LETTERS

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted through the Web (www.letter2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

Plant Patents and Agriculture

NORMAN E. BORLAUG RIGHTLY POINTS TO the crucial role of the Consultative Group on International Agricultural Research (CGIAR) in international agricultural research ("International agricultural research," Letters, 20 Feb., p. 1137) and makes a strong case for CGIAR to return to its original purpose, to feed the hungry. The Nuffield Council on Bioethics supports Borlaug's view that a combination of conventional plant breeding techniques and new techniques of biotechnology will best address the needs of small-scale farmers in developing countries. In particular, the Council has emphasized the important contribution of genetically modified (GM) crops, assessed on a case-by-case basis.

Image not available for online use.

The role of CGIAR in research on GM crops is strategically important. CGIAR holds one of the world's largest ex situ collections of plant genetic resources in trust for the global community, containing over 500,000 accessions of landraces and improved varieties of the world's major crops. The germplasm within the collections is made available without restriction to researchers around the world, on the understanding that no intellectual property (IP) protection is to be applied to the material as such.

However, further debate is required about the consequences of plant patents for access to germplasm. The collections of germplasm held by the CGIAR cannot be patented in "the form received." However, once a modification has been introduced, they may then be eligible for patenting. Patent protection for plants or seeds is frequently obtained by securing a broad patent that claims rights over the gene or gene vector. In effect, this may have the same outcome as patenting the whole plant. The holder of a patented variety may be able to prevent others from using it for breeding purposes.

This potential locking up of genetic variation would be contrary to the spirit and intent of plant variety rights. We consider that there is a strong case for the principle of the breeders' research exemption established for plant variety rights to be applied to patented varieties. We recommend that CGIAR closely monitor the impact of patents on the availability of germplasm to plant breeders.

Although seed companies and others are keen to use plant patents to protect new varieties, it is likely to erode the long-standing availability of germplasm between plant breeders. Although some may say that cross-licensing freely applied deals with this problem, it would appear to conflict with the need for stronger IP protection. Access to the unique resources of the CGIAR must not be jeopardized.

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CGIAR's Role in Agriculture

IN HIS ARTICLE ON THE FERMENT IN THE Consultative Group on International Agricultural Research (CGIAR) ("Lab network eyes closer ties for tackling world hunger," News Focus, 27 Feb., p. 1281), Dennis Normile explores some initiatives being considered within the CGIAR but misrepresents the nature of this unique body, and therefore the context in which these issues may be resolved. The CGIAR is not, as he writes, an association of research centers affiliated with the World Bank. Rather, it consists of the public and private donors who support 16 autonomous research centers. In words taken from its Web site, the CGIAR is a partnership that "includes 24 developing and 22 industrialized countries, 4 private foundations, and 13 regional and international organizations that provide financing, technical support, and strategic direction. The Food and Agriculture Organization of the United Nations (FAO), the International Fund for Agricultural Development (IFAD), the United Nations Development Program (UNDP), and the World Bank serve as cosponsors." The CGIAR has no formal corporate structure but makes decisions by consensus among the members at annual meetings chaired by a World Bank vice president. It is supported and advised by an office located at the World Bank, a Science Council composed of independent experts, and various other committees. Funding for centers is not pooled but flows directly from donor to center, so that group decisions can only be effective if they are reflected in the sum of individual donor decisions.

The donors making up the CGIAR collectively bear much of the responsibility for the present crisis. They expanded the goals to be addressed by the centers, but failed either to provide adequate resources for the broader program or to make changes in strategy and structure to accommodate the new goals within the funding available.

The boards and management of various centers and the bodies responsible for facilitating the operation of the CGIAR are discussing possible lines of action, some of them quite radical, as the article suggests. These proposals will be influential, as will the report from the Operations Evaluation Division of the World Bank cited in the article and the forthcoming study commissioned by the Rockefeller Foundation. Any decisions, however, will be made by the donor members of the CGIAR. Although all of them will have a say, the strongest voices will be the World Bank, reflecting both its financial and leadership roles; the European donors collectively, the United States, and Japan, because of their financial weight; and the developing countries, which now have a substantial presence at the table, although they provide relatively little funding.

It is to be hoped that when these decisions are made, they will respond to the needs of developing countries for agricultural research performed internationally, and also be doable with the resources that CGIAR donor members are willing to provide over time.

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Living and Nonliving Matter

IN THEIR PERSPECTIVE "TRANSITIONS FROM nonliving to living matter" (13 Feb., p. 963), S. Rasmussen *et al.* formulate the question: What is the difference between living and nonliving matter? They later reformulate this question as: What is the boundary between physical and biological phenomena? We suggest that the answers to those two questions are closer than the authors anticipate.

The fundamental difficulty seems to be a language barrier. In science, we assume that life obeys the laws of physics. Therefore, we have to find a translation from the language of biology into the more formal language of physics. Life in biology is defined by adaptation and reproduction in a cell-based system (*1*). In physics, a metastable spatial-temporal pattern would have the same attributes (*2*). A traditional formulation of physical laws based on individual parameter optimization, like energy, fails to describe systems with large configurational space corresponding to a single energy state (*3*). Such systems are called complex.

Proteins have glassy properties (*4*, *5*), i.e., they have a large number of conformational states corresponding to the same energies. Such systems (molecules) would be capable of adaptation. Physical systems with a unique ground state would not have the ability to adapt. Adaptation in biological systems requires that the system be complex. For example, there is no unique principle of protein folding [see discussion in (*6*, *7*)] or uniquely defined set of interactions between macromolecules (defined by energy minimization). There is rather an ensemble from which nature selects individual representatives to perform a particular function under a given set of conditions. Single-molecule experiments provide evidence of the existence of such ensembles. They invariably point to coexistence of molecules with significantly differing activities (*8*).

The transition from the physical to the biological realm is not quantitative, but rather qualitative. The deeper and more unique the energy minimum, the more "physical" the system gets. The more equi-energetic conformational states the system has, the more "biological" it becomes.

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Response

WE THANK STEC FOR HIS COMMENTS ON OUR Perspective, and we agree that living systems and many of their components are "complex" in general, in any reasonable definition of that term, and "glassy" in particular, in Stec's sense of "having a large number of conformational states corresponding to the same energies" (*1*). But these properties are not sufficient for life, that is, for localized molecular assemblages that regenerate, replicate, and build new functionality through evolution. Creating a real protocell will involve chemically integrating three key functions: a genetic system for the transmission of hereditary information, a metabolic system for extracting energy and materials from the environment, and a containment system for separating the protocell from its surrounding environment. And glassiness is insufficient to explain the essential mechanisms behind these key functions, much less their specific chemical details.

First, the transition to life depends critically on specific chemical properties. Assembling a protocell involves creating the appropriate synergy among its genetics, metabolism, and container, and this synergy hinges on the intrinsic properties of the component chemicals and their interactions. For example, even after a specific containment and metabolic chemistry have been shown to work together in the laboratory (*2*), it remains unclear how to achieve their cooperation with a genetic chemistry. General knowledge about the dynamics of complex systems no doubt helps, but only when combined with specific chemical knowledge. Stec's reference to clays illustrates this. We agree that clays might have played a significant role in the origins of life (*3*), and eventually it might even be possible in the laboratory to create living systems solely from inorganic building blocks (*4*), but many critical chemical details of such processes still elude us.

Second, although it might turn out that genetic, metabolic, and containment systems, and any protocell integrating them, can be viewed as glassy in Stec's sense, glassiness does not explain their functionality. We will illustrate this with an aspect of genetics, although similar arguments apply to energy transduction and the self-assembly of the components. Living systems undergo two different kinds of selection processes. When one state from an ensemble of equi-energetic states of a molecular system is favored by the conditions of the environment, the stabilization of this state by direct physical feedback illustrates the physical selection common in glassy and other complex physical systems, most of which are entirely devoid of life. But the adaptations essential for life are created through natural selection, which involves the heritability of functional properties (*5*). This process of differential replication of equi-energetic states due to their phenotypic functionality is consistent with thermodynamics, of course, but thermodynamics alone does not explain it (*6*). So, life requires mechanisms beyond mere thermodynamic glassiness.

The transition to life involves inheritable information taking control of the thermodynamic self-assembly and energy transduction processes of glassy systems, and our current understanding of this process is only sketchy. Knowledge of the general properties of complex systems is certainly helpful for understanding this transition, but is it not sufficient. The devil is in the details.

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References

1. See, for example, the many publications on these topics from the Center for Nonlinear Dynamics (CNLS) at Los Alamos National Laboratory (LANL) and the Santa Fe Institute (SFI). For more specific early complex systems studies of the origins of life, see, for example, (*7*, *8*).
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A Model for Promoting Research in Education

FOLLOWING ON J. HANDELSMAN *ET AL.*'S observations on reforming science education ("Scientific teaching," Policy Forum, 23 April, p. 521), our recent experience with drawing students into research at the University of Washington's Friday Harbor Laboratories suggests a model that seems to work. We've established research apprenticeship team training for about 50 undergraduates annually, funded largely by private and foundation sources, but we've had to work around some unexpected obstacles to do it, and there may be some lessons to be learned from identification of these obstacles.

Each team consists of faculty and graduate student mentors and five to eight undergraduates (any level, almost any background), all, including faculty, selected competitively from a national pool of applicants. Each team is immersed in research for a full academic quarter, living and working in a closely supportive team environment, without distractions. Students uniformly report the experience to be the highlight of their undergraduate career and a potent motivator for graduate work and professional commitment to research. The distinctive features of the model are a supportive team environment and the full-time focus on research.

The surprises have been the points of resistance. Some university leaders did not support the idea initially, perhaps because of perceived academic "turf" issues. Further, the formula (teams, focus, few distractions) does not match exactly the traditional National Science Foundation Research Experience for Undergraduates (REU) model, in which individual students work part-time with faculty in traditional research lab settings. NSF has repeatedly declined support of this new team-based model.

The good news is that the program is alive and well, and there are now are now over 200 alums. Further, there are several foundations with vision (notably the Washington Research Foundation, the Mary Gates Endowment, Achievement Rewards for College Scientists, and the Howard Hughes Medical Institute) that recognize the problem and are flexibly focused on fixing it.

We'd be happy to work with others interested in setting up similar programs at other institutions nationally.

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A Plea for Further Human Spaceflight

JAMES VAN ALLEN ("IS HUMAN SPACEFLIGHT now obsolete?," Letters, 7 May, p. 822) asks the proponents of human spaceflight not to "obfuscate the issues with false analogies to Christopher Columbus" or other explorers of similar caliber. However, in the same Letter, he allows himself to use the decline of high-altitude manned balloon flights as an example to support his point of view. Van Allen is entitled to his opinion, but he should at least apply the same standard to himself as he asks of others. Analogies to past history can be misleading, but they can also provide important insights. My own use of the past as a reason to support human space exploration is the observation that societies that stagnate have generally not survived for very long without outside help. As the inevitable globalization of Earth's social and economic systems progresses, humanity may one day, even accounting for all its current tribulations, become highly homogenized and on the path to such stagnation. Yes, analogies with the past may lead to the wrong conclusions, and so that bleak future may or may not happen. Space exploration and eventual attempts at settlements outside of Earth may or may not help prevent it, but considering the small cost of current or even proposed human space exploration efforts compared with total world government and private expenditures, it is a small price to pay to keep such programs going given their unproven, but potentially momentous importance to our collective future.

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CORRECTIONS AND CLARIFICATIONS

Editorial: "Climate change and climate science" by D. Kennedy (11 June, p. 1565). Editor-in-Chief Kennedy somehow misplaced a large mountain. Kiliminjaro is not in Kenya but in Tanzania, where its rapidly melting ice cap may threaten a significant source of tourism revenue.

News of the Week: "Genome resources to boost canines' role in gene hunts" by E. Pennisi (21 May, p. 1093). The dog that appears in the middle of the bottom row of the image is actually a mastiff, not a boxer as stated in the caption.

Random Samples: "Here thar be whorls" (7 May, p. 820). The map discussed in this item, the Carta Marina, was published in 1539, not 1519.

News of the Week: "Oldest beads suggest early symbolic behavior" by C. Holden (16 Apr., p. 369). The two beads mentioned in the story are 5 millimeters in diameter, not 35 millimeters.

News Focus: "New South Africa puts emphasis on reclaiming humanity's past" by J. Bohannon (16 Apr., p. 377). South African archaeologist Cedric Poggenpoel's name was misspelled in the article.