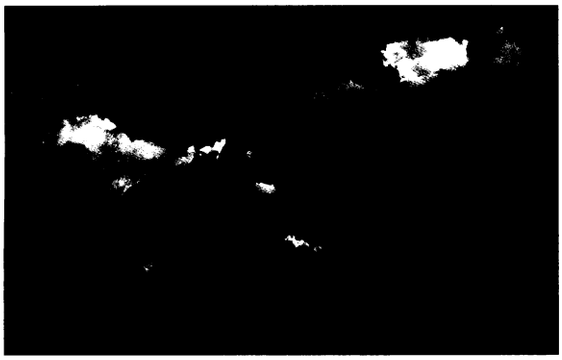
Readers criticize an editorial by Stephen Jay Gould as being "a sermon" and replacing one "crutch" with another. Gene therapy researchers discuss "clinical trials for patients with retinoblastoma," as well as where a cowboy hangs his hat. Speaking of clinical studies in general, readers state that "physicians, physician-scientists, and basic scientists all have contributed to biomedical research." And Earth scientists debate the magnitude of the seismic hazard in the New Madrid zone in the central United States

Science and "Truth"

It is amusing to see how quickly evolutionists fall into the trap of scientism (which is religiosity) when they declare that the theory of evolution has claim to "the truth." No reputable physicist or chemist would be presumptuous enough to characterize scientific discoveries, at least in the hard sciences, as "truth that will make us free," even when the evidence has become overwhelming (as it has for the Second Law of Thermodynamics or Einstein's theory of general relativity).

The editorial "Darwin's more stately mansion" by Stephen Jay Gould (*Science*'s Compass, 25 June, p. 2087) is a sermon in praise of the "evolutionary nexus," as he calls it. If Gould chooses to believe that he belongs to the species *Homo sapiens*, where he is "a little higher than the apes...," that is his prerogative. I and many of my physicist colleagues see intelligent design everywhere in nature and, compelled by the weight of such evidence, choose to believe that we are made "a little lower than the angels...," a quote which Gould takes from Psalm 8, but quickly dismisses as a "crutch."



Random or intelligent design?

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I ought to thank Gould for reminding me of the difference between good science and scientism. We should all take seriously the principle that "the confidence expressed in any scientific conclusion should be directly proportional to the quantity and quality of evidence for the conclusion" (*1*).

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References

1. *Teaching Science in a Climate of Controversy* (American Scientific Affiliation, Ipswich, MA, 1993), p. 23.

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Gould is right that the public would be better off if they understood the basis of all biological science. But I disagree that evolution, as a scientific theory, is "validated," at least in the classic sense of the scientific method. Evolution, when construed as the hypothesis that the properties of all species are set by the process of natural selection through survival and reproduction of the fittest, is, at best, a barely testable hypothesis.

Scientific hypotheses are most securely "validated" when (i) they make successful predictions; (ii) there are conceivable observations that could, in principle, refute them, but have not; and (iii) there is a comparably sensible competitor theory that is faring worse. None of these conditions is met by evolution, at least when it is construed as a statement about the natural world.

Don't get me wrong: I believe in evolution. But I would have a much stronger reason for my belief if Gould or others made a verifiable, falsifiable prediction about some as-yet-unobserved aspect of the natural world (and I don't mean about selectively bred fruit flies in laboratories) and put the hypothesis that evolution occurs by natural selection through survival of the fittest to an a priori test.

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Gould's editorial, with its many allusions to religious images, is puzzling. Has Gould appropriated the terminology of traditional religion as a prelude to creating an evolutionary religious faith? Or does he (consciously or unconsciously) recognize the existence of realities that transcend the empirical facts and that can only be expressed by words like "spirit" or "soul"?

If it follows from the statement "evolution is true" that "the comforts and crutches of traditional religious belief are false," then it behooves the evolutionary scientist to make his or her case. If "evolution is true" logically implies that "our species is *not* God's created image," then say so. Otherwise, a "pastoral effort" to win the minds and hearts of unbelievers that removes one crutch to replace it with another is open to severe criticism. (And do not forget the multitude who accept both the theory of evolution and the idea of man's spiritual destiny.)

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Although we probably can only ascribe spiritual significance to the biblical myth of creation, we must also be aware that man's thought and imagination are in a timeless realm—we cannot correlate either with what is happening in an hour in the timepiece on our wrist or over billions of years. Gould, therefore, should be more careful about overreaching with his laments and conclusions.

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Retinoblastoma Treatment

We take exception to the article "RAC nixes gene therapy treatment for retinoblastoma" by Ken Garber (News of the Week, 25 June, p. 2066). We strongly disagree with its portrayal of events at the 14 June meeting of the National Institutes of Health (NIH) Recombinant DNA Advisory Committee (RAC). At that meeting, members of our research team presented a proposed phase I clinical trial for patients with retinoblastoma that involves the use of suicide gene therapy. This therapy, which employs an adenoviral vector to deliver the herpes simplex thymidine kinase gene followed by treatment with ganciclovir, has been used to treat other tumors, including those of the central nervous system. Our proposed protocol will be the first use of this therapy to treat a malignancy of the eye. Current therapies for children with retinoblastoma include enucleation, chemotherapy, and radiation, all of which have damaging lifelong consequences, including blindness and increased onset of fatal second malignancies. The article by Garber does not accurately reflect either the outcome or the

collegial discussion that occurred at that RAC meeting. Our protocol was not "nixed" by the RAC. In fact, the RAC has encouraged us to proceed with the clinical study after addressing recommendations that evolved as a result of our discussion at that meeting. We intend to move forward after incorporating these recommendations.

Garber's article seems to trivialize the important ethical and scientific questions that were raised in this forum. Pedro Lowenstein presented interesting unpublished findings concerning the administration of viral vectors into rat brain. Thaddeus Dryja had some important views on the therapy of retinoblastoma that went far beyond the statement that enucleation is "gratifyingly tolerable" for the treatment of this disease. These ad hoc reviewers along with members of our clinical research team were

Retinoblastoma, a malignancy of the eye and a target for gene therapy

asked to present their views to the RAC and did so out of a sincere commitment to better the lives of children with cancer.

The article makes it sound as if the meeting was rife with contention and disagreement. Nothing could be farther from the truth. The meeting was handled like any other NIH review committee meeting and strongly adhered to the peer-review process so vital to the scientific community. Members from our team have great respect for the members of the RAC, the ad hoc reviewers, and the review process. In fact, one of the members of our research team, Estuardo Aguilar-Cordova, is currently a member of the RAC, but was not involved in the review process for this protocol.

Finally, a statement is attributed to Jan Wolff implying that some members of the gene therapy community are "cowboys." For those of us who have dedicated our careers to finding treatments for children with cancer that not only cure their disease but also avoid long-term toxicity and debilitation, we can only respond that when we enter our patients' rooms, we leave our hats and boots at the door.

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Seismic Hazard at the New Madrid Seismic Zone

In their report "Slow deformation and lower seismic hazard at the New Madrid seismic zone" (23 Apr., p. 619), Andrew Newman *et al.* analyze a regional network of Global Positioning System (GPS) velocity vectors in terms of a model developed for "infinitely long" strike-slip faults like the San Andreas, in the central United States (*1*). The apertures of the geodetic networks along the San Andreas are small with respect to the length of the fault, and far-field velocities approach the rate of relative plate motion. The exact opposite is the case in the study by Newman *et al.* The segmented fault system in New Madrid seismic zone is smaller than the scale of their regional geodetic network, and because the fault system they are studying is located within a stable continental interior, far-field velocities must approach zero (or extremely small values).

For these reasons, my colleagues and I made a detailed study in 1991 (*2*) of crustal strain with the use of a dense concentration of geodetic stations located astride a single major fault. Our repeated GPS measurements of this network in 1993 and 1997 appear to indicate lower rates of strain accumulation than we originally reported (*2*) on the basis of combined GPS and triangulation measurements. Lower rates of strain, however, do not necessarily imply lower seismic hazard for the region. It is quite possible that the strain energy released in the "storm" of large earthquakes that have been occurring in this area for the past few thousand years took hundreds of thousands, or even millions, of years to accumulate. If this is the case, a slow rate of strain accumulation over the past 6 years does not imply low seismic hazard.

The persistently high rate of seismic activity in the New Madrid Seismic Zone over the past few thousand years implies high seismic hazard in the foreseeable future.

To communicate any other message to the public would seem to be a mistake.

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2. L. Liu, M. Zoback, P. Segall, *Science* **257**, 1666 (1992).

Response

Our report examined two arguments widely cited to support assertions of high seismic hazard in the New Madrid zone, as illustrated by the National Seismic Hazard maps showing a higher hazard there than that shown for California. We found that both arguments seem incorrect.

First, our GPS measurements showed little or no far-field motion across the seismic zone, both near the fault and at distant sites. In contrast, Liu *et al.* (*1*) studied a network within ours, reported rapid strain accumulation comparable to that for the San Andreas fault, and interpreted this as consistent with an earthquake of magnitude 8 on the Richter scale occurring about once every 1000 years. Our observation of little or no resolvable motion, which Zoback and others now also find in their network, is independent of assumptions about fault mechanics. Both we and Liu *et al.* relate the inferred slip to earthquake recurrence through the standard steady-state assumptions criticized by Zoback. Although one might postulate alternatives, including time-dependent effects, the present data seem inadequate to require any explanation beyond that of little present motion.

Second, we revaluated an analysis by Johnston and Nava (*2*), which yielded a 550- to 1100-year recurrence for earthquakes with a magnitude greater than 8.3. We found that these data in fact correspond to a 14,000 +/– 7000 year recurrence for such earthquakes, or a 1,400 +/– 600 recurrence for magnitude 7 earthquakes. It thus appears that the largest New Madrid earthquakes are either smaller or less frequent than previously assumed. In our preferred model, these earthquakes are magnitude 7 (10 times smaller than one of magnitude 8). Similar proposals are being advanced by others based on fault lengths and geologic estimates of fault slip, both of which appear too small for magnitude 8 earthquakes. These observations have implications for seismic hazard estimates in the area. The predicted hazard depends on assumptions, many of which have considerable uncertainty because we have little seismological data from any but small earthquakes. For example, treating a magnitude 7 earthquake as one of magnitude 8 overpredicts the peak ground acceleration by a factor of two or more. Other factors contributing to the high values in the hazard maps include a model predicting higher ground motions than those estimated by alternative models, and parametrization of the largest earthquakes as occuring on widely separated faults, which increases the area of highest predicted hazard.

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