upwelling circulations in the ocean, yielding colder ocean surface temperatures and additional nutrients for biological growth.

The synergy of all these measurements makes the wind fields more valuable to science. Careful coordination of satellite research missions and ocean field programs (as in, for example, the World Ocean Circulation Experiment) were used in the past decade to maximize simultaneous data collection. These programs advanced our understanding of ocean circulation and atmosphere-ocean coupling while revealing the importance of temporal variability and trends. Given the difficulty of coordinating multiple satellite measurement programs and their vulnerability to system failure, even the best coordinated research missions are not a substitute for the sustained observing systems needed to understand and predict changes in climate and the role of ocean-atmosphere interactions in those changes. Considerable attention is now being focused on the design of sustained observing systems, including such programs as the Integrated Ocean Observing System and the National Polar-Orbiting Operational Environmental Satellite System (NPOESS).

Despite the phenomenal success of the SeaWinds scatterometer in measuring the small-scale wind patterns, the numerous advances made in understanding air-sea coupling with these observations, and a decade of experience with building, calibrating, and using the data for weather prediction, the future of this scatterometer is uncertain. Although the ESA-supplied advanced scatterometer (ASCAT) will be integrated into Europe's operational European Organisation for the Exploitation of Meteorological Satellites (EUMETSAT) MetOP missions, a scatterometer has not yet been included in any U.S.-planned monitoring system. Present NPOESS plans call for measurement of surface vector winds by polarimetric microwave radiometry (*8*), for which direction accuracy and all-weather measurement capability are not yet known. The low priority of wind directional accuracy is illustrated by NPOESS requirements: Wind speed is considered a key performance parameter (KPP), but wind direction is not. Further, no contingency plans exist for inclusion of scatterometers in NPOESS in the event that polarimetric radiometer measurements of vector winds prove inadequate for research or operational applications.

Wind and wind stress direction accuracy is critical to understanding the quantitative relationships between atmosphere and ocean and to operational requirements. For example, the upwelling shown in the figure as cold water near the coast is dynamically related to derivatives of the wind vectors, not to wind speed. For both atmospheric and ocean models, the dynamical boundary condition needed at the air-sea interface is stress, which requires the wind vectors. Wind stress magnitude is also not considered a KPP, and no directional accuracy requirement is specified for wind stress.

The European scatterometer measurements will be useful for many needs, despite lower spatial resolution and less coverage than SeaWinds. Nonetheless, proven, accurate, all-weather surface wind measurements need to be part of the U.S. operational program to improve weather and climate predictions. Given the long lead times required to plan and implement satellite observing systems, time is running out.

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EVOLUTION

Transitions from Nonliving to Living Matter

Steen Rasmussen, Liaohai Chen, David Deamer, David C. Krakauer, Norman H. Packard, Peter F. Stadler, Mark A. Bedau

All life forms are composed of molecules that are not themselves alive. But in what ways do living and nonliving matter differ? How could a primitive life form arise from a collection of nonliving molecules? The transition from nonliving to living matter is usually raised in the context of the origin of life. Two recent international workshops (*1*) have taken a broader view and asked how simple life forms could be synthesized in the laboratory. The resulting artificial cells (sometimes called protocells) might be quite different from any extant or extinct form of life, perhaps orders of magnitude smaller than the smallest bacterium, and their synthesis need not recapitulate life's actual origins. A number of complementary studies have been steadily progressing toward the chemical construction of artificial cells (*2*–*8*). The two back-to-back workshops (*1*)—one held jointly at Los Alamos National Laboratory (LANL) and the Santa Fe Institute (SFI), and the other in Dortmund, Germany, at the seventh European Conference on Artificial Life—strived to encompass the full spectrum of this research.

There are two approaches to synthesizing artificial cells. The top-down approach aims to create them by simplifying and genetically reprogramming existing cells with simple genomes. Although the two workshops included a notable top-down exemplar, they focused primarily on the more general and more challenging bottom-up approach that aims to assemble artificial cells from scratch using nonliving organic and inorganic materials.

Although the definition of life is notoriously controversial, there is general agreement that a localized molecular assemblage should be considered alive if it continually regenerates itself, replicates itself, and is capable of evolving. Regeneration and replication involve transforming molecules and energy from the environment into cellular aggregations, and evolution requires heritable variation in cellular processes. The current consensus is that the simplest way to achieve these characteristics is to house informational polymers (such as DNA and RNA) and a metabolic system that chemically regulates and regenerates cellular components within a physical container (such as a lipid vesicle).

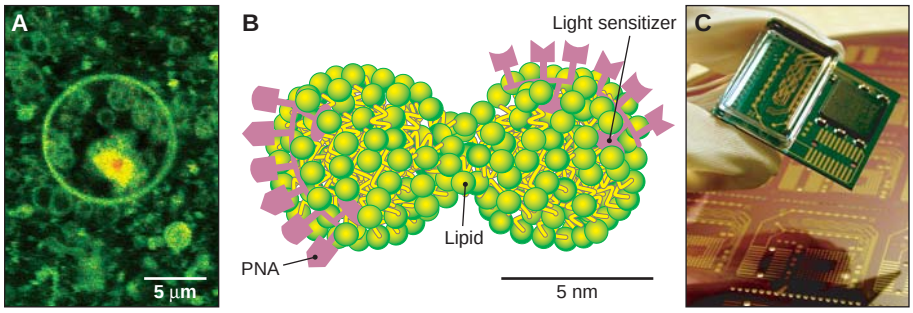
The workshops reviewed the state of the art in artificial cell research, much of which focuses on self-replicating lipid vesicles. David Deamer (Univ. of California, Santa Cruz) and Pier Luigi Luisi (ETH Zurich) each described the production of lipids using light energy, and the template-directed self-replication of RNA within a

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lipid vesicle. In addition, Luisi demonstrated the polymerization of amino acids into proteins on the vesicle surface, which acts as a catalyst for the polymerization process. The principal hurdle remains the synthesis of efficient RNA replicases and related enzymes entirely within an artificial cell. Martin Hanczyc (Harvard Univ.) showed how the formation of lipid vesicles can be catalyzed by encapsulated clay particles with RNA adsorbed on their surfaces (see the figure) (*9*). This suggests that encapsulated clay could catalyze both the formation of lipid vesicles and the polymerization of RNA.

Successfully integrating different chemical systems is a key challenge in artificial cell research. Steen Rasmussen (LANL) and Liaohai Chen (Argonne National Laboratory) presented a minimal protocell design in which a small lipid aggregate (for example, a micelle) acts as a container by anchoring a lipophilic peptide nucleic acid (PNA, an analog of DNA with a pseudopeptide backbone) on its exterior (see the figure) (*7*). Peter Nielsen (Univ. of Copenhagen) amplified the benefits of using PNA as the informational polymer in such a system, and Kim Rasmussen (LANL) described experimentally and theoretically the hybridization instabilities and charge transfer in DNA-like double-helix systems. In the Chen-Rasmussen protocell, light-driven metabolic processes synthesize lipids and PNA, with the PNA acting as both an information molecule and as an electron-relay chain. This is the first explicit proposal that integrates genetics, metabolism, and containment in one chemical system. Metabolism in this system has been shown to produce lipids, but experimental realization of the rest of the integrated system has not yet been achieved.

The workshops also included experiments that use the top-down approach to artificial cell construction. Hamilton Smith (Institute for Biological Energy Alternatives, Rockville, Maryland) described an ongoing project to first simplify the genome of *Mycoplasma genitalium* (the organism with the simplest known genome), and then augment it with genes that encode proteins with desired functions. This top-down approach will probably produce the first impressive results because it can adopt wholesale the proven capacity of nature's biochemistry to integrate the complex reaction pathways crucial to cellular life, and because it relies on mature laboratory technology for DNA sequencing, synthesis, and manipulation. However, in the long run, the bottom-up approach might provide access to biochemical systems that are incompatible with or inaccessible using existing cellular chemistry, thus yielding a more diverse set of artificial cells with a wider range of useful properties.



When is a molecular aggregate alive? Examples of new experimental, computational, and technological advances in the development of artificial cells. (**A**) Short RNA oligonucleotides (red) are adsorbed to a particle of montmorillonite (clay) and encapsulated within a fatty acid vesicle (green). The assembly of RNA within the vesicle is coordinated by the clay particle (*9*). (**B**) A model of a dividing protocell, with an integrated metabolic, genetic, and container system (*7*). This minimal system consists of a carboxylic acid micelle with hydrophobic photosensitizer molecules and a lipophilic PNA, which doubles as a simple gene and as part of the metabolic system (electron relay). (**C**) The biomodule shown may be used for adaptive screening of flow conditions to evolve artificially compartmentalized cells (*10*). This module is based on microfluidic technology with online monitoring and fine-grained computer feedback control of fluxes (via electrodes in fluidic channels driven by reconfigurable logic). Such a computational biomodule interface could also be used to program the chemistry of artificial cells so that they could conduct useful tasks.

An emerging frontier in the development of artificial cells is the use of combinatorial chemistry to aid in the search for suitable chemical systems. John McCaskill (Fraunhofer-Gesellschaft, Germany) described technology that could integrate different chemical systems by developing chemical reactions across multiple spatially separated micrometer-sized channels, which act as computer-controlled microreactors. This technology could also provide "life-support" for artificial cells and their precursors, creating stepping stones toward autonomous artificial cells and enabling them to be programmed to perform useful functions. Statistics that enable open-ended evolution to be identified in data from evolving systems were described by Norman Packard (ProtoLife Srl) and Mark Bedau (Reed College, Portland, Oregon). Open-ended evolution is characterized by a continued ability to invent new properties—so far only the evolution of life on Earth (data partly from the fossil record) and human technology (data from patents) have been shown to generate adaptive novelty in an open-ended manner. Packard explained how statistics could be coupled with McCaskill's technology to automate the search for chemical systems that might be useful for artificial cells. Gunter von Kiedrowski (Ruhr-Univ. Bochum, Germany) described a new set of chemical reactions that use molecular elements he called "tetrabots." Such tetrabots could provide an important step toward replicating more general, spatially extended, DNA-like nanoarchitectures.

Several presentations described broader issues underpinning artificial cell theory, simulation, and experiment. Stirling Colgate (LANL), David Krakauer (SFI), Harold Morowitz (George Mason Univ., Virginia), and Eric Smith (SFI) attempted to clarify the distinction between nonliving and living matter. They described how nonliving chemical reactions, driven by thermodynamics, explore the state of space in an ergodical fashion, and thus tend to conduct a random exhaustive search of all possibilities; in contrast, living systems explore a combinatorially large space of possibilities through an evolutionary process. This echoed a central workshop theme: how and when information becomes a dominant factor in the evolution of life, that is, how and when selection plays a greater role than thermodynamics in the observed distribution of phenotypes. Peter Stadler (Univ. Leipzig) reviewed selection using replicator network dynamics, a theoretical framework describing population growth produced by different kinetic conditions. Smith and Morowitz further described how the citric acid cycle of living cells might be a thermodynamic attractor for all possible metabolic networks, thus explaining its appearance at the core of all living systems. Universal scaling in biological systems was discussed by Geoff West (SFI) and Woody Woodruff (LANL), who explained why regular patterns can be found, for example, between an organism's weight and metabolic rate, regardless of whether the organism is a bacterium or an elephant. Shelly Copley (Univ. of Colorado, Boulder) explained how catalysts operate in living systems today and how these were likely to have evolved from

CREDIT: (A) M. M. HANCZYC/MASSACHUSETTS GENERAL HOSPITAL; (B) S. RASMUSSEN/LANL AND SANTA FE INSTITUTE; (C) P. WAGLER *ET AL.*/FRAUNHOFER GESELLSCHAFT BIOMIP

less efficient precursors. Andrew Shreve (LANL) presented a rich variety of self-assembled nanomaterials that display specific emergent properties of a mechanical, photonic, or fluidic nature.

Computational methods are now powerful enough to suggest new experiments. Yi Jiang (LANL) reviewed the state of the art for molecular multiscale simulations in which the challenge is to connect realistic but slow molecular dynamic simulations with less accurate but fast higher level simulations. Andy Pohorille (NASA Ames Research Center, California) used simulations to argue that nongenomic early organisms could undergo evolution before the origin of organisms with genes. Takashi Ikegami (Univ. of Tokyo) presented simulations of a simple and abstract model of metabolic chemistry that demonstrates the spontaneous formation and reproduction of cell-like structures.

The workshops started with some tension between the origin of life perspective and the more general concern with synthesizing the simplest possible artificial cells. However, the participants eventually agreed that different artificial cell proposals might suggest different prebiotic niches. The workshop ended with a road-mapping exercise on four interrelated issues: (i) What is the boundary between physical and biological phenomena? (ii) What are key hurdles to integrating genes and energetics within a container? (iii) How can theory and simulation better inform artificial cell experiment? (iv) What are the most likely early technological applications of artificial cell research?

In time, research on these forms of artificial life will illuminate the perennial questions "What is life?" and "Where do we come from?" It will also eventually produce dramatic new technologies, such as self-repairing and self-replicating nanomachines. With metabolisms and genetics unlike those of existing organisms, such machines would literally form the basis of a living technology possessing powerful capabilities and raising important social and ethical implications. These issues were elaborated by Bedau, who suggested that the pursuit of these new technologies should be guided by what he called a "cautious courage" perspective. All workshop participants agreed that useful artificial cells will eventually be created, but there was no consensus about when.

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PLANT SCIENCES

A *CONSTANS* Experience Brought to Light

John Klejnot and Chentao Lin

Each year during the spring, nature treats us to an amazing display of color and fragrance. Many plants bloom at this time of the year in response to seasonal changes of day length, a phenomenon called photoperiodism (*1*). Some plants, like Mendel's garden pea or today's experimental favorite *Arabidopsis*, flower more readily as days lengthen in the spring, whereas others such as rice or soybean prefer to flower when days get shorter in the fall. Since the discovery of photoperiodism in plants some 80 years ago (*1*), photoperiodic responses have been widely found in other organisms including mammals (*2*). How plants recognize photoperiods and respond to them by bringing forth blossoms has fascinated biologists for decades. On page 1003 of this issue, Valverde and colleagues (*3*) take us one step closer to understanding this phenomenon.

In plants, light signals are perceived by photoreceptors, which include phytochromes (phy) that respond to red/far-red light and cryptochromes (cry) that respond to blue/ultraviolet-A light (*4*). The light signals are "memorized" by the circadian clock and executed by transcription factors, which activate the floral meristem identity genes that initiate the transition from vegetative growth to reproductive development (*5*). Because neither the photoreceptors nor the circadian clock alone is sufficient to explain photoperiodic flowering, these components must somehow work together to measure day length changes (*5*). Almost a decade ago, Coupland's group discovered that an *Arabidopsis* gene called *CONSTANS* (*CO*) encodes a transcription factor that is critical for photoperiodic flowering (*6*). The CO protein activates the transcription of genes required for floral initiation, including a gene called *FLOWER LOCUS T* (*FT*) (*7*). The transcription of *CO* is governed by the circadian clock in a day length–dependent manner, and it has been hypothesized that a posttranscriptional regulatory mechanism must also be involved in regulating *CO* activity (*7*–*9*). Valverde *et al*. now show that the CO protein is ubiquitinated and then degraded by a protein complex called the proteasome, and that this process is regulated by both phytochromes and cryptochromes.

The researchers used transgenic *Arabidopsis* plants that constitutively express the *35S::CO* transgene independent of transcriptional control by the circadian clock and the *FT::LUC* reporter gene as a readout of *FT* promoter activity. They discovered that despite constitutive *CO* mRNA expression in the transgenic plants, the CO protein level was higher in the light phase of long days than in the light phase of short days, resulting in increased FT promoter activity during long days. Moreover, the abundance of CO protein and the activity of the *FT* promoter were greater in seedlings exposed to white, blue, or far-red light, relative to those exposed to red light or left in the dark. When recombinant CO protein was added to nuclear extracts of plant cells, it became ubiquitinated and degraded; degradation of CO was suppressed by proteasome inhibitors. Thus, CO is degraded in the dark via a ubiquitin/proteasome mechanism, and CO proteolysis is suppressed in light (blue and far-red).

To examine which photoreceptors are responsible for stabilizing CO in response to light, Valverde *et al.* crossed the *35S::CO* transgene into various photoreceptor mutant *Arabidopsis* plants. Analysis of the CO protein in the photoreceptor mutants showed that cry1/cry2 and phyA stabilize the CO protein in blue light and far-red light, respectively, and that phyB promotes CO degradation in red light. Apparently, these photoreceptors act to balance the abundance of CO protein in plants grown under conditions of natural light composed of different wavelengths (see the figure). Because both CO and FT activate flowering, these results also provide an explanation for why the *cry1cry2* and *phyA* mutants flower later than wild-type plants in blue light and far-red light, respectively; why the *phyB* mutant flowers earlier in red light; and how cry2 and phyA antagonize phyB action in white light to control flowering time (*10*, *11*). The

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