermediate oligomers may have served as a storage form of HCN and formaldehyde on the primitive Earth. Formaldehyde and glycoaldehyde also can be concentrated in the interlayer of double-layer hydroxide minerals that contain sulfite ion (Pitsch *et al.*, unpublished).

d. Stability of organics under geochemical conditions

Biomolecules of relevance to the origin and early evolution of life on Earth are inherently unstable in geologic environments. In the case of DNA, oxidation and depurination reactions limit the survival of substantial amounts of genetic information to only a few thousand years in most terrestrial environments. Peptides and proteins are completely hydrolyzed to free amino acids in $< 10^5$ years in temperate aqueous environments. On the early Earth, with an atmosphere containing little or no oxygen, oxidation reactions involving DNA would not have been important, so that depurination would have been the primary route of DNA decomposition. The Bada laboratory has found that DNA depurination and amino acid racemization take place at nearly the same rate in aqueous solution at neutral pH (*10*). Aspartic acid racemization rates can easily be measured in known-age geologic samples and thus may be useful in predicting the extent of DNA damage in natural environments. In samples with a D/L aspartic acid ratio < 0.1, DNA fragments containing more than 100 base-pairs remained intact, whereas in samples with higher D/L aspartic acid ratios, no DNA fragments of this length were preserved (*11*). In most geochemical environments, D/L aspartic acid ratios of 0.1 are attained in about 10^3–10^5 years, suggesting that this is the time limit for preservation of DNA-based genetic information in the absence of any repair mechanisms. This should be viewed as a constraint in the search for extinct DNA-based life on Mars.

Ribose and other sugars are known to be unstable in aqueous solution, although until recently no kinetic data were available concerning the decomposition of ribose in aqueous solution. The Miller laboratory measured the rate of ribose decomposition over a broad range of temperature and pH (*12*). The half-life of ribose at 100°C and pH 7.0 was found to be 73 minutes; at 0°C and pH 7.0 it was 44 years. These results strongly suggest that ribose is unlikely to have accumulated in the prebiotic environment, unless it was incorporated into more stable compounds soon after its synthesis. The other pentose and hexose sugars decompose at a rate that is roughly proportional to their free aldehyde content. Thus, it seems unlikely that *any* of the free sugars were abundant on the prebiotic Earth.

2. Chemical Nature of the First Genetic Material

a. Alternative nucleotide bases

a.1 Uracil and uracil analogues

Although an efficient prebiotic synthesis of the purines has long been known (*13*), the prebiotic synthesis of the pyrimidines has been more problematic. Cytosine has been synthesized from cyanoacetylene or cyanoacetaldehyde, but only in low yield (*14,15*). Recently, the Miller laboratory demonstrated that cytosine and uracil could be synthesized in 10 – 53% yield from cyanoacetaldehyde and urea, employing a drying lagoon model that allowed high concentrations of urea to be attained (*16*). They further showed that uracil reacts efficiently with formaldehyde to give 5-hydroxymethyl uracil. This reaction, which occurs for other pyrimidines as well, is rapid for a prebiotic synthesis and has a highly favorable equilibrium constant. These findings suggest that hydroxymethyl uracil may have been as important as uracil itself in prebiotic chemistry.

Hydroxymethyl uracil was shown to react with a variety of nucleophiles to produce the corresponding pyrimidine analogues (*17*). These analogues include compounds that are equivalent to many of the amino acids. For example, hydroxymethyl uracil reacts with NH_3 to give 5-aminomethyl uracil, which is an analogue of lysine. Comparable reactions with H_2S, guanidine, indole, and imidazole give rise to analogues of cysteine, arginine, tryptophan, and histidine, respectively. The substituted uracils form so readily that they might be considered to be as prebiotically plausible as uracil itself. Furthermore, their resemblance to many of the protein amino acids suggests a possible bridge between the RNA and DNA/protein worlds.

In order to explore the functional consequences of 5-substituted uracils for RNA catalysis, Xiaochang Dai in the Joyce laboratory carried out an *in vitro* evolution experiment in which the uracil residues of a ribozyme were replaced by 5-bromouracil residues. First, he replaced all 99 uridines within the *Tetrahymena* group I ribozyme by 5-bromouridine, resulting in markedly diminished phosphoester transfer activity. Then he constructed a population of random variants of this ribozyme and carried out five successive "generations" of *in vitro* evolution, selecting for restoration of phosphoester transfer activity. Activity was restored in the context of the bromouracil-containing ribozyme, even exceeding that of the non-brominated wild type. Furthermore, the evolved ribozyme had become dependent on bromouracil for its improved activity; if the evolved ribozyme was reverted to a non-brominated form, its catalytic activity was significantly decreased (Dai & Joyce, unpublished).

The Miller laboratory has studied the prebiotic synthesis of other potential nucleic acid bases that might offer an alternative to adenine, guanine, cytosine, and uracil during the early history of life on Earth. One such alternative is urazole (1,2,4-triazole-3,5-dione), which is produced readily from biuret and hydrazine (*18*). Urazole reacts with ribose and other sugars much more favorably compared to uracil, forms Watson-Crick pairs with adenine, and is transparent to UV light, making it an attractive potential precursor to uracil. Another potential alternative to uracil is dihydrouracil, which is synthesized readily from β-alanine and cyanate (*19*). Dihydrouridine occurs in the tRNA of most organisms, but is absent from the tRNA of most hyperthermophiles. This can be explained on the basis of a ring-opening reaction that occurs readily at 100°C and pH 7, resulting in cleavage of the ribose phosphate backbone.

a.2 Nicotinamide-containing nucleic acids

Nicotinamide mononucleotide (NMN) has been proposed as a "fossil" of the RNA world. Furthermore, it has been suggested that NMN could replace one of the purines in an informational polymer because it has hydrogen-bonding potential similar to that of adenine or guanine (*20*). Rihe Liu in the Orgel laboratory devised a novel method for preparation of NMN from NAD (*21*), then converted the product to nicotinamide nucleoside-5′-diphosphate (NMNDP). Attempts to polymerize NMNDP with polynucleotide phosphorylase proved unsuccessful, but, surprisingly, the reduced form of NMNDP was polymerized very efficiently (22). It also was possible to add a single residue of NMN to the 3′ terminus of an RNA or DNA molecule using terminal transferase and then incorporate additional standard nucleotides downstream from the NMN residue. This made it possible to study non-enzymatic template-directed synthesis reactions using either activated NMN as a monomer or NMN-containing oligomers as templates. It was found, however, that NMN cannot substitute for either AMP or GMP in these reactions. Thus, if NMN is a molecular fossil, it likely became attached to RNA by either noncovalent interactions or by ribozyme-mediated incorporation.

In order to test the latter possibility, Ronald Breaker in the Joyce laboratory prepared a truncated form of a group I ribozyme, and supplied nicotinamide adenine dinucleotide (NAD) as a substrate. The ribozyme was able to recognize the riboadenosyl portion of NAD and catalyze a self-incorporation reaction that resulted in covalent attachment of the coenzyme to the ribozyme (*23*). This brought the nicotinamide moiety into close proximity to the ribozyme active site, where it might be made to play a role in ribozyme function. RNA is likely to be able to exploit bound or incorporated coenzymes to carry out a broader range of chemical reactions compared to standard RNA. The presence of nicotinamide in the RNA world, for example, may have enabled RNA to perform oxidation/reduction reactions.

Breaker and Joyce also showed that the ribozyme could be made to self-incorporate dephosphorylated coenzyme A. Coenzyme A might have been useful in performing acyl transfer reactions in primitive metabolic pathways. In the Miller laboratory, both cysteamine and pantothenic acid, the building blocks of coenzyme A, have been synthesized under simulated prebiotic conditions (*24,25*). More recently, the pantetheine moiety of coenzyme A was prepared in about 5% yield by heating pantoyl lactone, β-alanine, and cysteamine at temperatures as low as 40°C (*26*). Each of these reactants are plausible prebiotic compounds and are highly soluble, and thus might have become concentrated in evaporating bodies of water on the primitive Earth.

b. Alternative backbones

b.1 Polyamide nucleic acid

The origin of the RNA world is not easily understood because it is difficult to envisage an efficient prebiotic synthesis of β-ribonucleotides and because it is unclear how RNA, even if available, could have replicated without the aid of a sophisticated catalyst. Recognition of these problems has prompted a search for simpler, alternative genetic systems that might have preceded RNA. One such possibility is polyamide nucleic acid (PNA), which resembles RNA in its ability to form double-helical structures stabilized by Watson-Crick pairing interactions, but has a backbone that is completely different and simpler than that of RNA. PNA is held together by amide rather than phosphodiester linkages (*27*). In collaboration with Peter Nielsen at the Panum Institute in Copenhagen, Christof Böhler in the Orgel laboratory has shown that polynucleotide templates facilitate the synthesis of complementary PNA oligomers. Conversely, PNA templates facilitate the synthesis of complementary oligonucleotides (*28*). This suggests that a transition between a PNA- and RNA-based genetic system could have occurred without loss of genetic information.

In addition to its chemical simplicity, PNA has the advantage of being achiral, thus avoiding the problem of enantiomeric cross-inhibition that greatly restricts the efficiency of template-directed polymerization of RNA in a racemic environment (*29*). Jürgen Schmidt in the Orgel laboratory studied the problem of enantiomeric cross-inhibition in the PNA-directed synthesis of complementary RNA. Cross-inhibition occurs in this system as well, suggesting that it is a general phenomenon not restricted to polynucleotide templates. However, when template-directed polymerization was initiated with a short oligonucleotide primer, enantiomeric cross-inhibition became much less severe, suggesting a possible enrichment mechanism for homochiral polynucleotides (Schmidt *et al.*, unpublished).

PNA can be viewed as a polymer of ethylenediamine monoacetic acid (EDMA), with the bases attached via an acetic acid linkage. The Miller laboratory carried out the synthesis of both EDMA and ethylenediamine diacetic acid from ethylenediamine, formaldehyde, and hydrogen cyanide. Beginning with 10^{-1}–10^{-4}M starting materials, EDMA was obtained in 11 – 79% yield. The prebiotic synthesis of ethylenediamine has not yet been demonstrated, but related compounds such as ethanolamine and cysteamine have been produced under plausible prebiotic conditions. Studies are currently underway to determine whether EDMA can be polymerized and whether the nucleotide bases can be attached to the poly-EDMA backbone.

The Joyce laboratory has shown that a ribozyme can be made to cleave an amide bond within the context of a polynucleotide analogue. Ribozymes that were evolved to cleave a target phosphoester were shown to cleave an unactivated, alkyl amide when that linkage was located either between two oligonucleotides or between an oligonucleotide and a peptide (*30*). The reaction is inefficient, with a rate acceleration of only about 10^2 as compared with the uncatalyzed reaction. Amide cleavage is Mg^{2+}-dependent and appears to proceed via an acyl intermediate, analogous to the aminoacyl-tRNA intermediate of biological protein synthesis. The fact that a single ribozyme catalyzes reactions involving phosphoesters and carboxyamides suggests a possible evolutionary route from the chemistry of RNA replication to that of protein synthesis during the early history of life on Earth.

b.2 With or without phosphate?

Consideration of PNA raises the possibility that the first genetic material may not have contained phosphate. This in turn raises the question as to whether phosphate itself is a prebiotically plausible compound. Keefe and Miller (*31*) have argued that there is no known efficient prebiotic synthesis of high energy phosphates or phosphate esters. All of the known processes, including the volcanic synthesis of P_4O_{10} (*32*), the synthesis of polyphosphate from phosphate minerals, and the use of high-energy organic compounds such as cyanamide or hydrogen cyanide (*33*), are inefficient and must compete with hydrolysis reactions. Attempts to find more efficient phosphate-polymerizing agents by spark discharge experiments and other prebiotic syntheses have so far proven unsuccessful (*31*).

The Arrhenius laboratory has shown that when phosphate is precipitated from sterile solutions that are at near-neutral pH and have a high Mg/Ca ratio, it does so in the form of whitlockite (protonated magnesium calcium phosphate), rather than apatite (*34-36*). Whitlockite is the thermodynamically stable phase, while apatite is a metastable phase that occurs in the presence of microorganisms. Upon heating, the amorphous whitlockite condenses to form linear polyphosphates. These in turn may give rise to trimetaphosphate, which has been shown to drive the phosphorylation of organic compounds such as glyceric acid (*37*). Stephen Mojzsis in the Arrhenius laboratory has demonstrated the existence of microaggregates of apatite intergrown with isotopically light graphite in sedimentary rocks from the Akilia Formation in southwest Greenland, dated at 3.86 billion years before the present. Because no other process is known to generate highly-fractionated light carbon, and this criterion is thus generally used to indicate bioorganic carbon, these carbonaceous apatite aggregates may establish a new earliest time point for the existence of life on Earth.

b.3 Aqueous polymerization reactions

Vera Kolb in the Orgel laboratory has developed a new method for studying the polymerization in aqueous solution of monomers that may have been important prior to the appearance of the RNA world. A [5′– ^{32}P]-labeled oligonucleotide that ends in a 3′-terminal amine is used as an initiator for the polymerization reaction. This initiator is extended by the addition of successive monomer units and the products are analyzed by polyacrylamide gel electrophoresis, relying on the 5′– ^{32}P label for visualization (*38*). In this way, the polymerization of ethylene-imine and co-polymerization of formaldehyde and urea have been studied. The later example is particularly relevant to prebiotic chemistry because it makes use of two prebiotically plausible monomers. Beginning with a 3′-amine-terminated oligonucleotide that had been treated with cyanate ion to generate a 3′-terminal ureido group, 4 – 5 successive subunits of formaldehyde-urea were added (*39*). With the combination of phenol and formaldehyde, much longer copolymers were obtained.

Richard Bruick in the Joyce laboratory similarly relied on an oligonucleotide that ends in a 3′-terminal amine to carry out attack on a thioester-linked oligonucleotide-peptide conjugate, resulting in attachment of the peptide to the attacking oligonucleotide via an amide linkage (*40*).

In this case the reaction involved a single addition and occurred in a template-directed fashion. An oligonucleotide template was used to specify a particular combination of amine-terminated oligonucleotide and oligonucleotide-conjugated peptide and to accelerate a reaction that is not detectable in free solution. A similar scheme might be used to carry out the synthesis of short peptides.

b.4 Polymerization on the rocks

In collaboration with James Ferris, an NSCORT Visiting Scientist, the Orgel laboratory has explored a new model for the prebiotic synthesis of long polymers (*41*). The central idea is that long, negatively-charged oligomers adsorb strongly and almost irreversibly to anion-exchange minerals, while monomers and short oligomers remain in the supernatant. Thus minerals may be used as a solid-phase support for chain elongation in an aqueous environment, without the need for covalent attachment. This idea is a general one that applies to polymers that are not necessarily related to nucleic acids.

Many of the experiments carried out to date have involved the polymerization of glutamic acid on the surface of hydroxylapatite or illite, although similar experiments have been carried out with aspartic acid and serine phosphate. Oligoglutamic acids that contain six or more subunits do not elute appreciably from the mineral surface over 24 hours, whereas monomers and shorter oligomers are readily washed away. Beginning with surface-adsorbed Glu_{10} , repeated "feedings" were carried out in which glutamic acid that had be activated with carbonyl diimidazole was allowed to bathe the surface for 24 hours before the supernatant was removed. This procedure was carried out repeatedly, resulting in the synthesis of long polyglutamic acids, up to about 50 subunits in length. A control reaction carried out in the absence of the mineral did not produce appreciable amounts of material longer than about the 9mer (*41*). Surface-tethered polymerization reactions provide a new method for generating a wide variety of homo- and heteropolymeric compounds with potential relevance to the origins of life. One can explore a large number of possible combinations of mineral surfaces, monomers, and activating agents.

b.5 RNA after all

In addition to a broad-based search for simpler, alternative genetic systems that might have preceded RNA, considerable attention continues to be directed toward RNA itself. Even if RNA was not the first genetic material, it is likely to have taken on the role of both genetic material and principal catalyst during the early history of life on Earth. Previous work by Eschenmoser and colleagues has shown that there is a favored route to ribose in the context of the formose reaction, provided one begins with formaldehyde and glycoaldehyde-phosphate and accepts ribose-2,4-diphosphate as the product (*42*). In the Arrhenius laboratory this result has been extended from the harshly basic conditions of the standard formose reaction to more prebiotically plausible conditions within the local environment of mineral interlayers (*43*). Yields of ribose 2,4-diphosphate, up to 43% relative to the input of glycoaldehyde-phosphate, were obtained using cobalt and manganese aluminum hydroxide minerals to adsorb the reactants from a dilute solution (≥ 20 μ M) at pH 7.5.

In the Orgel laboratory, work continues on the non-enzymatic template-directed synthesis of RNA. Recent studies have demonstrated that oligo(C) can be synthesized from activated cytidylate on single-stranded regions of a poly(G) template (*44*). If one employs a poly(7-deazaG) template, which has less propensity to form a tetrahelical structure compared to poly(G), the reaction is considerably more efficient (*45*). For replication to occur with a broad range of sequences, however, it may be necessary to enlist the help of a ribozyme. One approach to this has been taken by Luc Jaeger and Martin Wright in the Joyce laboratory, involving the construction of a catalytic motif comprised of a constant scaffold region of 220 nucleotides with attached random regions of 85 nucleotides. The scaffold region folds into a highly stable tertiary structure that has the propensity to bind an RNA duplex, while the random regions have the potential to form an active site about that bound duplex. *In vitro* evolution was used to obtain RNAs that catalyze the template-directed condensation between an oligonucleotide 5′-triphosphate and an oligonucleotide 2′(3′)-hydroxyl (Jaeger *et al.*, unpublished). This result is analogous to the work of Bartel and Szostak (*46*), in which ribozymes with RNA ligase activity were obtained starting from random-sequence RNAs.

Assuming that an RNA polymerase eventually came into existence on the primitive Earth, it would have been advantageous for that enzyme to be isolated within a protected microenvironment, for example, a lipid vesicle. Ajoy Chakrabarti, an NSCORT Visiting Postdoctoral Fellow from David Deamer's laboratory at the University of California, Santa Cruz, working together with Ronald Breaker in the Joyce laboratory, devised a model system to test this possibility (*47*). They encapsulated an RNA polymerase, polynucleotide phosphorylase, within liposomes comprised of dimyristoyl phosphotidylcholine. They then supplied a monomeric substrate, adenosine diphosphate, externally and relied on passive transport for delivery of the substrate to the encapsulated enzyme. Poly(A) was produced within the liposomes, as visualized by excitation fluorescence of ethidium bromide. Because of its large size (mean chain length ~ 100 nucleotides) and polyanionic character, the poly(A) remained trapped within the liposomes. In some ways, "polymerization in a bubble" resembles "polymerization on the rocks" in that both result in the preferential retention of long polymers. The principle of selective retention thus may be relevant to both prebiotic chemistry and the early history of life.

3. References Cited

1. Brinton, K. L. F. and Bada, J. L. (1996): *Geochim. Cosmochim. Acta* **60**, 349-354.
2. Bada, J. L., Brinton, K. L. F., McDonald, G. D. and Wang, X. S. (1996): *In Circumstellar Habitable Zones* (Doyle, L., ed.) Travis House Publications, in press.
3. Cronin, J. R., Pizzarello, S. and Cruickshank, D. P. (1988): In *Meteorites and the Early Solar System* (Kerridge, J. F. and Matthews, M. S., eds.) University of Arizona Press, Tucson, p.819.
4. Kroto, H. W. (1987): *Nature* **329**, 529-532.

5. Becker, L. R., Bada, J. L., Winans, R. E. and Bunch, T. E. (1994): *Nature* **372**, 507.
6. Becker, L. R., Bada, J. L., Winans, R. E., Hunt, J. E., Bunch, T. E. and French, B. M. (1994): *Science* **265**, 642-645.
7. Becker, L. R., Poreda, R. J. and Bada, J. L. (1996): *Science* **272**, 249-253.
8. Braterman, P. S., Arrhenius, G., Hui, S. and Paplawsky, W. (1995): *Orig. Life Evol. Biosphere* **25**, 531-538.
9. Arrhenius, T., Arrhenius, G. and Paplawsky, W. J. (1994): *Orig. Life Evol. Biosphere* **24**, 1-19.
10. Bada, J. L., Wang, X. S., Poinar, H. N., Paabo, S. and Poinar, G. (1994): *Geochim. Cosmochim. Acta* **58**, 3131-3135.
11. Poinar, H. N., Moss, M., Bada, J. L. and Paabo, S. (1996): *Science* **272**, 864-866.
12. Larralde, R., Robertson, M. P. and Miller, S. L. (1995): *Proc. Natl. Acad. Sci. USA* **93**, 8158-8190.
13. Oró, J. (1961): *Nature* **191**, 1193-1194.
14. Sanchez, R. A., Ferris, J. P. and Orgel, L. E. (1966): *Science* **154**, 784-785.
15. Ferris, J. P., Zamek, O. S., Altbuch, A. M. and Freiman, H. (1974): *J. Mol. Evol.* **3**, 301-309.
16. Robertson, M. P. and Miller, S. L. (1995): *Nature* **375**, 772-774.
17. Robertson, M. P. and Miller, S. L. (1995): *Science* **268**, 702-705.
18. Kolb, V. M., Dworkin, J. P. and Miller, S. L. (1994): *J. Mol. Evol.* **38**, 549-557.
19. House, C. H. and Miller, S. L. (1996): *Biochemistry* **35**, 315-320.
20. Kellogg, R. M. and Visser, C. M. (1988): In *Redesigning the Molecules of Life* (Benner, S. A., ed.) Springer-Verlag, Berlin, pp. 1-24.
21. Liu, R. and Visscher, J. (1994): *Nucleosides & Nucleotides* **13**, 1215-1216.
22. Liu, R. and Orgel, L. E. (1995): *Nucleic Acids Res.* **23**, 3742-3749.
23. Breaker, R. R. and Joyce, G. F. (1995): *J. Mol. Evol.* **40**, 551-558.
24. Miller, S. L. and Schlesinger, G. (1993): *J. Mol. Evol.* **36**, 302-307.
25. Miller, S. L. and Schlesinger, G. (1993): *J. Mol. Evol.* **36**, 308-314.
26. Keefe, A. D., Newton, G. L. and Miller, S. L. (1995): *Nature* **373**, 683-685.
27. Willung, P., Nielsen, P. E., Buchardt, O., Egholm, M. and Norden, B. (1994): *Nature* **368**, 561-563.
28. Böhler, C., Nielsen, P. E. and Orgel, L. E. (1995): *Nature* **376**, 578-581.
29. Joyce, G. F., Visser, G. M., van Boeckel, C. A. A., van Boom, J. H., Orgel, L. E. and van Westrenen, J. (1984): *Nature* **310**, 602-604.

30. Dai, X., De Mesmaeker, A. and Joyce, G. F. (1995): *Science* **267**, 237-240; see also *Science* **272**, 18-19, 1996.

31. Keefe, A. D. and Miller, S. L. (1995): *J. Mol. Evol.* **41**, 693-702.

32. Yamagata, Y., Watanabe, H., Saitoh, M. and Namba, T. (1991): *Nature* **352**, 516-519.

33. Keefe, A. D. and Miller, S. L. (1996): *Orig. Life Evol. Biosphere* **26**, 15-25.

34. Verbeeck, R. M. H., DeBruyne, P. A. M., Driessens, F. C. M., Terpstra, R. A. and Verbeek, F. (1986): *Bull. Soc. Chim. Belg.* **95**, 455-476.

35. Driessens, F. C. M. and Verbeeck, R. M. H. (1990): *Biominerals* (CRC Press, Boca Raton, FL) p. 427.

36. Gedulin, B. and Arrhenius, G. (1994): *In Early Life on Earth, Nobel Symposium No. 84* (Bengtson, S., ed.) Columbia University Press, New York, pp. 91-110.

37. Kolb, V. M. and Orgel, L. E. (1996): *Orig. Life Evol. Biosphere* **26**, 1-5.

38. Kolb, V. M. and Orgel, L. E. (1994): *J. Mol. Evol.* **38**, 433-437.

39. Kolb, V. M. and Orgel, L. E. (1995): *J. Mol. Evol.* **40**, 115-119.

40. Bruick, R. K., Dawson, P. E., Kent, S. B. H., Usman, N. and Joyce, G. F. (1996): *Chem. & Biol.* **3**, 49-56.

41. Ferris, J. P., Hill, A. R., Liu, R. and Orgel, L. E. (1996): *Nature* **381**, 59-61.

42. Müller, D., Pitsch, S., Kittaka, A., Wagner, E., Wintner, C. and Eschenmoser, A. (1990): *Helv. Chim. Acta* **73**, 1410-1468.

43. Pitsch, S., Eschenmoser, A., Gedulin, B., Hui, S. and Arrhenius, G. (1995): *Orig. Life Evol. Biosphere* **25**, 294-334.

44. Rembold, H. and Orgel, L. E. (1994): *J. Mol. Evol.* **38**, 205-210.

45. Rembold, H. and Orgel, L. E. (1994): *J. Mol. Evol.* **38**, 211-214.

46. Bartel, D. P. and Szostak, J. W. (1993): *Science* **261**, 1411-1417.

47. Chakrabarti, A. C., Breaker, R. R., Joyce, G. F. and Deamer, D. W. (1994): *J. Mol. Evol.* **39**, 555-559.

C. External Evaluation

1. Annual Review Committee

An Annual Review Committee receives a detailed report of progress and meets with the NSCORT PIs and Fellows each November. The Committee members are: Aloke Chatterjee, Benton Clark, Thomas W. Clarkson, David Des Marais, Donald De Vincenzi, Michael A. Meyer, Norman Pace, Julius Rebek, Alex Rich, John Rummel, William J. Schopf, Alan W. Schwartz and Ronald White. [For affiliations and addresses see Appendix II-C-1(1).]

The Committee has been effective and useful to the NSCORT program in the following ways:

- Preparation of the Annual Report provides an opportunity for self scrutiny and evaluation.

- Formal and informal interaction among the Committee members, PIs and Fellows contributes useful ideas and direction for all aspects of the program.

- Fellows gain useful experience preparing and presenting coherent summaries of their work and interacting with senior scientists.

- The informal dinner meeting introduces the Fellows to the significance of relaxed exchange among colleagues.

- The Reports of the External Review Committee have invariably suggested significant improvements in the program.

The complete report of the Annual Review Committee for 1995 is provided in Appendix II-C-1(2). Committee's *General Finding* states, "The NSCORT continues to be highly productive. Activities and research appear to be highly interactive and to provide value far beyond what would be obtained with individual grant support."

2. Three-Year Site Visit Review Panel

A 3-year Site Visit Review Panel was convened under the auspices of the American Institute of Biological Sciences and met in La Jolla, California on March 8-10, 1995. The following excerpts from that report attempt to provide an unbiased summary [see Appendix II-A-(2)].

Overall Evaluation: "This has been an outstanding program that is more than the sum of its parts. The science is excellent and the interaction among the research groups has been productive. The NSCORT has been able to attract excellent students, postdoctoral fellows, and visiting scientists. Communication between the groups appears to be working very well. There are some areas for improvement. The NSCORT could make better use of its associates and leverage its outreach with other organizations..."

> "The synergism among these five projects is strong, much stronger than one might expect given the five very independent and vigorous PIs."
>
> "In the area of education and training, a program of undergraduate, graduate and postdoctoral training is vigorous and productive."

"The very successful undergraduate program could further enhance the visibility of the NSCORT, if recruitment for the undergraduate fellowship could be more widely publicized."

"The NSCORT has been very successful in selecting talented graduate students and postdoctoral fellows from an international pool of applicants."

"The NSCORT should more vigorously explore possibilities that might help to improve this situation [placement of program graduates]."

"The education outreach effort aimed at secondary schools is excellent."

"... Dr. Edward Frieman, Director of Scripps Institution of Oceanography (SIO), stated that this was one of the most efficiently run multi-investigator organizations that he has been associated with."

"The NSCORT principals are leaders in the field in terms of publication numbers and, especially quality."

"The education through an NSCORT in Exobiology would certainly benefit from the more direct involvement of scientists working on the more "historical" aspects of the origin of life (e.g., phylogeny, microbiology, evolution of metabolic pathways, archaean fossils)."

"Progress has been outstanding at the research level and future research directions seem clear and relevant."

"The role of the 11 scientists named as "associates" in the NSCORT is not clear."

"The three participating institutions (UCSD-SIO, TSRI and Salk) have met their financial commitments."

"The funds have been and are being distributed and used well."

"The theme of the NSCORT for exobiology remains highly relevant to the NASA mission. Fundamental science should remain the predominant theme."

"This seems a good way for NASA to fund excellent research. NASA has gotten its money's worth."

D. Training and Education

1. Undergraduate, Graduate and Postdoctoral Fellows

A primary function of the NSCORT/Exobiology program is the training of young scientists to pursue research careers in Exobiology and related subjects. In addition to Fellowships for Graduate and Postdoctoral appointees, the program supports summer Fellowships for Undergraduate students. Graduate Student and Postdoctoral Fellows spend two to four years in a PI laboratory of their choice. Approximately 5 Fellows in each category are supported per year.

Subsequent to advertisements for Fellowships in the journals *Science* and *Nature*, and distribution of announcements through personal contacts, 143 applications for Fellowships have been received as of June 1996. From these, 15 Postdoctoral, 12 Graduate, and 30 Undergraduate applicants have been selected and have accepted Fellowships. Recipients of Fellowships have come from USA, Canada, China, England, France, India, Sri Lanka, Switzerland, Taiwan and Wales. The Fellowship Selection Process is summarized in Figure II-D-1.

In addition to direct funds for research and academic curricula, NSCORT supports a variety of educational activities for the Fellows:

- A bi-weekly Journals Club organized by the NSCORT Fellows.
- A bi-monthly Seminar-Discussion for NSCORT PIs, Fellows and Associates. Examples of discussion topics: "Life arose in a homogeneous global ocean"; "What simple experiment would you carry out to test for extraterrestrial life?"; "Was the first life autotrophic or heterotrophic?" etc.
- Seminars and Discussions by invited U. S. and foreign scientists (see below).
- U.S. and foreign visiting scientists to engage in collaborative research (see below).
- Courses in Chemical Evolution and other topics associated with Exobiology (see below).
- Field trips for Fellows: e.g., NASA Ames Research Center; JPL in Pasadena, CA; Death Valley (precambrian stromatolites); Baja California (cyanobacteria bioherms); Anza-Borrego desert (sedimentary environments); etc.

Undergraduate Fellowships

The NASA Specialized Center of Research and Training in Exobiology (NSCORT/ Exobiology) Summer Research Fellowship Program provides a ten week research experience for undergraduate college students majoring in chemical and/or earth sciences.

The Summer Research Fellowship features direct participation in the research activities of UCSD and Scripps Institution of Oceanography (SIO) faculties as well as an exploration of opportunities for graduate study at UCSD and SIO.

Summer Research Fellowships are offered on a competitive basis to students who have completed at least their junior year of college, are enrolled full-time at a college or university, and have a 3.0 or better grade point average. A complete Summer Research Fellowship application includes: a signed and completed application form, a Statement of Purpose, a current official undergraduate transcript, and the names, addresses and phone numbers of two faculty members who may be contacted for evaluation. Students receive a $2,500/(10-week) stipend and on-campus housing.

Research assignments are designed and supervised by a faculty Mentor in an area of the student's research interest, and require full-time commitment by the student. At the discretion of the students' Mentor, a final abstract or oral presentation may be required at the end of the Summer Research Fellowship [see Appendix II-D-1(1)]. Fellows attend seminars, discussions and meetings conducted under the auspices of the NSCORT program, and interact with the other NSCORT Fellows both formally and informally.

As of Summer 1996, 30 undergraduates representing the U.S. and 6 foreign countries have completed the Fellowship program.

Graduate Student Fellowships

Graduate students who have been admitted to the Ph.D. program in participating institutions (UCSD, TSRI and Salk) are eligible to apply for Fellowships in the Exobiology Training

Program.

The Graduate student is asked to submit a letter of application to the NSCORT Associate Director indicating his or her area of interest, institution and graduate program and to includ a proposed starting date and his or her preference of Principal Investigator. He or she should include a curriculum vitae, proposal for an area of thesis research, and the names of three academic references. Applicants should also directly contact an NSCORT Principal Investigator whose research activities are in the area of the applicant's interest. There should be an agreement that the Principal Investigator will sponsor and direct the academic program and research thesis of the applicant, if he/she is granted a Fellowship.

Applicants are evaluated competitively by the NSCORT Selection Committee following their initial graduate year, and if accepted, receive full tuition remission and a yearly stipend of $17,000 per year for three years of satisfactory performance.

Students fulfill the requirements of their parent institution and, in addition, participate in courses particularly relevant to Exobiology, attend seminars, discussions and meetings conducted under the auspices of the NSCORT program, interact with other NSCORT Fellows both formally and informally, and contribute to appropriate Outreach activities of the Exobiology program.

As of 1996, 12 graduate students representing the U.S. and 3 foreign countries have been enrolled in the Fellowship program. Six have completed their Fellowships and received a Ph.D. degree.

Postdoctoral Fellowships

Candidates with a Ph.D. degree or equivalent, preferably in geochemistry, chemistry, biochemistry or molecular biology, who have an interest in Exobiology or Exobiology-related research are eligible to apply for an NSCORT Postdoctoral Fellowship. Interested persons send resume/curriculum vitae with a statement of research interests and the names and addresses of at least three references to the Associate Director.

NSCORT/Exobiology Postdoctoral Fellows are introduced to the full range of activities of the Center and are expected to choose a research topic in the laboratory of one of the Scientific Staff. They participate in the Exobiology Seminar Program, the NSCORT Journals Club, Discussion Groups, and other organized activities, as well as contribute to the education of their graduate and undergraduate associates, and to the Outreach program.

Postdoctoral Fellows are normally appointed for two years, with an option for extension to accommodate timing for subsequent employment. Stipends range between $26,000 and $30,000 depending on number of postdoctoral years and experience.

As of 1996, 15 postdoctorals representing the U.S. and 8 foreign countries have been enrolled in the Fellowship program. Thirteen have completed their Fellowships. The following list summarizes the current placement of those Fellows who have completed their Fellowships.

Gene McDonald	Research Associate, Cornell University (September 1994)
Anthony Keefe	Postdoctoral NRC Fellowship Ames Research Center (June 1995)
Luann Becker	Postdoctoral NRC Fellowship Ames Research Center and UCSD (April 1995)

Ronald Breaker	Assistant Professor, Yale University (August 1995)
Niles Lehman	?Assistant Professor, California State University Long Beach (September 1995)
Michael Griffith	Isis Pharmaceuticals, Carlsbad, CA (July 1993)
Luc Jaeger	Assistant Professor, University of Strasbourg (January 1996)
Heinz Peter Muth	Patent Attorney, Germany (September 1993)
Ton Lee	Fisherman Pharmaceutical Corp., Taiwan (April 1995)
Stefan Pitsch	Eidgenössische Technische Hochschule Zurich, Switzerland (October 1995)
Ajoy Chakrabarti	Nexstar Pharamceuticals, San Dimas, CA (January 1996)
Kevin Walda	Manager, Analytical Facility, Scripps Institution of Oceanography, University of California, San Diego (April 1996)
Martin Wright	Postdoctoral, The Scripps Research Institute, La Jolla, CA

Fellowship Selection Process

The Fellowship Selection Process is summarized in Figure II-D-1.

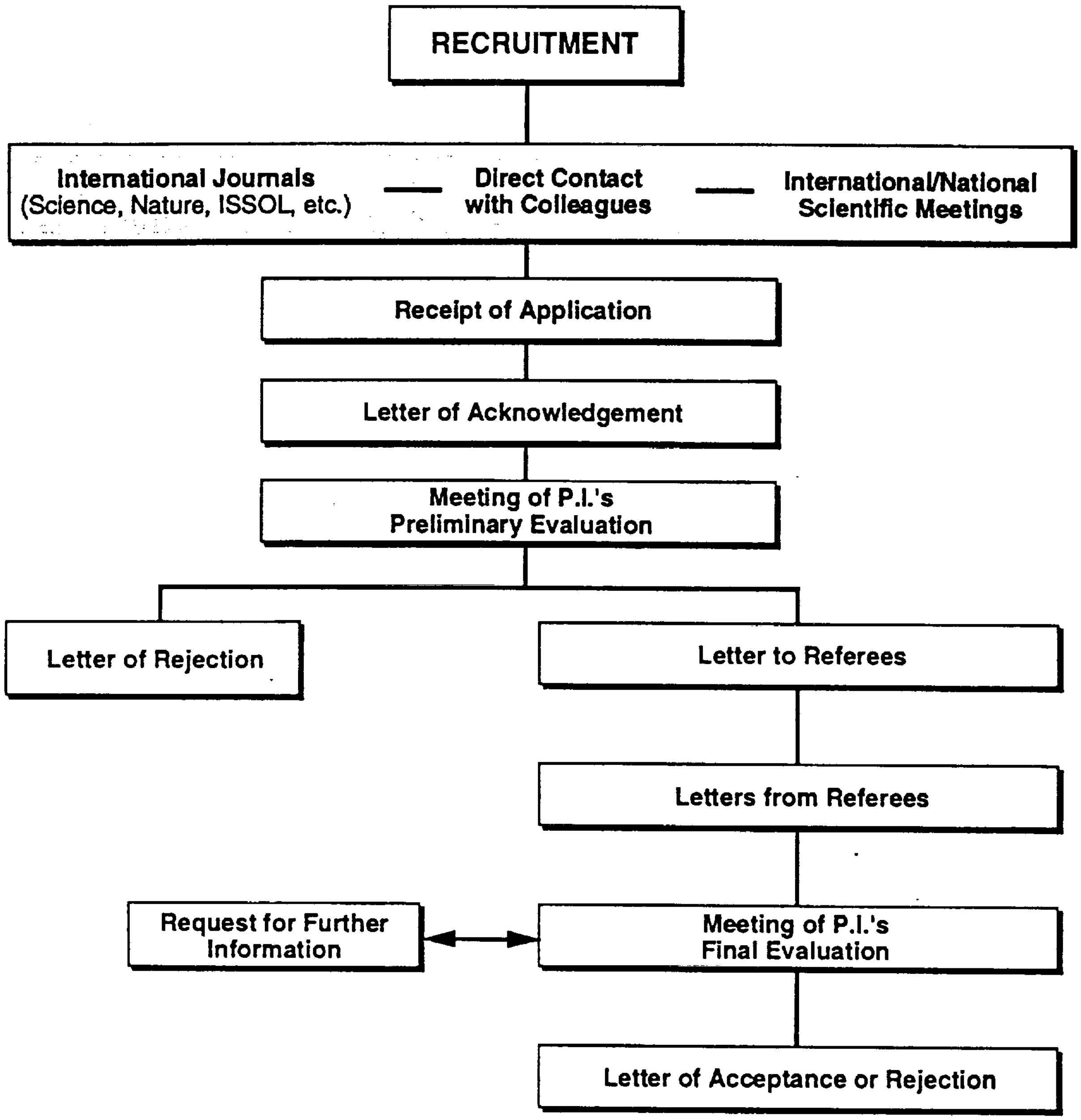
2. Courses and Seminars

The following courses in Chemical Evolution have been available to the NSCORT Fellows as of 1996.

e) Courses in Chemical Evolution

- Winter 1992 through 1996, Chem 122: Biochemical Evolution - S. Miller, L. Orgel & G. Joyce.
- Winter 1992, 1994, SIO 269: The Early Earth - J. Bada & M. Kastner; G. Arrhenius (see ref. 2)
- Fall 1994, SIO 269: Research in Molecular Evolution - G. Arrhenius
- Winter 1995, SIO 269: Crystal Surface Chemistry - G. Arrhenius
- Fall 1992-1996, ES 30: The Oceans - J. Bada, M.C. Hendershott & N.D. Holland
- Winter 1995, ES 102: Introductory Geochemistry - J. Bada & J. D. MacDougall
- Summer 1993, Molecular Evolution Seminar - R. Doolittle
- 1992-1996, Chem 293: Cosmochemistry Seminar Series ASK BADA for Quarter

NSCORT/Exobiology Fellowship Selection Process



- Applications summarized on receipt by Associate Director and distributed to P.I.'s
- Initial contact with applicants through Associate Director
- Applicants referred to direct contact with P.I.'s for specific research interests
- Accepted applicants referred to direct contact with P.I.'s for timing/laboratory arrangements
- Accepted applicants referred to Associate Director for administrative/residential arrangements

Figure II-D-(1)

The following Seminars and Discussions by invited U.S. and foreign scientists have been sponsored by NSCORT/Exobiology as of 1996.

Stanley Awramik	University of California, Santa Barbara
Herrick Baltscheffsky	University of Stockholm
Steven Benner	Eidgenössische Technische Hochschule
David Blake	NASA-Ames Research Center
Paul Braterman	University of North Texas
Ted Bunch	NASA-Ames Research Center
Chris Chyba	National Security Council
David Deamer	University of California, Davis
Victor Drits	Vernadski Institute of Geochemistry
Albert Eschenmoser	Eidgenössische Technische Hochschule
James Ferris	Rensselaer Polytechnic Institute
Peter Gogarten	University of Connecticut
Juan Granja	University of Santiago
Heinrich Holland	Harvard University
James Kasting	Pennsylvania State University
John Kerridge	NASA Headquarters
Vera Kolb	University of Wisconsin, Parkside
Antonio Lazcano	University of Mexico
Donald Lowe	Stanford University
Luigi Luisi	Eidgenössische Technische Hochschule
Michel Maurette	Centre de Spectrométrie Nucléaire et de Spectrométrie de Masse
Christopher McKay	NASA Ames Research Center
David Morrison	NASA Ames Research Center
Peter Nielsen	The Panum Institute
Andrew Pohorille	NASA-Ames Research Center
Julius Rebek	Massachusetts Institute of Technology
Alex Rich	Massachusetts Institute of Technology
Frank Seela	Universität Osnabrück
Jack Szostak	Harvard Medical School
Jonathan Trent	Argonne National Laboratory
Olke Uhlenbeck	University of Colorado
Eric Westof	Université de Strasbourg
Michael Yarus	University of Colorado, Boulder

In addition to these Seminars and Discussions by off-campus scientists, in each two month interval at least one seminar by local scientists on topics pertinent to Exobiology has been sponsored by NSCORT.

3. Visiting Scientists

U.S. and foreign Visiting Scientists have been sponsored by NSCORT/ Exobiology to come to the PIs' laboratories for periods ranging from a month to a year, and engage in collaborative research with the PIs and Fellows. Through 1995 they have included:

Paul Braterman	University of North Texas
Michael McConnell	Point Loma Nazarene College
Victor Drits	Vernadski Institute of Geochemistry
James Ferris	Rensselaer Polytechnic Institute
Juan Granja	University of Santiago
Bettina Heinz	Palomar College
Vera Kolb	University of Wisconsin, Parkside
Antonio Lazcano	University of Mexico
Michel Maurette	Centre de Spectrométrie Nucléaire et de Spectrométrie de Masse
David Usher	Cornell University

E. Knowledge Transfer and Outreach

NSCORT/Exobiology as a coordinated program not only communicates with Exobiologists nationally and internationally, but is able to introduce other potentially interested individuals and groups who would not otherwise come into contact with the discipline to the field of Exobiology These include members of the scientific community; primary, secondary and college students and teachers; and the general public. These activities are considered within the general mission of "Outreach". They include inviting individual students and researchers from allied fields to attend NSCORT meetings, seminars and discussions; providing opportunities for high school and junior college students and teachers to participate in Exobiology projects and to hear lectures by Exobiology specialists; establishment of Honorary and Adjunct Fellows to encourage broad participation in NSCORT programs; support and sponsorship of Exobiology agenda at national and international scientific meetings, and support of summer internships for undergraduate students.

NSCORT-invited lecturers give seminars and lead discussions in Exobiology that are open to the scientific community and, when appropriate, to the general public. Publications concerning Exobiology for both scientific and more general audiences are encouraged through NSCORT resources. Brochures and pamphlets are produced by the NSCORT Central Office describing the Exobiology programs and personnel.

NSCORT acts as a bibliographic and consultative resource for development of teaching materials.

In addition to the high school curricular segment on Exobiology, teaching materials are in preparation for the NASA Computer Bulletin Board for Teachers and the AAAS National Center for Science Education. In the public domain, NSCORT provides materials and expert consultation on Exobiology for newspaper and magazine articles as well as for television documentary programs. A summary of NSCORT/Exobiology Outreach activities was prepared for the NASA Life Sciences Education Programs Coordinator, Bonnie McClain, and is included in Appendix II-E.

The following outreach programs indicated by an asterisk (*) would not have occurred without the centralized, coordinated operation of NSCORT. Individual grants to PIs would not have been appropriate for support of these activities.

1. **Examples of outreach exchange within the professional community of Exobiologists (Appendix II-E-1).**
   a) Active collaboration with other NASA laboratories and extramural programs: L. B. Johnson Space Center, Houston; NASA Ames Research Center, Moffett Field; U.S. Geological Survey, Reston, VA; NIH National Center for High Resolution Electron-Microscopy, UCSD; The Geological Institute, Russian Academy of Sciences; University of North Texas; University of Wisconsin, Parkside; University of Copenhagen; Eidgenössische Technische Hochschule, Zurich; University of Mexico; University of California, Davis; University of California, Santa Barbara; University of California, Los Angeles; and Royal Institute of Technology, Stockholm.
   b)* Summary articles regarding NSCORT/Exobiology activities.
   c) Presentations by PIs and Fellows at national and international meetings and symposia: Winter Seminar, Klosters, January 1992, 1993; International Society for the Study of the Origin of Life (ISSOL), Barcelona, July 1993; Gordon Research Conference, August 1993; American Chemical Society, August 1993; Geological Society of America, October 1993; 1st International Circumstellar Habitable Zones Conference, January 1994; AAAS National Meeting , February 1994; American Chemical Society, March 1994; Fifth Symposium on Chemical Evolution and the Origin of Life, NASA Ames Research Center, April 1994; Frontiers in the Physics of the Origin of Life, June 1994; and ISSOL Meeting, Orleans, France, July 1996.
   d)* Sponsorship and support of sessions devoted to Exobiology at national and international conferences: International Society for the Study of the Origin of Life, Barcelona, July 1993; AAAS National Meeting , February 1994; American Chemical Society, March 1994; Gordon Research Conference, August 1994; Gordon Research Conference, January 1996; and ISSOL Meeting, July 1996.
2. **Examples of outreach exchange with the general scientific community (Appendix II-E-2).**
   a) Cooperative articles in journals of general scientific readership, e.g., *Scientific American, Science, Nature, American Scientist.*
   b) Lectures to scientists from other disciplines.
   c)* Brochures, pamphlets and Newsletter for distribution to potential Fellowship applicants, media, and other interested parties.
3. **Examples of outreach programs for high school and college (Appendix II-E-3).**
   a)* Involvement of high-school and college teachers in NSCORT/Exobiology laboratory research (e.g., Stephen Brown, La Jolla High School, Michael McConnell, College of Nazarene).
   b)* High School essay contest on Exobiology.
   c)* Sponsorship of Rincon Indian students at the Science Bowl, Navajo Indian Reservation in Chinle, Arizona (1994) and Shiprock, New Mexico (1995).
   d) Participation in SIO SURF Summer Program for undergraduates

e) Participation in NASA Planetary Biology Internship Program

f) Participation in UCSD Undergraduate Physics Research Center (UPRC)

g) Participation in UCSD Mentor Program for Undergraduates

h)* Lectures by NSCORT/Exobiology scientists to teachers and students

i)* Bibliographic and consultative assistance for secondary and college teachers through World Wide Web (Internet) and NASA Space Link.

j)* Exobiology Demonstration Teaching Module for high school teachers, available for circulation among local secondary schools. Includes bibliographic materials, laboratory apparatus, A/V aids, lecture notes, and student handouts. Presentations by NSCORT Fellows, NSCORT laboratory visits, etc. (see Appendix II-E-3-J).

4. Examples of outreach programs for primary/secondary education.

a)* Museum exhibit on Exobiology (in preparation).

b) Project "Dragonfly" (National Science Teachers Association plus University of Miami). Teaching materials, student journal and computer interaction (Leslie Orgel).

c)* National Science Teachers Association (NSTA) symposium on "Origins" at International Convention in San Francisco, December 1996 (Jeffrey Bada).

d)* Preparation of an elementary story-text (ages 6-12) "The Adventures of Percy the Proton". A Spanish translation will be made. (Appendix II-E-4-d)

5. Examples of outreach programs for the general public (Appendix II-E-5).

a)* NSCORT Central Office clearing house for bibliographic materials, interviews with scientists, and general orientation for media personnel.

Descriptions of research and other NSCORT/Exobiology associated activities appeared in local, national and international media from 1992 through 1996. Examples are: A 1993 one hour British TV program (Horizon: "Life is Impossible") emphasized NSCORT scientists. A *Time Magazine* article on Origin of Life, including NSCORT research, appeared October 11, 1993. Local San Diego media, UCSD in-house publications, and UCSD TV have carried descriptions of NSCORT activities.

A PBS NOVA television program, "The Search for the Origins of Life", currently in production by Geoffrey Haines-Stiles, will feature NSCORT scientists and laboratories. NSCORT personnel are providing consultation and editorial assistance.

Examples of TV interviews and programs, magazine and newspaper articles, and other media coverage are given in Appendix II-E-5.

b)* NSCORT maintains a Home Page on the World Wide Web (http://www-chem.ucsd.edu/~nscort/nscort/Nscort.html).

c)* Public lectures by local and extramural Exobiology scientists, e.g. David Brin, "The Great Silence: Is Anybody Out There?", April 16, 1996.

NASA NAGW-2881: FINAL REPORT

The Chemistry of Early Self-Replicating Systems
January 1, 1992 through December 31, 1996

Appendices

NSCORT/Exobiology
Duties of the Office of the Associate Director

1. PREPARATION AND CONTROL OF BUDGET

The Office shall be responsible for preparing detailed yearly budget requests for submission to NASA. Throughout the year, the Office will monitor expenditures, distribute funds through the Cal Space Business Office to participating entities and coordinate the overhead and budgeting policies of the three NSCORT Institutions.

2. PREPARATION OF ANNUAL REPORT, INTERIM REPORTS, BROCHURES

The Office shall be responsible for the timely acquisition of research reports from the PIs and other budgetary and programmatic data to be included in the Annual Report to NASA. Preparation and distribution of this report shall be completed by the Office no later than October 1.

The Office shall be responsible for interim ad hoc reports to NASA and other administrative bodies throughout the year.

The Office shall be responsible for preparation and distribution of brochures, announcements, and other communications describing the NSCORT/Exobiology program and for advertising lectures, meetings and other functions.

3. COLLECTION AND MAINTENANCE OF RECORDS

The Office shall be responsible for the accession and cumulative maintenance of all records and materials pertinent to the NSCORT/Exobiology program. This will include bibliographic reprints, professional activities of the PIs and Fellows, awards, etc.; yearly biographies of Fellows; articles from general scientific and public media; outreach activities involving professional exobiologists, the broad scientific community, college, primary and secondary education and the general public.

4. ORGANIZATION OF LOCAL, NATIONAL AND INTERNATIONAL MEETINGS

The Office shall be responsible for organizing seminar programs, meetings and symposia, including the itinerary of visiting speakers, and for resolving administrative problems of visiting scientists. The Office shall be responsible for administrative aspects of site selection, travel, accommodations, etc. as appropriate for meetings related to the NSCORT/Exobiology program. This shall include preparation and distribution of materials for the Annual Review Committee and for the 5 year Grant Renewal Committee.

The Office shall arrange for approximately bi-monthly PI meetings, preparation of agenda, taking and distribution of minutes, etc.

5. ADMINISTRATIVE ASPECTS OF NSCORT FELLOWSHIP PROGRAM
(see: NSCORT Fellowship Selection Process)

The Office shall be responsible for communication with Fellowship applicants concerning the Program, receipt and distribution of Fellowship applications, and preparation and implementation of appointments (see Table 1).

The Office shall act as an interface between NSCORT Graduate and Postdoctoral Fellowship appointees, as well as undergraduate summer program students, and the appropriate administrative structures of UCSD, The Scripps Research Institute, and The Salk Institute for Biological Studies. This will include academic and personal advice to students and postdoctoral personnel.

The Office shall be responsible for official communications with applicants and appointees concerning the structure of the NSCORT Fellowship Training Program, academic requirements, criteria for reappointment, stipends, and other general matters pertinent to successful completion of the program.

The Office shall be responsible, in consultation with the Principal Investigators, for preparing advertising/announcement materials concerning the NSCORT program for appropriate distribution to applicants and appointees.

Throughout the Fellows' tenure, the Office will oversee budgetary disbursement and control for salaries, overhead and support.

The Office will be responsible for coordination and arrangements for communal activities of Fellows, e.g., Journal Club, Bi-monthly Seminars, Summer Intern Program.

6. LIAISON WITH EXTRAMURAL PROFESSIONAL ORGANIZATIONS

The Office shall be responsible for liaison with other NASA entities (Ames Research Center, Johnson Space Center, other NSCORT's, etc.) and with professional organizations including AAAS, Gordon Conferences, ACS, AGU, ISSOL, International Conference on Circumstellar Habitable Zones.

7. DEVELOPMENT AND COORDINATION OF OUTREACH PROGRAMS

The Office shall be responsible for liaison with public media, e.g., arrange interviews, distribute materials, provide consultation. The Office shall provide consultation and guidance for educational programs, e.g., primary and high school Exobiology curricula, NASA Computer Bulletin Board for Teachers, AAAS National Center for Science Education, Institute for Advanced Studies in Biology, and International Space University.

8. SEARCH FOR EXTRAMURAL FUNDS

The Office shall be responsible for investigating sources of funding to supplement the NASA grant, especially in the area of Outreach and Education. Such sources include other governmental agencies (e.g., NSF), private foundations, and local individuals/organizations.

National Aeronautics and
Space Administration

Headquarters
Washington, DC 20546-0001

MAY 22 1995

Reply to Attn of: UL

Stanley L. Miller, Ph.D.
Department of Chemistry, 0317
University of California, San Diego
9500 Gilman Drive
La Jolla, California 92093-0317

Dear Dr. Miller: Stanley

Thank you very much for hosting the site visit review of your Center's operations and accomplishments and for providing all of the information requested by the review team. Because of your kindness and cooperation, the review was smooth and successful; I appreciate your responsiveness.

With this letter, I am enclosing a copy, for your use, of the final, sit-visit report provided by the American Institute of Biological Sciences. NASA is in the process of reviewing this report and of deciding whether to continue funding a Center in this research area for five additional years, beginning in late 1996 or early 1997. We will let you know our decision as soon as it is reached.

I hope that your final 18 months of activity are as productive as the first three and one-half years have been and I look forward to our own future interactions.

Sincerely,

Ron

Ronald J. White, Ph.D.
Senior Program Scientist
Life and Biomedical Sciences and Applications Division

Enclosure

cc:
SLC/M. Meyer (w/o enclosure)

SITE VISIT REPORT **PRIVILEGED COMMUNICATION**

PANEL:	NSCORT: THIRD YEAR SITE VISIT REPORT
DATE:	March 8-10, 1995
DIRECTOR:	Stanley Miller
INSTITUTION:	University of California, San Diego
TITLE:	Exobiology

Individual Projects

Project: Chemical Reactions of Nucleotide Bases with Other Possible Primitive Earth Compounds (Dr. Stanley Miller)

Dr. Stanley Miller, who derives almost all of his extramural funding from the NSCORT, has had a productive 3 years, with 15 publications, 4 accepted, 3 submitted, and a variety of projects currently under way. Much of his work centers on the chemical stability of possible prebiotic compounds to establish whether they are likely candidates for important players in early chemical evolution. Due to its non-selectivity, the formose reaction is not a likely process for the formation of ribose. Still, they have shown that even if a viable route to ribose formation or formation of an appropriate derivative such as a ribose-2,4-diphosphate were found, these compounds, along with other sugars, decompose at such a rate ($t_{1/2}$=73 minutes at 100C for ribose at pH7) that they are too unstable to have been used under prebiotic conditions unless they were utilized immediately. They have also shown that a proposed FeS/H_2S medium, while strongly reducing, does not reduce CO_2 to form amino acids or nucleic bases, at least under the reaction conditions studied; this draws into question the robustness of such a process as proposed by Wächtershäusen.

Another project concerned with the prebiotic synthesis of potential nucleic bases centers on the possibility that urazole was an attractive precursor base to uracil. Urazole is formed under prebiotic conditions from hydrazine and biuret and reacts with ribose and other sugars more readily than uracil does. Other properties that make urazole an attractive precursor to uracil are its ability to form hydrogen bonds with adenine and its transparency in the ultraviolet region.

Using a dried beach model of prebiotic synthesis to increase concentrations, they demonstrated efficient synthesis of cytosine and uracil from cyanoacetaldehyde and urea. They also showed that uracil.reacts with formaldehyde to form 5-hydromethyluracil, which in turn reacts with a number of nucleophiles to form most of the side chains found in the common amino acids.

Another project demonstrated that the pantheine portion of coenzyme A can be produced under prebiotic conditions from pantoyl lactone, β-alanine, and cysteamine, all of which are compounds with high water solubility. There is some indication that the cysteamine is required for effective amide bond formation to form the dimer of β-alanine at 40C, which is much milder than other systems.

Finally, based on the stability of polynucleotides and other factors, Miller has proposed that the evolution from the prebiotic soup to cyanobacteria may have taken less than 10 million years, far faster than current models would indicate.

Project: Accretion of Organic Material on the Primitive Earth (Dr. Jeffrey Bada)

Dr. Jeffrey Bada derives approximately two-thirds of his extramural funding from the NSCORT. All three of his major projects address the possible sources, stability, and composition of the organic material available for prebiotic chemistry. Using the presence of α-amino isobutyric acids (Aib) and the D/L ratio of amino acids as markers, they have reinvestigated lunar samples and analyzed polar ices, seawater, and interplanetary dust particles to estimate the flux of organic material. SNC meteorites were examined for possible sources of D-amino acids using the same techniques, but neither Aib nor excess D-amino acids were found.

In an exciting study, they found fullerenes (both C_{60} and C_{70}) at impact sites. The 1.85-billion-year-old Sudbury impact structure has 10^{13}-10^{14}g of C_{60} present, which is consistent with efficient production under shock conditions in a nonoxidizing environment. The K/T boundary sediments also contain fullerenes but in much smaller amounts, probably due to the increased oxygen content at the time of impact. Other possible sources of fullerenes, such as meteorites, are currently under investigation. The results thus far, suggest that the production of organics upon impact could have included significant quantities of carbon, balancing the global carbon budget in prebiotic times and eliminating the need for high levels of carbon dioxide.

A third project addresses the stability of biomolecules on the primitive Earth. While pursuing collaborative studies with Dr. Miller on amino acid stability at hydrothermal vents, Dr. Bada has used D/L ratios of amino acids, especially aspartic acid, to estimate the stability of DNA under geochemical conditions. This approach assumes that DNA fragmentation occurs by hydrolytic depurination. As an interesting example, insects entombed in an amber matrix with ages varying from <100 years to 130 million years, show very little racemization of their amino acids, indicating that preservation of DNA is viable in this anhydrous environment. This would have significant implications for any attempt to establish when DNA became a major genetic player if appropriate DNA samples can be found. It also has implications for nonterrestrial studies.

Project: Formation, Concentration and Growth of RNA Precursor Molecules (Dr. Gustaf Arrhenius)

This is a four-part program with good progress being made in all parts.

1. Surface processes in concentration, ordering and oligomerization. Dr. Arrehenius, in collaboration with A. E. Eschenmoser (Zurich), has been able to concentrate phosphate esters on positively charged mineral surfaces, thus producing high yields of aldohexose phosphates, and ultimately the sugar phosphate component of p-RNA, proposed as the precursor of modern RNA. This work is proceeding nicely.

2. Prebiotic geochemistry of phosphate

Phosphate is considered a key molecule in the origin of life. Naturally occurring magnesium calcium phosphate is protonated, and Dr. Arrehenius has found that upon heating, short polyphosphate polymers are formed. Furthermore, phosphate oligomers are concentrated to the order of 10M by sorption onto surface active minerals. Work proceeds on oligopeptides with Dr. Orgel.

3. Biomarkers in the oldest geological record

Dr. Arrhenius is analyzing banded iron formations dating back to around 3.7 billion years. Apatite is found in association with graphite, suggesting the presence of life on Earth as early as 3.87 billion years ago. This technology will be applied to the study of inclusions in SNC meteorites (with Dr. Bada) believed to have been transported from Mars to Earth.

4. Ammonia and nitriles

In collaboration with Professor Siegel, they have studied the formation of cyanohydrin from cyanide and formaldehyde. The cyanohydrin undergoes hydrolysis/condensation to form dimers and trimers. This laboratory effort is proceeding well, supported by an active and talented group of postdoctorals, fellows, and students. The work is important and relevant to the origin of life field and serves to bridge geology and prebiotic chemistry.

Project: Catalysis of Nucleic Acid Replication by Mineral Surfaces (Dr. Leslie Orgel)

This laboratory continues to be a productive center for exobiology, and Dr. Orgel remains an intellectual leader of the NSCORT. His laboratory has concentrated on the fundamental mechanisms of polymerization preceding RNA. They have developed an easy method for synthesizing $[^{32}P]$-labeled oligonucleotides and polymerizing formaldehyde/urea, formaldehyde/phenol, and ethyleneimine in aqueous solutions. Using gel electrophoresis, they have examined the oligopolymerization of aspartic acid, glutamic acid, and o-phosphoserine. Micelles of cetyltrimethylammonium bromide catalyze the polymerization reaction. Based on the finding that oligonucleotides with an amide-linked backbone (PNAs) form stable helical complexes with oligonucleotides, they have used these PNA templates to oligomerize ribo G residues. PNA monomers also can be polymerized on a ribo polymer. Prelimary experiments involving polymerization of DNA on PNA primers and PNA on DNA primers suggest the possibility of the takeover of one genetic system by another.

Dr. Orgel emphasized that his group is committed to investigating basic mechanisms and developing new techniques that will, in the long-term, lead to more relevant polymerization reactions. His long term strategy is highly appropriate in exobiology research.

Project: Evolution of Protein Synthesis in the Context of a Genetic System Based on RNA Genomes and RNA Catalysis (was: "Directed Evolution of RNA and Proteins") (Dr. Gerald Joyce)

The project aims to study the transition from the "RNA" to the "protein-world." Using the directed *in vitro* evolution of RNA molecules, Joyce's group succeeded in evolving RNAs and DNAs with novel catalytic properties. In particular, RNAs that hydrolyze or form peptide bonds were generated. These experiments not only show the power of Darwinian evolution in the test tube, they also provide impressive documentation of the variety of catalytic properties that were possible in an RNA (or DNA) world.

In collaboration with David Deamer's group at UC Davis, Dr. Joyce's group is currently working to encapsulate catalytic RNAs and the amplification machinery in vesicles. If successful, this encapsulation would allow for the directed evolution of more complex systems involving self replication and/or translation. It would also have great potential for the development of new catalytic agents important for biotechnology. This facet of Dr. Joyce's approach is now funded through a grant from the NIH.

Integration of Projects into an Effective NSCORT

The synergism among these five projects is strong, much stronger than one might expect given the five very independent and vigorous PIs. Although some of the PIs had collaborated before the NSCORT was established, numerous new collaborative projects have been initiated, and it is clear that there is substantial interaction among the various groups. While there could be better communication between PIs about future directions for research emphasis, the current arrangement is working quite well. This positive situation is probably due in large part to the equal distribution of funds and fellowships among the five PIs, precluding internal competition at the Center.

Education and Outreach

In the area of education and training, a program of undergraduate, graduate and postdoctoral training is vigorous and productive. The caliber of students and postdoctorals is high, and they are immersed in learning and laboratory work. The summer student population seems somewhat internally derived. It would probably be more productive to broaden the search for participants to include institutions on a more national scale. This would mean more of an effort on the part of NASA management, but the outcome would be more in line with the NSCORT intent. The summer internship program allowed a total of 17 undergraduate students to participate in research projects in the PIs' laboratories. Also, undergraduate courses on Biochemical Evolution, The Early Earth, a Cosmochemistry Seminar Series, and a summer seminar on Molecular Evolution were offered at UCSD and SIO, and included material relevant to exobiology. This very successful undergraduate program could further enhance the visibility of the NSCORT, if recruitment for the undergraduate fellowship could be more widely publicized.

The NSCORT has been very successful in selecting talented graduate students and postdoctoral fellows from an international pool of applicants. The high level of interaction among the PIs, students, and postdoctoral fellows is a result of biweekly journal clubs, bimonthly seminar/dinner discussions, field trips, roundtable discussions, and seminars with outside speakers. Journal clubs and seminars might benefit from having spaces designated as central "homes" for their activities. The institutions of the NSCORT should provide such space, as originally proposed.

Although general lab rotation was not established for incoming graduate students, interaction among the different laboratories was evident, especially in the research of the more advanced graduate students and postdoctorals. Many students and postdoctorals from the laboratories of the PIs' that were not funded directly by the NSCORT participated in the Center's activities, as well. Training and interaction would be strengthened if students and postdoctorals from the laboratories of the Center's associated scientists also would participate. The focus of the Center on prebiotic chemistry certainly contributed to the synergism between the groups; in order to incorporate other aspects of exobiology into training and education, the seminar series included speakers that represent these other areas. Some of the visiting scientists also represented other approaches.

However, the education through an NSCORT in exobiology would certainly benefit from the more direct involvement of scientists working on the more "historical" aspects of the origin of life (e.g., phylogeny, microbiology, evolution of metabolic pathways, archaean fossils). One way to achieve this goal would be through a real involvement of the associated faculty. Also some students and postdoctorals indicated their preference for a broadened program of symposia and seminars. These could include cosmochemistry, planetary evolution, self-assembling systems, etc. Students and post doctorals should understand the basis for NASA's interest in and support of Origin of Life work. It is not clear that they do. Seminars on the subject would help.

The organization of special symposia and conferences at national and international meetings has been quite successful and should continue as planned.

The role of the 11 scientists named as "associates" in the NSCORT is not clear. It would seem, at least in some cases, that their direct involvement would be desirable and beneficial.

Technology transfer from research laboratory to commercial enterprise is occurring, particularly in the area of analytical techniques. Transfer to the pharmaceutical industry is a possibility that will be pursued.

Qualified postdoctorals are having increasing difficulty obtaining appropriate permanent or tenure track appointments; this appears to be a national trend. In recognition of this problem, efforts to aid placement of NSCORT program graduates were a priority in the original NSCORT proposal. However, the actual efforts do not appear to exceed the usual. Placement of graduates from Dr. Joyce's laboratory has been more successful, probably reflecting the "cutting edge" character of this research and its relationship to biotechnology. The U.S. students in particular seemed rather disheartened concerning job opportunities in exobiology-related areas. The NSCORT should more vigorously explore possibilities that might help to improve this situation.

The education outreach effort aimed at secondary schools is excellent but limited. The program for grades 9-12 at La Jolla High School is well-organized and knowledgeably run by Steve Brown, a teacher at that school. He is highly motivated, articulate, and quite knowledgeable through his participation in NSCORT laboratory work. This activity could be furthered by participation of NSCORT graduate students and postdoctorals in seminars and special lectures at the school. It could also be broadened to include other schools and communities. NSCORT staff, however, feel that existing funds are inadequate to significantly broaden the program. This may well be true, but the site team commends the effort to date.

Effectiveness of Quality Control

While the five PIs meet regularly with the associate director, the internal management has been delegated to the latter individual. This arrangement is working quite well and allows the PIs to focus on the science and the evaluation and selection of fellows. There appear to be remarkably few problems from the perspective of both the PIs and the institutional official. In his introductory remarks, Dr. Edward Frieman, director of SIO, stated that this was one of the most efficiently run multi-investigator organizations that he has been associated with.

The major quality and programmatic evaluation is provided by the External Advisory Committee, which is chaired by Benton C. Clark, Martin Marietta Astronautics. Committee members have expertise in a wide variety of areas. The advisory committee spends one intense day each year reviewing the program. Their recommendations have been taken seriously by the NSCORT and their implementation has enhanced the program. This continued active involvement of the advisory committee is strongly encouraged.

Performance/Effectiveness of the NSCORT Director

Dr. Stanley Miller's success in fostering a collaborative atmosphere between the five research groups is evidenced by the obvious synergism in the activities of the Center. The appointment of Robert Tschirgi as associate director proved very fortunate. He and administrative assistant, Lois Lane, effectively oversee the day-to day operation of the Center, including budget coordination, administration of the fellowship program, and the various outreach activities.

One of the few complaints was that the flow of information between the administration and the students and postdoctorals could be improved by a more direct dispersion of information.

Impact of External Knowledge Transfer

The exobiology community is very aware of the activities of this NSCORT. The NSCORT principals are leaders in the field in terms of publication numbers and, especially, quality. Cooperation and collaboration with NASA Centers (in particular, the Ames Research Center and the Lunar Planetary Institute at the Johnson Space Center) is well-established and mutually productive frpm student to postdoctoral to PI. This is commended, and its continuance is encouraged.

Progress has been outstanding at the research level and future research directions seem clear and relevant. Plans in the other areas are not as clear.

Institutional Support for the NSCORT

The three participating institutions (UCSD-SIO, TSRI, and Salk) have met their financial commitments. Their waiver of overhead on fellowships continues to be extremely helpful, allowing the leveraging of funds that can be devoted to the pursuit of the scientific projects. The area of major concern is the NSCORT's relationship with CalSpace. The 1994 annual report of the External Review Committee states the problem very well and points out "the apparent inability of CalSpace/UCSD to meet the facilities support level that was promised in the original NSCORT grant application." They recommend that this facilities issue be resolved "prior to the national evaluation for continuation of the Exobiology NSCORT, which will be made in February - March 1995." According to the association director, CalSpace had not responded to this recommendation at the time of this review. It is strongly encouraged that this matter be positively resolved before application for renewal.

Budget Analysis

The present allocation of funds to the laboratories seems satisfactory.. The present plan of equal distribution to the laboratories is probably the simplest and easiest for planning purposes. The funds have been and are being distributed and used well. NASA has gotten its money's worth. The reduced institutional overhead charge on NSCORT is a real benefit to research as compared with individual grants. This is a major enabler for the NSCORT funding method at NASA. In addition, we see real synergism in this program between closely collaborating laboratories. This seems a good way for NASA to fund excellent research.

Overall Evaluation and Recommendations

This has been an outstanding program that is more than the sum of its parts. The science is excellent and the interaction among the research groups has been productive. The NSCORT has been able to attract excellent students, postdoctoral fellows, and visiting scientists. Communication between the groups appears to be working very well.

There are some areas for improvement. The NSCORT could make better use of its associates and leverage its outreach with other organizations, such as the educational programs of the National Science Foundation.

The theme of the NSCORT for exobiology remains highly relevant to the NASA mission. Fundamental science should remain the predominant theme. As the previous NASA Research Announcement had sufficient thematic breadth to encompass all disciplines in exobiology and to provide each potential Center ample opportunity for creativity, we do not see any reason for change.

The NSCORT should be encouraged to reapply for renewal. Their concentration on the basic science underpinning the disciplines of exobiology is providing the foundation necessary for a long term strategy to understand the mechanisms for the origin of life. As they plan for renewal, consideration should be given to the demographics of the group and the future composition of the research teams. This may be an opportunity to broaden the scope by more active participation of the associates and by introducing more biological science, for example.

APPENDIX II-B
NSCORT-Related Publications, 1992-1996
(NASA NAGW-2881 Final Report)

Jeffrey L. Bada

a. Peer-Reviewed Journals

*Bada, J. L. and G. D. McDonald, 1996. Detecting amino acids on Mars. *Anal. Chem.*, **68**, 668A-67.

*Poinar, H. N., M. Hoss, J. L. Bada and S. Paabo, 1996. Amino acid racemization and the preservation of ancient DNA. *Science* **272**, 864-86.

*Becker, L., R. J. Poreda and J. L. Bada, 1996. Extraterrestrial helium trapped in fullerenes in the Sudbury impact structure. *Science* **272**, 249-253.

*Brinton, K. L. F. and J. L. Bada, 1996. A reexamination of amino acids in lunar soils: implications for the survival of exogenous organic material during impact delivery. *Geochim. Cosmochim. Acta* **60**, 349-354.

Bada, J. L. and G. D. McDonald, 1995. Amino acid racemization on Mars: Implications for the preservation of biomolecules from an extinct Martian biota. *Icarus* **114**, 139-143.

*Bada, J. L., 1995. Origins of homochirality. *Nature* **374**, 594-595.

*Keefe, A.D., S.L. Miller, G.D. McDonald and J.L. Bada, 1995. Investigations of the Prebiotic Synthesis of Amino Acids and RNA Bases from CO_2 Using FeS/H_2S asa Reducing Agent. *Proc. Natl. Acad. Sci. USA* **92**, 11904-11906.

McDonald, G. D. and J. L. Bada, 1995. A search for endogenous amino acids in the Martian meteorite EETA79001. *Geochim. Cosmochim. Acta* **59**, 1179-1184.

Bada, J. L., S. L. Miller and M. Zhao, 1995. The stability of amino acids at submarine hydrothermal vent temperatures. *Origins Life Evol. Biosphere* **25**, 111-118.

*Zhao, M. and J.L. Bada, 1995. Determination of a-Dialkylamino Acids and Their Derivatization with a Chiral Adduct of O-Phthaldealdehyde. *J. Chromat. A* **690**, 55-63.

*Becker, L., J. L. Bada, R. E. Winans, and T. E. Bunch, 1994. Fullerenes in the Allende meteorite. *Nature* **372**, 507.

Bada, J. L., C. Bigham and S. L. Miller, 1994. Impact melting of frozen oceans on the early Earth: Implications for the origin of life. *Proc. Natl. Acad. Sci. USA* **91**, 1248-1250.

Becker, L. J. L. Bada, R. E. Winans, J. E. Hunt, T. E. Bunch and B. M. French, 1994. Fullerenes in the 1.85 billion-year-old Sudbury impact structure. *Science* **265**, 642-645.

Bada, J. L., X. S. Wang, H. N. Poinar, S. Paabo and G. Poinar, 1994. Amino acid racemization in amber-entombed insects: implications for DNA preservation. *Geochim. Cosmochim. Acta* **58**, 3131-3135.

Sagan, C., B.N. Khare, W.R. Thompson, G.D. McDonald, M.R. Wing and J.L. Bada, 1993. Polycyclic Aromatic Hydrocarbons in the Atmospheres of Titan and Jupiter. *Astrophysical Journal* **414**, 399-405.

Becker, L. T. P. Evans and J. L. Bada, 1993. Synthesis of $C_{60}H_2$ by rhodium-catalyzed hydrogenation of C_{60}. *J. Org. Chem.* **58**, 7630-7631.

Becker, L., G. D. McDonald and J. L. Bada, 1993. Carbon onions in meteorites. *Nature*, **361**, 595.

Miller, S. L. and J. L. Bada, 1993. Comment on "Summary and implications of reported amino acid concentrations in the Murchison Meteorite". *Geochim. Cosmochim. Acta* **57**, 3473-3474.

Zenobi, R., J.-M. Philippoz, R.N. Zare, M.R. Wing, J.L. Bada and K. Marti, 1992. Organic Compounds in the Forest Vale, H4 Ordinary Chondrite. *Geochim. Cosmoschim.Acta* **56**, 2899-2905.

Wing, M.R. and J.L. Bada, 1992. The Origin of Polycyclic Aromatic Hydrocarbons in Meteorites. *Origin of the Life and Evolution of the Biosphere* **21**, 375-383.

b. Conference Volumes/Book Chapters

Wang, X.S., H.N. Poinar, G.D. Poinar and J.L. Bada, 1995. Amino Acids in the Amber Matrix and in Entombed Insects. In: "**Amber, Resinite and Fossil Resins**" (Eds. K. Anderson and J.C. Crelling) *ACS Symposium Series* **617**, pp. 255-262.

*Bada, J.L., K.L.F. Brinton, G.D. McDonald and X.S. Wang, 1996. A Search for Extraterrestrial Amino Acids in Polar Ice: A Progress Report. In: "**Circumstellar Habitable Zones**" (Ed. L. Doyle) Travis House Publications, pp. 299-304

Bunch,xxxxxxxx, 1996. In: "**Circumstellar Habitable Zones**" (Ed. L. Doyle) Travis House Publications, pp.

c. General Interest Articles

Bada, J.L., 1995. Cold Start. *The Sciences* **35** (# 3): 21-25.

d. Abstracts of Papers at National/International Meetings

Bada, J. L., Brinton, K. and McDonald, G. "The Exogenous Delivery of Amino Acids to the Modern Earth: an Evaluation from Poal Ices" *ISSOL Meeting*, Orleans. France, 1996, *Origins Life Evol. Biosphere* **26**, 217-218 (1996).

Keefe, A. D., Miller, S. L., McDonald, G. and Bada, J. L. "An Experimental Investigation of the Iron-Sulfur World" *ISSOL Meeting*, Orleans, France, 1996, *Origins Life Evol. Biosphere* **26**, 230-231 (1996).

Bada, J. L., Arrhenius, G. Miller, S. L., Orgel, L and Joyce, G. "The NASA Specialized Center of Research and Training (NSCORT) in Exobiology" *ISSOL Meeting*, Orleans, France, 1996, *Origins Life Evol. Biosphere* **26**, 318-319.

Becker, L. and Bada, J. L. "Proof of Exogenous Delivery of Organics to the Early Earth in the Sudbury Impact Structure" *ISSOL Meeting*, Orleans, France, 1996, *Origins Life Evol. Biosphere* **26**, 331 (1996).

Wang, X. S. and Bada, J. L. "The Geochemical stability of DNA" *ISSOL Meeting*, Orleans, France, 1996, *Origins Life Evol. Biosphere* **26**, 411 (1996).

Bada, J. L. "Amino Acid Homochirality on Earth and Mars" *ISSOL Meeting*, Orleans, France, 1996, *Origins Life Evol. Biosphere* **26**, 518-519 (1996).

Hamilton, H.H. and Bada, J.L. "Amino Acid Preservation in Dinosaur Remains: A Critical Assessment" Amer. Chem. Soc. National Meeting, August, 1995. *Amer. Chem. Soc. Abst. of Papers*, **210 GEOC,** 085 (1995).

Becker, L., Bada, J.L. and Bunch, T.E. "PAHs, Fullerenes and Fulleranes in the Allende Meteorite" *Lunar and Planetary Science Conference* **XXVI, Vol. 1**, 87 (1995).

Becker, L., Bada, J.L. and Bunch, T.E. "Fullerenes in the K/T Boundary: Are They a Result of Global Wildfires?" *Lunar and Planetary Science Conference* **XXVI, Vol. 1**, 85 (1995).

Becker, L. and Bada, J.L. "Fullerenes in the Sudbury Impact Structure: Implications for the Earth's Early Carbon Cycle?" AGU National Meeting, December, 1994. *EOS Trans.* **75**, 410 (1994).

McDonald, G.D. and Bada, J.L. "A Search for Extraterrestrial Amino Acids in a Martian Meteorite" American Astronomical Society Meeting, Washington, D.C., September, 1994. *Bull. Amer. Astron. Soc.* **26**, 1179 (1994).

Wang, S. X., Bada, J.L., Poinar, H.N. and Poniar, G.D. "Amino Acids in the Amber Matrix and in Entombed Insects" Amer. Chem. Soc. National Meeting, August, 1994. *Amer. Chem. Soc. Abst. of Papers*, **208 GEOC**, 015 (1994).

Bada, J.L. and Wang, S.X. "Amino Acid Fenton-Type Reactions on the Primitive Earth" Amer. Chem. Soc. National Meeting, March, 1994. *Amer. Chem. Soc. Abst. of Papers*, **207 GEOC**, 039 (1994).

Becker, L., Evans, T.P. and Bada, J.L. "Synthesis of $C_{60}H_2$ by Rhodium-Catalyzed Hydrogenation of C_{60}" Amer. Chem. Soc. National Meeting, March, 1994. *Amer. Chem. Soc. Abst. of Papers*, **207 ORGN**, 419 (1994).

McDonald, G.D. and Bada, J.L. "A Search for Extraterrestrial Amino Acids in a Martian Meteorite" Amer. Chem. Soc. National Meeting, March, 1994. *Amer. Chem. Soc. Abst. of Papers*, **207 GEOC**, 013 (1994).

Bada, J.L. "Sources and Stability of Organic Compounds on the Early Earth" *American Association for the Advancement of Science Annual Meeting*, San Francisco, CA, February 20-24, 1994.

Bada, J.L., Brinton, K.L.F., McDonald, G.D. and Wang, X.S. "A Search for Extraterrestrial Amino Acids in Polar Ice: A Progress Report" *1st Annual International Conference on Circumstellar Habitable Zones*, NASA Ames, January 19-21, 1994.

Brinton, K and Bada, J.L. "The Use of the Ninhydrin Reaction for the Elimination of Protein Amino Acids in Cosmogeochemical Samples" *ISSOL Meeting*, Barcelona, Spain, 1993, *Origins Life Evol. Biosphere* **24**, 125-126 (1994).

Bada, J.L., Bigham, C. and Miller, S.L. "Impact Melting of a Frozen Ocean on the Early Earth and the Implications for the Origin of Life" *ISSOL Meeting*, Barcelona, Spain, 1993, *Origins Life Evol. Biosphere* **24**, 273-274 (1994).

Bada, J.L. "Amino Acid Stereochemistry in Cosmogeochemical Samples and the Origin of Amino Acid Chirality on Earth" *ISSOL Meeting*, Barcelona, Spain, 1993, *Origins Life Evol. Biosphere* **24**, 286-287 (1994).

Bada, J.L., Miller, S.L. and Zhao, M. "Amino Acid Stability in Hydrothermal Vents" *ISSOL Meeting*, Barcelona, Spain, 1993, *Origins Life Evol. Biosphere* **24**, 364-365.

McDonald, G.D. and Bada, J.L. "Inhibition of Amino Acid Metabolic Enzymes by a-Aminoisobutyric Acid" *ISSOL Meeting*, Barcelona, Spain, 1993, *Origins Life Evol. Biosphere* **24**, 301-302 (1994).

Brinton, K.L.F., Bada, J.L. and Arnold, J.R. "A Reexamination of Amino Acids in Lunar Soil" *Lunar and Planetary Science Conference* **XXIV**, 193-194 (1993)

Miller, S.L. and J.L. Bada. "The Strecker Cyanohydrin Reaction and the Synthesis of Amino and Hydroxy Acids in the Murchison Meteorite". *29th Meeting of the Committee on Space Research, The World Space Congress,* Washington, D.C., August 28, Sept. 5, 1992.

Bada, J.L. and M.-X. Zhao. "Extraterrestrial Sources of Organic Compounds on the Early Earth and Their Significance" *29th Meeting of the Committee on Space Research, The World Space Congress*, Washington, D.C., August 28-Sept. 5, 1992.

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NSCORT-Related Publications, 1992-1996 (NASA NAGW-2881 Final Report)

Gustaf Arrhenius

a. Peer-Reviewed Journals

Arrhenius, T., Arrhenius, G. and Paplawsky, W.J. (1994) "Archean geochemistry of formaldehyde and cyanide and the oligomerization of cyanohydrin." *Orig. of Life* **24**, 1-19.

Kuma, D., Usui, A., Paplawsky, W., Gedulin, B. and Arrhenius, G. (1994) "Crystal structures of synthetic 7Å and 10Å manganates substituted by mono- and divalent cations." *Mineralog. Mag.* **58**, 423-445.

Mojzsis, S., Nutman, A.P. and Arrhenius, G. (1994) "Evidence for a marine sedimentary system at >3.87 Ga in southern West Greenland." EOS, Transactions of the *Amer. Geophysical Union* **75**, 690.

Braterman, P.S., Arrhenius, G., Hui, S. and Paplawsky, W. (1995) "Preferential uptake of ammonium ions by zinc ferrocyanide." *Orig. Life Evol. Biosphere* **25**, 531-538.

Pitsch, S., Eschenmoser, A., Gedulin, B., Hui, S. and Arrhenius, G. (1995) "Mineral induced selective formation of sugar phosphates." *Orig. Life Evol. Biosphere* **25**, 294-332.

* Dickens, J., Irvine, W.J. Ohishi, M. Arrhenius, G., Pitsch, S., Bauder, A., Muller, F. and Eschenmoser, A. (1996) "A search for interstellar oxiranecarbonitrile (C_3H_3NO)." *Orig. Life Evol. Biosphere* **26**, 97-110.

* Mojzsis, S.J., Arrhenius, G., McKeegan, K.D., Harrison, T.M., Nutman, A.P., and Friend, C.R.L. (1996) "Evidence for life on Earth before 3,800 million years ago." *Nature* **384**, 55-59.

* Arrhenius, G. and Mojzsis, S. (1996) "Extraterrestrial life: Life on Mars - then and now." *Current Biology* **6**, 1213-1216.

b. Book Chapters/Conference Proceedings

Arrhenius, G., Gedulin, B. and Mojzsis, S. (1993) "Phosphate in models for chemical evolution." *Chemical Evolution and Origins of Life*, C. Ponnamperuma and J. Chela-Flores, eds. (A. Deepak Publ., Hampton, VA), pp. 25-50.

Fan, G., Mojzsis, S. and Arrhenius, G. (1993) "Confocal study of microaggregates in 2.5 billion year old sediments." *Proc. 51st Annual Meeting of the Microscopy Society of America*, ed. G.B. and C. Rieder, San Francisco Press.

Gedulin, B. and Arrhenius, G. (1994) "Sources and geochemical evolution of RNA precursor molecules; the role of phosphate." *Early Life on Earth, Nobel Symposium 84*, ed. S. Bengtson, Columbia Univ. Press, 91-110.

Arrhenius, G., (1995) "Molecular evolution toward life." *Symposium, Life, Earth, and the Universe*, Faculty of Science and Technology, Univ. of Uppsala.

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NSCORT-Related Publications, 1992-1996 (NASA NAGW-2881 Final Report)

Gerald F. Joyce

a. Peer-Reviewed Journals

Lehman, N. and Joyce, G. F. (1993): Evolution *in vitro* of an RNA enzyme with altered metal dependence. *Nature* **361**, 182-185.

Joyce, G. F. (1993): Evolution of catalytic function. *Pure & Appl. Chem.* **65**, 1205-1212.

Lehman, N. and Joyce, G. F. (1993): *In vitro* evolution: analysis of a lineage of ribozymes. *Current Biol.* **3**, 723-734.

Tsang, J. and Joyce, G. F. (1994): Evolutionary optimization of the catalytic properties of a DNA-cleaving ribozyme. *Biochemistry* **33**, 5966-5973.

Breaker, R. R. and Joyce, G. F. (1994): Emergence of a replicating species from an *in vitro* RNA evolution reaction. *Proc. Natl. Acad. Sci. USA* **91**, 6093-6097.

Joyce, G. F. (1994): *In vitro* evolution of nucleic acids. *Curr. Opin. Struct. Biol.* **4**, 331-336.

Breaker, R. R., Banerji, A. and Joyce, G. F. (1994): Continuous *in vitro* evolution of bacteriophage RNA polymerase promoter elements. *Biochemistry* **33**, 11980-11986.

Cadwell, R. C. and Joyce, G. F. (1994): Mutagenic PCR. *PCR Methods Appl.* **3**, S136-140.

Breaker, R. R. and Joyce, G. F. (1994): Inventing and improving ribozyme function: rational design versus iterative selection methods. *Trends Biotechnol.* **12**, 268-275.

Chakrabarti, A. C., Breaker, R. R., Joyce, G. F. and Deamer, D. W. (1994): Production of RNA by a polymerase protein encapsulated within phospholipid vesicles. *J. Mol. Evol.* **39**, 555-559.

Breaker, R. R. and Joyce, G. F. (1994): A DNA enzyme that cleaves RNA. *Chem. & Biol.* **1**, 223-229.

Dai, X., De Mesmaeker, A. and Joyce, G. F. (1995): Cleavage of an amide bond by a ribozyme. *Science* **267**, 237-240; see also *Science* **272**, 18-19, 1996.

*Breaker, R. R. and Joyce, G. F. (1995): Self-incorporation of coenzymes by ribozymes. *J. Mol. Evol.* **40**, 551-558.

*Breaker, R. R. and Joyce, G. F. (1995): A DNA enzyme with Mg^{2+}-dependent RNA phosphoesterase activity. *Chem. & Biol.* **2**, 655-660.

*Bruick, R. K., Dawson, P. E., Kent, S. B. H., Usman, N. and Joyce, G. F. (1996): Template-directed ligation of peptides to oligonucleotides. *Chem. & Biol.* **3**, 49-56.

*Tsang, J. and Joyce, G. F. (1996) Specialization of the DNA-cleaving activity of a group I ribozyme through *in vitro* evolution. *J. Mol. Biol.* **262**, 31-42.

b. Book Chapters

Joyce, G. F. and Orgel, L. E. (1993) Prospects for understanding the origin of the RNA world: in *The RNA World* (Gesteland, R. F. and Atkins, J. F., eds.) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pp. 1-25.

Joyce, G. F. (1994) Foreward: in *Origins of Life: The Central Concepts* (Deamer, D. W. and Fleischacker, G. R., eds.) Jones and Bartlett Publishers, Boston, pp. xi-xii.

Breaker, R. R. and Joyce, G. F. (1994) Minimonsters: evolutionary byproducts of *in vitro* RNA amplification: in *Proceedings of the NATO Conference on Self-Reproduction of Supramolecular Structures*, Maratea, Italy, September 12-16, 1993 (Fleischaker, G. R., Colonna, S. and Luisi, P. L., eds.) Kluwer Academic Press, Dordrecht, The Netherlands, pp. 127-135.

*Joyce, G. F. (1995) The RNA world: life before DNA and protein: in *Extraterrestrials, Where are They?* (Zuckerman, B. and Hart, M. H., eds.) Cambridge University Press, Cambridge, pp. 139-151.

*Tsang, J. and Joyce, G. F. (1996) *In vitro* evolution of randomized ribozymes: in *Methods in Enzymology*, Vol. 267 (Abelson, J., ed.) Academic Press, Orlando, pp. 410-426.

c. General Interest

Joyce, G. F. (1992): Directed molecular evolution. *Sci. Am.* **267(6)**, 90-97.

Joyce, G. F. (1993): Climbing Darwin's ladder. *Current Biol.* **3**, 703-704.

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NSCORT-Related Publications, 1992-1996 (NASA NAGW-2881 Final Report)

Stanley L. Miller

a. Peer-Reviewed Journals

Miller, S. L. and Schlesinger, G. (1993) "Prebiotic Syntheses of Vitamin Coenzymes: I. Cysteamine and 2-Mercaptoethanesulfonic Acid (Coenzyme M)" *J. Mol. Evol.* **36**, 302-307.

Miller, S. L. and Schlesinger, G. (1993) "Prebiotic Syntheses of Vitamin Coenzymes: II. Pantoic Acid, Pantothenic Acid, and the Composition of Coenzyme A" *J. Mol. Evol.* **36**, 308-314.

Miller, S. L. and Bada, J. L. (1993) Comment on "Summary and implications of reported amino acid concentrations in the Murchison meteorite" by Shock, E.L. and Shulte, M.D., *Geochim. Cosmochim. Acta* **57**, 3473-3474.

Bada, J. L., Bigham, C., and Miller, S. L. (1994) "Impact Melting of Frozen Oceans on the Early Earth: Implications for the Origin of Life" *Proc. Natl. Acad. Sci. U.S.A.* **91**, 1248-1250.

Kolb, V. M., Dworkin, J. P., and Miller, S. L. (1994) "Alternative Bases in the RNA World: The Prebiotic Synthesis of Urazole and Its Ribosides" *J. Mol. Evol.* **38**, 549-557.

Lazcano, A. and Miller, S. L. (1994) "How Long Did It Take For Life to Begin and Evolve to Cyanobacteria?" *J. Mol. Evol.* **39**, 546-554.

Keefe, A. D., Lazcano, A., and Miller, S. L. (1995) "Evolution of the Biosynthesis of the Branched-Chain Amino Acids" *Origins of Life Evol. Biospherė* **25**, 99-110.

Bada, J. L., Miller, S. L., and Zhao, M. (1995) "The Stability of Amino Acids at Submarine Hydrothermal Vent Temperatures" *Origin of Life Evol. Biosphere* **25**, 111-118.

Keefe, A. D., Newton , G. L., and Miller, S. L. (1995) "A Possible Prebiotic Synthesis of Pantetheine, a Precursor to Coenzyme A" *Nature* **373**, 683-685.

Robertson , M. P. and Miller, S. L. (1995) "Prebiotic Synthesis of 5-Substituted Uracils: A Bridge Between the RNA World and the DNA-Protein World" *Science* **268**, 702-705.

Robertson , M. P. and Miller, S. L. (1995) "An Efficient Prebiotic Synthesis of Cytosine and Uracil" *Nature* **375**, 772-774.

*Larralde, R., Robertson, M. P. and Miller, S. L. (1995) "Rates of Decomposition of Ribose and Other Sugars: Implications for Chemical Evolution" *Proc. Nat. Acad. Sci. U.S.A.* **92**, 8158-8160.

*Keefe, A. D., Miller, S. L., McDonald, G., and Bada, J. (1995) "Investigation of the Prebiotic Synthesis of Amino Acids and RNA Bases from CO2 Using FeS/H2S as a reducing agent" *Proc. Nat. Acad. Sci. U.S.A.* **92**, 11904-11906.

*Miller, S. L. and Lazcano, A. (1995) "The Origin of Life - Did It Occur at High Temperatures?" *J. Mol. Evol.* **41**, 689-692.

*Keefe, A. D. and Miller, S. L. (1995) "Are Polyphosphates or Phosphate Esters Prebiotic Reagents? *J. Mol. Evol.* **41**, 693-702.

*Keefe, A. D. and Miller, S. L. (1996) "Potentially Prebiotic Syntheses of Condensed Phosphates" *Orig. Life Evol. Biosphere* **26**, 15-25.

*Lazcano, A. and Miller, S. L. (1996) "The Origin and Early Evolution of Life: Prebiotic Chemistry, the Pre-RNA World, and Time." Cell **85**, 793-798.

*House, C. H. and Miller, S. L. (1996) "The Hydrolysis of Dihydrouridine and Related Compounds" *Biochemistry* **35**, 315-320.

*Keefe, A. D. and Miller, S. L. (1996) "Was Ferrocyanide a Prebiotic Reagent?" *Orig. Life Evol. Biosphere* **26**, 111-129.

*Robertson , M. P. and Miller, S. L. (1996) "Prebiotic Synthesis of Diaminopyrimidine" *J. Mol. Evol.* **43**, 543-550.

b. Chapters in Books and Conference Volumes

Miller, S. L. (1993) "The Prebiotic Synthesis of Organic Compounds on the Early Earth": In *Organic Geochemistry: Principles and Applications*, (M.H. Engel and S.A. Macko, eds.). Plenum Press, New York, pp. 625-637.

Miller, S. L. (1995) "Prebiotic Synthesis of Organic Compounds. A Short Review and New Results" *Microbiologia SEM* **11**, 161-172.

Miller, S. L (1995) "La Seintesis Prebiotica De Compuestos Organicos Como Paso Hacia El Origen De La Vida": in *Origenes De La Vida En El Centenario De Aleksandr Ivanovich Oparin*, (F. Moran, J. Pereto & Moreno, eds.) Editorial Complutense, Madrid, pp. 43-81.

*Miller, S. L. and Lazcano, A. (1996) "From the Primitive Soup to Cyanobacteria: It May Have Taken Less Than 10 Million Years" *Proc. Intl. Conf. on Circumstellar Habitable Zones*, (Doyle, L. R, ed.) Travis House Publications, Madrid, CA, pp. 393-404.

c. General Interest Articles

Miller, S. L. (1992) "Whence Came Life?" *Sky & Telescope* **83**, 604.

d. Abstracts of Papers at National/International Meetings

*Miller, S.L. "From the Primitive Atmosphere to the Prebiotic Soup to the Pre-RNA World." Symposium in RNA Today, Princeton, NY May 9-10, 1996.

*Miller, S.L. (1996) "Endogenous Synthesis of Prebiotic Organic Molecules." *Orig. Life Evol. Biosphere* **26**, 201-201.

*Marquez, C., Lazcano, A., Miller, S.L., Oro, J. (1996) "Fuller Deuterated Aliphatic Hydrocarbons Obtained from Iron Carbide Treated with DCl and D_20." *Orig. Life Evol. Biosphere* **26**, 450-451.

*Larralde, R., Robertson, M.P. and Miller, S.L. (1996) "Kinetics of the Decomposition of Ribose and Other Sugars: Implications for Chemical Evolution." *Orig. Life Evol. Biosphere* **26**, 355-356.

*Levy, M. and Miller, S.L. (1996) "The Prebiotic Synthesis of N^6-Methyladenine, 1-Methyladenine and 1-Methylhypoxanthine." *Orig. Life Evol. Biosphere* **26**, 249-350.

*Dworkin, J.P. and Miller, S.L. (1996) "The Relative Reactivity of Deoxyribose and Ribose: Did DNA Come Before RNA? *Orig. Life Evol. Biosphere* **26**, 412-413.

*House, C.H. and Miller, S.L. (1996) "The Hydrolysis of Dihydrouridine and Related Compounds." *Orig. Life Evol. Biosphere* **26**, 357-358.

*Nelson, K.E. and Miller, S.L. (1996) "The Prebiotic Synthesis of Ethylenediamine Monoacetic

Acid, the Repeating Unit of Peptide Nucleic Acids." *Orig. Life Evol. Biosphere* **26**, 345-346.

*Keefe, A.D., Miller, S.L. McDonald, G. and Bada, J. (1996) "An Experimental Investigation of the Iron-Sulfur World." *Orig. Life Evol. Biosphere* **26**, 230-232.

*Bada, J.L., Arrhenius, G., Miller, S.L., Orgel, L. and Joyce, G. (1996) "The NASA Specialized Center of Research and Training (NSCORT) in Exobiology." *Orig. Life Evol. Biosphere* **26**, 318-319.

---

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NSCORT-Related Publications, 1992-1996 (NASA NAGW-2881 Final Report)

Leslie E. Orgel

a. Peer-Reviewed Journals

Harada, K. and Orgel, L.E. (1993) "Unexpected substrate specificity of T4 DNA ligase revealed by in vitro selection" *Nucleic Acids Res.* **21**, 2287-2291.

Rembold, H. and Orgel, L.E. (1994) "Single-strand regions of poly(G) act as templates for oligo(C) synthesis" *J. Mol. Evol.* **38**, 205-210.

Rembold, H. and Orgel, L.E. (1994) "Polycytidylate and poly(7-deazaguanylate): a pair of complementary templates" *J. Mol. Evol.* **38**, 211-214.

Kolb, V. and Orgel, L.E. (1994) "Oligonucleotides as probes for studying polymerization reactions in dilute aqueous solution", *J. Mol. Evol.* **38**, 433-437.

Harada, K. and Orgel, L.E. (1994) "In vitro selection of optimal DNA substrates for ligation by a water-soluble carbodiimide", *J. Mol. Evol.* **38**, 558-560.

Zieboll, G. and Orgel, L.E. (1994) "The use of gel electrophoresis to study the reactions of activated amino acids with oligonucleotides", *J. Mol. Evol.* **38**, 561-565.

Orgel, L.E. (1995) "Unnatural selection in chemical systems" *Acc. Chem. Res.* **28**, 109-118.

Kolb, V. and Orgel, L.E. (1995) "Oligonucleotides as probes for studying polymerization reactions in dilute aqueous solution. II. Polycondensations", *J. Mol. Evol.* **40**, 115-119.

Silveira, M.H. and Orgel, L.E. (1995) "PCR with detachable primers", *Nucleic Acids Res.* **23**, 1083-1084.

Bohler, C., Nielsen, P.E. and Orgel, L.E. (1995) "Template switching between PNA and RNA oligonucleotides", *Nature* **376**, 578-581.

*Liu, R. and Orgel, L.E. (1995) "Enzymatic synthesis of polymers containing nicotinamide mononucleotide", *Nucleic Acids Res.* **23(18)**, 3742-3749.

*Schmidt, J., Nielsen, P.E. and Orgel, L.E. (1996) "Separation of "uncharged" oligodeoxynucleotide analogs by anion-exchange chromatography at high pH" *Anal. Biochem.* **235**, 239-241.

*Bohler, C., Hill, Jr., A.R. and Orgel, L.E. (1996) "Catalysis of the oligomerization of O-phospho-serine, aspartic acid, or glutamic acid by cationic micelles", *Orig. Life Evol. Biosph.* **26**, 1-5.

*Kolb, V. and Orgel, L.E. (1996) "Phosphorylation of glyceric acid in aqueous solution using trimetaphosphate", *Orig. Life Evol. Biosph.* **26**, 7-13.

*Ferris, J. P., Hill, Jr., A. R., Liu, R. and Orgel, L. E. (1996) "Synthesis of long prebiotic oligomers on mineral surfaces" *Nature* **381**, 59-61.

*Hill, Jr., A.R. and Orgel L.E. (1996) "Oligomerization of negatively-charged amino acids by carbonyldiimidazole" *Orig. Life Evol. Biosph.* **26**, 539-545.

b. Chapters in Books

Joyce, G.F. and Orgel, L.E. (1993) "Prospects for Understanding the Origin of the RNA World": in *RNA World* (Ray F. Gesteland and John F. Atkins, eds.).Cold Spring Harbor, New York, Cold Spring Harbor Laboratory Press, Chapter 1, pp. 1-25.

c. General Interest Articles

Orgel, L.E. (1994) "The origin of life on the earth", *Scientific American* **271**, 52-61.

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Report of the External Review Committee for the NSCORT for Exobiology
November, 1995

An intensive day of review was conducted on Nov. 3, 1995 for the NASA Specialized Center of Research and Training (NSCORT) in Exobiology. The meeting was held in at the Martin Johnson House of the Scripps Institution of Oceanography. The meeting was hosted by Dr. Jeffrey Bada, the new director of the NSCORT. At this meeting, the format recommended from the preceding year's review was adopted. This consisted of short presentations by each of the Principal Investigators summarizing their overall work, followed by suitably brief, yet detailed presentations by those students and fellows who have received significant funding from the NSCORT. The complete agenda is documented elsewhere and will not be repeated here.

The members of the External Review Committee in attendance were DesMarais, Rich, Schwartz, Schopf, DeVincenzi, Rummel, Clark and Meyer. The General Finding of the committee was that the NSCORT continues to be highly productive, and that several recommendations from the previous review have been implemented and shown to be effective. The following additional findings and recommendations should be considered.

General Finding: The NSCORT continues to be highly productive. Activities and research appear to be highly interactive and to provide value far beyond what would be obtained with individual grant support.

1. Research

Finding: Scientific research is now, if anything, even more synergistic and promising than the previous high level. Significant progress is being made along many different fronts. Broad questions are being investigated as well as detailed problems of specific biochemical nature. Several competing theories of prebiotic chemistry are being examined by laboratory investigation, where feasible, with reportable, publishable results.

Recommendation: Continue on this general path, with sensitivity to maintaining a breadth that will engage the interests of a significant fraction of the total exobiological community.

2. Education and Training (General)

Finding: Summer student program opportunities could be more extensively documented.

Recommendation: The organization should quantitatively document the efforts that went into publicizing opportunities and selecting participants for summer positions with the NSCORT.

November 22, 1995

Finding: The work of Steve Brown within the La Jolla High School program appears to be excellent in many different respects.

Recommendation: The NSCORT should assist Mr. Brown in obtaining additional support of this effort through State or National resources which are ear-marked for education. In addition, there may be opportunities for NSCORT-funded students and fellows to contribute their time to these efforts.

3. Public Outreach

Finding: Public outreach is mainly implemented from within the NSCORT organization.

Recommendation: The NSCORT should leverage this effort by enlisting the help of existing organizations which specialize in reaching the public and students. For example, the Reuben H. Fleet Science Museum has on-going programs which could be influenced to include exobiology aspects of the NASA space and exobiology programs to educate the public and inspire students.

Finding: The student fellows were again polled for their involvement in giving talks to lower-level students and/or the general public. Only three had done so. When asked how many would be willing to do so if asked, nearly a unanimous raising of hands occurred.

Recommendation: Provide a mechanism for opportunities by these energetic workers to spread the word, as well as to serve as training and experience for developing their presentation, organizational, and communications skills. Steve Brown agreed during this meeting to facilitate this opportunity for a large number of the fellows. However, the Director of the NSCORT should monitor this activity to ensure that it is being successfully pursued. The Advisory Committee feels that this activity could be an important component of the successful completion of the work by students and fellows. In addition, each should understand and become proficient in explaining the relevance and potential benefits of this research to the general public, as well as the reasons behind the interest of NASA in supporting such work.

4. Professional outreach
Finding: It is our understanding that the NSCORT has decided to reduce the number of "associates" to five, but to increase their role and participation.

Recommendation: We endorse this move to make this position more significant, and hopefully in the long run more effective. The selections of Russell Doolittle, Marina Fomenkova, and J. William Schopf considerably broadens and strengthens the program.

It is suggested that some designation other than 'associates' may be more appropriate, but the key ingredient is to facilitate some level of participation by outside investigators in the NSCORT. Although only a small amount of resources can be targeted to this, a variety of creative uses of these persons could be mutually beneficial to the NSCORT objectives as well as the careers or programs of these individuals. If resources were sufficient, the NSCORT may wish to consider providing subsistence for visiting associates (e.g., housing by NSCORT, salary by sabbatical leave from a home institution) in return for contributing to the educational coursework in exobiology.

5. Outreach -- Technology Transfer
Finding: A specific request in last year's report, that the NSCORT consider and advise on the applicability of research to transfer of technology for the benefit of the public, was not responded to in a detailed manner. Applications relevant to pharmaceutical interests were referenced, but not explained or described in detail.

Recommendation: Although this is not a primary goal of the original NSCORT, it is nonetheless an interest of NASA and the U.S. Government. A modest effort should be placed into simply documenting any current results as well as potential future results on the transfer of information, techniques, data, and/or discoveries made under this work to the use by the private sector to develop marketable items or to the general knowledge which can serve for the betterment of human well-being. Investigators are very well placed to make these connections and to emphasize the potential importance of Origins of Life research to these goals.

6. Student Fellows
Finding: In the private session with students and fellows, there was agreement that the previous situation of some lack in breadth of topics in symposia has been accommodated.

Recommendation: The Journal Club, the student-independent research activities, and the student-led symposia should all be supported in suitable ways (e.g., time allocations for these activities, funds for dinners, and willingness for the P.I.'s to maintain a hands-off posture, as appropriate).

7. CalSpace Involvement
Finding: The Advisory Committee is gratified to see that the situation identified in the previous report concerning the level of support of NSCORT by CalSpace has improved significantly.

Recommendation: It is very important that the CalSpace commitment given in the original proposal be continued, and that additional mutual benefits be exploited wherever possible, including, but not limited to, assistance by CalSpace in achieving the maximum leverage on Outreach through the publicizing of successes in Exobiological research, the availability of the World Wide Web Home Page, and the community outreach projects in the state of California.

8. Synergy
Finding: A number of activities appear to be stronger than solely the sum of their parts.

Recommendation: It is recommended that the NSCORT office make a comparison of that level of activities that would occur if only individual research support had been obtained, with that which is occurring now. This would include not only staff research activities, but the numbers and intensity of student involvement, the student special programs, and the outreach to other professionals, educational institutions and the public at large. Wherever possible, quantitative comparisons should be made (with-NSCORT versus without-NSCORT).

Third Annual
Summer Student Symposium

NSCORT Exobiology Journals Club

August 10, 1995

Martin Johnson House
Scripps Institution of Oceanography
La Jolla, California

**NASA Specialized Center of Research and Training (NSCORT)
Exobiology**

Gustaf Arrhenius—Scripps Institution of Oceanography
Jeffrey Bada—Scripps Institution of Oceanography
Gerald Joyce—The Scripps Research Institute
Stanley Miller—University of California, San Diego
Leslie Orgel—Salk Institute for Biological Studies

Program of Papers Presented at the Third Annual Summer Student Symposium

NSCORT Exobiology Journals Club

August 10, 1995

Martin Johnson House
Scripps Institution of Oceanography
La Jolla, California

Chairs: Jason Dworkin and Anthony Keefe

Time	Author and Title		Page
2:00	**Vera Kolb**[1] Double Layer Hydroxide Minerals as a medium of Phosphorylating Agents and Organic Substrates	Arrhenius (SIO)	3
2:20	**Matthew Levy** The Prebiotic Synthesis of 1-Methyladenine and 6-Methyladenine	Miller (UCSD)	4
2:40	**Healy Hamilton** Amino Acid Preservation in Dinosaur Remains: a Critical Assessment	Bada (SIO)	5
3:00	BARBECUE		
4:00	**Kevin Nelson** The Prebiotic Synthesis and Ring-Opening Polymerization of Ethylenediamine Monoacetic Acid	Miller (UCSD)	6
4:20	**Aaron Eppler** Biomolecule and Amino Acid Detection Using Matrix-Assisted Laser Desorption Mass Spectrometry	Bada (SIO)	7
4:40	**Shibin Zhang** Catalytic Mechanism of the Oligonucleotide Formation from the 5′-Phosphrimidazolide of Adenosine in Na^{+}-Montmorillonite	Arrhenius (SIO)	8

Time	Author and Title		Page
5:00	**Uday Kishore**[2] Polymerization of Activated Adenosine Monomers on a PNA Template	Orgel (Salk)	9
5:20	**Chloe Zubieta**[3] Adsorption and Reaction of 3′-5′-cAMP and 2′-3′-cAMP in $Mn_2Al(OH)_6{\cdot}Cl$	Arrhenius (SIO)	11
5:40	**Guru Khalsa** Early Biochemical Pathways: Branched-Chain Amino Acids	Miller (UCSD)	12
6:00	ADJOURN		
Appendix	**Joel Dacks** Modified Uracil in RNA and the Prebiotic Synthesis of Lipids	Miller (UCSD)	13
	NSCORT Exobiology Summer Fellows 1992-1995		15

[1] Visisting Scientist
[2] Planetary Biology Intern
[3] SURF summer student

Summary of Training, Education, and Outreach Activities of the NSCORT in Exobiology

Training (Definition: Training includes learning opportunities and information dissemination designed primarily for your NSCORT members.)

***Total number of students participating in NSCORT since its establishment.**

Post-Docs 15 Graduates 11 Undergraduates 30

***Number of students participating in NSCORT during 1995-1996 academic year.**

Post-Docs 9 Graduates 6 Undergraduates 7

***Does NSCORT have a Journal Club?**

Yes x No ____

If yes, who participates?

**Faculty x Post-Docs x Graduates x Undergraduates x

***Does NSCORT sponsor a Seminar Series?**

Yes x No ____

If yes,

The Seminar Series is scheduled:

Weekly ____ Monthly x Other ____ (explain)

The Seminar Series is open and announced to:

NSCORT staff x Campus community x General Public ____

The Seminar Series is held:

On campus x Off campus x (explain) The NSCORT/exobiology program is conducted at three separate and independent institutions, UCSD, SALK and TSRI (The Scripps Research Institute) in proximity at La Jolla, Ca. Seminars are held at all three sites.

***Does NSCORT host an annual symposia?**

Yes ____ No x

If yes, what is its purpose?

NSCORT Internal Information/Goal-Setting Exchange ____

Summary research presentation for NSCORT and invited guests ____

Training Workshop for NSCORT and interested professional community ____

Other (explain) ____

***Does NSCORT sponsor a summer internship program for students?**

Yes x No ____

**By invitation only.

If yes, identify student status and briefly describe program.

Post-Doc ____

Program description:

Graduate ____

Program description:

Undergraduate _x_

Program description: Tutorial research in PI laboratories; Journals Club; Summer Symposium (presentation of papers on research)

High School

Program description:

*** Has NSCORT developed and staffed an academic course based upon NSCORT research?**

Yes _x_ No ____

If yes, please include a copy of the course description and outline with this completed form and provide the following information: (see page 8 for course description)

Number of times the course has been offered _4_

Total number of students who have completed the course _93_

Course is open to:

NSCORT trainees _x_ Post-Docs ____ Graduates _x_

Undergraduates _x_ Other ____ (explain)

***Does NSCORT sponsor or staff a training program other than those referred to on this form?**

Yes ____ No _x_

If yes, please include a title and description of each program on a separate paper and return with this completed form.

Education (Definition: Education includes education information or activities designed for grades K-14

that benefit students other than your NSCORT trainees, and participation by NSCORT members in professional association conferences, etc.)

***State the number of NSCORT-related presentations and/or demonstrations in which NSCORT members have participated since it was established.**

Education K-12 20 Education 13+ 8 Professional Associations 44

***State the number given since January 1995.**

Education

K-4 1 5-8 4 9-12 3 13+ 10

Professional associations

Local meetings ____ State/Regional Conferences 4

National Conferences 9 International Conferences 8

Please name the National and International Conferences in which NSCORT has participated. Winter Seminar, Klosters; American Chemical Society; Gordon Research Conference on the Origin of Life; Symposium on the Origin of Homochirality in Life; Royal Swedish Academy of Sciences; University of Uppsala; American Society for Biochemistry & Molecular Biology; Gordon Research Conference on Nucleic Acids; Gordon Research Conference on Solid State Physics and Ceramics; International Union of Geodesy and Geophysics; International Union of Geophysics; The Keystone Center, "Scientist to Scientist Colloquium"; The Year of Louis Pasteur International Symposium, Rockefeller University; Keyston Symposium on Molecular & Cellular Biology; Table Ronde Roussel Uclaf, Paris; ISSOL, Orleans

*** State the number of NSCORT-related articles that have been published in educational and/or professional journals.**

Total number to this date 167 Total number since January 1995 54

***Has NSCORT developed or assisted in development of a teaching module or curriculum materials suitable for grades K-12?**

Yes x No ____

If yes, provide the following information

Title of module/curriculum: Exobiology for High School Students

Targeted grade level: 9-12 Targeted subject or discipline: Exobiology

Amount of class time to complete the module/curriculum 15 hours

Is the module/curriculum available for replication? No

Provide a name and phone number for a contact person who will answer further inquiries about the module/curriculum. Steve Brown, La Jolla High School, 450 Nautilus Street, La Jolla, CA 92037. Phone (619) 454-3081 ext. 230; Email address: stephenebr@aol.com

____

*If NSCORT has association with or has developed any education activity or program other than those referred to in this form, please name the activity or program and provide a brief description. Provide this information on a separate paper and return with this completed form.
(see attached page 6)

Outreach (Definition: Outreach includes activities that extend NSCORT information to business and general public audiences.)

* List the number of NSCORT-related presentations and/or demonstrations given to business and/or general public audiences since your NSCORT was established. 3

*List the number given since January 1995.

Business ____ General public 3

*List the number of NSCORT-related media-outreach opportunities in which NSCORT members have participated since your NSCORT was established.

Radio 0 Television 13 Newspaper 32

General audience magazine 26

*List the number of NSCORT-related media-outreach opportunities since January 1995.

Radio 0 Television 5 Newspaper 11

General audience magazine 11

*Does NSCORT have a Homepage?

Yes x No ____

If yes, please give address: http://www-chem.ucsd.edu/~nscort/NSCORT.html

If yes, please give a brief description of the purpose of this page. Include comments on how/if information will be up-dated on a regular basis, intended audience, who is responsible for editing or posting the information, etc. Is the posted information downloaded frequently, do you have an average of hits per month? Provide this information on a separate paper and return with this completed form.

*Do NSCORT members respond via internet and e-mail to general public inquiries?

Yes x No ____

***Which of the following NSCORT materials are available? (Please send copies with this completed form.)**

Brochure _x__ Flyer ____ Booklet _x_ Newsletter _x_

Annual Report _x_ Slide Presentation ____ Video ____

Other ____ (explain)

***If NSCORT has participated in any type of Outreach other than what is referred to in this form, please identify the Outreach and provide a brief description.**

(see attached page 7)

Name of person(s) completing this form: Dr. Robert Tschirgi

Date: 5-14-96

Thank you for sending the completed form and accompanying materials to me at the following address by June 15, 1996.

Bonnie J. McClain
NASA Life Sciences Education Programs Coordinator
c/o USRA
300 D Street, SW Suite 801
Washington, D.C. 20024

Continued from page 4

Other NSCORT/exobiology Educational Activities and Programs

1. *Evening Discussion/Seminars*: Approximately 6 evening meetings/year with invited guest speakers, followed by round table discussion. Topics range from "The Scientific World View" to "Photochemistry of Jupiter and Titan Atmospheres." PIs, Fellows and selected guests are invited.

2. *Field Trips for Fellows*: Approximately 12 field trips have been provided for Post-doctoral and Graduate Fellows. These have included visits and presentations at NASA Ames Research Center in Moffett Field, California; attendance at the "Creation and Earth History Museum in Santee, California; study of Cambrian fossil fauna at Marble Mountain, California; study of geologic stratification of Grand Canyon, Arizona; and view of Comet Hyakutake, Anza Borrego Desert, California.

3. *Sponsorship and Support Sessions Devoted to Exobiology at National and International Conferences are as follows*:

   International Society for the Study of the Origin of Life, Barcelona, July 1993
   AAAS National Meeting, February 1994
   American Chemical Society, March 1994
   Gordon Research Conference, August 1994
   Gordon Research Conference, January 1996

4. *Visiting Scientist Program*: Eleven senior visiting scientists from Mexico, France, Chile, and Sweden as well as the U.S. have conducted cooperative research projects with NSCORT/exobiology PIs and Fellows, and presented seminars/discussions.

Continued from page 5

Other NSCORT/exobiology Outreach Activities

1. *High School Essay Contest*: During 1993, an Exobiology essay contest was implemented in selected San Diego High Schools.

2. *Sponsorship of Rincon Indian high school students to attend NSF Science Bowl (3 years).*

3. *Sponsorship of Public Lectures*: Topics included "The Great Silence: Is Anybody Out There? The great debate over whether humanity is alone in the cosmos," by David Brin, PhD and "To Boldly Go: America's Next Era in Space," by Leslie E. Orgel, PhD.

4. *Museum Exhibit*: A museum exhibit on Exobiology is planned at the "Stephen Birch Museum and Aquarium" on the UCSD campus, and at the "Rueben Fleet Space Theatre and Science Center," in downtown San Diego.

J. L. Bada

Chemistry 122 - Biochemical Evolution
Winter Quarter, 1995
M W F 2-3 PM
3050 York Hall

LECTURE SCHEDULE

M	Jan 9	Introduction. On the abundance of life in the universe.
W	Jan 11	The big bang and the origin of the elements.
F	Jan 13	Formation of the solar system.
M	Jan 16	HOLIDAY.
W	Jan 18	The primitive atmosphere.
F	Jan 20	Prebiotic synthesis - amino acids.
M	Jan 23	Prebiotic synthesis - purines, pyrimidines, sugars.
W	Jan 25	Other prebiotic syntheses. Stability of organic compounds.
F	Jan 27	Carbonaceous chondrites and interstellar molecules.
M	Jan 30	Organic synthesis on other planets.
W	Feb 1	Polymerization processes.
F	Feb 3	Template polymerizations. (Leslie Orgel)
M	Feb 6	Origin of optical activity.
W	Feb 8	Primitive enzymes and RNA enzymes.
F	Feb 10	MIDTERM.
M	Feb 13	Transfer RNA. Membranes.
W	Feb 15	Self-replicating systems. (Gerald Joyce)
F	Feb 17	Precambrian fossil record.
M	Feb 20	HOLIDAY.
W	Feb 22	History of O_2 in the atmosphere. Origin of biochemical synthesis.
F	Feb 24	Primitive fermentation schemes. Methane bacteria.
M	Feb 27	Origin of photosynthesis.
W	Mar 1	Nitrogen fixation and nitrate metabolism.
F	Mar 3	Origin of citric acid cycle. Origin of eukaryotic organisms.
M	Mar 6	Introduction to protein evolution. Origin of the genetic code.
W	Mar 8	Gene duplication.
F	Mar 10	Calculation of homologies.
M	Mar 13	Examples of protein evolution.
W	Mar 15	Examples of protein evolution.
F	Mar 17	Review and Discussion.
W	Mar 24	FINAL 7-10 PM

NSCORT/exobiology WWW Homepage

The NSCORT/exobiology Homepage is still in the construction phase, and if it fulfills its intent of constantly broadening its mission, will always be under construction.

Information contained in the Homepage is continually reviewed by the PIs or a designated postdoctoral Fellow in each laboratory. The research materials are updated approximately monthly, and personnel descriptions modified as required by turnover and curriculum vitae changes.

The intended audience for the present incarnation of the Homepage is primarily postdoctoral fellows and graduate students interested in Exobiology as a career focus. Mature scientists in allied fields will find the information of interest, though no attempt is yet being made to include extensive details of research results.

The office of the Associate Director is responsible for editing and posting information, and for oversight direction of the technical assistant (Dr. Kevin Walda) who creates and maintains the Homepage.

A primary activity currently under development will be the inclusion of materials for downloading by high school science teachers, providing a teachers' manual, student syllabus and handouts, instructions for laboratory experiments, pictures, bibliographic references, etc. comprising a self-contained High School Teaching Module on Exobiology. During the summer 1996, Stephen Brown (La Jolla High School science teacher, email address stephenebr@aol.com) and Danny Quizon (Career Technician, La Jolla High School) will be in charge of preparing this module.

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WHAT'S EVOLVING AT THE LA JOLLA NSCORT?

Over the past three years considerable progress has been made in harnessing the power of Darwinian evolution to develop macromolecules that exhibit desired chemical properties. For example, Andrew Ellington and Jack Szostak (Harvard University Medical School) generated a population of 10^{13} random-sequence RNA molecules and subjected them to a selection constraint such that only those molecules that could bind to an organic dye were amplified to produce molecular "progeny." The progeny, in turn, were subjected to the same selective amplification procedure, and the process was repeated for six "generations." In the end, Ellington and Szostak obtained RNA molecules that bound to the dye with high affinity and specificity.

On a recent visit to the La Jolla NSCORT (NASA Specialized Center for Research and Training) in Exobiology, Szostak presented the latest and most dramatic example of a test-tube evolution experiment. Szostak and graduate student David Bartel wished to develop an RNA molecule that catalyzes the condensation of template-bound oligonucleotide 5'-triphosphates. This chemistry proceeds spontaneously, but is so achingly slow ($t_{1/2}$ = 33 yr) that even prebiotic chemists who are used to thinking on the geological time scale would tend to doubt its significance. However, Bartel and Szostak attached random sequences to the template, and began evolving towards improved catalytic activity. After ten generations of selective amplification, coupled with the occasional introduction of fresh mutations, they obtained RNAs that could accelerate the spontaneous reaction by more then 10^6 fold ($t_{1/2}$ = 5 min). This is the first time that a new enzyme has been developed starting from a random sequence.

Two investigators from the La Jolla NSCORT also have been heavily engaged in test-tube evolution research. Gerald Joyce and co-workers at the Scripps Research Institute have been using *in vitro* evolution techniques to direct existing RNA enzymes toward the expression of novel catalytic behaviors. In one series of experiments, begun by research technician Amber Beaudry and now continued by Scripps graduate student Joyce Tsang, an RNA-cleaving ribozyme was used as a starting point to develop ribozymes that cleave DNA. The evolving population has now reached the 27th generation and has accumulated, on average, 17 mutations compared to the starting molecule. The starting molecule has barely detectable DNA-cleavage activity, with catalytic efficiency (k_{cat}/K_m) of only about 36 M^{-1} min^{-1}. However, individual ribozymes isolated after the 27th generation have a catalytic efficiency of 10^6 M^{-1} min^{-1} and promote DNA cleavage at a rate that is 10^{12} fold greater than the spontaneous reaction.

Kazuo Harada, working with Leslie Orgel, has completed a study of the optimal sequences for template-directed ligation with DNA ligase or a chemical activating agent. It is clear that high levels of fidelity cannot easily be achieved in template-directed ligation reactions except under very special conditions. This is important in evaluating theories that propose self-replication based on systems of short oligonucleotides.

Activities associated with Jack Szostak's visit to the La Jolla NSCORT included a roundtable discussion involving NSCORT principal investigators, postdoctoral fellows, and graduate students. Steven Benner (ETH, Zurich), on sabbatical at Cal Tech and a previous NSCORT visitor, also joined the discussion. The chief topic concerned nucleic acid analogues that may have relevance to the origins of life and that might be replicatable and evolvable in the laboratory. From the discussion it was clear that *in vitro* selection is now established as a powerful technique for finding catalytic oligonucleotides. Nucleic acid chemistry is extending the range of potentially self-replicating molecules available for investigation by *in vitro* selection. It is likely that the combination of these two approaches will teach us a great deal about the transition from chemistry to biology. ☐

Gerald F. Joyce
and Leslie E. Orgel
(USA)

EXOBIOLOGY SYMPOSIUM AT THE SAN DIEGO ACS MEETING

On March 13 and 14, 1994 a symposium was held at the American Chemical Society (ACS) meeting in San Diego as part of the Geochemistry Division. This symposium was organized as part of the outreach program of the NASA Specialized Center of Research and Training (NSCORT) in Exobiology located at UC San Diego. The symposium covered most topics relating to the origin of life with lively discussion following many of the talks. A great deal of information was exchanged both during the discussions and among the participants afterwards. The three half-day sessions are briefly described here.

There was standing room only for the first morning session which was devoted to Mars, potential organic inputs from space, and impacts. After some introductory remarks by the organizer and session chair S. Miller (UC San Diego) the session got underway. The first speaker, D.L. DeVincenzi (NASA Ames) discussed the future of Mars exploration and exobiological perspectives thereof. This was followed by L. Allamandola's (NASA Ames) presentation on the chemistry occurring on the surface of interstellar ice grains at around 10K, from simple molecules to polycyclic aromatics. The next talk, given by M. Bernstein (NASA Ames) (with L.J. Allamandola, S.A. Sandford and S. Chang), was in a similar vein and concerned the synthesis of hexamethylenetetramine in irradiated ice at 10K from mixtures of CO, H_2O, CH_3OH and NH_3. This is unexpected as formaldehyde was not one of the reactants.

After the break T. Bunch (NASA Ames) discussed recent findings on NASA's long duration exposure facility in which 'Buckminsterfullerenes' were found in cosmic dust impact craters. This is the first direct evidence of their extraterrestrial occurrence. This was followed by G. McDonald (Scripps Inst. of Oceanography) (with J.L. Bada) who reported on recent work on Antarctic meteorite EETA 79001. An analysis of the D/L ratio of the amino acids within this showed them to be of terrestrial origin. It was suggested that earlier studies conducted on organic carbon from the same meteorite also only observed terrestrial contamination. J. Cronin (Arizona State Univ.) (with S. Pizzarello, X. Feng and S. Epstein) described studies of the isotopic enrichments in ^2H, ^{13}C, and ^{15}N in organic compounds in the Murchison meteorite. It was suggested that this may indicate mild thermal aqueous processing of the parent body with decarboxylation of amino acids. The final talk of the morning session was given by S. Chang (NASA Ames) who suggested that some organic compounds synthesized by irradiation of interstellar ice grains could have survived the protosolar collapse and ended up as constituents of the prebiotic soup.

The afternoon session, "The RNA World and Before" presided over by Gene McDonald, opened with Antonio Lazcano's (UNAM) (with S. Miller) presentation on the time required for life to arise. From a consideration of the time required for the entire ocean to pass through hydrothermal vents and approximate calculations of the rate of gene duplications, it was suggested that it could have taken as little as 10 million years to go from the prebiotic soup to the cyanobacteria observed at 3.5 billion years in the Warrawoona formation. R. Breaker (Scripps Clinic) (with G.F. Joyce) next described recent work on the *in vitro* evolution of ribozymes to cleave DNA and to do so in the presence of Ca^{2+} rather than Mg^{2+}.

The afternoon continued with L. Orgel (Salk Institute) discussing the template directed polymerization of activated mononucleotides. He described how GC oligonucleotides with more than 60% G could direct the synthesis of complementary strands. However, these are then unable to direct the synthesis of themselves as they are less than 60% G and so no further replication is possible. A. Kanavarioti (UC Santa Cruz) (with E.E. Baird), in her studies of the kinetics of the template directed synthesis of poly(G) by poly(C) from activated mononucleotides, reported that she found that the rate of reaction increases with a decrease in the concentration of the template. She suggested that this was due to an increase in template occupancy.

J. Ferris (Rensselaer Univ.) (with Z.P. Ding, K. Kawamura and K.J. Prabahar) described the oligomerization of the 5-phosphoroimidazolide of adenosine in the presence of montmorillonite which results in oligomers up to the decamer.

The penultimate talk of the day was given by R. Shapiro (New York Univ.) in which the prebiotic role of adenine was reconsidered. Adenine can be the product of oligomerization of HCN and is often given as an example of a molecule central to modem biology that would have been in the prebiotic soup. It was pointed out that synthesis conditions for adenine would have been rare on the early Earth, and that adenine hydrolyzes and reacts with electrophiles relatively quickly.

The first day of the Symposium ended with a presentation by A. Keefe (UC San Diego) (with S.L. Miller) who discussed the concentration of polyphosphates in the prebiotic ocean. Taking into account the small amounts emitted from lava and perhaps formed by the heating of phosphate rock as well as the rate of hydrolysis, it was concluded that the steady state oceanic concentration of condensed phosphates was less than 10^{-8} M. This is not sufficiently concentrated to be utilized for polymerization reactions and so it was suggested that other free energy sources need to be considered for the first organism.

The final session, convened on the morning of the second day, and chaired by G. McDonald, opened with J. Bada (UC San Diego) (with X. Wang) speaking on Fenton–type reactions of amino acids. In this study the decomposition rates of both amino–isobutyric acid and alanine were measured in the presence of Fe^{2+} and H_2O_2. The rate of decomposition of aminoisobutyric acid was much faster and it was suggested that this may be one of the reasons that it was not incorporated into proteins. M. Robertson (UC San Diego) (with J.P. Dworkin and S.L. Miller) then discussed the prebiotic synthesis of some alternative bases to A, U, G and C which may have played a role in the pre–RNA world. Many potential pyrimidines can be formed under prebiotic conditions and these have functionalities equivalent to the 20 amino acids. If incorporated into RNA these would have greatly expanded the versatility of RNA to act catalytically.

J. Dworkin (UC San Diego) (with V.M. Kolb and S.L. Miller) spoke next on the prebiotically plausible syntheses of the compounds urazole and guanazole as well as their reaction with ribose and other sugars to readily form nucleosides, something that AUGC will not do without an input of energy.

Measurement of the rate of decomposition of ribose was described next by R. Larralde (UC San Diego) (with S.L. Miller). It was suggested that ribose was unlikely to have been a constituent of the first genetic material as it is too unstable. Art Weber (SETI Inst.) then discussed the prebiotic polymerization of dimercaptopropanol on the surface of iron (II) hydroxide oxide. Polymers up to the 15–mer were synthesized and it was suggested that these or similar disulfide polymers may have played a role in the first organism.

G. Ertem (Rensselaer Polytechnic) (with J.P. Ferris) reported on studies in which the template directed synthesis of poly(G) from activated monomers in the presence of poly(C) and montmorillonite. Oligomers of up to 20 units were detected.

T. Lee (Scripps Inst. of Oceanography) (with G. Arrhenius et al.) next presented their work on the sorption of phosphate esters of simple aldehydes into double layer hydroxide minerals. Dissolving the minerals yielded hexose triphosphates and pentose diphosphates in up to 7% yield. The last talk of the session and the symposium was given by R. Minard (Univ. Of Illinois) (with C.N. Matthews, et al.) who described the study of HCN polymers using a variety of analytical techniques.

In some cases the symposium speakers described a broad overview of their topics, and others presented their latest unpublished results. Symposia at national ACS meetings acquaint a wider audience of chemists with the current progress in exobiology than those who attend ISSOL and other specialized meetings. ❐

Stanley L. Miller and Anthony D. Keefe
(UC San Diego)

Fifth Symposium on Chemical Evolution and the Origin of Life
NASA Ames Research Center, Moffett Field, California, April 25-29, 1994

THE NSCORT/EXOBIOLOGY PROGRAM

Stanley Miller*, Jeffrey Bada, Gustaf Arrhenius, Leslie Orgel and Gerald Joyce
University of California, San Diego
La Jolla, California 92093-0317

As part of its ongoing support for research on the origin of life and related topics, the NASA Specialized Center of Research and Training (NSCORT) in Exobiology was established in 1992. The center is affiliated with the California Space Institute of the University of California, San Diego. The director is Dr. Stanley Miller and the associate director is Dr. Robert Tschirgi. Researchers affiliated with the NSCORT are located at the University of California, San Diego, Salk Institute and The Scripps Research Institute.

The goals of the center are to carry out research at the forefront of origin of life studies, to train young scientists for careers in the exobiology/origin of life field, and to undertake public education activities in exobiology. Symposia on current topics in origin of life research sponsored by NSCORT-Exobiology have been held at the 1994 national meetings of the American Association for the Advancement of Science and the American Chemical Society.

Three of the five research groups which make up NSCORT-Exobiology are affiliated with the University of California at San Diego. Dr. Stanley Miller is currently involved in work on aqueous prebiotic chemistry, including the synthesis of nucleic acid components and condensed phosphates. Dr. Jeffrey Bada is analyzing amino acids, polycyclic aromatic hydrocarbons and other organic compounds in meteorites. Efforts are also underway to measure the concentration of extraterrestrial amino acids in seawater and polar ice in order to evaluate the influx of extraterrestrial organics to the early Earth. The work of Dr. Gustaf Arrhenius involves the possible role of clay and hydrotalcite minerals as catalysts or templates for prebiotic chemical reactions, as well as the role of phosphate minerals in prebiotic chemistry.

The remaining two NSCORT-Exobiology research groups are those of Dr. Leslie Orgel at the Salk Institute, and Dr. Gerald Joyce at The Scripps Research Institute. Dr. Orgel's focus is on the template-directed non-enzymatic polymerization of nucleotides to produce oligonucleotides and short nucleic acids which could have served as early informational and catalytic molecules. Dr. Joyce's exobiology-related work involves the use of molecular biological techniques to direct the evolution of catalytic RNA molecules in response to changes in environmental conditions.

INSTITUTIONAL PROFILE

Novel Center Seeks to Add Spark to Origins of Life

LA JOLLA, CALIFORNIA—For more than 4 decades, a small band of researchers has been trying to explore a question that is about as fundamental as you can get: How did life begin? So far, they have only nibbled at the edges of the topic. Part of the problem is simply the difficulty of peering 4 billion years into the past, which is roughly when life on Earth likely originated. But another, more human, dilemma has held back origin of life studies, too: It isn't really a field. There is no degree in the discipline; although there is an international society, it has all of 300 members; and funding for origin of life studies is pathetic. Still, despite this harsh climate, an intellectual primordial soup made up of five leading origin of life researchers and their 20 students is now simmering here, and it may yet give life to a bona fide field.

The spark that could start off a self-perpetuating academic process was a decision 3 years ago by the National Aeronautics and Space Administration (NASA) to designate this "exobiology" group as a NASA Specialized Center of Research and Training (NSCORT). This "virtual" center is aimed at encouraging collaboration among the five participants and their students, who belong to four separate institutions. It has already enlivened the discipline: Since NASA began funding the center 3 years ago, the group has published a bevy of high-profile papers and thrown fuel on a number of long-smoldering debates. "It's a terrifically excellent group," says William Schopf, a geologist at the University of California, Los Angeles, who has helped review this NSCORT. "They're pushing the limits of problems that are of high quality."

If it seems odd that the space agency is spending nearly $1 million a year to investigate the origin of life, NSCORT member Stanley Miller of the University of California, San Diego, stresses that looking for life on other planets is part of NASA's mission. And, says Miller, "if you're going to search for life on other planets, understanding how it started on Earth is essential." Miller and his NSCORT colleagues are tackling a diverse set of issues, ranging from the chemistry of Earth's early atmosphere, to the notion that life may have been seeded from space, to the conditions that might give rise to robust RNA molecules.

Even without NASA's help, the five principal investigators (PIs)—all chemists of different stripes—would be in the forefront of origin of life studies. In addition to Miller, the group consists of Leslie Orgel at the Salk Institute for Biological Studies, Gustaf Arrhenius and Jeffrey Bada from the Scripps Institution of Oceanography, and Gerald Joyce of the Scripps Research Institute. "These are all-stars," says Schopf. "You'd assume they'd be affecting the field regardless." Yet you would not necessarily assume that they would be collaborating, because some of the PIs share little intellectual common ground—which sits fine with Orgel. "Why have several people in a field if you all think the same thing?" he asks.


SUSAN R. GREEN

Life from space? NSCORT head Jeffrey Bada examines ice core for signs of extraterrestrial organics.

The five PIs hook up with each other to do specific experiments, as they see fit. But the NSCORT's most important contribution, says Schopf, is that these researchers have been able "to attract a coherent group of students." And, by all accounts, it's the intermingling of the students—who mix it up at a biweekly journal club to which the PIs specifically are "disinvited"—that makes the NSCORT tick. "I think it's worked extremely well for the younger people," says Orgel.

Spark of life. San Diego's status as world headquarters for origin of life studies is linked strongly to Miller, who rose to fame in 1953 while still a graduate student in the lab of Nobel Prize-winning chemist Harold Urey. The so-called Miller-Urey experiment simulated the prebiotic atmosphere by mixing molecules they presumed were present on the early Earth: methane, ammonia, hydrogen, and water. They then zapped this soup with an electrical charge to mimic lightning, which in turn produced small amounts of amino acids—the building blocks of proteins, which are critical to all living things. "[That study] had a tremendously important role in making chemists aware that the whole question of origin of life could be approached by lab experiments," says NSCORT's Arrhenius. "It became an acceptable field."

Yet today, Arrhenius and many other researchers dismiss the experiment itself because they contend that the early atmosphere looked nothing like the Miller-Urey simulation. Basically, Miller and Urey relied on a "reducing" atmosphere, a condition in which molecules are fat with hydrogen atoms. As Miller showed later, he could not make organics in an "oxidizing" atmosphere.

Arrhenius's objection "starts from the observation that Earth now has such a high proportion of water," he says, noting that H_2O is a strong oxidizing agent. "And there's no theory to say the early Earth was deficient in water." Indeed, he believes it had much more water than was simulated in the Miller-Urey experiment. Also, methane and ammonia are easily obliterated by ultraviolet light, which makes it difficult to see how they could have hung around long enough to form organics.

Others balk at the notion of a reducing atmosphere because of what is known as the "faint young sun" paradox. As geologist James Kasting of Pennsylvania State University explained 2 years ago in *Science* (12 February 1993, p. 920), the sun likely had about 30% less luminosity when Earth was formed. If the planet had the same atmosphere as today, its mean surface temperature would have been below the freezing point of water; it would be a giant iceball. As geologic evidence suggests that Earth had liquid water early in its history, Kasting and others maintain that Earth's early atmosphere must have been rich in carbon dioxide (CO_2), which, through the greenhouse effect, would have kept the surface toasty. But these high levels of CO_2, a neutral agent, also would have prevented a Miller-Urey scenario.

Not that the first biomolecules had to have formed in an environment exposed to the atmosphere. One alternative explanation to the Miller-Urey scenario for life's origin focuses on deep-sea vents that cycle hot fluid in a reducing environment. Another is the theory promoted by A. Graham Cairns-Smith of the University of Glasgow in Scotland that life began as inorganic clays that passed on information in their crystalline structures. The NSCORT researchers are skeptical of both ideas, but they do take more seriously a proposal first made by the late British crystallographer John Desmond Bernal that minerals might have acted as catalysts to help build the first organic molecules.

Life from space. Then again, the building blocks for life might not have taken shape on Earth at all. A possibility that Arrhenius strongly favors and Orgel says he'd choose "if I really had to" is that comets, meteorites, and interplanetary dust particles shuttled in the organic molecules from which life on Earth evolved.

Bada, who heads NSCORT and is himself a former Miller graduate student—and who shares many of his mentor's views—puts little stock in this idea, yet he has been seriously investigating the possibility. Bada's working hypothesis is that if significant quantities of extraterrestrial organic molecules arrived 4 billion years ago, the supply should have continued at a reduced level in the recent past. To address this question, he has relied on α-aminoisobutyric acid (AIB), which is the most common amino acid found in meteorites containing carbon but is rarely found on Earth. He reasoned that if he repeatedly found AIB in polar ice, a medium that contains minuscule amounts of confusing terrestrial organic matter, that would strengthen the argument for an extraterrestrial origin.

In five dozen ice samples dating back more than 6000 years, Bada's group has only found one with high AIB levels. "This suggests to me that [extraterrestrial organics] would not have been important on the early Earth," says Bada. The one positive sample, he says, supports the idea that "delivery of organics to the Earth was not very robust and was very episodic."

Miller, who still believes his original work is valid, insists that no one knows what Earth's early atmosphere contained. "There's no evidence," says Miller. And he argues that the faint young sun paradox would not exist if the oceans went through several freeze-thaw cycles. As Miller, Bada, and Charles Bigham in his lab postulated in the 15 February *Proceedings of the National Academy of Sciences* last year, only the upper layer of the early Earth's oceans might have been frozen over, with the bottom layers constantly heated by radioactive decay from Earth's interior. Giant fiery meteorites, or bolides, might have repeatedly struck the upper ice layer, melting huge holes in the ocean surface. This could have created a plausible setting for the origin of life by freeing into the atmosphere methane, hydrogen, and ammonia that had been produced by hydrothermal vents on the ocean's floor. Then again, life might have started in the ocean itself if the bolides contributed organics and the ocean surface then refroze, trapping concentrations of methane and ammonia in the water. "That's where some interesting chemistry can take place," says Bada.

The pre-RNA world. Wherever and however the "interesting chemistry" took place, the organic molecules it spawned would ultimately have formed larger molecules able to hold information and copy themselves—the first life forms. What they might have looked like is another focus of NSCORT's "intensely experimental" approach, says Scripps Research's Joyce.

Joyce cut his scientific teeth as a graduate student in the lab of Orgel, who in the late 1960s was a co-proponent of the theory that life began with RNA, genetic material that today is best known as an intermediary in the process that transforms DNA into proteins. Orgel and others postulated that life more likely began in what has become known as the "RNA world" because RNA was easier to synthesize than DNA and because it made sense that the more stable DNA could eventually evolve from RNA. Their proposal required that some early form of RNA must have behaved as an enzyme, a critical function that would allow the molecule both to store genetic information and to act as a catalyst to help other RNA molecules copy themselves. In 1983, the University of Colorado's Thomas Cech and Yale's Sidney Altman independently made a breakthrough that lifted enzymatic RNA out of the speculative realm: They found that enzymatic RNAs, now called ribozymes, exist on Earth today.

The scenario that life began with ribozymes raises significant problems, too, however. RNA is a complex molecule that contains the sugar ribose linked on one side to a phosphate and on the other to bases known as purines (adenine and guanine) or pyrimidines (cytosine and uracil). As Orgel puts it, "There were no chemical supply houses on the primitive Earth." What's more, even if the ingredients had been present, the chemical steps needed to assemble them would have been difficult if not impossible in a prebiotic world, Orgel has shown. "The central problem is to see how you get to the RNA world," he says.

Miller's lab has been interested in fashioning a pre-RNA that does not rely on the traditional pyrimidines and purines. For example, he reported last year in the *Journal of Molecular Evolution* that urazole, a mimic of the pyrimidine uracil, binds much more easily with ribose.

Another possible pre-RNA that the NSCORT researchers have been studying is the peptide nucleic acid, or PNA, which Peter Nielsen of Denmark's Panum Institute and co-workers first reported in *Science* (6 December 1991, p. 1497). Like DNA and RNA, this synthetic molecule forms a double helix, but it uses simple amides rather than complicated ribose-phosphates for its backbone. Working with Nielsen, Orgel and Christof Böhler in his lab reported in the 17 August *Nature* that pieces of RNA can provide the template for pieces of PNA and vice versa. This demonstrates that "genetic takeover" of a pre-RNA by RNA could have occurred.

Yet Orgel is far from convinced that PNA preceded RNA. "Even PNA still looks fairly complex," he says. Building off Bernal's original idea, Orgel's and Arrhenius's labs are now collaborating in attempts to synthesize other pre-RNAs by using mineral surfaces to construct molecules with simple backbones.

The evolution of creation. Over at Scripps Research, Joyce is addressing a question further downstream. Rather than concentrating on where the original material came from, Joyce wants to unravel how RNA by itself could have been a life form. Which raises a fundamental question: What is life?

"The origin of life is synonymous with the origin of Darwinian selection," says Joyce. In Joyce's view, life is defined by repeated cycles of replication and mutation. Using the tools of molecular biology, he grows large populations of RNAs—on the order of 10^{14}—and attempts to select for the traits that the molecule ultimately would need to be a life form all by itself. For example, Joyce has shown that with "directed evolution" he can select for ribozymes that cleave DNA and incorporate other "coenzymes." But he envisions much fancier tricks. "We would like to teach the ribozyme to take over replication," says Joyce.

As with everyone else in NSCORT, Joyce firmly believes that while science may not unravel the precise origin of life, it is constantly moving closer to a plausible explanation. "Life will be made in the lab," predicts Joyce. "There's a reasonable chance it will be made by the end of the decade. ... It isn't something we need to talk about sitting in front of the fireplace sipping brandy. It's doable." Especially if the NSCORT succeeds and spawns a new generation of origin of life–ologists to take up the cause.

–Jon Cohen

THE NSCORT EXOBIOLOGY PROGRAM

Principal Investigator	Affiliation	Research Area
Gustaf Arrhenius	Scripps Institution of Oceanography	Formation and growth of RNA precursors
Jeffrey Bada	Scripps Institution of Oceanography	Organic material on primitive Earth
Gerald Joyce	Scripps Research Institute	Evolution of protein synthesis using RNA
Stanley Miller	University of California, San Diego	Nucleotides on primitive Earth
Leslie Orgel	Salk Institute for Biological Studies	Catalysis of nucleic acid replication by minerals

J. L. Bada

CalSpace News

Volume 1, Number 2 | The Newsletter of the California Space Institute | July 1, 1994

NSCORT / Exobiology

An Introduction

Among the many CalSpace projects and programs is the *NASA Specialized Center of Research and Training (NSCORT) in Exobiology*. Established by a NASA grant in January of 1992, the NSCORT program functions under the directorship of Dr. Stanley Miller, Professor of Chemistry, UCSD, as a joint undertaking of investigators at UCSD, The Scripps Research Institute (TSRI), and The Salk Institute for Biological Studies (SALK).

NSCORT's focus is the field of exobiology, or the study of the origins of life and the forms it might take elsewhere in the universe. This eclectic field includes disciplines ranging from astrogeophysics to molecular biology, and is a prime example of a scientific discipline requiring close interaction among several arenas of research.

Overall policy and research directions for NSCORT are managed by the Scientific Staff, composed of Professors Stanley L. Miller, Gustaf Arrhenius and Jeffrey L. Bada (Scripps Institution of Oceanography, UCSD), Gerald F. Joyce (TSRI), and Leslie E. Orgel (SALK).

Each member of the Scientific Staff heads one of the five NSCORT research laboratories. Dr. Miller's group is studying the chemical reactions of nucleotide bases with other possible primitive Earth compounds. The compounds formed by these reactions are the potential precursors of the RNA world, which is believed to have existed on the primitive Earth before the DNA world.

Two research groups are located in the Marine Research Division at SIO. In one laboratory, Dr. Arrhenius is exam-

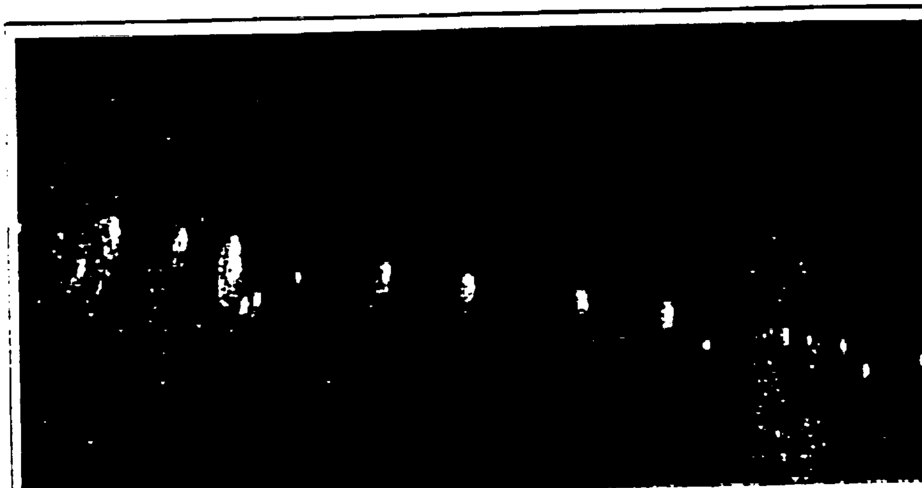
(see NSCORT page 2)

CalSpace Researcher Studies Comet Shoemaker-Levy 9

Collision with Jupiter expected mid-July

Comet Shoemaker-Levy 9, already split into many pieces, will strike the planet Jupiter in the third week of July, 1994. It is an event of tremendous scientific interest but, unfortunately, one which is not likely to produce a spectacular visual display for the general public. Nevertheless, it is a unique phenomenon and secondary effects of the impacts will be sought after by both amateur and professional astronomers.

The impact of comet Shoemaker-Levy 9 into Jupiter represents the first time in human history that people have discovered a body in the sky and have been able to predict consequences to a planet more than seconds in advance.



A mosaic containing two new Wide-Field Camera (WFC) images and one Planetary Camera (PC) image (resampled to the same resolution as the WFC images) of the comet taken in January 1994. Twenty nuclei are visible here, while one more is slightly outside of the field-of-view (to the right). Each nucleus has its own coma and tail. Notice that some of the nuclei are now significantly displaced from the "train," which is defined by the imaginary line connecting most of the bright nuclei. The width and height of this image project to distances of 605,000 kilometers (376,000 miles) and 126,500 kilometers (78,600 miles), respectively, at the comet.

Lucy McFadden, CalSpace Associate Research Scientist and a National Science Foundation Visiting Professor currently at the University of Maryland, has observed the comet before its demise. She and her colleague, Mike A'Hearn, have imaged the comet at visible and infrared wavelengths from telescopes at Kitt Peak in Tucson, Arizona, Mauna Kea Observatory in Hawaii, and Cerro Tololo in Chile. McFadden and A'Hearn have looked at the comet every month since January with the goal of characterizing the comet in terms of particle size and composition.

The impact will deliver more energy to Jupiter than the largest nuclear warheads ever built, and up to a significant fraction of the energy delivered by the impact which is generally thought to have caused the extinction of the dinosaurs on Earth, roughly 65 million years ago. Earth-bound observers are taking this opportunity to observe and study

(see Comet page 2)

Comet... (continued from page 1)

the comet's collision with a planet to gain more understanding of one of the fundamental physical processes within the solar system—impacts. The discovery has spawned scientific thinking about the frequency with which comets fragment and the implications related to the inventory of small bodies in the Solar System and how they modify the surfaces and atmospheres of the planets.

The 22 identified fragments and smaller debris in comet Shoemaker-Levy 9's orbit will hit Jupiter in the southern hemisphere, at latitudes between 47-49 degrees between July 16, and July 22, 1994. The fragments will approach the atmosphere at an angle roughly 45 degrees from the vertical. The impacts will occur on the back side of Jupiter as seen from Earth, in an area that is also in darkness. This area will be close to the limb of Jupiter and will be carried by Jupiter's rotation to the front, illuminated, side less than half an hour after the impact. The grains in the tail of the comet will pass behind Jupiter and remain in orbit around the planet.

It is generally expected that nearly every observatory in the world will be observing events associated with the impact. These observatories will include several Earth-orbiting telescopes (Hubble Space Telescope, International Ultraviolet Explorer, Extreme Ultraviolet Explorer) and several interplanetary spacecraft (Galileo, Clementine, and Voyager 2).

- contributed by Alan Chamberlain and Lucy McFadden

NSCORT.. (cont'd from page 1)

ining the formation, concentration, and growth of RNA precursor molecules. To conduct this research, the formation of organic molecules by plasma processes in the upper atmosphere is modeled experimentally. The resulting compounds are then followed through processes of selective concentration, ordering, and growth under control of surface active minerals.

Meanwhile, Dr. Bada is exploring the accretion of organic material on the primitive earth. This study involves a search of sea water and arctic ice for extraterrestrial organic compounds arriving on Earth in meteorites and comets. It is thought that the amount and nature of these compounds will indicate the importance of extraterrestrial input on the primitive Earth.

In the Chemical Evolution Laboratory at SALK, Dr. Orgel is looking at the catalysis of nucleic acid replication by mineral surfaces. This investigation searches for simple catalysts (including mineral surfaces) that might increase the efficiency of RNA—essential for first life-forming reactions—replication.

Finally, at TSRI's Department of Molecular Biology, Dr. Joyce researches the evolution of protein synthesis in the context of a genetic system based on RNA genomes and RNA catalysts. In this research, chemical compounds are being caused to evolve under laboratory conditions that demonstrate the capability of RNA as a catalyst.

Eleven NSCORT post-doctoral fellows and 5 graduate student fellows, as well as 10 adjunct fellows, work on these five projects. An annual summer program is also conducted for 5 undergraduate fellows.

Included as Associates of NSCORT are scientists from the La Jolla area who work in fields related to the origins of life and who wish to participate in the major activities of the Center. The Associates include: Dr. Russell F. Doolittle, Dr. M. Reza Ghadiri, Dr. John F. Kerridge, and Dr. Mark H. Thiemens.

Administrative and liaison activities for NSCORT are handled by the Associate Director, Dr. Robert Tschirgi. In collaboration with the Scientific Staff, Dr. Tschirgi is also involved in coordinating education and outreach programs.

Past educational programs for high school and college students and teachers have included an essay contest on exobiology, sponsorship of Rincon Indian students at the Science Bowl, participation in summer programs and internships for undergraduates, lectures for high school and college teachers in Mexico and the U.S., and development of teaching materials on exobiology.

The NSCORT Outreach Program provides information concerning exobiology to the general scientific community through lectures, cooperative articles in journals of general scientific readership, such as *Scientific American* and *American Scientist*, as well as in-house produced brochures and pamphlets.

National and international scientists working in areas pertinent to exobiology are invited to give seminars and lectures. Some of these scientists then go on to conduct collaborative research in an NSCORT laboratory.

Among its many other activities, NSCORT also sponsors a bi-weekly Fellow's Journal Club programmed and conducted by the post-doctoral and graduate student fellows. In addition, a tri-monthly dinner meeting brings Fellows and PIs together in a seminar/discussion format.

For more information about NSCORT programs and research activities, please contact the NSCORT Administrative Offices at (619) 534-1891.

- contributed by Robert Tschirgi

The NSCORT/Exobiology Logo. The formation of primary self-replicating molecules is symbolized by the presence of energy, water, and atmosphere. The initial atmosphere, with its necessary chemical components, appears as the background of wind and cloud. A lightening bolt represents the energy required to propel the nascent compounds toward increasing order, replication, and evolution. Water, essential for all known life, falls as drops. The double-helix of RNA/DNA emphasizes the subsequent evolution through the genetic code.

Summer '95 Volume 1.1

NSCORT/exobiology

NASA Consortium of UCSD, SALK, and TSRI located at La Jolla, California

PERSONNEL

Top Brass

Since its inception in 1992, Dr. Stanley Miller has served as Director of the NSCORT/ exobiology Center. Through his leadership, the program has achieved international renown. It is a testimony to Dr. Miller's stature as a founder and developer of the "Origin of Life" field. Following his appointment as Research Professor of Chemistry in 1994, Dr. Miller requested that he be relieved of the Director's duties to devote more time to research and training. As a Principal Investigator in NSCORT, he will continue his contributions to the program.

As of July 1, 1995, Dr. Jeffrey Bada, Professor of Marine Chemistry, SIO (UCSD), one of the original five NSCORT founders, will assume the post of Director.

Each of the five PIs maintains an independent laboratory studying an aspect of exobiology. They are: Profs. Stanley Miller, Department of Chemistry, UCSD; Jeffrey Bada, Marine Research Division, SIO; Gustaf Arrhenius, Marine Research Division, SIO; Gerald F. Joyce, The Scripps Research Institute (TSRI), and Leslie Orgel, Salk Institute for Biological Studies (SALK).

Eleven Associate Members of NSCORT/exobiology are: Drs. Russell F. Doolittle, UCSD; Marina Fomenkova, Cal Space Institute; M. Reza Ghadiri, TSRI; John F. Kerridge, UCSD; Mark H. Thiemens, UCSD; Thomas Ahrens, California Institute of Technology; David Stevenson, California Institute of Technology; K. C. Nicolaou, TSRI; Jay Siegel, UCSD; William J. Schopf, UCLA, and Charles Perrin, UCSD.

Administrative personnel are Dr. Robert Tschirgi, Associate Director, and Lois Lane, Administrative Assistant.

NSCORT / EXOBIOLOGY LOGO

Exobiology is the study of the conditions, substances and reactions from which arise the self-duplicating, evolving systems called life, and their distribution throughout the universe. In this endeavor, the mechanisms for life's most arcane processes will be explored, with consequent unpredictable bounties for medicine, biology and technology.

The formation of primary self-replicating, evolving molecules is symbolized by energy (lightning bolt), water and atmosphere. The double helix of RNA/DNA represents subsequent evolution through the genetic code.

GRANT RENEWAL

Site Review

March 9, 1995 an external Site Visit Review Panel to evaluate NSCORT/exobiology accomplishments met with PIs, Fellows and Staff. Brief addresses by Dr. Edward Frieman, Director of SIO, and Dr. Sally Ride, Director of The California Space Institute assured the Panel of support for NSCORT by these parent institutions.

The Panel consisted of members from Woods Hole Marine Biological Laboratory; University of Connecticut; UC Davis; NASA Kennedy Space Center, and the American Institute of Biological Sciences. Two observers from NASA Washington Headquarters were in attendance.

This is the third year of the NASA grant that sponsors NSCORT, and the Review Panel is the first step in determining whether the grant will be renewed for another five-year period beginning in 1997. Renewal will be in competition with other academic institutions and dependent on NASA budgetary priorities.

The final report from the Panel concludes: "This has been an outstanding program that is more than the sum of its parts. The science is excellent and the interaction among the research groups has been productive. The NSCORT has been able to attract excellent students, postdoctoral fellows and visiting scientists." "NASA has gotten its money's worth."

The Mission

NSCORT: NASA Specialized Center of Research and Training. There are several NSCORT programs located at universities, industries and space centers around the country, each with a different focus of research and training. For example, the Purdue University NSCORT is dedicated to Bioregenerative Life Support Systems to sustain human life in space, and the University of Rochester/University of Colorado/ Martin Marietta Corp./Center for Space and Advanced Technology consortium focuses on Space Environmental Health.

The NASA/exobiology program was activated January 1, 1992. It is a consortium of scientists at three institutions in the La Jolla (San Diego), California area. The administrative recipient of the NASA grant is the California Space Institute, Scripps Institution of Oceanography (SIO), University of California, San Diego (UCSD). The program partners—The Salk Institute for Biological Studies (SALK), and The Scripps Research Institute (TSRI)—receive their assigned funds to support research and training in Exobiology through the central NSCORT office at UCSD.

In 1991, the Principal Investigators (PIs) (see *Top Brass*, pg. 1) responded to the opportunity from NASA to establish an integrated NSCORT for Exobiology. Such a unified program would allow greater synergy of research efforts and broader cooperative educational and outreach programs.

The specific aims of the NSCORT/exobiology program are:

- The support and training of Postdoctoral, Graduate and Undergraduate Fellows.
- The support of research by PIs and Fellows.
- The dissemination and exchange of information concerning Exobiology within the scientific community, pre-college and college students, and the general public.

The advantage of the NSCORT consortium over independent, research grants is primarily the promotion of interaction among the Fellows and PIs. NSCORT contributes support and sponsorship for a variety of communal activities including a Bi-weekly Journal Club, a Bi-monthly Seminar-Discussion dinner, seminars and discussions by international scientists, visits to other institutions (e.g. NASA Ames), collaborative research, field trips and a yearly discussion/dinner with the Review Committee members.

...So Far

During the first three years of the NSCORT/exobiology program:

- One hundred and forty scientific papers have been published.
- Twenty-nine seminars and discussions by invited national and international scientists have been given.
- Eight national and international visiting scientists have collaborated in research projects.
- Fourteen collaborative research projects with other national and international laboratories have been undertaken.
- NSCORT scientists have made presentations at ten national and international scientific meetings.
- NSCORT has sponsored five sessions devoted to Exobiology at national and international conferences.
- NSCORT has received over 125 applications for Fellowships representing 22 nationalities. Sixteen postdoctoral, 10 graduate and 22 undergraduate Fellowships have been awarded.

In addition to communication with the scientific community through articles in general scientific literature (e.g. *Scientific American, American Scientist, Omni*), NSCORT creates and distributes pamphlets and brochures on Exobiology; presents posters at meetings of primary and secondary school science teachers; develops teaching modules for high school science classes; supports Native American high school Science Bowl participants; maintains a Computer Bulletin Board for students and teachers interested in Exobiology; contributes to primary school educational programs such as *Dragonfly*; acts as a bibliographic and consultative resource for development of teaching materials, and provides materials and expert consultation on Exobiology for newspaper and magazine articles as well as television documentary programs.

Honors and awards:

Stanley Miller: Ireland Scholar and Lecturer, U. of Alabama at Birmingham (1994).

Gerald Joyce: Co-recipient, National Academy of Sciences Award in Molecular Biology (1994) and the Pfizer Award in Enzyme Chemistry(1995).

Leslie Orgel: Silliman Lecturer at Yale University (1994) and Urey Medal from ISSOL (1993).

Gustaf Arrhenius: Svante Arrhenius Prize and the Academy Medal from Akademiya Tvorchestva (Russia) (1992).

Research

The only life currently known to exist is on planet Earth. Therefore, the Exobiology research program focuses on the conditions, substances and chemical reactions of primitive Earth and its extraterrestrial environment, beginning about 4.6 billion years ago.

The themes of research in the laboratories of the NSCORT/exobiology program are:

- Plausible chemistry under plausible prebiotic conditions.
- Earth based syntheses and inputs from space.
- Nature of first genetic material.
- RNA/DNA/protein evolution under laboratory conditions.

Dr. Jeffrey Bada's lab is studying the accretion of organic material on the primitive earth. A search is being made of sea water, polar ice, lunar soils and meteorites from Mars for extraterrestrial organic compounds. The amount and nature of these compounds will indicate the importance of extraterrestrial input on the primitive Earth.

Dr. Gustaf Arrhenius' lab is studying the formation, concentration and growth of RNA precursor molecules. The formation of organic molecules by plasma processes in the upper atmosphere is modeled experimentally. The resulting compounds, some with possible role in the emergence of life, are being followed through processes of selective concentration, ordering and growth under control of surface active minerals.

Dr. Stanley Miller's lab is studying the chemical reactions of nucleotide bases with other possible primitive Earth compounds. The compounds formed from nucleotide bases reacting with products of prebiotic processes are potential precursors to the genetic material of the pre-DNA, probably RNA, world.

Dr. Leslie Orgel's lab is studying the catalysis of nucleic acid replication by mineral surfaces. The replication of RNA—essential for first life-forming reactions—does not occur efficiently in solution, without the presence of enzymes. Simple catalysts (including mineral surfaces) might increase the efficiency of this type of reaction.

Dr. Gerald Joyce's lab is studying the evolution of protein synthesis in the context of a genetic system based on RNA genomes and RNA catalysts. Chemical compounds are being caused to evolve under laboratory conditions that demonstrate the capability of RNA as a catalyst.

News From the Labs.......

Bada Lab

Dr. Luann Becker attended the Second Ames Dust Workshop on "The connection between interstellar and solar system dust and molecules" held April 27-28, at the NASA Ames Research Center in Moffett Field, CA. The meeting was a blend of astrophysicists, chemists, and geologists offering new insights on the composition and origin of interstellar and stellar dust molecules. Much of the discussion was focused on polycyclic aromatic hydrocarbons (PAHs), derived from stellar environments, as the dominant component of dust. Dr. Becker's identification of fullerene structures in the Allende Meteorite (Becker et al., 1993), similar to Onion-type grains from WC stars, supports the theory that fullerenes are a ubiquitous form of carbon in certain stellar environments. These studies raise many interesting questions concerning the delivery of exogenous carbon to early Earth and the role it may have played in the origins of life.

Miller Lab

The Miller group has been very busy of late; we are now up to a total of 8 group members. So far this year we have received visits by Antonio Lazcano, Albert Eschenmoser and Stefan Pitsch. Antonio Lazcano is collaborating with us on a number of papers. Albert Eschenmoser was treated to presentations by Michael Robertson on the instability of ribose, by Jason Dworkin on Urazole as a potential base in the pre-RNA world, and by Anthony Keefe on the prebiotic synthesis of pantetheine and an investigation of Wächtershäuser's iron sulfur world. Stefan Pitsch presented at one of our group meetings. In addition, Anthony Keefe gave an invited lecture to the exobiology division of NASA Ames in February on the prebiotic synthesis of pantetheine and also was invited by the Arrhenius group to defend why he felt phosphates cannot have played a part in the first organisms.

Arrhenius Lab

The Arrhenius group is currently working on the problem of concentration and mineral surface-induced reaction of formaldehyde. This study is spearheaded by Drs. Stefan Pitsch and Ram Krishnamurthy, Postdoctoral Fellows from ETH (Zürich, Switzerland); Professor Vera Kolb, visiting from the University of Wisconsin, is carrying out related phosphorylation studies.

Professor Jay Siegel, NSCORT Associate at UCSD, and Professor Paul Braterman, visiting from the University of North Texas, are continuing the study of cyanide reactions in the presence of formaldehyde and with ferrous ion producing ferrocyanide-mineral complexes.

The role of charged surface active minerals in concentration and oligomerization is also investigated by Drs. Ton Lee and Malchis Arrhenius in collaboration with Professor Leslie Orgel, using amino acid phosphate esters as probes. Shibin Zhang, together with Professor J.P. Ferris, is trying to find the structurally related cause of nucleic acid oligomerization in the clay mineral montmorillonite.

Selected Recent Publications

Arrhenius Lab

Gedulin, B. and G. Arrhenius, "Sources and geochemical evolution of RNA precursor molecules: the role of phosphate," In *Early Life on Earth, Nobel Symposium 84*, ed. S. Bengtson, 91-110, Columbia University Press, 1994.

Mojzis, S., A.P. Nutman and G. Arrhenius, "Evidence for a marine sedimentary system at >3.87 Ba in southern West Greeland." *EOS, Trans. Am. Geophys. Union* 75, 44, 690, 1994.

Bada Lab

Bada, J.L., "Origins of Homochirality." *Nature* 374, 594-595, 1995.

Bada, J.L. and G.D. McDonald, "Amino acid racemization on Mars: Implications for the preservation of biomolecules from an extinct Martian biota." *Icarus* 114, 139-143, 1995.

Joyce Lab

Breaker, R.R. and G.F. Joyce, "A DNA enzyme that cleaves RNA." *Chem & Biol* 1, 223-229, 1994.

Dai, X., A. De Mesmaeker and G.F. Joyce, "Cleavage of an amide bond by a ribozyme." *Science* 267, 237-240, 1995.

Miller Lab

Keefe, A.D., G.L.Newton, and S.L. Miller, "The prebiotic synthesis of Pantetheine: a precursor to coenzyme A." *Nature* 373, 683-685, 1995.

Robertson, M.P. and S.L. Miller, "Prebiotic synthesis of 5-substituted uracils: a bridge between the RNA and DNA/protein worlds." *Science* 268, 702-705, 1995.

Orgel Lab

Kolb, V. and L.E. Orgel, "Oligonucleotides as probes for studying polymerization reactions in dilute aqueous solution." *J Molecular Evolution* 38 433-437, 1994, and "Oligonucleotides as probes for studying polymerization reactions in dilute aqueous solution, II: Polycondensations." *J. Molecular Evolution* 40, 115-119, 1994.

Harada, K. and L.E. Orgel, "In vitro selection of optimal DNA substrates for ligation by a water-soluble carbidiimide." *J. Molecular Evolution* 38, 558-560, 1994.

Outreach

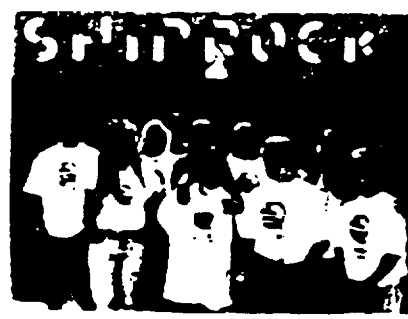
A significant mission of NSCORT/exobiology as a coordinated program is to introduce other potentially interested individuals and groups to the field of Exobiology who might not otherwise come in contact with the discipline. These "outreach" activities fall into three categories: 1) professional and general scientific community; 2) college, high school and primary education; and 3) the general public.

Programs for the professional community of exobiologists:

- Collaboration with other NASA laboratories and extramural programs.
- Summary articles regarding NSCORT/exobiology activities.
- Presentations at National and International symposia.
- Sponsorship of Exobiology sessions at National and International meetings.

Programs for the general scientific community:

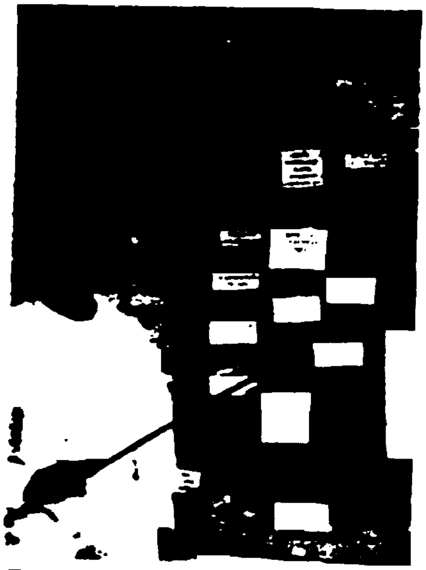
- General scientific readership articles, e.g. *Scientific American, Nature, Omni.*
- Lectures to scientists from other disciplines.
- Brochures and pamphlets describing NSCORT/exobiology.



Rincon Indian High School students wearing NSCORT/ exobiology T-shirts at All-Indian Science Bowl Contest, Shiprock, New Mexico.

Programs for high school and college science teachers and students:

- Involvement of teachers in NSCORT/exobiology research laboratories.
- High school teaching modules and essay contest.
- Support of Rincon Indian high school student Science Bowl.
- Research internships for undergraduate college students.
- Extramural lectures by NSCORT scientists to teachers and students.
- Consultative assistance for teachers through NASA Space Link and other BBS.



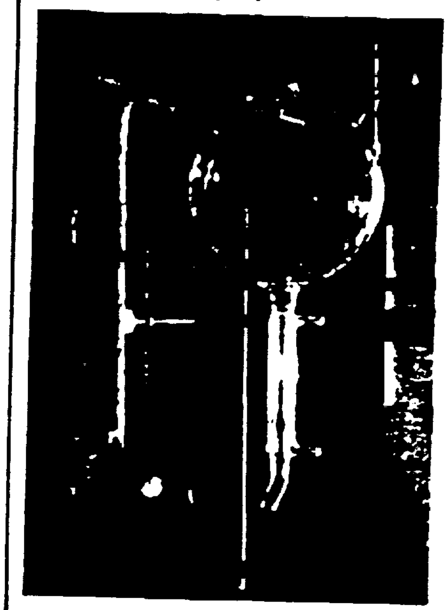
Flavia Bergs, La Jolla High School student, demonstrating classic Miller-Urey experiment (Steve Brown, teacher).

Programs for primary and secondary education, and the general public:

- Poster exhibits at National Science Teachers Association meetings.
- Contribution to pupil-scientist interaction through programs such as *Dragonfly*.
- Contributions to local, national and international media, e.g., TV documentary "Life is Impossible"; Time Magazine article "Origin of Life"; NOVA TV program "The Search for the Origins of Life".

Recent outreach activities:

- Lectures by Dr. Stanley Miller at El Colegio de la Frontera Norte, (Tijuana and Ensenada, Mexico); at the UC Irvine Summer Science Institute, and at Point Loma Nazarene College.
- Lectures by Dr. Leslie Orgel at the BSCS Educational Research and Development Organization, Colorado College.
- Lectures by Dr. Gerald Joyce to San Diego high school science teachers.
- Development of an Exobiology teaching module in cooperation with Mr. Stephen Brown, La Jolla High School.
- Lecture by Dr. Jeffrey Bada to San Diego State University students and teachers.
- Talk by Dr. Gustaf Arrhenius to pupils of the Torrey Pines Elementary School at Science Discovery Day.



Duplicate of 1953 Miller-Urey primitive atmosphere spark apparatus for generating prebiotic compounds.

Publications of general interest:

- Orgel, Leslie E. "The Origin of Life on Earth," *Scientific American* 271, 52-61 (1994).
- Bada, Jeffrey L. "Cold Start," *The Sciences* 35, 21-25 (1995).
- Miller, S.L. & Lazcano, A. "How Long Did It Take for Life to Begin and Evolve to Cyanobacteria?," *Journ. of Molecular Evolution* 39, 546-554 (1994).
- Joyce, Gerald F. "Directed Molecular Evolution," *Scientific American* 267, 90-97 (1992).

:-) :-) :-) :-) :-) :-)

Fellows

Sharon Wang, Anthony Keefe, Michael Robertson, Karen Brinton, Jason Dworkin, Gene McDonald and Stephen Mojzsis were among the NSCORT Fellows visiting the Arroyo Tapiada Caves.

The NSCORT/exobiology program provides funding for stipends and benefits, fees, and research expenses to support post-doctoral, graduate and undergraduate student Fellowships. In addition to regular Fellowships, there are Adjunct Fellowships (funded from other budget categories of NSCORT monies) and Honorary Fellowships (unfunded). Currently, there are 9 post-doctoral Fellows plus 3 Adjuncts and 1 honorary; 4 graduate student Fellows, plus 5 Adjuncts; and 6 Undergraduate Fellows plus 2 Adjuncts.

NSCORT Fellows Anthony Keefe, Michael Robertson and Jason Dworkin at Arroyo Tapiada Caves

Fellowships are solicited through national and international scientific publications and are evaluated competetively by a committee of the five NSCORT PIs. Pending yearly review, postdoctoral Fellowships are committed for two years and graduate Fellowships for three.

Current Fellows:

- **Arrhenius laboratory**... *Postdoc:* Ram Krishnamurthy, Ton Lee, Stefan Pitsch. *Graduate:* Stephen Mojzsis (Adjunct), Sarah Richards-Gross (Adjunct). *Undergraduate:* Shibin Zhang (Adjunct), Chloe Zubieta (SURF summer student).
- **Bada laboratory**... *Postdoc:* Kevin Walde (Adjunct). *Graduate:* Karen Brinton, Sharon Wang, Luann Becker (Adjunct). *Undergraduate:* Aaron Eppler (summer 1995), Healy Hamilton (summer 1995).
- **Joyce laboratory**... *Postdoc:* Ajay Chakrabarti, Luc Jaeger, Terry Sheppard (Fall, 1995), Martin Wright. *Graduate:* Richard Bruick (Adjunct), Xaio-Chang Dai (Adjunct).
- **Miller Laboratory**... *Postdoc:* Anthony Keefe. *Graduate:* Jason Dworkin. *Undergraduate:* Christopher House (Adjunct), Michael Robertson (Adjunct), Joel Decks (summer 1995), Guru Khalsa (summer 1995), Matthew Levy (summer 1995), Kevin Nelson (summer 1995).
- **Orgel laboratory**... *Postdoc:* Jürgen Schmidt, Christof Böhler (Adjunct), Michael Silveira (Adjunct). *Graduate:* Rihe Liu. *Undergraduate:* Uday Kishore (Planetary Biology Intern, summer 1995).
- **Cal Space Institute**... *Postdoc:* Alan Chamberlin (Honorary).

Fellows who have completed or are completing their Fellowships this year are continuing their careers through a variety of placements:

Luann Becker: NRC Fellowship, Ames Research Center and UCSD

Ron Breaker: Assistant Professor, Yale University

Ton Lee: Fisherman Pharmaceutical Corp., Taiwan

Michael Griffith: Isis Pharmaceuticals

Chris House: Graduate Student, UCLA

Luc Jaeger: Assistant Professor, University of Strasbourg, France

Anthony Keefe: NRC Fellowship, Ames Research Center

Rosa Larralde: Graduate Student, Harvard

Niles Lehman: Postdoctoral Fellow, University of Oregon

Gene McDonald: Research Associate, Cornell University

Heinz Peter Muth: Patent Attorney, Germany

Michael Robertson: Graduate Student, Indiana University

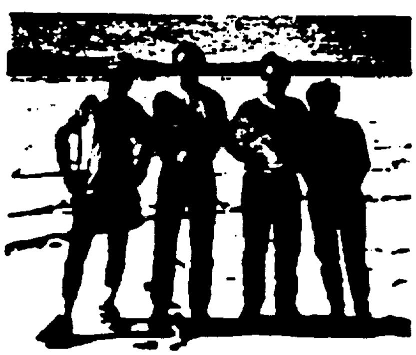
The NSCORT Journals Club

Anthony Keefe and Jason Dworkin

The NSCORT/exobiology Journals Club meets every second Wednesday and the members take turns presenting topics. In order to facilitate discussion among the Fellows, the PIs are specifically disinvited.

Steve Mojzsis gave the first 1995 presentation on evidence from ancient zircons indicating the presence of an ocean prior to 4.2 Ga. Luc Jaeger described the tertiary structure of RNA based on his PhD studies. Rihe Liu summarized the alternative backbones that have been utilized in the manufacture of anti-sense DNA pharmaceuticals, and whether they could have been utilized in the pre-RNA world. Sharon Wang presented Kanavarioti's view of how the RNA world could have become established. Tony Keefe presented a talk on quantum theory and the origin of life, in which suggestions were made that the early universe existed in a linear superposition of all possible quantum states until the first one arose containing a conscious observer, causing collapse to this single possibility and necessitating the appearance of life. Most recently, Chris House discussed the possibility that cyclic AMP could have been the precursor to ATP. Chris has been able to cyclize AMP in 0.15% yield.

In addition to seminars, the Club also makes relevant field trips, including the microbial mats in San Quintin, Mexico (with the Schopf group from UCLA), Bristol Dry Lake to consider concentration mechanisms, and the Marble Mountains to view evidence of Cambrian stromatolites, trilobites, brachiopods and archeocyathids.



Tony Keefe, Michael Robertson, Jason Dworkin and Pepita Larralde at Bristol Dry Lake

A recent excursion to the Creation and Earth History Museum in Santee exposed the Fellows to the origin of life dogma held by a reputed 47% of Americans (*U.S. News & World Report*, December 23, 1991). The depth of ignorance and circular logic were astonishing to the Fellows. They agreed on the great need for educational outreach to the community by physical scientists, historians and anthropologists.

An excursion is planned to tour JPL to see the manufacture and control of unmanned spacecraft. A special tour of the Palomar Observatory is also scheduled.

NSCORT Fellows Michael Robertson, Karen Brinton, Anthony Keefe, Jason Dworkin, and Steve Mojzsis at Amboy Crater

Summer Research Program

The NSCORT/exobiology Summer Research Fellowship Program is a ten week research experience for undergraduate college students majoring in chemical and/or earth sciences. It features direct participation in research activities of UCSD and Scripps Institution of Oceanography (SIO) faculties as well as an exploration of opportunities for graduate study at UCSD and SIO.

Summer Fellowships are offered on a competitive basis to students who have completed at least their junior year of college, are enrolled full-time at a college or university, and have a 3.0 or better grade point average. Research assignments are designed and supervised by a faculty Mentor in conjunction with the student's research interest, and require full-time commitment by the student. At the discretion of the student's Mentor, a final abstract or oral presentation may be required at the end of the summer program.

Students receive a $2,500 (10-week) stipend and campus housing. Application requires a completed Application Form, Statement of Purpose, official undergraduate transcript and two faculty references.

Summer Fellowship Program
NSCORT/exobiology Office
University of California, San Diego
La Jolla, CA 92093-0216

☺☺☺☺☺☹

Calendar

Visitors.......

- April 18, 1995: Mrs. Bonnie McClain, Outreach Coordinator and Development Assistant, Purdue University NSCORT, discussed Purdue Outreach programs.
- May, 1995: Prof. Antonio Lazcano, Professor of Microbiology, University of Mexico, Visiting Scientist in Miller lab.
- January-May 1995: Dr. James Ferris, Professor of Chemistry, Rensselaer Polytechnic Institute, President of ISSOL, Visiting Scientist in the Orgel laboratory.
- Fall, 1995: Dr. Bevan French, Smithsonian Institution, Washington, DC, Visiting Scientist in the Bada laboratory.
- July-August, 1995: Prof. Paul Braterman, Dept. of Chemistry., U of North Texas.
- May-August, 1995: Prof. Vera Kolb, Dept. of Chemistry, University of Wisconsin, Visiting Scientist in Arrhenius laboratory.
- June-August, 1995: Prof. Bettina Heinz, Dept of Chemistry, Palomar College, San Diego, Visiting Scientist in Arrhenius laboratory.
- Summer, 1995: Dr. Dilip Kondepudi, Assoc. Prof. of Chemistry, Wake Forrest University, Visiting Scientist in the Miller and Bada laboratories.

Seminars, Courses.........

- Winter 1994: "The Early Earth" (SIO 269), J. Bada and M. Kastner.
- Winter 1994: "Biochemical Evolution" (Chem 122), S.L. Miller, G.F. Joyce & L.E. Orgel.
- Fall & Winter 1994: "Physics and Chemistry of Surfaces: Course I & II" (SIO 269), G. Arrhenius.
- May 3, 1995: NSCORT Evening Discussion Seminar, Dr. James Ferris, Moderator, 6:00 p.m., San Francisco.Santa Cruz Room, UCSD Price Center. Invitation only.
- May 19, 1995: Seminar/Discussion, Prof. James Kasting, Department of Geosciences, Penn State University, 2:00 p.m., 4500 Hubbs Hall, SIO. Seminar open; Discussion by invitation only.
- May 22, 1995: Prof. Kurt Bostrom, Geochemistry Dept., University of Stockholm, "Biological vectors of trace elements", 1600 h, IGPP, Munk Conference Room.
- June 2, 1995: 7th Annual Society of Fellows Research Symposium, TSRI.
- June 7, 1995: Chemistry Evening Discussion, TSRI (Joyce lab presentations).
- Fall, 1995: "Surface Chemistry." (SIO 269), G. Arrhenius.

Meetings at Home and Away...

- Bi-monthly: Fellows Journals Club, 4502 Pacific Hall, Revelle College, UCSD.
- August 10, 1994: 2nd Annual Summer Student Meeting, UCSD / SIO. Keynote speaker: Dr. Gene McDonald
- May 11, 1995: Presentation of work on DNA enzymes (Joyce lab) at Table Ronde Roussel-Uclaf, Paris.
- May 24, 1995: American Society for Biochemistry and Molecular Biology, San Francisco, presentation on amidase ribozymes (Joyce lab) and receipt by Dr. Gerald Joyce of Pfizer Award in Enzyme Chemistry presented by the Division of Biological Chemistry of the American Chemical Society.
- June 14, 1995: Gordon Research Conference on "Nucleic Acids", New Hampton, NH, (Joyce lab presentations).
- July 2-14, 1995: Invited lecture "Ocean-atmosphere interaction in the first billion years" by Gustaf Arrhenius, XXI General Assembly, IUGG, International Union of Geodesy and Geophysics, Boulder, CO.
- August 6-11, 1995: "Scientist to Scientist Colloquium", The Keystone Center, Keystone, CO. (G. Joyce presentation).
- August 16, 1995: 3rd Annual Summer Student Meeting, UCSD / SIO.
- September 13, 1995: "The Year of Louis Pasteur International Symposium", Rockefeller University, NY. (G Joyce presentation).
- October 14, 1995: Indiana Molecular Biology Symposium IX, G. Joyce presentation.
- October 16, 1995: Jean Mitchell Watson Honorary Lecture, University of Chicago, given by G. Joyce.
- November 3, 1995: Annual NSCORT Review Committee, La Jolla.
- January 7-12, 1996: Gordon Conference "Origin of Life", Ventura, CA. Gerald Joyce, Chair (NSCORT co-sponsor).
- March/April 1996: Two-day visit by NSCORT Fellows to NASA Ames.
- July 1-5, 1996: Fifth International Symposium on Bioastronomy, Capri, Italy.
- December 27-30, 1996: National Science Teachers Association International Convention, San Francisco, CA. Symposium on "Origins of Life," J. Bada.
-

Final Word

(The Bada hypothesis as interpreted by RDT)

Life arose in arctic snow,
And not at the equator,
If you doubt it, watch it grow,
In your refrigerator.

The NSCORT/exobiology News is published surreptitiously two to four times a year at the Central Office of NSCORT/exobiology. To be placed on the mailing list or otherwise communicate with the perpetrators, write or phone:

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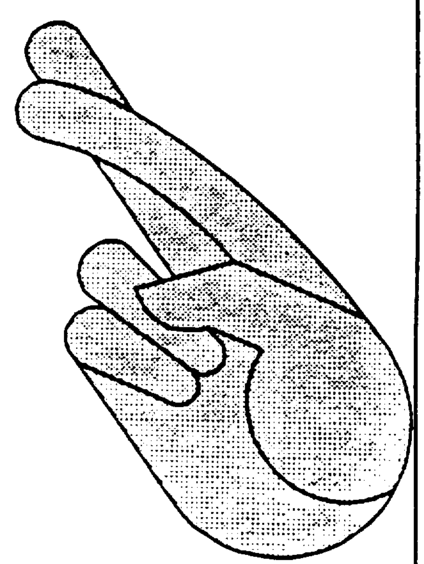
Editor: Prefers to remain anonymous, but can be contacted at the above address.

Robert Ischingi, Associate Director



NSCORT/ Exobiology

The *NASA Specialized Center of Research and Training (NSCORT) in Exobiology* is comprised of laboratories at the University of California, San Diego, The Salk Institute, and The Scripps Research Institute. These laboratories are both independently and collaboratively engaged in exobiology-related research.

Studies such as this—concerning the origins of life on Earth and the possibility of life elsewhere in the universe—are highly interdisciplinary in nature and draw upon the principles and techniques of paleobiology, molecular biology, biochemistry, organic chemistry, geochemistry, and geophysics.

One of the major questions in origins-of-life research is the relative contribution of terrestrial synthesis versus extraterrestrial sources (e.g. interplanetary dust particles and impacting meteorites) to the inventory of organic materials on the prebiotic Earth. To explore this question, the laboratory of Jeffrey Bada at Scripps Institution of Oceanography has undertaken an investigation of the amino acid content of polar ice core samples. Measured flux rates are extremely low, suggesting that ongoing delivery of interplanetary dust particles is not a major source of organic material on Earth.

The laboratory of *Stanley Miller* (Department of Chemistry, UCSD) has focused on terrestrial prebiotic synthesis. A number of biologically relevant compounds have been synthesized under simulated prebiotic conditions. This group has been active in pinpointing the difficulties that must have been overcome if nucleic acids were to have been available to biological systems on the primitive Earth. Perhaps life, at least nucleic-acid-based life, was not possible until the Earth's surface had cooled to more modest temperatures.

Steven Mojzsis in Gustaf Arrhenius' laboratory at SIO views the origins of life from a different perspective. Observations suggest that an operating cycle of marine sedimentation and mineralization was present before 3.87 billion years ago. Thus, the availability of liquid water is considered a necessary prerequisite for the origins of life.

The laboratories of Leslie Orgel at Salk Institute and Gerald Joyce at Scripps Research Institute have focused more on laboratory models of primitive biological systems than on the historical problem of life's origins. Rehe Liu, an NSCORT graduate student in the Orgel laboratory, has synthesized nucleoside analogues that contain nicotinamide in place of the standard bases. And, Xiaochang Dai in the Joyce laboratory has achieved an advance in the test tube that may recapitulate an advance that was made by evolving RNA molecules during the early history of life on Earth.

J. L. Bada

NASA Specialized Center of Research & Training (NSCORT) in Exobiology

Another CalSpace program is the *NASA Specialized Center of Research and Training (NSCORT) in Exobiology*. Established in January of 1992, the NSCORT program functions under the directorship of Dr. Stanley Miller, Professor of Chemistry, as a joint undertaking of investigators at UCSD, the Scripps Research Institute (TSRI), and the Salk Institute for Biological Studies (SALK).

NSCORT's focus is the field of exobiology, or the study of the origins of life and the forms it might take elsewhere in the universe. This eclectic field includes disciplines ranging from astrogeophysics to molecular biology, and is a prime example of a scientific discipline requiring close interaction among several arenas of research.

The primary function of the NSCORT/Exobiology education program is the training of young scientists to pursue research careers in exobiology and related subjects. Toward this end, the majority of the NASA grant's budget is devoted to fellowship support for graduate students and postdoctoral trainees. A summer program also provides laboratory experience at the undergraduate level.

Since its inception, NSCORT has granted 11 postdoctoral, 5 graduate student, and 19 undergraduate fellowships. In addition, 11 Adjunct Fellows have been appointed who participate in the education activities. Seminars and discussions by local and visiting scientists, biweekly Journal Club meetings, field trips, visits to off-campus laboratories, and attendance at scientific meetings are some of the vehicles used to provide community interaction among the Fellows.

Another segment of the NSCORT/Exobiology mission is to provide "outreach" activities which foster knowledge and understanding of this field throughout the scientific and public communities. Outreach activities include sponsorship of sessions devoted to exobiology at national and international conferences, articles in journals of general scientific readership, development of a high school curriculum on exobiology, and participation in various internship programs for teachers and students.

Inquiries about NSCORT/Exobiology programs and research activities should be addressed to Dr. Robert Tschirgi, Associate Director, NSCORT.

UNIVERSITY OF CALIFORNIA, SAN DIEGO

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NASA SPECIALIZED CENTER OF RESEARCH
AND TRAINING IN EXOBIOLOGY (NSCORT)
CALIFORNIA SPACE INSTITUTE, UCSD
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EXOBIOLOGY

SAN DIEGO CITY SCHOOLS

Mr. Stephen E. Brown
Science Teacher

LA JOLLA HIGH SCHOOL
750 Nautilus St. La Jolla, CA 92037
454-3081

The Exobiology Logo

The formation of primary self-replicating molecules is symbolized by the presence of energy, water and atmosphere. The initial atmosphere with its necessary chemical components appears as the background of wind and cloud. A lightning bolt represents the energy required to propel the nascent compounds toward increasing order, replication and evolution. Water, essential for all known life, falls as drops. The double helix of RNA/DNA emphasizes the subsequent evolution through the genetic code.

A CONSORTIUM OF:

The University of California, San Diego (UCSD)
The Salk Institute for Biological Studies (SALK)
The Scripps Research Institute (TSRI)

EXOBIOLOGY MINI-COURSE PILOT

Requirements:

- Attendance at 8 one hour seminar group discussions.
- Participation in developing a high school pilot mini-course in exobiology.
- Outside reading of eight *Scientific American* level research articles.
- Summary essay on topic of "Exobiology" due in January 1995.

Benefits:

- Exposure to current scientific research.
- Credit towards "Science Research Techniques" (SRT)
- Boost your G.P.A.
- Looks great on your transcripts for college admissions
- Letter of recommendation from LJHS and UCSD upon completion of summary essay.

*See Mr. Baron for sign up.
*See Mr. Brown for more details.

Course Outline/Syllabus

Themes/Areas of Research

1. **Solar system:** Evolution , origin and present state, exploration, cosmochemistry, nature of interstellar space, planetary chemistry, biogenic composition, molecular signals from space, molecules as interstellar probes.

2. **The "Origin of Life" as a Scientific Research Field:** Central concepts — Time, plausibility, temperatures, substrates, sites for possible chemical evolution, sources of prebiotic organic material, carbonaceous chondrites, infall, accretion, submarine hot springs, primitive earth atmosphere and ocean chemistry, constraints on development, annihilation by impactors, ozone, oxygen histories, ammonia, analytical techniques in exobiology research, chromatographic methods, PCR amplification, two-step laser mass spectrophotometry.

3. **Early-Earth Environment:** Geochemistry, prebiotic chemistry and evolution, understanding earth by comparison with other planetary compositions, experimental design and concepts involved with synthesis of prebiotic molecules, extraterrestrial organic matter in polar ices, modern oceans, lunar soils.

4. **Molecular Biology/Self-Assembly of Supramolecular Systems:** Self-replicating molecules, molecular attraction forces, optical activity, membrane models, plasmalemma, lamellae, phospholipid bilayer, surface phenomena (hydrophylic and hydrophobic forces), permeability, solute transport, facilitated diffusion, selective accumulation, encapsulation, vesicles, protocells, proteinoid microspheres.

5. **Energetics of Life's Origins:** Bio-energetics, sources of energy, energy yields, utilizations, transformations, catalytic pathways, enzymes and non-enzymatic pathways, photochemistry, electrochemistry, evolution of ion transport mechanisms, PROON gradients, pH and phase separation, charge separation, free energy, prebiotic respiration, glycolysis and photosynthesis, submarine hot springs, primitive pigment systems, photoreactive membranes and centers, surface metabolism before enzymes and templates, phosphates and bond energy.

6. **Bio-Information Molecules:** Macromolecular precursors, early-evolution of nucleic acids, nucleotides, purines, pyrimidines, base pairings, enzyme functioning, PNA, the RNA world, genetic molecular amplification to proteins, genetic apparatus, template directed polymerization, RNA polymerase, the primitive gene, ancestral genetic systems, functions of hereditary materials, possible formation and evolution, mineral catalysts, thermal copolymerization of amino acids to protein-like products, autocatalytic sets of proteins, early transcription from RNA to DNA, nucleic acid polymerases, ribosomes, biocatalyses reflect cell evolution.

7. **Searching for Evidence of Life Beyond Earth:** Definition of "Life", cosmic origin and evolution, the big bang, biogenic elements, molecules and compounds, chemical and prebiotic evolution, formation of the solar system, SETI and HRMS.

SPACE OUTLOOK

WISCONSIN
Space Grant Consortium

Volume 5, No. 2

July, 1995

HIGHER EDUCATION

HIGHER EDUCATION INCENTIVES PROGRAM

The Wisconsin Space Grant Consortium is delighted to announce that three outstanding undergraduate teachers have received Higher Education Incentive Grants for 1995-96.

Professor Vera Kolb, Department of Chemistry, UW-Parkside to develop a two-semester 1995-96 space sciences lecture series for the entire campus in coordination with the UW-Parkside Departments of Physics, Chemistry, and Geology and the Lectures and Fine Arts Programs. The featured speaker will be distinguished marine chemist Jeffrey Bada from the Scripps Institute of Oceanography.

How to Build A Space Science Community

Vera Kolb
Department of Chemistry
UW-Parkside
WSGC Institutional Representative

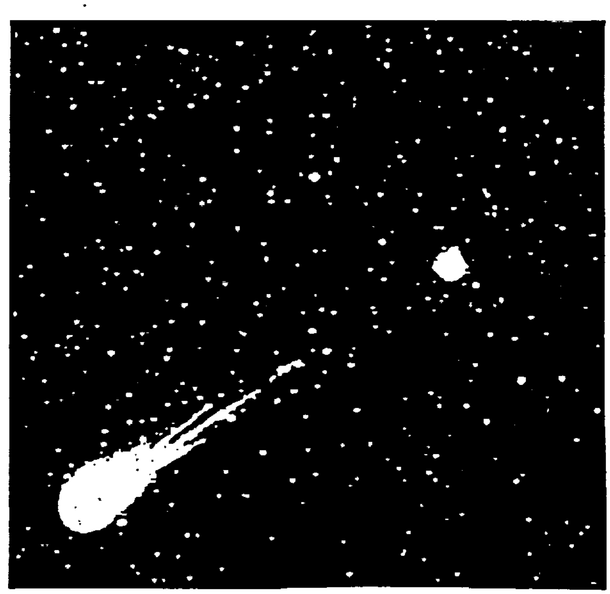
From 1992-1994, I was on a sabbatical leave at the Salk Institute in San Diego, California, doing research on the origins of life on Earth. My research was sponsored by the NASA Specialized Center for Research and Training (NSCORT) in Exobiology. It was a really exciting time for me. In addition to doing very important research, I had an opportunity to attend most interesting seminars on various aspects of space science: from meteorites to climate on early Earth, from chemistry in primordial soup to chemical evolution in the test tube, from interstellar chemistry to search for life elsewhere in the universe. These seminars were sponsored by the NSCORT, California Space Institute, the Salk Institute, University of California-San Diego, the Scripps Institute of Oceanography, and the Scripps Research Institute.

After returning to Parkside, I knew that I was going to miss the excitement of the weekly seminars I had gotten used to. It was an easy and enjoyable way to learn space science. Also, I was anxious to recruit research students and connect with my colleagues who might have an interest in space science. Where was I to start?

I decided to organize a space science seminar series and see if there would be interest in it. First, I recruited our physicist Jim McCrickard, whom I knew had an interest in space sciences since he teaches astronomy. Jim and I put the program together. I called the speakers, Jim reserved the lecture rooms and was in charge of the audio-visual equipment. We made a flyer, and advertised in the science departments and in our classes.

We had three internal and three outside speakers. The latter were sponsored by the WSGC. The topics were arranged in a bottom-to-top approach. We started with the origin of the universe, moved to the age of the Earth and evolution of planets, provided a necessary break with a lecture on science fiction, moved to the origins of life on Earth, and finished with the biomedical aspects of weightlessness.

To our great surprise and delight, the series has been a huge success. The attendance, by both faculty and students, was great. We had at least 60 people per lecture, but some lectures drew crowds of 100 or more people. It was also gratifying to see our emeriti professors attending. The discussion period after each lecture was lively, with many interesting questions from the students and professors in the audience.



The lecture series helped build the space science community at Parkside. I discovered that there are chemists, biologists, geologists, and physicists at Parkside who have both interest and expertise in some aspects of space science. Students have been an eager and enthusiastic audience. Four students have joined my laboratory and have carried out space-related research this past semester.

If you wish to have your own space-science series, we hope that our positive experience will encourage you to implement it. Good luck.

Certificate of Appreciation

Presented to

NASA Center of Specialized Research and Training in Exobiology at the California Space Institute, UCSD

With thanks for generously supporting the 1995 National Science Teachers Association National Meeting

Space Life Sciences Outreach Coordinator

8/8/95
Date

JUNIOR SCIENCE & HUMANITIES SYMPOSIA

May 6, 1996

Professor Robert Tschirgi
UCSD
LaJolla, CA 92093

Dear Professor Tschirgi:

On behalf of the U.S. Army Research Office and the Office of Naval Research, please accept my thanks for your support of the U.S. Army and Navy sponsored 34th National Junior Science and Humanities Symposium, held April 25 - 28, 1996, in San Diego.

Your support as a judge of the National student research paper competition was a valuable contribution to our program. Many of our participants commented on the outstanding conduct of the National JSHS judging. Even the student competitors commented on the fairness of the competition and your sincere interest in their research. Your support allowed us to provide a positive learning experience not only for the student competitors but also for the many other talented students who were in the audience. Your contributions are sincerely appreciated.

Again, thank you for your invaluable support of the U.S. Army and Navy's 34th National Junior Science and Humanities Symposium. I hope you enjoyed your participation!

Sincerely,

Doris Ellis Cousens
Director, National JSHS

Funded by the Departments of the Army and Navy
Administered by The Academy of Applied Science
P.O. Box 2934 ◆ Concord, New Hampshire 03302-2934 ◆ Tel. 603/228-4520 ◆ FAX 603/228-4730

Robert H. Rines, President
Doris Ellis Cousens, Director, National JSHS, Email: cousensaca@aol.com
Kate Trojano, Business Administrator, National JSHS, Email: ktacademy@aol.com

JUNIOR OCEANOGRAPHERS CLUB

Tuesday, May 21, 1996
7:00 pm
Stephen Birch Aquarium Museum

Speaker: Steve Mojzsis
Scripps Institution of Oceanopgrahy
Geological Research Division/UCSD

Title: "How Old is the Earth?"

The question of the age of the Earth, and of life on Earth, has been asked by every culture since the beginning of humanity. Lately, new clues about when life could have arisen on our planet are being uncovered by scientists. Join graduate student, Steve Mojzsis, from the NASA NSCORT/Exobiology Center at SIO for an historial review of what we know, and a preview of what we can learn about the age of life on planet Earth.

NSCORT/Exobiology Outreach

Elementary Grade Level Education

"The Adventures of Percy the Proton"

created and written by
Quinn Maughan at UCSD Chemistry
QMaughan@chem.ucsd.edu

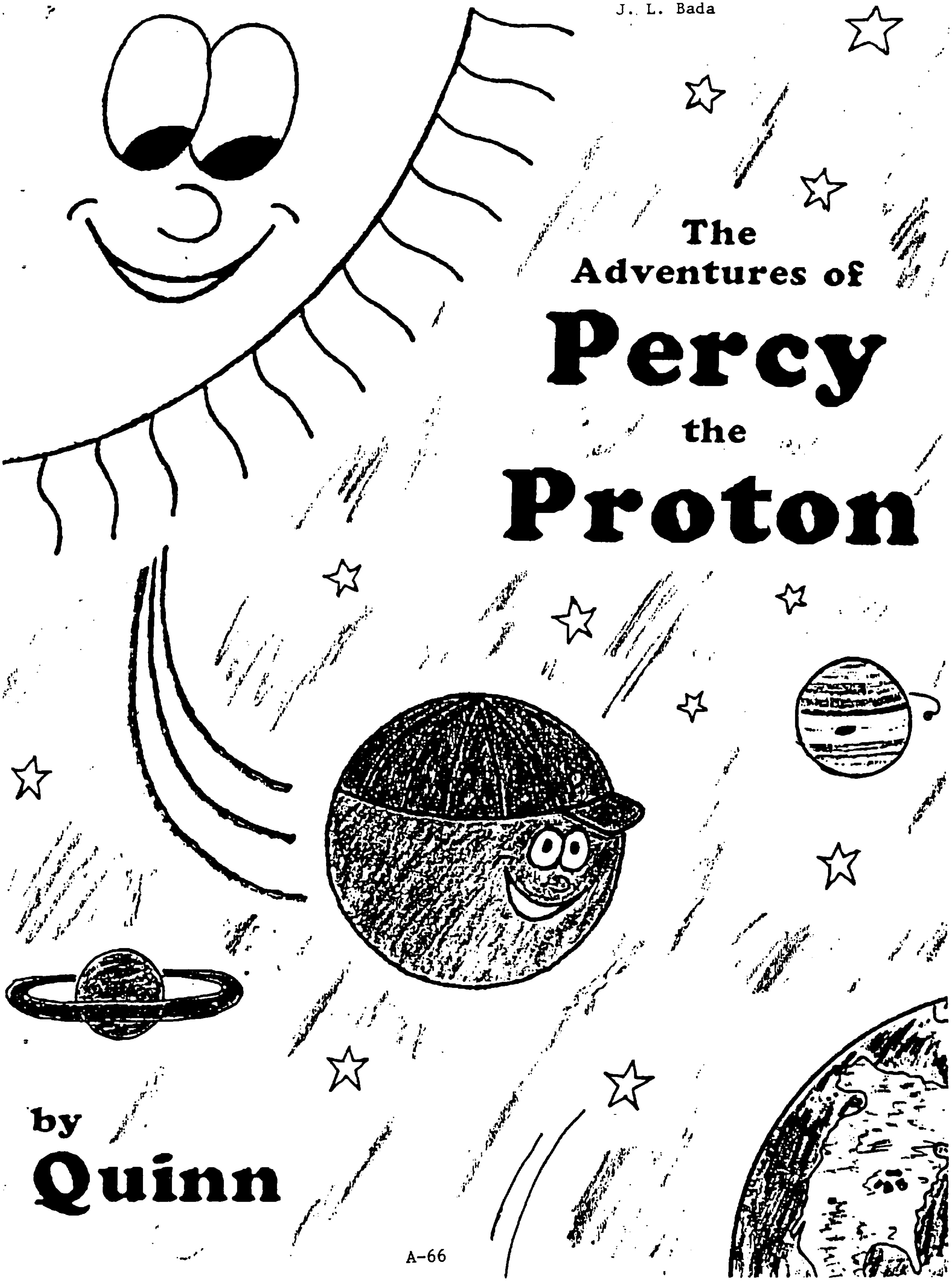
classroom pilot tested by
Stephen Brown at La Jolla High School
http://www.sdcs.k12.ca.us/schools/ljhs/home.html

Summary:

One hundred and fifty secondary level science students, ages 15-17, at La Jolla High School were presented with the educational story: "The Adventures of Percy the Proton". Each student was also presented with a pre-test and post-test questionnaire along with its introduction. The data compiled from these questionnaires has shown a significant increase in the understanding of basic atomic structure and formation of the universe, sun, and Earth, for the majority of these students.

Our intentions are to administer this same lesson at the elementary grade level and identify appropriate reading level effectiveness comparisons. The written student feedback will be used to modify and extend the depth of the subject content included in the introductory story as well as in additional stories to follow. These will be used for additional classroom trials. This elementary grade level lesson will be enriched with student activities relating to the understanding of science as our trial effectiveness increases. "The Adventures of Percy the Proton" is to become a principal component of our broader outreach efforts and will be translated for our Spanish speaking students for additional trials.

Our entire NSCORT/Exobiology outreach program will be available to classroom teachers via the internet by accessing: "chem-net" at the url: http://grove.ucsd.edu/~jyeh/intro.html.



The Adventures of Percy the Proton

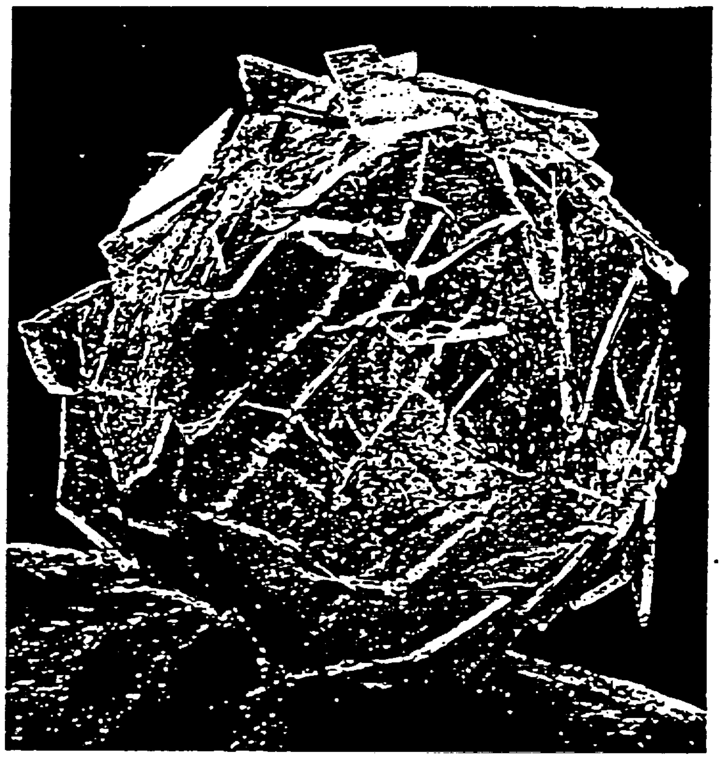
by Quinn

THE SCIENCES
MAY/JUNE 1995

COLD START

The first life may have evolved out of a chilled organic soup that brewed under a thick layer of ice

BY JEFFREY L. BADA



Andy Goldsworthy, Thin Ice, Frozen Scaurwater, Dumfreisshire, *10–11 January 1987*

SOME STORIES are so compelling they bear retelling many times. So it is with scientific stories about the beginnings of life. Forty-two years ago, at the University of Chicago, a young graduate student named Stanley L. Miller set out to reproduce the conditions that gave rise to life on earth. With a simple circuit of glass tubing he connected two flasks. Into one flask he poured water, an early ocean in miniature; into the other he released a mixture of methane, ammonia and hydrogen, to represent primeval air. He zapped the atmosphere nonstop with an electric arc, the laboratory equivalent of lightning. When he turned off the spark a week later, the miniature ocean had turned the color of tea. Chemical analysis showed that it was loaded with organic compounds, including several amino acids, the building blocks of proteins—key players in the processes of life.

The scientific community was jubilant. "If God didn't do it this way," Miller's adviser, the Nobel laureate chemist Harold C. Urey, remarked half jokingly, "he missed a good bet." The bet he had in mind was an atmosphere with a strong tendency to trigger chemical reactions by donating electrons—in chemical terms, a reducing environment. Later, Miller as well as other scientists, including the planetary astronomer Carl Sagan of Cornell University, ran similar experiments with various reducing mixtures of gases and with other sources of energy, such as ultraviolet light. The almost invariable result: a rich organic brew—prebiotic soup.

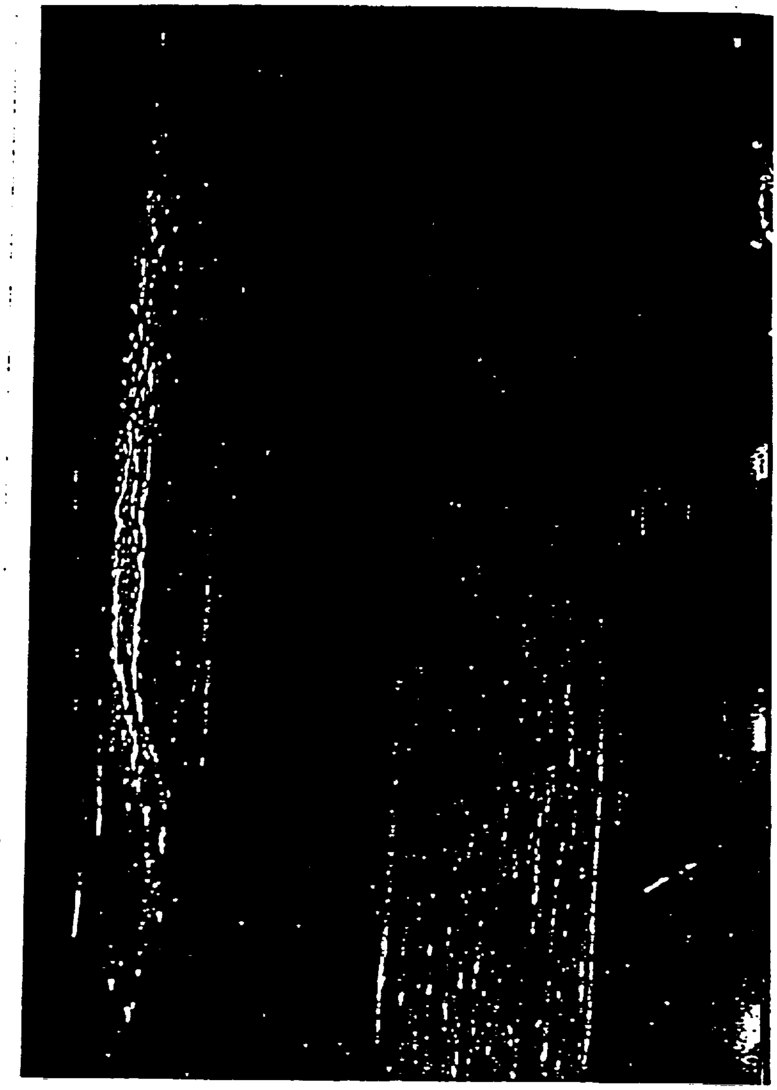
Then came the backlash. Biochemists showed that to turn even the richest prebiotic soup into a single-celled organism would take more than time and good wishes. Some even suspected that proteins, and thus amino acids, had played little or no role in the earliest organisms. Atmospheric chemists, meanwhile, had found what they considered fatal flaws in the mixtures of gases that Miller and his successors had used in their reactions. In the real atmosphere, they pointed out, methane and ammonia would have quickly disintegrated under the influence of ultraviolet light. Most came to favor a more stable mixture of gases with drastically different chemical properties.

In recent years many investigators studying the origin of life have taken an approach different from the one Miller took: they have worked backward in time to determine how the intricate machinery of the living cell might have arisen from simpler precursors. Most workers now believe that some of the most fundamental features of modern cells (including the genetic code based on DNA and a biochemistry dependent on enzymes made of proteins) did not exist in the earliest life. Many biochemists now speak of an RNA world—a realm of life in which, before the first modern cells emerged 3.5 billion years ago, all of the major functions of life were carried out by ribonucleic acids, chemical cousins of DNA. [See Christian de Duve's article "Prelude to a Cell," *The Sci-*

ences, November/December 1990.] Some investigators are trying to trace life back further still, into even more exotic pre-RNA worlds in which the processes of life were conducted by a much different set of organic polymers.

Stanley Miller's back-to-basics approach is still thriving, however. In the NASA Specialized Center of Research and Training in Exobiology, Miller and I and colleagues at the University of California, San Diego, and the Scripps Research Institute and the Salk Institute for Biological Studies in La Jolla, are investigating the conditions that gave rise to life on earth. We start with a simple premise: that at least 3.8 billion years ago organic molecules in the earth's ocean initiated the self-replicating chain reaction that can be regarded as the beginning of life. Then we ask: Where did the prebiotic soup come from? How could the earth and its atmosphere and oceans have developed into a reactor capable of producing it? What sort of reactor would have brewed the *best* prebiotic soup? What other steps would have been necessary to set the stage for the origin of life?

Our work so far has thrown out some clear challenges to the conventional wisdom. Among other surprising conclusions, Miller and I believe that life on earth started in what at first glance looks like a most unlikely place: in a frigid ocean, under hundreds of feet of ice.



IN MANY WAYS, THE EARTH ON WHICH LIFE emerged 3.8 billion years ago was an alien world. It was a young planet, having condensed from dust and gas only 700 million years earlier. Its surface was probably about 97 percent water. There was no oxygen in its atmosphere. Its interior was more radioactive, and thus hotter, than it is today. The sun, however, was much cooler, shining (according to the latest models of stellar evolution) 20 to 30 percent less brightly.

The early earth was violent, subject to frequent collisions with comets, meteorites, asteroids and other debris left over from the formation of the solar system. According to a scenario known as the impact-frustration hypothesis, the bombardment was fierce enough at first to boil the seas, killing off any early organisms; only about four billion years ago did things settle down. Then life developed swiftly and never died out.

All of those characteristics place important constraints on chemical models of the early earth. The persistence of life is particularly important: it implies that for almost four billion years the overall temperature of the earth has stayed between zero and one hundred degrees Celsius, the freezing and boiling points of water.

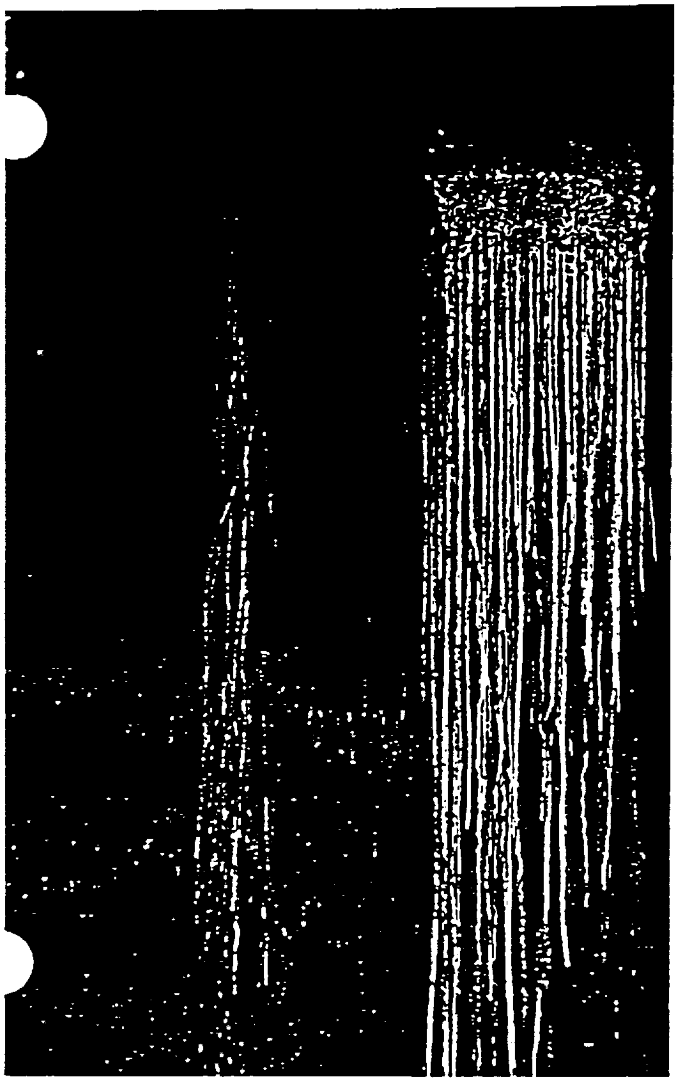
The lower end of that temperature range is particularly dangerous, because the earth, once frozen, would be hard to thaw. Ice is more than three times as reflective as water (in technical terms, it has a higher albedo), and once it forms, it repels heat that otherwise would melt it. If the earth were to freeze tomorrow, it would take a star 30 percent more luminous than the sun to melt it. For that reason most theorists take it as axiomatic that the earth has never frozen, and models of atmospheric evolution almost always include a generous dollop of greenhouse gases—especially in the days of the faint young sun.

Both methane and ammonia are greenhouse gases, and in theory, a Miller–Urey atmosphere could trap enough heat to keep the earth from freezing. The problem is that each gas would quickly break down under sunlight. That is why most atmospheric scientists now favor an early atmosphere of nitrogen and carbon dioxide, similar to the atmosphere today but with two major differences: it was free of oxygen (a later by-product of life), and it included thousands or even tens of thousands times as much carbon dioxide (necessary to offset the lower solar luminosity).

THE ONLY THING WRONG WITH THE CARBON dioxide–nitrogen atmosphere is that it is useless for engendering life. Chemically it is all but inert. Pump it into Stanley Miller's flasks and jolt it with electricity (an experiment that Miller and others have tried), and you will get . . . carbon dioxide and nitrogen—nothing more exciting than that.

So where on earth did prebiotic soup come from?

The answer, according to some biochemists and planetary scientists, is that it came from *nowhere* on earth. Conditions on the early earth were too hostile, they say: life, or



Pat Steir, Waterfall of the Fundiments, *1990*

the chemical precursors of life, must have come from outer space. That idea surfaced early in this century, when the Swedish physicist and chemist Svante A. Arrhenius proclaimed with almost missionary zeal a hypothesis he called panspermia (seeds everywhere): life, he said, had drifted to earth in a cloud of space-faring spores or microorganisms. In 1981 the English molecular biologist and codiscoverer of the structure of DNA, Francis H. C. Crick, proposed an even more radical hypothesis: directed panspermia, the idea that the seeds of life were sent to earth by intelligent extraterrestrials. Such ideas are impossible to test, and they beg the real question: How did the supposed seeding organisms, intelligent or otherwise, come to exist?

Other investigators have suggested that what came from space was not life itself but the raw ingredients of life, organic molecules. That possibility is worth investigating. Simple organic molecules such as hydrogen cyanide (HCN) and even ethyl alcohol (C_2H_5OH) have been detected spectroscopically in interstellar dust clouds, and more complicated organic molecules—including amino acids—have been found in the kind of meteorites known as carbonaceous chondrites. The Murchison meteorite, which fell near a small town in Australia in 1969, contains at least seventy-four amino acids, including eight or more of the twenty amino acids that make up proteins in organisms on earth.

Did extraterrestrial molecules stock the prebiotic soup? To test that possibility my colleagues and I have investigated whether extraterrestrial molecules are still falling to earth or have done so in the geologically recent past. As an indicator of such molecules we tested for alpha-amino-isobutyric acid (AIB), an amino acid that is extremely rare on the earth but common in some extraterrestrial bodies that have fallen to earth. We searched for this amino acid in ice cores from Antarctica and Greenland and in fallout from two major impacts: the 1908 Tunguska event, in which an object from space exploded over Siberia with the force of a small nuclear blast; and the famous sixty-five-million-year-old impact at the Cretaceous–Tertiary (KT) boundary, which may have caused the extinction of the dinosaurs.

Unfortunately for the theory of extraterrestrial seeding, in all the samples we checked the amounts of AIB deposited were either undetectable or pitifully small. Only one ice sample, approximately 4,500 years old, showed detectable quantities of AIB. Ice samples dating from 1908 showed no traces of it, indicating that the Tunguska object did not deliver an appreciable organic signal to the earth.

In sediments from the KT boundary, we measured about 0.00005 gram of AIB for every square centimeter of the KT-boundary surface. If similar amounts of AIB were distributed over the entire surface of the earth (a generous assumption), then, in chemical terms, they would have created a two-billionths molar solution of AIB. That is like stirring a teaspoonful of sugar into a six-foot-deep swimming pool the size of a football field—too dilute a soup, in my opinion, for any kind of organic chemistry. The 4,500-year-old event recorded in the ice would have created a similarly dilute AIB solution. Even if (as Sagan and his colleagues have estimated) cosmic debris struck the prebiotic earth at 10,000 times the present levels, the resultant prebiotic soup would still have been much too weak, I believe, to engender life.

AT BEST, THEN, THE LIFE-FROM-SPACE HYPOTHesis comes off as a desperate attempt to explain how life could have formed in a fundamentally hostile environment. It would make far more sense to take the obvious given—that life exists—and ask under what conditions it was most likely to form. As the Miller–Urey experiment showed, a reducing environment gives rise to organic molecules in concentrations orders of magnitude higher than does even the most optimistic alternative scenario. The logical follow-up is to ask another question: How could such an environment have come about?

The scenario we propose rests on a small but critical leap of logic. The Miller–Urey experiment assumed that the key ingredients for any earthly prebiotic soup must have originated in the earth's atmosphere. The most important reactions in its abiotic synthesis, however, took place not in air but in water. The amino acids in Miller's reacting vessels, for instance, came about via a reaction pathway known as the Strecker synthesis, developed in 1850 by the German–Norwegian chemist Adolph Friedrich Ludwig Strecker:

An Early Earth?

Jupiter's moon Europa could be a good model of what our planet looked like four billion years ago

"THE PAST IS A FOREIGN COUNTRY," THE ENGLISH WRITER L. P. Hartley observed in his novel *The Go-Between.* For Jeffrey Bada and other proponents of an ice-covered early earth, however, the past might well be orbiting around another planet. Searching for evidence to bolster their theories, they have combed the solar system for worlds that might shed light on the geophysical and geochemical processes that once held sway closer to home. One of the most promising candidates is a frigid body slightly smaller than the earth's moon and five times as far from the sun as the earth is. It is Europa, the next-to-innermost large moon of the planet Jupiter.

In February, Europa made headlines when astronomers studying images from the Hubble Space Telescope concluded that oxygen is present in its atmosphere. The oxygen is a byproduct of water vapor rising from the material on Europa's surface: a thick shell of slightly dirty, rock-hard H_2O—water ice. It is the ice, not the oxygen, that excites Bada and other investigators. As Europa orbits Jupiter, tidal stresses from the giant planet's varying gravitational pull squeeze the moon, causing internal friction. In the early 1980s the planetary scientist Ray T. Reynolds of the NASA Ames Research Laboratory in Moffett Field, California, and other investigators showed that, in theory, the friction should generate enough heat to maintain a layer of liquid water beneath the surface. The result could be a global ocean capped with a frozen ceiling kilometers or even tens of kilometers thick.

In short, Europa might resemble a scaled-down working model of Bada and Miller's frozen earth. That could be a godsend for theorists trying to trace the evolution of our planet—if the hidden ocean is really there. Is it? Nobody can be sure, Reynolds cautions, but there is some tantalizing circumstantial evidence. Images transmitted back to the earth in the 1970s by Pioneer and Voyager space probes revealed that the icy surface of the Jovian moon is scored with dark lines that look like fissures. Apart from that, however, Europa is amazingly smooth—a sharp contrast to the meteor-pocked exteriors of its neighboring moons Ganymede and Callisto.

"There should be craters of all ages on the surface, and we don't observe them," Reynolds says. "What that means is that something is removing them."

That something could be a sign of a sub-Europan ocean. If liquid water does flow beneath the surface, then, Reynolds suspects, the relatively warm ice above it would tend to creep, gradually erasing large craters. Small craters could perish more dramatically, when fractures in the ice reach the ocean, unleashing geysers of cold steam that recondense in a rain of frost. In principle, such geysers could be detected from the earth by a sharp rise in the water content of Europa's atmosphere. No one has ever seen anything like that, but Reynolds says he will be looking hard at the high-resolution images the *Galileo* space probe will send back when it reaches the Jovian system in early December.

All of which is a far cry from saying that Europa does, or could, harbor life. On the contrary, says Doyle T. Hall, an atmospheric scientist at Johns Hopkins University and a member of the team that discovered the oxygen: every part of Europa is hostile if not inimical to life. The atmosphere is negligible. The ocean, if one exists, is swathed in perpetual darkness and burdened with immense pressure from the overlying ice. And in between, on the moon's surface, lies a radioactive hell.

"Europa is orbiting inside Jupiter's magnetic field, and inside that magnetic field there are a lot of energetic particles—radiation to you and me," Hall says. "If you could magically go there and stand on Europa, it would probably be like getting a chest X ray every second or two. Basically, any organic matter on the surface is going to be torn apart."

That's a pity, because in some respects Europa has the makings of an attractive piece of real estate. Five billion years from now, Reynolds says, the sun will enter the red-giant phase of stellar evolution. As it swells to engulf Mercury and Venus, its heat will turn the earth into a cinder and, somewhat later, melt all the ice on Europa. "It won't last very long, but it looks as if there will be a period of a few hundred million years, very far in the future, when there may be oceans on Europa."

—PAMELA SUE FROST

gaseous hydrogen and methane reacted to produce slightly more complex molecules called aldehydes and ketones, and hydrogen cyanide, a lethal poison today. Those molecules then reacted with ammonia *in water* to produce amino acids. The reducing environment needed to pave the way for life was not the atmosphere but the ocean.

We propose that on the prebiotic earth, the atmosphere and the ocean were divided at least sporadically into two separate reacting vessels. How could that have come about? Easily. Suppose the early atmosphere had the "wrong" composition, too thin a blanket of greenhouse gases to keep the warmth of the faint young sun from leaking away into space. Suppose the ocean froze. Suppose, contrary to the conventional wisdom, that the whole earth was sheathed in ice. What then?

For one thing, the ocean would not have frozen all the way to the bottom. Even today, radioactive decay in the earth's interior causes heat to flow outward through the ocean bottom, warming the waters at a rate of about eight-hundredths of a watt for every square meter of ocean floor. Four billion years ago the heat flow may have been about three times as strong. If the surface temperature of the ice was minus forty degrees Celsius, a simple calculation balancing the heat flow from the ocean floor to the atmosphere shows that the ice layer would have been about 300 meters thick. Most of the ocean, to an average depth of several kilometers, would have stayed liquid (albeit at a bracing minus two degrees Celsius).

The icy water could easily have steeped into a prebiotic broth. Methane and ammonia bubbling up through hydrothermal vents could have provided the raw ingredients for processes such as the Strecker synthesis. The cold would have prolonged the life spans of organic molecules, making it much more likely that a chemical complex would participate in a productive reaction. The important organic building block hydrogen cyanide, for instance, lasts an average of 1,000 years at fifty degrees Celsius but a hundred times as long at zero degrees Celsius. Trapped under the ice, the molecules would accumulate year after year, century after century, forming a rich fertilizer for organic synthesis.

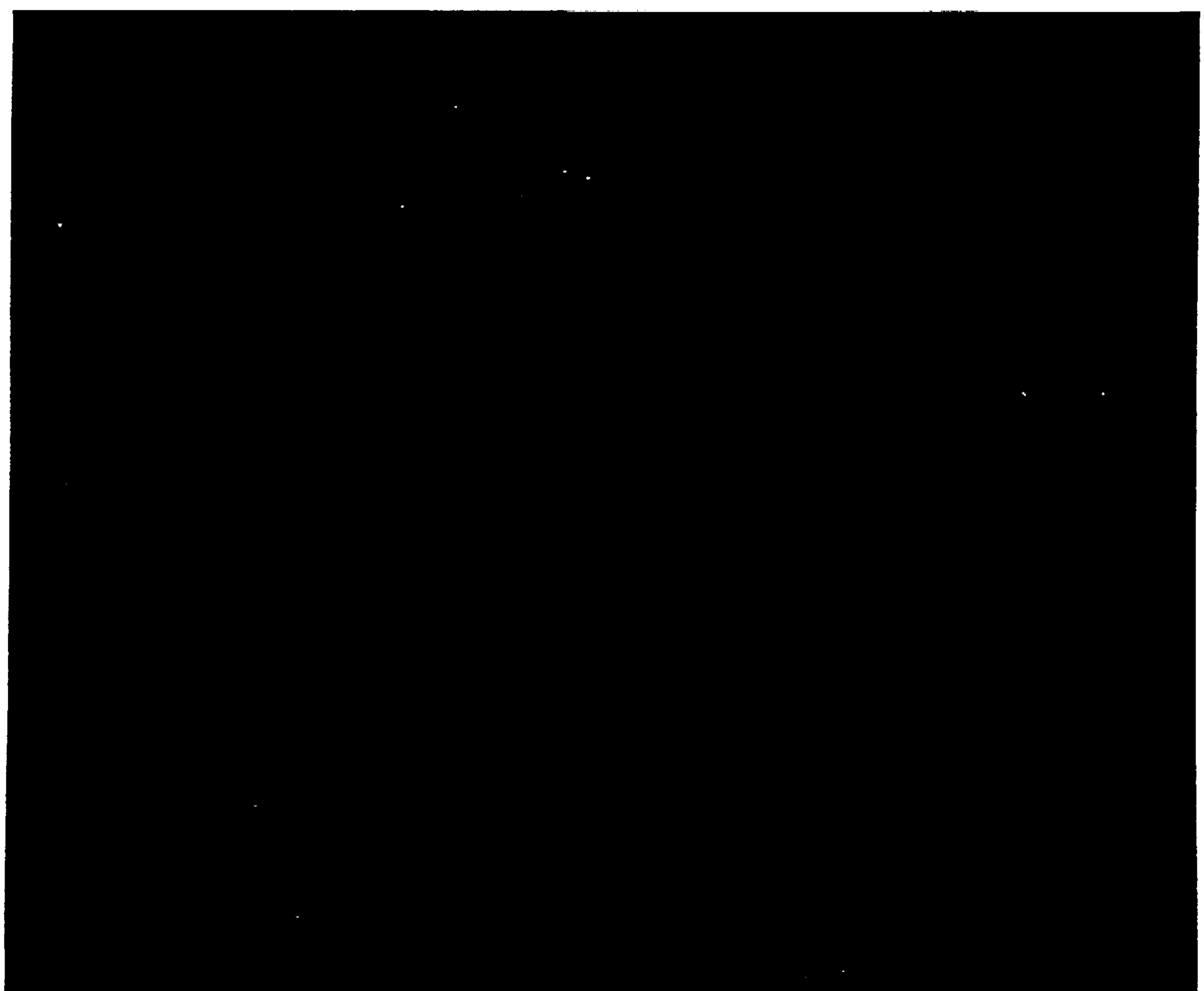
Under such a scenario, what goes on above the ice becomes much less important than what goes on underneath it. Theorists may pick and choose from a wide variety of possible atmospheres, ranging from a classical Miller–Urey mixture to the currently favored carbon dioxide–nitrogen, only with much more moderate levels of carbon dioxide. Thinking the unthinkable has its rewards.

WHAT ABOUT THE ALBEDO EFFECT? A FEW paragraphs ago I said that a frozen ocean would stay frozen forever. Yet only last week I left my office in La Jolla and went running on the beach, and the ocean was anything but frozen. What drove away the ice?

Only one answer is possible, and it arrives trailing a pleasing dose of irony. Cosmic collisions could have done the job. According to a model by the geophysicist Norman Sleep of Stanford University and his associates, when an extraterrestrial object strikes the earth, 75 percent of its kinetic energy ends up buried at the site of impact or dispersed into space; the rest of the energy heats the atmosphere. A simple calculation shows that a chunk of debris a hundred kilometers across could have melted all the ice on earth. It is possible that a much smaller body—similar to the one that struck the earth at the KT boundary—could have melted the ice, if it made a large enough hole. Thanks to the albedo effect, such a hole would gather heat, widen, suck in more heat, and widen further, triggering a runaway melt.

If a global ice shell did exist, there is no way of knowing the exact circumstances of its demise. Perhaps one impact was enough to melt it forever. Perhaps the earth passed through several cycles of impacts and freezes, each new melt enabling a fresh burst of gases to bubble out of solution into the atmosphere; each new freeze ratcheting the prebiotic soup toward greater chemical sophistication. In that case, the vision of life under ice starts to look a little like panspermia-through-the-looking-glass, with extraterrestrial visitors cast not as instigators but as liberators. It also makes a nice coda to the impact-frustration hypothesis, framing the emergence of the first organisms in the silence between two cosmic drum rolls: a long one that boils the oceans and delays the advent of life; then a short one that thaws the ice and sets life free. •

JEFFREY L. BADA is a professor of marine chemistry at the Scripps Institution of Oceanography, University of California, San Diego. *He thanks Robert J. Coontz Jr. for editorial assistance in preparing this article.*



William Baziotes, Opalescent, *1962*

This is one of a series of "Public Forum Lectures" given at NASA Headquarters in Washington, DC to establish the future direction of the NASA mission. This "Science of Life" lecture was given by Leslie Orgel on January 23, 1995.

TO BOLDLY GO: AMERICA'S NEXT ERA IN SPACE

"Signs of Life"

Leslie E. Orgel

The Salk Institute for Biological Studies
Post Office Box 85800, San Diego, CA 92186-5800, U.S.A.

The big question is, "Is there life elsewhere in the Universe?"

Tonight I consider one aspect of the problem — How do you recognize life if it doesn't communicate with you or try to eat you? I discuss this from the point of view of an organic chemist. Lyn will discuss other approaches.

First we need to say what would count as life. Roughly speaking — something with too much organized complexity to have arisen by chance and which must, therefore, have arisen by natural selection.

We are unlikely to recognize life if it is not dependent on carbon chemistry — so we look where the light is and analyze for organic molecules.

The signs of life are then the appearance of organic compounds with more specificity than can be accounted for by the straightforward organic chemistry of a planetary environment. Examples: Optically active compounds — pure compounds where we expect mixtures — specific sequence polymers where we expect random copolymers. (On the earth we would see proteins rather than random mixtures of peptides.)

NASA's likely contributions:

Mars landings to see what is there.
Laboratory simulation to see what to expect.
Studies of organic chemistry on Titan and on comets to verify our ideas about abiotic synthesis.
Studies of the Origins of Life on our own Planet — for comparison.

Dr. LynnMargolis was co-lecturer for this topic.

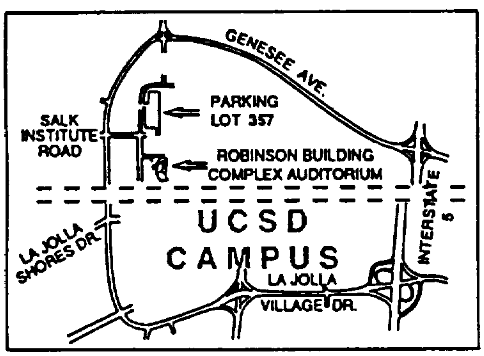
PUBLIC LECTURE

The Great Silence: Is Anybody Out There? The great debate over whether humanity is alone in the cosmos.

Featured Speaker: David Brin, Ph D

Robinson Building Complex Auditorium
International Relations and Pacific Studies
Marshall College
University of California, San Diego

Tuesday, April 16,1996
3:30 pm ~~ Refreshments
4:00-5:00 pm ~~ Lecture



Free reserved parking is available in Lot 357
Enter UCSD/Marshall College on
Salk Institute Road (East) and follow
"Brin Lecture" directional signs.

Sponsored by
The NASA Specialized Center of Research
& Training (NSCORT) in Exobiology
University of California, San Diego
La Jolla, California

Additional information:
NSCORT Central Office (619) 534-1891

David Brin, Ph.D has a triple career as scientist, public speaker and author. His novels, such as *The Postman* and *Startide Rising* have appeared on the New York Times Bestseller List and have won widespread literary acclaim, as well as multiple "Hugo" and "Nebula" awards. As a lecturer, Brin is in demand to give talks about various aspects of technology and the human future. (His 1990 novel, ***EARTH***, is widely credited as including one of the best prognostications of the worldwide data networks of tomorrow. Brin was a fellow at the California Space Institute. More recently he has been a research affiliate at the Jet Propulsion Laboratory and participated in interdisciplinary activities at UCLA's Center for the Study of Evolution and the Origin of Life.

THE SAN DIEGO UNION-TRIBUNE • SUNDAY, JANUARY 8, 1995

Virus-cutter DNA may be within reach

By DAVID GRAHAM, Staff Writer

DNA, the genetic blueprint of life, now can be even more than a template from which future generations are shaped, thanks to some manipulations by La Jolla scientists.

The master molecule can be changed so that it takes on new duties, acting like a pair of molecular scissors that can cut other molecules. And researchers think the new DNA molecule might be used as a drug that can attack cancers and potent viruses, such as AIDS or herpes.

Wound in strands inside the body's cells, DNA holds the instructions for building every organ in the body. It is the genetic inheritance of future generations.

But it had never been known to cleave other molecules until chemists at The Scripps Research Institute forced ordinary DNA to "evolve" in test tubes to take on the new role.

"Nature never obliged us with DNA that acts like an enzyme (and cuts), so we obliged ourselves and made one," said Gerald Joyce, a Scripps biochemist.

The discovery was reported in the British journal *Chemistry & Biology*.

Beyond the intellectual excitement of manipulating the basic material of life, scientists believe the discovery opens the possibility of new drugs that attack viruses in fundamental ways.

In recent years, researchers seeking to thwart viruses have experimented with a copy of DNA the body makes, called RNA, that acts like a molecular scissors in the body to help build tissues and organs at the microscopic scale.

In this approach, the RNA attaches to a part of the genetic material of a virus or of the gene that contributes to cancer. It then snips the genetic material in a chemical reaction so that the virus or cancerous cell cannot reproduce.

The scissors-like RNA is carefully chosen so it will recognize and chop only the specified material, which also happens to be an RNA, and spare healthy tissue in the body. A person receives the drug as a simple injection.

The approach is a potentially elegant one because it attacks disease at a more fundamental level, but RNA tends to degrade quickly in the body, before it can kill sufficient virus particles.

The DNA chemical is "a million times" more stable, raising the possibility of a more effective drug, Joyce said.

"What he's done is a real advance," said biochemist David Ecker, a vice president of Isis Pharmaceuticals Inc., a Carlsbad biotechnology company pursuing similar drug strategies against viral infections and inflammation.

Because DNA is more stable, drugs made with it might last longer in the body, and fewer doses might be required.

UCSD biologist Flossie Wong-Staal is attempting to treat AIDS patients by using an RNA scissors to snip the virus' genetic information.

Joyce and colleague Ronald Breaker found the new DNA by taking 100 trillion strands of DNA and exposing them to RNA and asking, "Who among you can cleave RNA?"

The DNA strands, comprised of four basic chemicals, were produced in random combinations by a machine.

After a few hours, Joyce found thousands of the strands that in fact could cling to the RNA and could cause a chemical reaction that would cut it. He then repeated the experiment with the successful strands until he isolated eight that were particularly fast.

"We had a DNA molecule that could cut RNA at a rate of one a minute," Joyce said.

The designed DNA is different from most found in cells because the designed DNA has only a single strand. That found in nature has the double helix shape identified by Nobel laureates James Watson and Francis Crick. Crick is now the interim president of the Salk Institute in La Jolla.

Joyce's work is related to other experiments in which he is trying to understand how life could have begun on Earth from inert chemicals.

He is testing the genetic material RNA to see if it can be coaxed to start making copies of itself. Such molecules that replicate themselves would be considered alive.

Despite the newly demonstrated ability of DNA to cleave molecules, Joyce said it probably was not the seminal molecule for life. But many believe RNA could have been. RNA is a "hotter molecule," much better at producing chemical reactions that likely would be necessary for rudimentary life forms, Joyce said.

Experiment Creates a Synthesis That May Have Abetted the Dawn of Life

By MALCOLM W. BROWNE

It is very unlikely, scientists agree, that the precise chemical pathways from which life arose will ever be known. But it may at least be possible to identify some of the chemical steps that might plausibly have played roles in the origin of life, and three biochemists believe they have found just such a step.

In a paper scheduled for publication today by the British journal Nature, those biochemists — Dr. Stanley L. Miller of the University of California at San Diego and two associates there — describe a way they have discovered to synthesize pantetheine from a mixture of chemicals not derived from a living organism.

Pantetheine in the body is a precursor of coenzyme A, a substance that is essential to the metabolism of both simple and complex creatures and that plays a key part in building the chemical bonds that hold proteins together.

Scientists believe that because coenzyme A is involved in so many fundamental enzyme reactions at every level of life, it must have become biologically important very early in the history of life.

The object of Dr. Miller's experiment was to determine whether pantetheine (pronounced panta-THEE-een) could be synthesized reasonably easily from chemicals presumed to have existed before life began. His group found that the reaction from the mixing and warming of three such prebiotic chemicals — pantoyl lactone, beta-alanine and a sulfur-containing compound called cysteamine — yielded pantetheine, which is the major component of the coenzyme A molecule.

"We cannot know whether this synthesis mirrors what actually happened at the dawn of life," Dr. Miller said, "but it looks like a possibility."

His group found that the reaction that yielded pantetheine could be made to proceed at a temperature as low as 104 degrees Fahrenheit — "a discovery," he said, "that came as a pleasant surprise."

For 42 years, Dr. Miller has explored the chemistry of life's origins, sometimes with dramatic results. In a landmark experiment in 1953, when he was a graduate student of Dr. Harold Urey, he created a kind of genesis-in-miniature by passing an electric spark through a sealed glass vessel containing a mixture of simple gases: methane, ammonia, carbon dioxide, hydrogen and water vapor. The ingredients reacted to form various amino acids, the molecular building blocks of proteins, which in turn are the building blocks of living organisms.

Another step in the exploration of 'the prebiotic soup.'

Since then, Dr. Miller has created 13 of the 20 known amino acids, using laboratory apparatus containing different mixtures of gases possibly duplicating those of the earth's atmosphere some four billion years ago.

In the latest experiment, Dr. Miller, Dr. Anthony D. Keefe and Gerald L. Newton dissolved the three reactant chemicals in water and then concentrated them by evaporation. They then heated the dry mixture, analyzed the result and found that they had synthesized a significant quantity of pantetheine.

"Pantoyl lactone, beta-alanine and cysteamine are all extremely soluble in water," Dr. Miller said, "and that fact might have caused them to separate from less soluble compounds and become very concentrated in ancient lagoons where water evaporated."

Dr. Miller concluded that pantetheine could have been a component of what he calls "the prebiotic soup," the solution of chemicals from which life spontaneously arose.

Other biochemists are not in unanimous agreement with this interpretation. Another possibility was proposed in a comment published by Nature from Dr. James P. Ferris, a chemist at Rensselaer Polytechnic Institute. "Perhaps," he wrote, "most coenzymes were not synthesized readily from their component parts on the primitive earth but are the products of an early form of life."

In any case, the riddle of life's origin is shrouded in a myriad of mysteries besides the problem of coenzymes' creation. One mystery awaiting explanation is how enzymes themselves came into being, and how these complex proteins developed the ability to direct and control the synthesis of other proteins from simple amino acids. Another suite of mysteries has to do with the origins and evolution of two nucleic acids — ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) — which not only replicate themselves but also direct the assembly of proteins into complete living organisms.

A few scientists, including Dr. Francis Crick of the Salk Institute in San Diego, who was the co-discoverer of the double spiral structure of DNA, believe that the creation of life was so complex that its seeds may have come to earth from some distant point in the universe. Dr. Miller and most other scientists, however, argue that this merely begs the question of life's chemical origin; the mystery is merely transferred from the earth to some other planet.

"I don't want to exaggerate the importance of our work on the prebiotic synthesis of pantetheine," Dr. Miller said, "but it's another step toward understanding how life might have arisen."

THE NEW YORK TIMES NATIONAL THURSDAY, FEBRUARY 23, 1995 A9

POPULAR SCIENCE APRIL 1995 • 35

ORIGINS OF LIFE

FLYING BUCKYBALLS

Fullerenes, the carbon molecules that so intrigue scientists, have been discovered in the debris from two asteroid impacts. The finds mean that the molecules—called "buckyballs" because their structure resembles the geodesic domes designed by Buckminster Fuller—may have played a role in the evolution of life on Earth.

Researchers from NASA and the University of California at San Diego found a mother lode of buckyballs at a two-billion-year-old asteroid impact site in Sudbury, Ontario. Another team from Rice University found fullerenes in ash deposits that fell to the ground in New Zealand 65 million years ago, after the impact in Mexico that probably spelled doom for the dinosaurs.

The fullerenes may have been ferried in on asteroids or comets, or they may have been created when the tremendous heat of the impacts transformed other forms of carbon, says Jeffrey Bada, a chemist studying the Canadian site.

If fullerenes existed on Earth billions of years ago, they may have played a role in the development of life, he says. The molecules are good catalysts for chemical reactions.—*David Graham*

THE SAN DIEGO UNION-TRIBUNE Thursday, June 29, 1995

C B-3

UCSD scientists offer clues to origins of life

By DAVID GRAHAM
Staff Writer

All life may have started in an "RNA world," in which chemical snippets in drying lagoons started making copies of themselves.

But without a new insight from some University of California San Diego scientists, it was hard for theorists to account for all the chemicals that would have been necessary to build ribonucleic acid (RNA) strands on primeval Earth.

In work reported today in the research journal *Nature*, the scientists think they can explain how two key components of RNA could have been made on early Earth. It could have happened in lagoons and drying pools on beaches, UCSD chemist Stanley Miller said.

RNA is similar to DNA, deoxyribonucleic acid, the genetic code of life, and exists in the body to carry out the instructions of DNA. But at the dawn of Earth, RNA chemicals may have been the first simple life forms — able to store information about themselves and make copies of themselves, in essence forming generation after generation.

Miller and research fellow Michael P. Robertson showed how two of the four key chemical components of RNA — cytosine and uracil — could have been available in sufficient quantities to make RNA. It probably was necessary for ocean water to concentrate in evaporating pools in order to produce sufficient quantities of the chemicals to form RNA, Miller said.

Through a series of simple chemistry experiments, they showed how the two could have been synthesized starting with one other common chemical in the drying pools of ocean water.

"It makes it (RNA creation) really quite plausible," said Miller, who is famous from experiments in the 1950s that gave insights into how life could have arisen from inert chemicals on Earth.

"Once you get all the right conditions, it works like a charm."

The study does not prove life began with self-replicating RNA or that it had to be made of the four chemicals it is today, Miller said, but the experiment does bolster the theory.

Starting with cyanoacetaldehyde, which could have been created by lightning striking the ancient pools, and urea, which would have been concentrated in the evaporating water, Miller heated the chemicals to yield cytosine, one of the four primary components of RNA. Cytosine then reacts with water to produce uracil, another of the four primary components.

The other two chemicals that comprise RNA are guanine and adenine. Other experiments had previously shown how these two chemicals could have been present on early Earth.

THE NEW YORK TIMES SCIENCE TUESDAY, JULY 4, 1995

Chemist Adds Missing Pieces To Theory on Life's Origins

All four chemical bases of RNA can arise in nature.

By MALCOLM W. BROWNE

No one has yet shown how life originated on Earth, and the chance that science will ever unlock all the details of the process seems vanishingly small. But as molecular biologists discover how nature may have built unaided the maze of tiny bridges that led from inanimate chemicals to living creatures, hopes brighten that the ancient pathway to life may one day be at least dimly revealed.

The latest news about the quest comes from Dr. Stanley L. Miller of the University of California at San Diego, a pioneer in the reconstruction of "prebiotic" chemical reactions — the primeval chemistry of the young Earth that is presumed to have given rise to life. Dr. Miller and a colleague, Dr. Michael P. Robertson, report in a pair of papers that they have found a way that nature could have created several vital building blocks that had seemed beyond the reach of prebiotic chemistry.

The achievement, they believe, strengthens the theory that the first living creatures were able to synthesize protein and reproduce without the help of the DNA (deoxyribonucleic acid) that makes up the genes of advanced organisms, including human beings. Instead, scientists theorize, primitive viruses and one-celled organisms may have depended solely on RNA (ribonucleic acid) to guide and catalyze their growth and reproduction. According to this theory, which has been gradually accepted during the last 20 years by most biologists, the early "RNA world" evolved into the present system, in which both RNA and DNA play important roles in life processes.

Speculation that the primitive earth was an RNA world arose in 1982, when Dr. Thomas Cech of the University of Colorado disclosed the discovery (for which he was later awarded a Nobel prize) that RNA molecules alone, without the help of outside enzymes, could induce themselves to split up and splice themselves together in new arrangements. This meant that primitive forms of life (like the single-celled tetrahymena animals with which Dr. Cech experimented) could have come into being without any need by nature to invent complex

Continued on Page 22

Robert Burroughs for The New York Times

Dr. Stanley L. Miller in the laboratory at the University of California at San Diego.

Chemist Adds Missing Pieces To Theory on the Origins of Life

Continued From Page 19

He uses simple gases to make 13 of 20 essential amino acids.

protein enzymes.

Since a landmark experiment Dr. Miller performed in 1953 with the late Dr. Harold C. Urey, the discoverer of deuterium, Dr. Miller has devoted his life to the quest for life's origins. In the Miller-Urey experiment, a sealed flask was filled with a mixture of methane, ammonia, carbon dioxide, hydrogen and water vapor — all substances presumed to have been rich in the Earth's early atmosphere. Through this mixture an artificial lightning bolt was passed for several weeks, at the end of which a brownish sludge that formed in the flask was found to contain amino acids of the kind necessary to build proteins. Since then, experimenting with different mixtures of simple gases and conditions, Dr. Miller has created 13 of the 20 amino acids essential to life.

But one problem the theory has had to confront was a possible shortage in the primeval oceans of two key pieces in the structure of an RNA molecule, known as cytosine and uracil. Dr. Miller and Dr. Robertson believe they have solved the difficulty.

In companion pieces in the journals Science and Nature , the two scientists report that both substances might have been produced by the lifeless young oceans in ample quantities by a process involving the evaporation of sea water in tropical lagoons, the freezing of sea water in polar regions and the mixing of their products in the open ocean.

The freezing part of the process could have increased sea water concentrations of hydrogen cyanide, Dr. Miller believes. Cyanide is a deadly poison to animals, but it was an essential precursor to many of the molecules from which primitive life arose.

The evaporative part of the process, Dr. Miller said, could have concentrated the traces of urea that accumulate in sea water as a result of reactions in the atmosphere caused by lightning flashes. In experiments, Dr. Miller and Dr. Robertson showed that when the concentration of the simple chemical urea in sea water is high enough, it reacts with another quite common component of sea water that also owes its formation partly to lightning bolts. Under these conditions, the scientists found, the reaction between urea and the second chemical, known as cyanoacetaldehyde, yields fairly large amounts of cytosine, which is one of the nucleotide bases (or "letters") the DNA and RNA molecules use to spell out the genetic "words" controlling protein production and the growth and reproduction of organisms.

A bonus of this discovery is that cytosine, which is itself an essential component of both DNA and RNA, reacts in the presence of water to form uracil, one of the four essential "letters" in RNA. (Uracil is not an ingredient of DNA, which utilizes another nucleotide base, thymine, in its place). Relatively large amounts of two other essential bases in the four-letter alphabets of DNA and RNA, adenine and guanine, are believed to have formed in ample amounts from the polymerization of naturally occurring ammonium cyanide in a slightly alkaline solution.

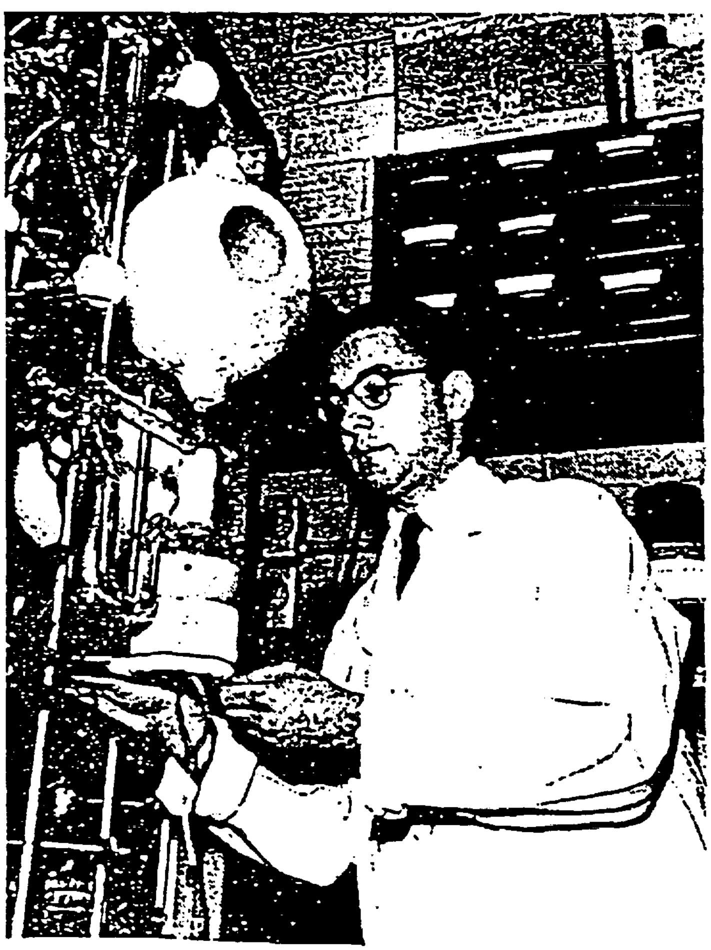
Because of the new experiments, it now appears plausible that all four RNA nucleotide bases could have been created in nature by ordinary atmospheric, oceanic and geological processes from simple, naturally occurring ingredients.

In another series of experiments, Dr. Miller and Dr. Robertson have carried the discovery a step further.

One of the many chemicals that lightning bolts are believed to have created as they ripped through the early Earth's atmosphere is formaldehyde, which presumably rained into the primeval oceans. When uracil reacts with formaldehyde it forms an important intermediary substance known as hydroxymethyluracil, which in turn can react with a large variety of chemicals that biologists assume to have been present in the primeval oceans. The results, Dr. Miller and Dr. Robertson report, are molecules that incorporate "side chains," molecular branches connected to chains of atoms, that are also found in most of the 20 amino acids used by organisms to make proteins.

This coincidence implies, the scientists said, that the catalytic activity of RNA — its ability to promote the synthesis of many different kinds of protein — may have been much greater in the infant Earth than had been assumed. The RNA world may therefore have been much richer in variety than scientists had supposed.

But a daunting array of problems still blocks understanding of the origin of life. One of these concerns the

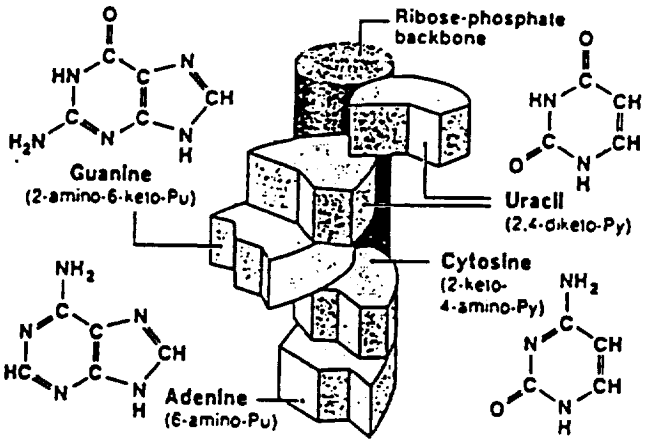


Associated Press/Wide World Photo

Dr. Stanley L. Miller as a 23-year-old graduate student in 1953.

Building Blocks of RNA

It is now known that all four components of RNA can be produced by natural processes on the face of the earth, a finding that has profound implications for scientists' thinking about the origins of life.



Source: "A Guided Tour of the Living Cell," de Duve (Scientific American Books)

The New York Times

origin of the molecular backbone of RNA — a current concern of Dr. Miller's.

The backbones of RNA and DNA are both sugar phosphates containing five-sided rings of carbon atoms, but there is a slight difference between them. In the case of DNA, double strands of pentose sugar are wrapped helically around each other and connected by pairs of nucleotide bases. The backbone of RNA, however, is a single strand of ribose phosphate — a pentose sugar containing an additional oxygen atom. To this backbone are attached the four nucleotide bases.

The problem in imagining how RNA got started, Dr. Miller said, is that ribose is unstable, particularly when it is warm.

Dr. Miller said he is preparing a new paper describing experiments that show that half of any quantity of ribose decays in a little over an hour

Could the RNA world, predecessor of life as we know it, arise naturally?

at the boiling point of water. Even at the freezing point, the half life of ribose is only 44 years. This, he said, implies that high-temperature settings, including a primitive earth heated by the impact of an asteroid, seem less plausible as cradles of life, if it is assumed that early life came about in an RNA world — one in which the creation and survival of the ribose-phosphate backbone was crucial.

Some scientists, including Dr. Francis Crick, co-discoverer of the double-helical structure of DNA, have suggested that life had too little time to originate on the primitive earth, given only a "prebiotic soup" of simple chemicals. They have proposed that life might have reached the earth in the form of spores sent out from some distant planet.

But Dr. Miller and most other molecular biologists regard this idea, called "panspermia," as begging the question; the origin of life on that hypothetical distant planet still must be explained somehow.

Dr. Christian de Duve, a Belgian microbiologist awarded the 1974 Nobel prize for his investigation of the structures of cells, dismisses the panspermia notion as unnecessary.

"If you equate the probability of the birth of a bacterial cell to that of the chance assembly of its component atoms," Dr. de Duve wrote in his textbook, "A Guided Tour of the Living Cell," "even eternity will not suffice to produce one for you. So you might as well accept, as do most scientists, that the process was completed in no more than one billion years and that it took place entirely on the surface of our planet."

The hard part, he wrote, was getting from the simplest chemicals to the first specialized cells, after which "it took no more than 150,000 generations for an ape to develop into the inventor of calculus."

As to whether some guiding hand was needed for the process, Dr. de Duve commented:

"The answer of modern molecular biology to this much-debated question is categorical: chance, and chance alone, did it all, from primeval soup to man, with only natural selection to sift its effects. This affirmation now rests on overwhelming factual evidence."

But the succession of chances that created life did not operate in a vacuum, he said. "It operated in a universe governed by orderly laws and made of matter endowed with specific properties. These laws and properties are the constraints that shape evolutionary roulette and restrict the numbers that can turn up. Among these numbers are life and all its wonders, including the conscious mind."

GAZETTE

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New look at origins of life

Latest theory suggests that life began beneath a frozen sea

MATT CRENSON
DALLAS MORNING NEWS

DALLAS – In a 1953 paper, Stanley Miller described how a simple apparatus could generate some of the crucial building blocks of life. Working in the University of Chicago laboratory of Harold Urey, Miller filled a flask with ammonia, methane, hydrogen and boiling water. Then he generated electrical sparks meant to simulate lightning.

After a week, the water in the flask had turned "deep red and turbid," Miller wrote in the journal Science. Dissolved in the water were amino acids – the basic components of proteins.

Those experiments formed the foundation for modern research into the origins of life and stimulated many of the major theories that prevail today.

But four decades later, Miller and his colleagues don't think those early experiments really reproduced the conditions of life's earliest development. Most origin-of-life researchers think that the atmosphere was predominantly carbon dioxide and nitrogen, not methane and ammonia. Lightning has been left behind as a probable catalyst for the origin of life. And Miller now proposes that life formed in a freezer, not a boiling cauldron.

Unsolved problem

"The origins of life remain one of the major unsolved problems of this century," origin-of-life researcher Jeffrey Bada said at a recent scientific meeting.

Research during the past three decades has cast doubt on old ideas about how life began, but it hasn't erected anything that's much more convincing. Current theories of life's origin rely more on plausible arguments than hard scientific evidence.

"There's no evidence for anything, so it's a wide open field," said Bada, a chemist at the Scripps Institution of Oceanography in La Jolla, Calif.

The only hard evidence lies in the most ancient rocks on Earth. Geologists have found fossil bacteria in 3.5 billion-year-old rocks from Australia and southern Africa, and some think they may be able to see signs of life in rocks in Greenland that are as old as 3.8 billion years.

The fossils are of organisms advanced enough that a microbiologist would find them familiar to today's species, said Andrew Knoll, a paleontologist at Harvard University in Cambridge, Mass. So life must have been well under way by 3.5 billion years ago. And biochemically, that life was strikingly similar to life today.

To: Leslie Orgel
From: Chris Lash
} saw this on the Internet last night.

THE TIMES

May 2 1996 BRITAIN

Scientists deliver origin of species in a global pizza

BY NIGEL HAWKES
SCIENCE EDITOR

LIFE did not begin in a primordial soup but on the surface of a primordial pizza, according to the latest theory.

For more than a century biologists interested in the origins of life have assumed, following Charles Darwin, that the best place for simple molecules to come together to form more complex ones was "a warm little pool". Unfortunately, experiments have failed to show that this happens. While chains of molecules can grow in solution in water, they also break up, so that molecules are split off as fast as they can be linked. It appears impossible to create in this way chains of DNA-like molecules long enough to hold genetic information.

For half a century scientists have tried to reproduce conditions that allowed life to begin, by experiments in which simple chemicals present in the early Earth have been encouraged to form bigger ones. The molecules of life are very large, so a process in which small molecules can be added one by one to form very long chains, or polymers, is required.

Now Leslie Orgel of the Salk Institute for Biological Sciences in San Diego and colleagues have suggested a change in the recipe. Reporting in *Nature*, they say that mineral surfaces such as clay provide a better substrate for the formation of long chains. Chains more than ten links long cannot form in water, while on clay or other minerals it is possible to produce 55-link chains. Such chains can go on growing by successive "feedings" with raw material, washed on to the minerals periodically by rain or tide.

The process described by Dr Orgel and his colleagues involves mixing small molecules with minerals so that they attach to the mineral surface, then separating the solids out and mixing them with a fresh supply of the small molecules. In this way, they show, long chains can be built up link by link. The team envisages the precursors of life forming in colonies on the hard surface of the minerals, dotting it like the fillings on the top of a pizza.

"Minerals on the primitive Earth would have provided a 'library' of surfaces for the exploration of molecular evolution," they say. In this way, DNA-like chains and protein-like molecular chains can be created. What is still missing is the ability of any of the chains so far produced to copy themselves, an essential feature of life.

Next page: Appeal is launched for Bronze Age site

Neil Morgan

How did life begin? Don't take E.T.'s word

The red planet Mars is getting a big push these days. Everybody's looking at Mars. You'll be hearing a lot more about Mars. The fun of being Jeffrey Bada is explaining what an exobiologist thinks about, including Mars.

Bada talks with the guileless charm of a native San Diegan who took his banjo along to Harvard. When he returned, as a chemist at Scripps Institution of Oceanography, he took up a study that's fascinated man since long before Aristotle's time: How did life begin?

N among all the exotica in which most of us dertrained, exobiology must be added to th... ...iences for which this city is becoming a world center.

If you're less than enthralled — muttering, perhaps, about what earthly practical purpose such knowledge could serve — you will be putting in your earplugs to fend off future newsbreaks from NASA. Three years ago the National Aeronautics and Space Administration designated Bada, four San Diego colleagues and their 20 students as a NASA Specialized Center of Research and Training. (Clumsy bureaucrats named it NSCORT.)

NASA sends a modest $1 million a year to San Diego for exobiology, the branch of biology investigating the existence of living organisms elsewhere in the universe. NASA cares.

Dr. Daniel Goldin, chief administrator for NASA, says a major NASA goal is to discover the origin and distribution of life within the universe.

"That's exobiology," Bada says. "That's what we do here in San Diego."

Despite E.T. and a coterie of real-life space watchers and scientific listeners, and notwithstanding perennial reports from isolated areas about flying saucers and bizarre creatures, there has in all recorded world history been no verifiable contact with extraterrestrial intelligence.

S... exobiologists concentrate their study on th... litions, substances and chemistry of pr... ...ve Earth from about 4.6 billion years ago.

But NASA and its San Diego sleuths do not rule out an outside chance.

In 2001 NASA will send an unmanned probe to Mars to search for evidence of life, past or present.

In 2005, another probe is planned to bring back a sample of Mars.

"If we are to find life in the solar system," Bada says, "Mars is really our only hope. If life ever existed on Mercury and Venus, it was totally obliterated by the heat. We used to fantasize about life on our moon, but we know now it is a sterile object. Some people still fantasize about making Mars the next colony of man."

Bada's colleagues are all major figures of science. They are Stanley Miller of UCSD, Gustaf Arrhenius of SIO, Gerald Joyce of Scripps Research Institute, and Leslie Orgel of the Salk.

Yet they are not beyond sponsoring a lecture April 16 by science-fiction author David Brin, a San Diegan who has his own Ph.D. in physics. His title is "The Great Silence: Is Mankind Alone in the Cosmos?"

It's a question that haunts these scientists.

"It would be glorious to prove that the origin of life took place somewhere else, too," Bada says. "Our definition of life is linked with intelligence and has only one requirement: A system incapable of perfect replication. This is synonymous with our definition of evolution. Naked molecules replicating imperfectly would be to us a sign of life."

But what would these scientists do if a sample of Mars suggested life there? The odds may seem impossibly high, but it would answer many questions, Bada says, "about the origin of life on Earth. Is the life we have on Earth a universal biochemistry? Or is the molecular architecture of Earth unique?"

Would these exhilarated scientists hold the predictable news conference to announce life on Mars?

Bada laughs, wondering, too. "Would we talk about the fear of contaminating Earth with Martians? We'd certainly quarantine that sample to make sure whatever's there doesn't get out. In the same way, we don't want to contaminate Mars by introducing material from Earth. There's ethics in science."

But a scheduled NASA orbiting probe of Europa, a satellite of Jupiter, rings of unseasoned ethics. Europa interests exobiologists because it may have similarities to Earth. It is totally white and smooth, with a surface of ocean ice beneath which there may be liquid. Europa's rocky core is probably like Earth's core long ago.

NASA plans to fire a kind of stinger missile from its probe into Europa's ice and then orbit its instruments through the cloud they believe will rise.

Suppose some Europan rose up through that cloud waving a STOP THE BOMB banner?

All "Star Trek" stuff, and Bada is beyond that. He admits to having once enjoyed the series. But now he finds it "really awfully anthropomorphic. The basic flaw is that they're distorted but they still look human and think like humans. And probably thinking like humans is unique to humans."

Bada is much more intrigued these days by the uniquely intelligent dolphins. One hypothesis holds that the dolphin may have been more intelligent than man 10 million years ago before man underwent an "explosive evolution."

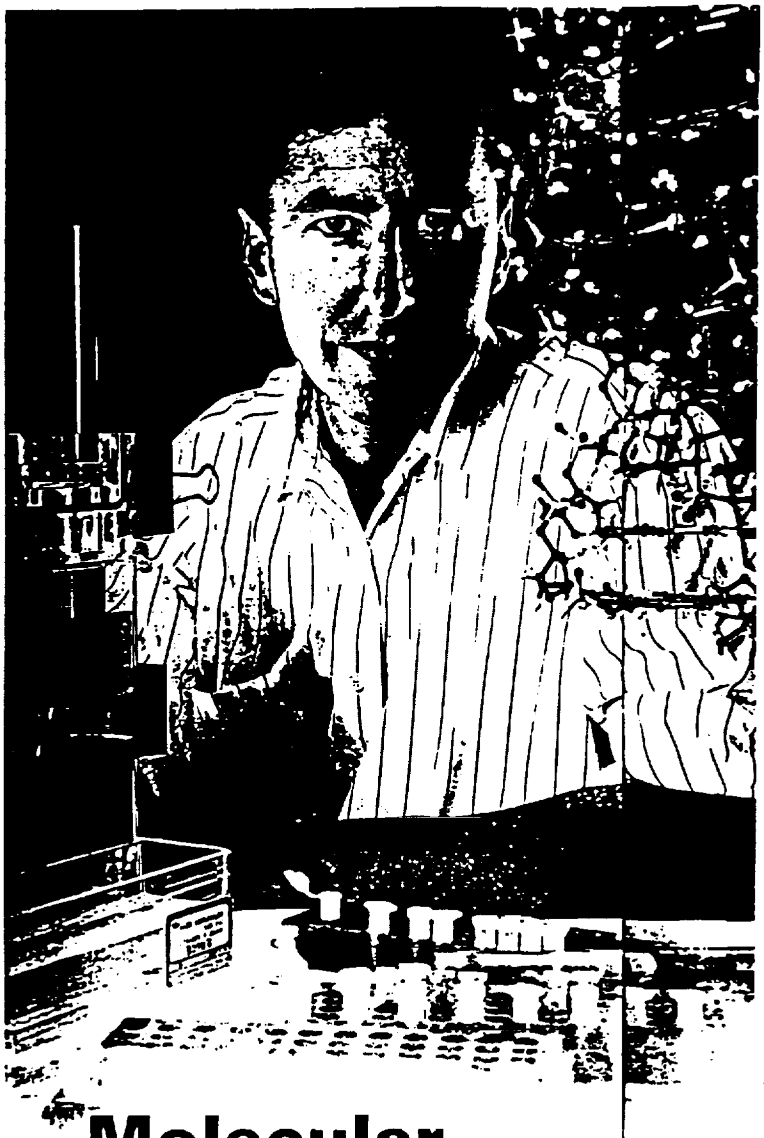
The dolphin, already the smartest creature in the seas, had no evolutionary need to grow smarter, while man's brain became his tool for survival.

Bada and his group have published a succession of research papers that have made them much the most visible exobiologists in the science. SRI's Joyce recently told the magazine *Science* that "life will be made in the lab. There's a reasonable chance it will be made by the end of the decade. . . . It's doable."

About 400 scientists from around the world will convene in Orleans, France, this summer to discuss the origins of life. Not assuming any immediate breakthrough, they have scheduled their following conference at San Diego in 1999

NEIL MORGAN'S column appears Sundays, Tuesdays and Thursdays.

J. L. Bada
TSRI QUARTERLY
(The Scripps Research Institute)
Fall 1995, Volume Two, Number Three, Pages T2,3



Molecular Evolution at Warp Speed

In Gerald Joyce's lab, they make the DNA that nature doesn't.

J. L.Bada
TSRI QUARTERLY
(The Scripps Research Institute)
Fall 1995, Volume Two, Number Three. Pages T2,3

SCIENTIST AT WORK

DNA gets a lot of credit for being the material from which life derives, the font from which flows all the information needed to create an organism. But it isn't exactly a worker bee. At least, not until recently.

The key players in molecular biology—DNA, RNA and proteins—have long been viewed as having limited, but complementary roles: RNA is the courier of genetic information copied from and stored in DNA; proteins are the catalysts for a medley of chemical actions and reactions.

Enter test-tube evolution. Called "the technology of the future" by Nobel prize-winning biophysicist Manfred Eigen, it is part chemistry, part biology, part simple lab procedure and part drama. And it's happening right now, at a pace that seems furious for a process rooted in the principles of Darwinian evolution.

Last fall, TSRI biochemist Gerald Joyce, M.D., Ph.D., accelerated the already fast-paced field of molecular evolution when he followed the Darwinian recipe to evolve, in four days' time, the first DNA that got up and performed—one capable of cleaving RNA, an ability that has powerful and fascinating promise. This discovery was first published in *Chemistry & Biology* in December 1994.

In 1981, the discovery by Nobel prize-winning biochemist Thomas Cech at the University of Colorado of a natural RNA enzyme that could cleave other RNA molecules shattered pre-existing notions and inspired speculation about the presumed limitations of DNA.

"We think of DNA as being just the egg," says Joyce, "the genetic information. But it was tempting to speculate whether DNA could be an enzyme too."

It occurred to Joyce and Ronald Breaker, Ph.D., then a postdoctoral fellow in Joyce's lab at TSRI, that their work in test tube evolution with RNA might be applied to the search for a DNA enzyme. This, however, would be a different ballgame: previously, the scientists had induced RNA to evolve a new function by either starting with one of nature's own RNA enzymes or with one they had made themselves. But nature has not yet provided DNA enzymes.

Starting with random sequences of DNA, Joyce and Breaker attempted to evolve what nature had not.

"We took 100 trillion strands of DNA and attached all 100 trillion of them to a support," Joyce says. "All 100 trillion of them are holding on, just kind of waggling there in the breeze." Then the two researchers posed their challenge: Who among you can cleave RNA?

"We said, 'Okay, now do this cut.'"

Because "the cut" was between the molecule and the solid to which it was attached, any molecule that met the challenge fell off. Achievers in that first batch of randomly selected molecules were rare, but those that accomplished the task were amplified, and their progeny challenged to perform the same task, faster. By the fifth generation, the scientists had evolved DNA molecules that could fall off in only one minute.

"Once we had them, we determined their genetic sequence and gave them a more difficult task," Joyce says. "They had to grab an RNA sequence, cut it, find another one . . . repeating this cycle once per minute."

"And, literally, four days later we had a catalytic DNA."

Joyce's research is the kind of science for which the cliché "far-reaching implications" was coined. The National Institutes of Health (NIH) supports his work because of its therapeutic potential for the treatment of AIDS, and NASA because of its implications for origins of life theory. And his discoveries have been reported in *Time, The Wall Street Journal, Scientific American* and *The Economist*, among others.

The research performed in Joyce's lab may yield new treatments against powerful viruses like AIDS and herpes. Because HIV itself evolves very fast, its treatment will require a drug that can race along with it, perhaps one based on a fast-evolving enzyme capable of keeping pace. Viruses like AIDS must produce RNA to make the proteins required to build new virus particles—RNA that could be targeted by an enzyme capable of interrupting the process.

"RNA enzymes can cleave RNA, but DNA is a million times more stable. We wanted the best of both worlds—DNA that could actually cleave RNA. There wasn't one in nature, so we had to make it."

While several biomedical companies are exploring this possibility with RNA enzymes, DNA, the stable molecule that has recently evolved the ability to "grab an RNA sequence, cut it, find another one; grab it, cut it, find another one . . ." could prove far more effective.