SCIENCE

Published by the **American Association for the Advancement of Science (AAAS),** *Science* serves its readers as a forum for the presentation and discussion of important issues related to the advancement of science, including the presentation of minority or conflicting points of view, rather than by publishing only material on which a consensus has been reached. Accordingly, all articles published in *Science*—including editorials, news and comment, and book reviews—are signed and reflect the individual views of the authors and not official points of view adopted by the AAAS or the institutions with which the authors are affiliated.

The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objectives are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, to advance education in science, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

Membership/Circulation
Director: Michael Spinella
Fulfillment: Marlene Zendell, *Manager*; Mary Curry, *Member Service Supervisor*; Pat Butler, Helen Williams, Laurie Baker, *Member Service Representatives*
Promotions: Dee Valencia, *Manager*; Hilary Baar, Angela Mumeka, *Coordinators*
Research: Kathleen Markey, *Manager*; Robert Smariga, *Assistant*
Financial Analyst: Jacquelyn Roberts
Administrative Assistant: Nina Araujo de Kobes
***Science* Member Services**
Marion, Ohio: 800-347-6969;
Washington, DC: 202-326-6417
Other AAAS Programs: 202-326-6400

Advertising and Finance
Associate Publisher: Beth Rosner
Advertising Sales Manager: Susan A. Meredith
Recruitment Advertising Manager: Janis Crowley
Advertising Business Manager: Deborah Rivera-Wienhold
Finance: Leslie Gelder, *Manager*
Marketing Manager: Laurie Hallowell
Traffic Manager: Tina Turano
Recruitment: Michele Pearl, *Operations Manager*; Dan Moran, *Traffic Manager*; Debbie Cummings, Celeste Wakefield, Angela Wheeler, *Sales*
Marketing Associate: Allison Pritchard
Reprints Manager: Corrine Harris
Permissions Manager: Arlene Ennis
Sales Associate: Carol Maddox

ADVERTISING SALES: East Coast/E. Canada: Richard Teeling, 201-904-9774, FAX 201-904-9701 • **Southeast:** Mark Anderson, 305-856-8567, FAX 305-856-1056 • **Midwest:** Donald Holbrook, 708-516-8882, FAX 708-516-8883 • **West Coast/W. Canada:** Neil Boylan, 415-673-9265, FAX 415-673-9267 • **UK, Scandinavia, France, Italy, Belgium, the Netherlands:** Andrew Davies, (44) 457-838-519, FAX (44) 457-838-898 • **Germany/Switzerland/Austria:** Tracey Peers, (44) 270-760-108, FAX (44) 270-759-597 • **Japan:** Mashy Yoshikawa, (3) 3235-5961, FAX (3) 3235-5852
Recruitment: 202-326-6555, FAX 202-682-0816
European Recruitment: AnneMarie Vis, (44) 0223-302067, FAX (44) 0223-302068
Send materials to *Science* Advertising, 1333 H Street, NW, Washington, DC 20005.

■

Information for Contributors appears on pages 40–42 of the 1 January 1993 issue. Editorial correspondence, including requests for permission to reprint and reprint orders, should be sent to 1333 H Street, NW, Washington, DC 20005.

LETTERS

Use of NSFNET

Christopher Anderson's article about the privatization of the National Science Foundation's NSFNET (News & Comment, 21 May, p. 1064) mentions an Office of Technology Assessment report which says that most U.S. researchers use computer networks only for electronic mail and suggests that the benefits of Internet to scientific collaboration are yet to be realized. Earth scientists, and seismologists in particular, however, are already making extensive use of NSFNET and Internet facilities for the rapid distribution of large data sets and for collaboration between researchers at widely separated institutions. We are concerned about plans that could restrict the high-speed NSFNET backbone to a select group of scientists and could encourage a system of charges that hampers access by the wider research community.

The Incorporated Research Institutions for Seismology (IRIS) supports an automatic system that gathers data, through Internet and phone modem, from up to 27 globally dispersed broadband digital seismic observatories, including stations in Russia, Western Europe, Australia, and Japan, and at the South Pole. Whenever a significant earthquake occurs around the globe, researchers can obtain data by Internet from the IRIS Data Management Center within hours. Data from this system was critical in the planning of the aftershock surveys that followed the 19 October 1989 Loma Prieta earthquake in the San Francisco Bay area and the 28 June 1992 Landers earthquake in Southern California. On 21 May 1992, the Chinese detonated a high-yield (Richter magnitude, 6.6) nuclear explosion underground. University seismologists in the United States augmented the automatically retrieved data set for this explosion with digital waveforms from the IRIS open seismic station in Obninsk (outside of Moscow) by a satellite telemetry link and sent the data across the United States on the Internet system. Within a day of the explosion, scientists in Russia, California, and Colorado had analyzed the data in a collaborative effort.

The utility of the current academic networking system is a direct consequence of its fairly uniform software protocols and its low cost to individual users. Easy access to large shared databases and seamless collaboration between distant researchers are becoming essential to modern research. We trust that, as the National Science Foundation and Internet respond to pressures for expansion and privatization, access restrictions and burdensome charging structures do not curtail these healthy trends.

Jeffrey Park*
Department of Geology and Geophysics, Yale University, New Haven, CT 06511–8130

*Cosigners: Tim Ahern, The IRIS Consortium; Thomas Boyd, Colorado School of Mines; Goran Ekstrom, Harvard University; John Filson, U.S. Geological Survey; Karen Fischer, Brown University; Charles Langston, Pennsylvania State University; Jonathan Lees, Yale University; Arthur Lerner-Lam, Columbia University; Alan Levander, Rice University; Guy Masters, University of California, San Diego; Guust Nolet, Princeton University; Thomas Owens, University of South Carolina; Gary Pavlis, Indiana University; Robert Phinney, Princeton University; Paul Richards, Columbia University; David Simpson, The IRIS Consortium; Stewart Smith, University of Washington; Brian Stump, Southern Methodist University; Frank Vernon, University of California, San Diego; Terry Wallace, University of Arizona; and Francis Wu, State University of New York, Binghamton.

■

Whither Directed Mutation?

In their letter of 28 May (p. 1222), Richard E. Lenski and John E. Mittler made several misleading statements about the experiments that John Cairns and I have published (*1*, *2*). The relevant results can be summarized as follows. In most of our experiments we used a strain of *Escherichia coli* that cannot use lactose because of a frameshift mutation affecting the *lacZ* gene. When these Lac^- cells were plated on medium with lactose as the sole source of carbon, Lac^+ revertants, scored as colonies, appeared after 2 days and continued to appear for a week or more. Early-appearing Lac^+ revertants had a Luria-Delbrück distribution, indicating that they arose during nonselective growth before plating, from which we calculated a mutation rate of 1.4×10^{-9} per cell per generation. Later appearing revertants had a Poisson distribution, as they should if they arose after plating, and appeared at a constant rate of 2.2×10^{-8} per cell per day. Lac^+ revertants did not accumulate if the cells were starved in the absence of lactose or in its presence if the cells were also deprived of another requirement for growth (*1*).

Lenski and Mittler state that our methods were not sufficiently sensitive to detect the growth of Lac^- cells in the presence of lactose or the death of cells (both Lac^- and

Lac$^+$) in its absence. However, if the continuous appearance of Lac$^+$ revertants was a result of normal generation-dependent mutations, the number of cells would have had to increase 50- to 100-fold during the course of our experiments. Similarly, to account for the failure of Lac$^+$ cells to accumulate in the absence of lactose, the population would have had to decline nearly 10-fold during a 4-day period of starvation. We would have detected such gross population changes had they occurred (*1*).

Lenski and Mittler state that we did not investigate whether starvation would affect the "time course of colony formation after lactose was provided." Yet, we showed repeatedly (and with three different Lac$^-$ alleles) that the time course of appearance of Lac$^+$ colonies was unaffected by starvation for periods of up to 4 days (*1*, *2*).

Lenski and Mittler imply that we did not take into account the fact that our population of Lac$^+$ revertants included cells with different growth rates on lactose. However, we have discussed in detail the distribution of growth rates among the Lac$^+$ revertants (*1*). We demonstrated, by statistics and by direct observation, that the proportion of fast- and slow-growing revertants was the same among the population of Lac$^+$ revertants appearing long after lactose selection was applied as among the population of Lac$^+$ revertants that arose during nonselective growth. Thus, the late appearing revertants were not simply slow growers.

Lenski and Mittler suggest that our late-arising Lac$^+$ revertants were not a result of a single mutational event, but of an initial mutation conferring an intermediate phenotype that allowed a cell to grow slowly on lactose, followed by a mutation to the final Lac$^+$ phenotype. Any low-frequency event can be modeled as the product of two or more higher frequency events, but such modeling must be constrained by the actual data. To account for mutants appearing at frequencies of 10^{-9} to 10^{-8} per cell, this model requires that both the initial and the final mutation rate be extremely high. In particular, the mutation rate from the intermediate to the final phenotype must be of the order of 10^{-5} per cell per generation (*3*). The occurrence of such a high mutation rate would itself be worthy of investigation. Furthermore, Lenski's model (*3*), and others that assume that mutants arise simply because a population of cells is increasing with time, predicts that the rate at which mutants appear should also increase with time, whereas we find that the rate of appearance of new Lac$^+$ revertants is constant (*1*, *2*).

Patricia L. Foster
Department of Environmental Health, Boston University School of Public Health, Boston University School of Medicine, Boston, MA 02118

References

1. J. Cairns and P. L. Foster, *Genetics* **128**, 695 (1991).
2. P. L. Foster and J. Cairns, *ibid.* **131**, 783 (1992).
3. R. E. Lenski, M. Slatkin, F. J. Ayala, *Proc. Natl. Acad. Sci. U.S.A.* **86**, 2775 (1989).

Response: Foster calls our earlier remarks (*1*) about a paper by Cairns and Foster (*2*) misleading. We do not think they were. We do not have sufficient space for a detailed rebuttal; however, several general points bear on this controversy.

Mutational events cannot be witnessed directly, so their rates must be inferred indirectly from the population dynamics of mutant genotypes and their progenitors. Therefore, experiments intended to demonstrate the existence of directed mutations require a careful accounting of population dynamics and appropriate controls. The complicated experiments reported by Cairns and Foster (*2*) do not convincingly address these problems. We have investigated experimentally two other studies purporting to demonstrate directed mutation and, in both cases, the apparent directedness of certain mutations (under conditions where the resulting phenotype was advantageous) disappeared when we performed additional analyses and controls that took into account alternative hypotheses (*3*, *4*).

The alternative explanations (to that of directed mutation) reflect processes that are likely to be quite general (*5*). The issue, therefore, is not whether these processes are relevant, but whether they are of sufficient magnitude to explain the observed dynamics without invoking directed mutation. The alternative hypotheses are not mutually exclusive; several effects may combine to produce a much larger discrepancy than could be explained by any single process (*5*). These alternative explanations [references *9–11*, *48*, and *51* cited in our article (*5*)] were published well before Cairns and Foster (*2*) published their paper. Thus, Cairns and Foster had the opportunity to present (and, if appropriate, refute) these alternative explanations in a cogent fashion. However, they did not cite any of these papers or discuss alternative explanations.

Even if real, the phenomenon of directed mutation would not require any reverse flow of information by which a cell might "instruct" itself to produce appropriate mutations. Several models proposed for directed mutation [references *8*, *17*, and *40* cited in our article (*5*)] invoke subtle biases in mutational processes that could, if verified, explain this phenomenon on the basis of random molecular events. And experimental results reported recently by Foster and Cairns (*6*) seem to exclude the instruction-