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"ORIGINS OF LIFE IN THE UNIVERSE" CENTER

White Paper to the Harvard Task Force on Science & Technology

(December, 2004)

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1. Initiative Plan

SUMMARY: Throughout recorded history there are a few big questions that have always occupied people's minds – the origin of life is one of them. Understanding the origin of life and its diversity, on Earth and beyond, has become a problem that can be tackled by the methods of modern science. Our **vision** is to create a world-class center for research and education on the origins of life in the Universe (hereafter, Origins Center). This highly inter-disciplinary center will encompass everything from planet formation and detection to the origin and early evolution of life. Our educational **mission** is to provide a home for the increasing number of Harvard students interested in pursuing this inter-disciplinary theme, to work towards establishing a new concentration, and help the development of young scientists in this nascent field.

Our goal is to make Harvard a world leader in Origins research. In the long term (10 years plus), we envision an inter-disciplinary Origins Center in a new building close to other Centers and departments, in Allston or Cambridge. In the short term, we are ready to begin work immediately. We suggest a modest internally funded program with 5-10 postdoctoral fellows and a prebiotic chemistry lab co-located in adjacency to the Biology, EPS, DEAS and Chemistry departments to support our collaborative research and to create the initial home of the Origins Center.

A. Overview of the initiative

Our initiative is an inter-disciplinary synergy among 5 distinct areas (see Figure 1). These areas are represented by faculty (our team) who have known each other, attend our seminar series, work along the theme of our proposal, and collaborate on some projects (thick arrows in Fig. 1). Rather than describing the five areas in some order of preference, below we have chosen to follow the *path from stars to life*.

A.1. Astronomy: exoplanets & their environments

The search for origins would naturally begin with the building blocks – the formation of the elements, the planets, and – in more general terms, the astrophysical environments that could be biologically hospitable. The discovery of planets and planetary systems around other stars (exoplanets, for short) has led to the creation of a new field that is poised to become one of the defining aspects of astrophysics in the 21st century. The new discoveries have already raised many new questions, some of which are fundamental to planet formation and the diversity of planetary environments. To date the astrophysics community has led the search and study of exoplanets, but the field is maturing quickly and already demands synergy between astrophysics, geophysics, cosmochemistry, and traditional Solar system planetary science.

Planet formation and survival are among the fundamental unresolved questions of planetary astrophysics. The challenge is to understand the physics as we move from the single example (and datum) of

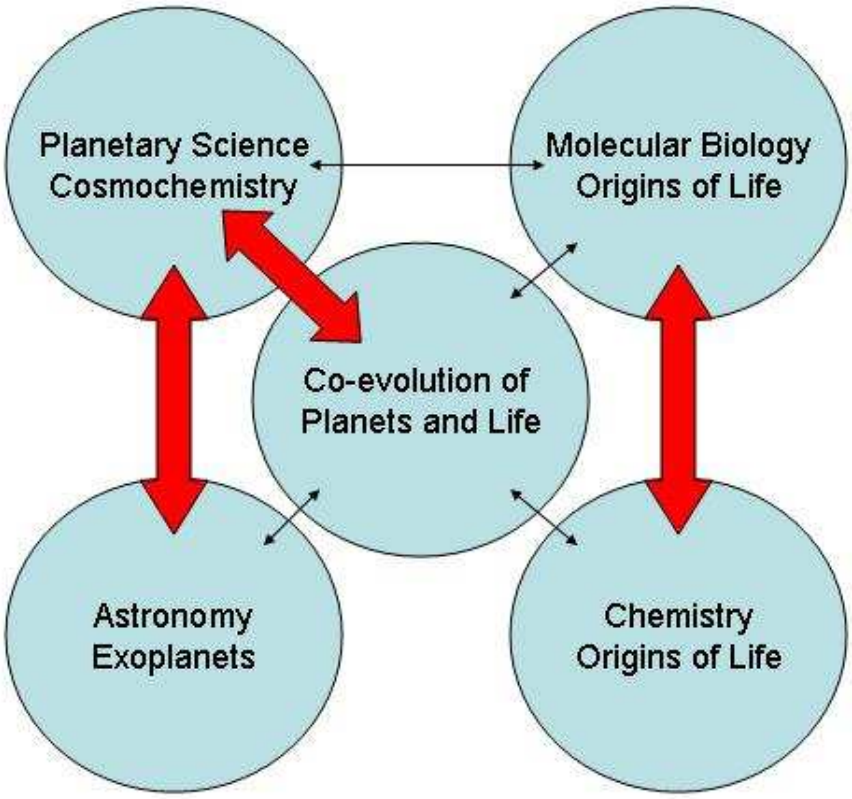

Fig. 1.— Schematic diagram of the five areas of the Origins Center team with connecting arrows for existing connections.

the Solar System to the diversity of planetary systems already discovered. It is a question with venerable history – the 250-years-old Kant-Laplace model, and a bright future – the quest for Earth-like planets, which might also harbor life. Planet formation is a complex and multi-faceted problem. The astrophysics and cosmochemistry groups are already collaborating on a coupled model for the evolution of solids in protoplanetary disks and the timeline for their eventual growth into planets.

We already have a world-class effort in innovative planet discovery. In separate efforts, our team members Noyes, Charbonneau, Sasselov and their groups have discovered several exoplanets, and remotely probed the planetary atmosphere of one of them. We have become a leading location for the search of exoplanets with the new transit method (four of our planet discoveries, including the first one, have been accomplished with it). The goal now is to detect more such exoplanets and understand their physical parameters, and to push the discovery space to smaller-size planets. We are involved with NASA space missions like Kepler and TPF (Terrestrial Planet Finder), to discover and study Earth-like planets – the ultimate goal in this grand endeavour. On the theoretical side, this has already motivated collaborative work with the planetary science group on models for larger (than Earth) terrestrial planets.

A.2. Planetary Science: Cosmochemistry & planetary environments

The processes that lead to the formation of habitable planets begin in the domain of astronomy (above), but are completed and fully understood in the domain of planetary science. Isotopic and chemical analyses of extraterrestrial materials are the observational basis for inferring the processes and events in both the early solar system for pre-solar system processes and origins of planetary systems. A number of important questions relating to the early evolution of the terrestrial planets and asteroids may be investigated by utilizing exinct as well as long-lived radionuclide chronometers. The major activities led by team member Jacobsen will be: i) to conduct such isotopic and chemical studies of extraterrestrial materials, ii) to continue developing cosmochemical models to aid in interpretation of the results as well as in planning of new experiments, and iii) to develop new techniques and instruments to more fully utilize isotopic and chemical systems that will be of importance for research on origins of planetary systems.

Analysis of extraterrestrial materials will include samples returned from planetary missions as well as samples landing on Earth (meteorites and cosmic dust). We are particularly interested in working on samples that will likely be returned from Mars within the next 10 years in addition to meteorites inferred to come from Mars. We are also interested in returned samples of cometary dust (Stardust Mission: sample return – January 2006) and asteroidal samples when they become available. In the meantime and for honing new techniques, the emphasis will continue to be placed on work on lunar samples and meteorites. The existence of pre-solar grains in meteorites has now been well established for about a decade and during this time a number of fundamental discoveries were made. However, there is much work still to be done on this type of material.

The fundamental areas of research activities in Cosmochemistry will be as follows: (i) the time scales and processes that occurred during the earliest stages of formation of our solar system and their application to the understanding of the formation of planetary systems in our galaxy; (ii) the time scales and processes in proto-planetary and planetary formation and evolution, such as the time scale and functional shape of accretion and core formation for the terrestrial planets (see Figure 2); (iii) the origin of the Moon, testing of the giant impact hypothesis for the origin of the Moon; (iv) early planetary differentiation processes, such as the importance of magma oceans, proto-atmospheres, and crust formation and how this might lead to a habitable planet; and (v) composition of comets, cometary dust, importance to early

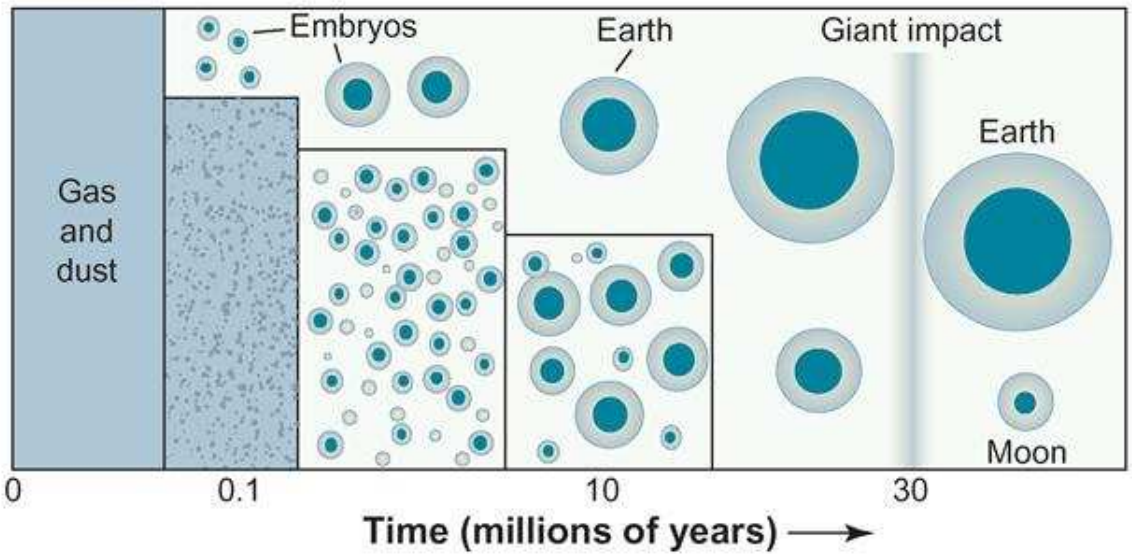

Fig. 2.— Formation of the Earth (Jacobsen 2003): the first new solid grains formed from the gas and dust cloud called the Solar Nebula some 4567 million years ago. Within 100,000 years, the first embryos of the terrestrial planets had formed. Some grew more rapidly than others, and within 10 million years, about 64% of Earth had formed; by that time, proto-Earth must have been the dominant planet at 1 astronomical unit (the distance between Earth and the Sun). Accretion was effectively complete at 30 million years, when a Mars-sized impactor led to the formation of the Moon. The figure is not to scale.

ocean-atmosphere evolution.

The above effort, in collaboration with the astronomy group, aims to understand how and where planets, in particular habitable planets form. It anticipates playing a major role in the study of returned samples from comets (2006) and Mars (c.2014). The other large effort is to study the surfaces and atmospheres of exoplanets, as well as their bulk characteristics. This is in anticipation of the NASA space missions Kepler (2007-2011) and TPF (c.2015). Collaborations have begun along these lines, e.g. in modeling terrestrial planets larger than the Earth, thus different from the Solar System examples, but very likely to be among the planets discovered by Kepler and TPF. The cosmochemistry group plans to collaborate with the group in the area of co-evolution of planets and life (team member Knoll) on the physicochemical conditions in the early atmosphere-ocean system. These areas explore one of the big questions in our theme: the origin of the organic matter on the early Earth (transported in from comets, generated in situ, etc.).

A.3. Co-Evolution of Planets and Life

All of the initiatives outlined in this white paper revolve about the central observation that life is a planetary phenomenon. Life on Earth was born of planetary processes and has been sustained through time by tectonic and other planetary processes that recycle biologically important materials and regulate environment. Moreover, life has expanded and diversified through time to provide a set of planetary processes important in their own right. Of fundamental importance, sedimentary rocks deposited throughout our planet's history record the history of terrestrial life and environment (Figure 3).

In the future, experimental approaches to the origin of life will benefit from closer coordination with Earth scientists who can specify the range of relevant environmental conditions. How did seawater and atmospheric composition, pH, and redox state constrain the chemical pathways that led to self-replicating systems on Earth? Indeed, as current missions expand our understanding of other planetary surfaces, we can begin to conduct experiments that provide more general perspectives on the emergence of life. (For example, the recent discovery – in part by our team member Knoll – that surface environments on the young Mars were acidic and perhaps strongly so (see Figure 4) urges lines of experimentation never before contemplated by students of prebiotic chemistry.) The search for Earth-like planets beyond our solar system and, especially, the characterization and interpretation of their atmospheres by remote sensing also requires that we understand the historical relationship between biology and atmospheric chemistry on Earth.

We have just entered an era of renewed planetary exploration and it is likely that questions of life and environment will play a significant role in shaping missions by NASA and its international partners over the next two decades. This effort will be guided by our experience in reconstructing Earth's biological and environmental history from the rock record, a field in which Harvard has long played a leading role – and one that is integral, as well, to Harvard's recently inaugurated Microbial Sciences Initiative. The new Origins Center should support both research and education in this inherently interdisciplinary field, facilitating new lines of work that arise through collaboration with planetary scientists and molecular biologists interested in life's origins. Because we have no assurance that terrestrial organisms exhaust the possibilities of life, however, we need to think hard about how we might recognize traces of an unfamiliar biology. Extraterrestrial structures or molecules can be accepted as presumptive evidence of biology only if we can eliminate the alternative hypothesis that they formed by physical processes. Biology might vary from planet to planet, but physics and chemistry should be the same, providing a consistent yardstick for biological assessment.

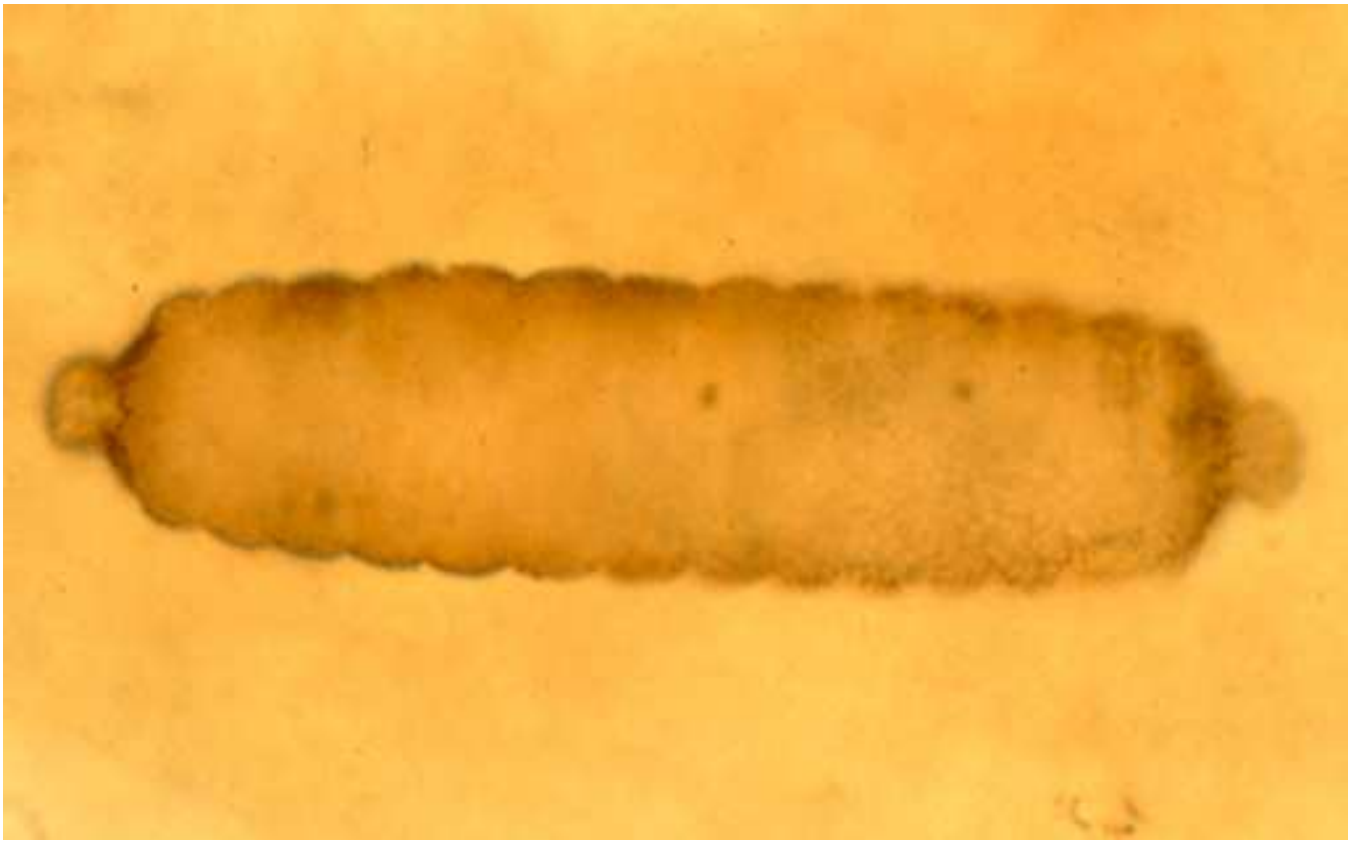

Fig. 3.— A fossil cyanobacterium preserved in ca. 1.5 billion year old sedimentary rocks from northern Siberia (A.Knoll). Sedimentary rocks record Earth's biological and environmental history, permitting us to investigate the origin and evolution of life in the context of planetary development. (Cross-sectional diameter of the fossil is 15 microns.)

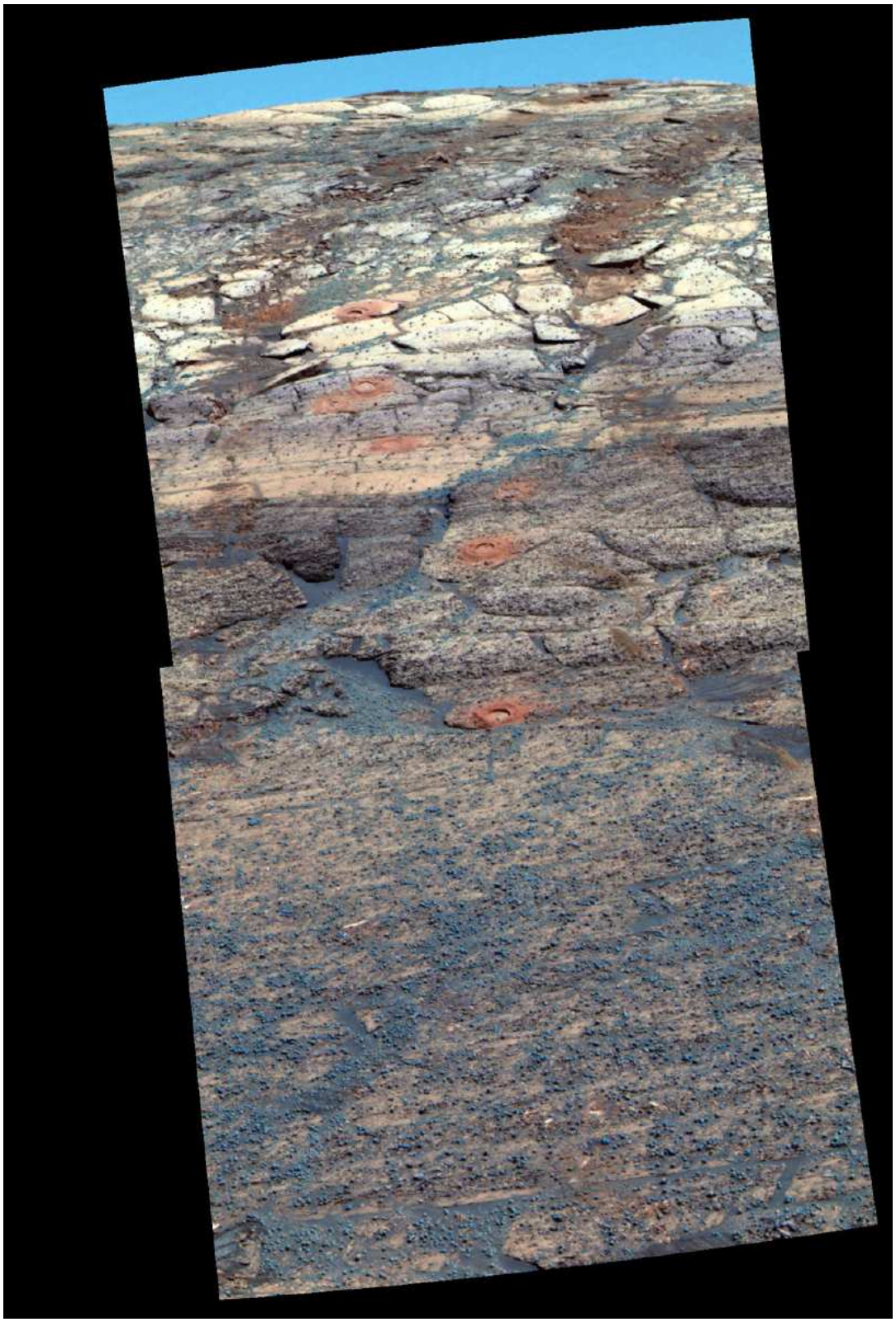

Fig. 4.— The inner surface of Endurance crater in Meridiani Planum, Mars. The image clearly shows distinct layers of sedimentary rock in the local stratigraphy, as well as both rover tracks made during descent into the crater and circular holes where chemical analyses were performed. Members of our team expect to take part in continuing planetary missions, basing exploration strategies in part on our experience in deciphering Earth's early geological record.

By what pathways and at what rates did the small inorganic chemicals present at planetary birth react to form molecules of the prebiotic soup, how did those molecules assemble into larger structures, and how did those structures become the earliest, self-replicating, self-improving proto-cells?

This initiative will focus on one of the most important unsolved problems in the origin of life: understanding the step in which *chemicals* become the earliest, self-replicating $proto - cells$. We understand, very generally, how chemicals present in the atmosphere of the prebiotic Earth might have been converted into organic molecules (even quite complicated organic molecules). We understand how a primitive cell might evolve into a more sophisticated cell, and how the mechanism of nucleic-acid-based inheritance provides a mechanism for allowing a cell to change its attributes. We do *not* understand how solutions of chemicals could spontaneously give rise to self-replication and the other characteristics (energy dissipation, adaptation) of living cells.

The step between "chemicals" and "self-replicators" is chemistry, but chemistry of a type that has been relatively little explored. *The* key issue is: can one find a plausible route from chemicals that might have been present in these prebiotic solutions to the components required for the existence of early cells? We acknowledge at the outset the obvious: that no studies can ever *prove* how life emerged, since it is impossible to replicate and revisit its birthplace. A *plausible* path would, however, complete a chain of logical links extending from compounds present in the atmosphere of a primitive earth to us, and fundamentally focus – by confirming that it was possible for self-replicating systems to arise spontaneously – our view of our origins.

The formation of the prebiotic soup may have had extraterrestrial origins such as photochemical reactions in nebulae and the transport by comets to planets or, alternatively, chemical reactions on planets may have led to the formation of a prebiotic soup. The attraction of the latter pathway is that, if feasible routes can be found, high volumes of organic material can be formed. Two cutting-edge possibilities are chemistry at the surface of minerals and chemistry inside atmospheric particles. Photoelectrochemistry on mineral surfaces, leading to the formation of reduced organic molecules, has the potential to play a central role in the prebiotic syntheses of building blocks for biomolecules. Atmospheric particles are another likely candidate of unique chemical reactors for prebiotic reactions. As individual particles evaporate, chemical reagents are concentrated while there is simultaneous a high solar flux to promote photochemistry. Experimental evaluation of these possibilities is currently absent. Even if there were a compelling explanation for the formation of prebiotic molecules, there would still be the unsolved problem of how these molecules assemble into useful structures such as membranes or photosystems. Precursors to photosystems I and II are needed, which could have been Fe and Mn transition metals complexed by ligands. Possibilities with regard to structural stability, kinetics of formation, and efficiency of photochemical reactions should be investigated. In addition to an energy source, protocells would need structure and containment to overcome the effects of dilution and entropy, i.e., we must understand how micelles and membranes could arise spontaneously from the prebiotic soup.

One question to be addressed by this initiative is, "Is RNA the only molecule capable of encoding its own synthesis, responding to its environment, and improving?" Modern organisms must use protein catalysts (enzymes) to aid in the copying mechanism of RNA and we are curious if these very central aspects of life can be achieved with simple molecules that can be synthesized in the lab. If so, then it is plausible that self-replicating, evolving molecules may have formed from the prebiotic molecules present on the early Earth. The development of synthetic self-replicating molecules will allow us to study: 1. What

are the necessary building blocks for self-replication? 2. What may have emerged before an RNA world? 3. How do these molecules improve their properties? 4. How might molecules with such properties be useful in new technologies? By working in close collaboration with researchers investigating the conditions present on the primitive Earth, we will be able to more accurately choose starting materials and conditions that reflect what may have been present at a certain time in Earth's history. We will also explore what may have come before an RNA world. What chemistry may have preceeeded RNA, but still had the capability to carry information and act as catalysts? Answering these questions will require a unique collaborative effort between scientists involved in prebiotic chemistry, biochemistry, astrophysics, and geochemistry.

A.5. Molecular Biology: Origin of Life

The last area of investigation is the culmination of the effort to unravel the origin of life with a highly interactive molecular biology lab. The strategy is to learn about how Darwinian behavior can emerge from chemistry by trying to build simple systems that evolve spontaneously. The goal is to make, by a combination of design and evolution, informational molecules that can catalyze their own replication. An example would be an RNA sequence that acts both as a template to store and transmit information, and also as an enzyme to catalyze the chemistry of replication. The other half of the program is some kind of membrane compartment that provides spatial localization, but is also a self-replicating system. Then we have to figure out how to bring these two replicating systems together so that we have a real cell-like system with all the elements required for Darwinian evolution. By trying to build complex systems like this, we really bring the gaps in our understanding into focus, so we are forced to work on the hard problems such as how cell division could occur, before the machinery for cell division evolved. Looking forward in evolutionary time, one goal is to try and explain why biology is the way it is, i.e. why and how did protein synthesis evolve, and why are membranes so universally used in energy storage and transduction?

Team member Szostak is leading a vigorous program with several collaborations. This kind of work obviously connects with prebiotic chemistry and planetary science, as well as requiring interactions with physical chemists and people who can help with advanced instrumentation not normally used by molecular biologists. The program is already very inter-disciplinary. One example is the continuing work with Dave Weitz's lab in DEAS, which specializes in colloid science, optical technology and more recently microfluidics. They were very helpful in Szostak's initial work with vesicles including vesicle analysis by light scattering (see Figure 5). Team member Scot Martin and Szostak have discussed some collaborative work to analyze the properties of vesicles made from the amphiphilic molecules generated in their photochemical CO2 reduction experiments.

More extensive interactions with people working on prebiotic chemistry would potentialy be very helpful. For example, if they had a better understanding of prebiotic phosphate activation chemistry, Szostak's lab could use the appropriate chemistry in their in vitro evolution experiments that are aimed at generating self-replicating nucleic acids. Similarly, a better understanding of early planetary environments would be helpful in evaluating the significance of experiments on ice-eutectic phase reactions (this is the phenomenon that some reactions greatly speed up when frozen, due to the concentration of solutes in the small liquid regions between ice crystals), and also experiments that involve mineral surface catalysis of chemical transformations and vesicle assembly reactions. Szostak interacts with Sunny Xie's lab in Chemistry, and collaborates on an application of RNA in vitro evolution with Verdines' lab. With respect to interactions with the astronomers and astrochemists, these will be less direct but one can still envision some important interactions, such as discussions of biomarkers for remote sensing, i.e. TPF and exoplanet life detection.

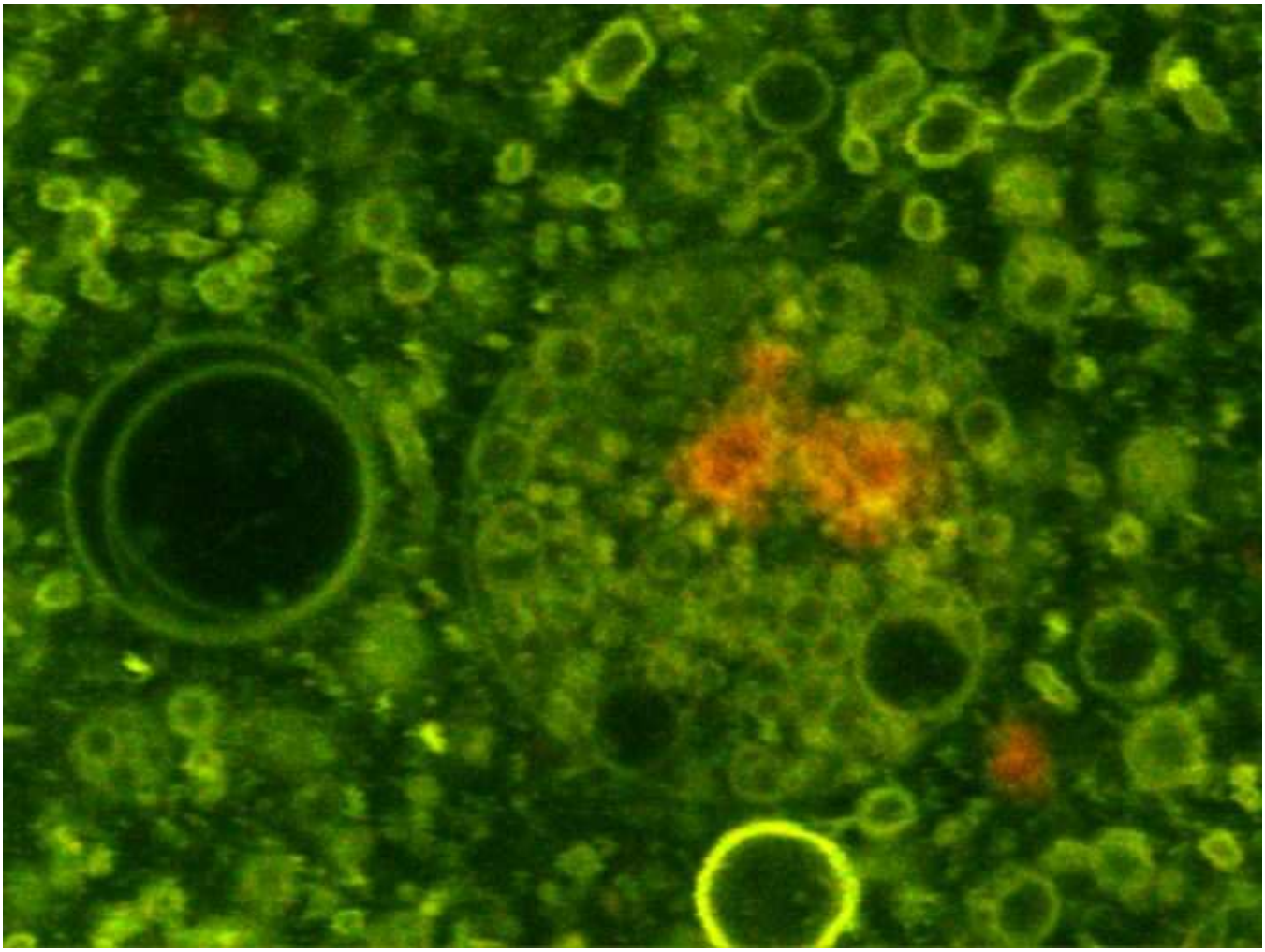

Fig. 5.— RNA (red) adsorbed onto clay, inside a large vesicle (green) assembled through the action of the clay. It illustrates how clay particles can bring together the key components of a simple celli (Szostak 2004).

In summary, the team is conducting research in an emerging field which is inherently inter-disciplinary. The work will be greatly strengthened by closer interactions, which would create a center with no equivalent elsewhere.

B. Educational mission

Creating the Origins Center will answer a need among our Harvard undergraduates which has caught the attention of several of our team members. We meet an increasing number of students who are interested in inter-disciplinary studies related to the origin of life and habitable environments. This has already prompted team members Knoll and Sasselov to develop a core course bridging biology and astronomy of exoplanets. Other team members are planning similar cross-boundary courses on the origin of life. The EPS and Astronomy departments have just began a joint effort – the Center for Planetary Astrophysics, which facilitates joint programs for undergraduate and graduate students, as well as collaborative research. Not surprisingly, its initiators and members are all team members for the Origins Center. We propose to fund undergraduate research in our Origins Center labs, as well as inter-disciplinary projects by graduate students at Harvard. We expect our programs to become among the most popular both for students interested in the physical and in the life sciences. As a long-term goal, we will work toward developing a new concentration.

With the creation of the Origins Center, we will enhance our ongoing seminar series, as well as venture into more outreach among the non-science concentrators, and further – the public in general. We already have experience with public lecture series in our team and regularly drawn very large crowds to their public lectures, and we could expect a thriving public interest in our ongoing research.

2. Initiative Organization and Timing

A. Organizational structure

Our team represents five distinct areas of expertise (see Figure 1). Sasselov from Astronomy serves as the leader of the entire initiative, Jacobsen leads the planetary sciences and cosmochemistry area, Lecar – the astronomy area. The origin of life area is led by Szostak from the molecular biology side, by Knoll from the side of co-evolution of planets and life, and by Shair and Martin from the chemistry side. Here is the whole team in alphabetical order: Alcock (Center for Astrophysics), Bloxham (Earth and Planetary Science), Charbonneau (Astronomy), Friend (Chemistry & Chem. Biology), Hernquist (Astronomy), Holman (Astronomy-SAO), Jacobsen (Earth and Planetary Science), Knoll (Biology & Earth and Planetary Science), Lecar (Astronomy-SAO), Loeb (Astronomy), Martin (DEAS), Mukhopadhyay (Earth and Planetary Science), Noyes (Astronomy), O'Connell (Earth and Planetary Science), Ruvkun (Medical School-MGH), Sasselov (Astronomy), Shair (Chemistry & Chem. Biology), Stewart-Mukhopadhyay (Earth and Planetary Science), Szostak (Medical School-MGH), Whitesides (Chemistry & Chem. Biology).

We believe in our success as a team because we realize that we represent a critical mass for launching this area. While there is a lot of work to be done in strengthening some areas and in collaboration, the necessary expertise and enthusiasm is already present at Harvard, and in our team in particular. Note that our team has a very important representation from both FAS and the Medical School.

B. Staging & Resources

Our initiative to create an Origins Center is a "grassroots" effort based on the already ongoing research of many of our team members on the origins theme. Therefore we are ready to begin the work for the new Center immediately. In fact, a long delay would not be prudent as there is increased interest in the theme at other institutions.

We propose a two-stage plan to build this initiative to its intended size. First, **in the short-term** (over the next 5−10 years) an internally funded program creating an initial Origins Center on campus. The core of this center will be about 10 postdoctoral fellows (in equilibrium), i.e. two from each of our 5 areas. The postdocs will be located in offices which are next to each other, in an area with a new prebiotic chemistry lab. The chemistry and biology postdocs will work in the new lab which will be co-directed by Szostak and our Chemistry faculty. This area should have a visitor office and a common area for meetings of the team. The area should be in the vicinity of the Chemistry, Biology, and Earth and Planetary Science departments. The core of co-located postdocs will accomplish simultaneously two things: boost the (collaborative and otherwise) research in the areas where we currently lag behind, and create the intellectual atmosphere by drawing the faculty on our team to spend more time at the Origins Center (and together). This will also help facilitate our recruiting efforts.

Second, beginning in the short term, but with a **long-term** view, we propose to start building the Origins Center by recruiting new faculty – at least 5 senior and 5 junior faculty over the next 10−15 years. All of them would be recruited on the basis of moving at the appropriate time into the collaborative environment of the Origins Center. We already have candidates in mind for prebiotic chemistry, planetary science, molecular phylogeny, etc. Recruiting would follow the standard pattern involving a search committee and departmental affiliation, but the search committees should contain members of the Origins Center to ensure that he recruited faculty are of the highly interactive and multi-disciplinary nature to make the Origins Center a success.

Finally, the Origins Center, in its own building perhaps on Allston campus, will become the location of all the new faculty hires, new labs, postdoctoral fellows, as well as multi-user instrumentation. It will be a center where we will host conferences and workshops.

Other Resources by Area

Some resources, like graduate student support funds, are general for the Origins Center. Others are particular to the different 5 areas and some are described below.

In the **Astronomy** area the two critical facilities are more computing power (the planet formation effort) and a new lab for advanced large-telescope instruments (for the planet characterization effort). The former could be secured through the Inst. for Theory and Computation. The latter is crucial in our goal to be part of the large national (and international) plans to build a new generation of telescopes capable of imaging exoplanets. We could be leaders in such efforts if we are capable to design and build the specialized instrumentation necessary for such studies. The Harvard-Smithsonian Center for Astrophysics has an excellent record in building spectrographs and cameras of outstanding quality, and the Origins Center could benefit from it by providing the lab and resources. By developing the specialized instrumentation to characterize newly detected exoplanets, we will capitalize on the huge investment in spaceborn detection techniques by NASA over the upcoming 15 years, and may enable the CfA to compete successfully to host the operations center for one of these upcoming missions.

In the **Planetary Science** area the major research tools will be high precision and high sensitivity mass spectrometry, combined with ultra low-level chemistry applied to extraterrestrial samples. The focus is on building an Extraterrestrial sample analysis facility, consisting of ultraclean laboratories with (i) mass spectrometers for precise isotopic measurements of extraterrestrial samples, (ii) equipment for elemental analysis (electron probe, ICP and GD mass spectrometers), and (iii) imaging (SEM and NanoSIMS) of extraterrestrial samples. Part of this work will likely involve instrument development in cooperation with one or several high tech companies. It is expected that the proposed work will lead to improvement of

techniques that may have significant applications in other fields of earth and planetary sciences as well as medical and pharmaceutical sciences. A small facility for storing and preparing extraterrestrial samples is also needed as well as ultraclean chemical separation laboratories for separating trace quantities of elements from extraterrestrial samples. To operate the laboratories effectively one needs support for a small group of relatively permanent senior research scientists (3) (research associates and staff scientists), post-doctoral fellows (3), technicians (3) and graduate students (3).
Some equipment and renovations will be needed immediately to get ready for the comet Wild sample return in 2006.

In the **Co-Evolution of Planets and Life** area the main resources needed are new faculty appointments in geobiology and planetary dynamics, with the necessary funds for field work and seed money for new initiatives.

In the **Chemistry & Molecular Biology Origin of Life** areas, the crucial resources are a new prebiotic chemistry lab to begin with, and then more faculty in several areas, e.g. in prebiotic chemistry, molecular phylogeny, etc. These are also the areas with highest potential for technology spin-offs and technology development. For example, Szostak's lab is currently working on new aspects of protein synthesis that may some day allow for the coded synthesis of small molecules on the ribosome – a technology with obvious applications in drug discovery.

3. Rationale

Harvard could become a leader in an emerging discipline which bridges the physical and the life sciences. By its inter-disciplinary nature it is also a new way to further the educational goals of the University. The field is maturing quickly and there is increased interest in the theme at other institutions. For example, NASA has a large, but much more narrow, effort – the Astrobiology Institute, which is more focused on providing support for NASA's roadmap of future space missions and does not address (and fund) the central issues in understanding the origin of life. Universities, like Colorado and Washington, have initiated small programs, also limited to astrobiology. However, the idea is in the air, and we at Harvard should act soon, if we are to be leaders.

Indeed, the major risk in evaluating our initiative is the risk of not acting now and allowing the emerging competitors to achieve the scientific breakthroughs elsewhere. The future of the field seems now well assured. The search for planets in the early stages of formation, and possibly in various stages of the early evolution of life, is just beginning, and is an aspect of the exploration of our galaxy that will continue indefinitely, at least for hundreds of years. Similarly, the ability to design and build new life-forms, a by-product of efforts to understand the origin of life, will really open the door to synthetic biology - a discipline that may take generations to mature, and which could be a truly transforming technology.