A reader urges caution about having confidence in a Nuclear Test Ban Treaty. Researchers assert that, mathematically, the physical properties of DNA are more like links of overcooked spaghetti than a chain of rigid uncooked pieces: "in reality, there are no hinges interspersed with rigid regions (unless perhaps one reduces to a single base pair–level description)." Phylogenetic analyses of whales are explored. The editor of the *Thomas A. Edison Papers* comments on the nature of Edison's workshops and research. Scientific journal prices are decried. And the ability of epidemiological studies to identify risks from silicone breast implants is questioned.

Confidence in Nuclear Deterrence

One must admire the determination and idealism expressed by Sidney Drell *et al.* (Policy Forum, *Science*'s Compass, 19 Feb., p. 1119) for trying to achieve the controversial political goal of a Comprehensive Test Ban Treaty (CTBT). However, the U.S. nuclear stockpile cannot be known to be free of unanticipated problems without experimental testing of the explosive itself. Changes creep into the system as time passes. "Confidence" is a relative, not an absolute, term. The consequence of mistaken untested confidence regarding a nuclear weapon issue could involve human lives. By analogy, in Drell's field, the complete testing of postulates at a high energy–physics facility is often required before wide acceptance is possible. Unanticipated results are not infrequent.

Recruitment and retention of top-notch scientists and engineers who are qualified to assess the amalgamation of the many technical fields that enter nuclear explosive performance will be difficult indeed unless they can test their work. To complicate the issue, any technical ambiguity in an assessment will have to stand up to enormous political pressures to postpone or ignore bad news ("clear warning signs of unanticipated problems").

It is not surprising that many have concluded that a CTBT is not in the U.S. national interest.

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DNA: Uncooked, *al Dente*, or *Scotti*?

A recent Random Samples contribution "Locked but not knotted" (12 Feb., p. 931) describes a mathematically interesting result about locked, unknotted hexagons. We believe, however, that the statement that DNA is like "chains or loops of linked rigid pieces, like bits of uncooked spaghetti joined by hinges," rather than the more familiar "overcooked spaghetti" is misleading.

Piece-wise linear models of polymers were introduced by Kuhn in the 1930s to provide a tractable model simpler than the continuous description that he knew was closer to reality. His approximation and subsequent refinements have successfully allowed relatively simple mathematical and numerical treatments of physical phenomena in DNA. However, the effective physical properties of DNA are relatively uniform along the backbone and, in reality, there are no hinges interspersed with rigid regions (unless perhaps one reduces to a single base pair–level description).

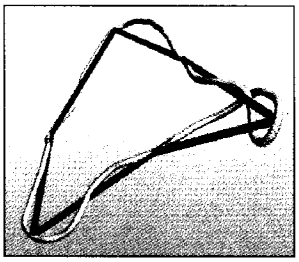

Fig. 1. DNA model.

Electron microscopy of DNA has shown that on the wide range of viewable length scales the double helix appears as a continuous curve (Fig. 1). Any such smooth curve (in yellow) can be well approximated by n line segments, with n sufficiently large (the case $n = 6$ shown in red seems inadequate). The question of how large n needs to be depends on the smoothness of the underlying curve, or whether the spaghetti is cooked *al dente* or *scotti*. For models of DNA, this smoothness depends on the number of base pairs represented by the continuous curve (2686 for the data shown).

We know of no realistic application involving a piece-wise linear model of a DNA loop where the number of links, n, can be as few as 6. Moreover, any conclusion that depends sensitively on n—for example, rigidity—for $n = 6$, which disappears for $n = 7$, cannot be physically pertinent for DNA.

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Response

The point of Stasiak *et al.* that DNA does not resemble a polygon of 6 or 7 rigid segments is absolutely correct. Such a model may be more realistic for an artificially synthesized polymer, and several mathematicians I spoke with suggested that this might be an interesting project for chemists to work on (similar to the synthesis of "rotaxanes," in which two loops are geometrically linked without being topologically linked). For DNA, the best model may indeed be one that depends on the details of how the spaghetti is cooked, as Stasiak *et al.* suggest.

The mathematical treatment of large molecules with a certain amount of rigidity is still very much in its infancy. If mathematicians continue to study models of molecules that are in some respects outdated or oversimplified, the reason is that there are still interesting questions about them that have not been answered. The mathematicians I spoke with felt that the shape presented by Jason Cantarella was a useful step toward understanding the effect of rigidity on conformation. The conclusion: Rigidity matters.—**Dana Mackenzie**

Whale Origins

In a recent book review (*Science*'s Compass, 12 Feb., p. 943) of the volume *The Emergence of Whales: Evolutionary Patterns in the Origin of Cetacea* (edited by J. G. M. Thewissen) (*1*), John E. Heyning writes, "[m]ost analyses of the morphological data indicate that perissodactyls (horses, tapirs, rhinos) form the sister taxon to cetaceans" and cites four phylogenetic analyses (*2*) of paleontological data. All of these predate work in the *The Emergence of Whales*. In fact, chapter 6 of the Thewissen volume (*3*) explicitly *supports* the idea that artiodactyls are more closely related to cetaceans than are perissodactyls on the basis of a maximum parsimony analysis of morphological data.

Again, on the subject of whether or not perissodactyls are the extant sister taxon of cetaceans, Heyning writes, "[i]n all the molecular analyses this potential relationship either has not been fully explored or, in some cases, has been excluded by the designation of perissodactyls as an outgroup." This statement is contradicted by a

Early whale evolution poses difficulties for taxonomists.

chapter in the Thewissen volume by J. Gatesy (*4*). Gatesy's analysis is one of the most densely sampled molecule-based phylogenies for mammals, and I would not characterize it as having "not fully explored" the position of perissodactyls. More important, Gatesy's figure 16 shows that he did not designate perissodactyls as an outgroup. There are three mammalian orders (Primates, Camivora, and Rodeniia) at lower nodes on the tree than Perissodactyla.

Hotly debated areas of genuine incongruence do persist between molecular and morphological phylogenetic analyses of cetaceans—in particular, on the issue of artiodatctyl monophyly. However, there are places where consensus has emerged.

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3. J. Geisler and Z. Lou, in (*1*), pp. 163–212.
4. J. Gatesy, in (*1*), pp. 63–111.

Response

Challenging dogma inherently evokes critique; I address each point in order. My statement that most recent phylogenetic analyses of morphological data sets show a relationship of cetaceans to a perissodactyl/paenungulate clade is correct as cited. While the excellent paper by Geisler and Lou (*1*) in the *Emergence of Whales* does result in a cetacean/artiodactyl clade, it does not de facto negate previous studies. This is because each of these studies has used a slightly different suite of morphological characters, making comparisons among studies problematic at best. A concrete example is that Geisler and Lou examined only a limited selection of soft tissue characters, not incorporating such characters as the outpocket off the Eustachian tube, which forms an air sinus in the peribullar region. This derived character is uniquely shared by cetaceans, perissodactyls, and hyraxes (*2*). One problem for all morphological studies to date has been that there have been inadequate investigations of several key morphological features. I have found that some pivotal characters failed to meet muster as derived characters, whereas others are demonstrably not homologous, and others have been overlooked altogether.

My second point, that outgroup selection has not been fully explored in most molecular analyses, also withstands scrutiny. The chapter by Gatesy (*3*) represents one of the most exhaustive and methodologically sound phylogenetic studies I have read to date. Nonetheless, Gatesy (*3*, p. 81) explicitly states that he used perissodactyls as one of his outgroups in some of his analyses based on the assumption of a cetacean plus artiodactyl clade. If perissodactyls are the sister taxon to cetaceans, then their use as an outgroup will incorrectly root the tree, with potentially cascading impacts on the entire phylogeny. Virtually all analyses have shown that ungulates form a monophyletic clade, with artiodactyls, cetaceans, and perissodactyls clustering in a polytomy at the basal node. Nonetheless, an undeniable problem is that it is unclear which order of mammals represents the sister taxon to the ungulates, which should serve as the most appropriate outgroup to properly root the tree. This dilemma is no less profound for the morphological data than it is for the molecular data.

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Edison's Laboratory

The issues raised by John J. Gilman in his 15 January letter (*Science*'s Compass, p. 327) prompt me to respond both to his remarks and to Bettyann Holtzmann Kevles's review (*Science*'s Compass, 11 Dec., p. 1997) of my book, *Edison: A Life of Invention* (*1*). The book's arguments are actually much closer to those suggested by Gilman than those represented in the review. In her effort to distill a 500-page book into a short review, Kevles chooses language that oversimplifies my analysis of Edison's laboratories and research methods.

I would never use the term "overgrown workshop" to describe Edison's laboratories. In fact, I discuss at some length how he combined the tradition of machine shop invention with laboratory research to construct a new institution—the industrial research laboratory. In addition, I point out how the first of these laboratories at Menlo Park was seen as new by his contemporaries, who then tried to emulate his example. I also note that, during the last quarter of the 19th century, Edison had the finest and best-equipped private research laboratories in the United States. Moreover, Edison pioneered the use of research teams that combined skilled mechanics, able to construct and modify new technologies, with laboratory researchers using the best electrical and chemical apparatus available to investigate and test the materials and mechanical and electrical elements that made up these devices.

The research that went on in Edison's laboratories was certainly much more than mere tinkering, another term I would never use to describe Edison's work. It may be that Kevles and I disagree over the extent to which Edison's research, which was largely empirical, represents research rather than tinkering. But I would argue that much scientific and technological research is primarily empirical. Throughout the book, I discuss at length how the research undertaken by Edison both drew on the best scientific knowledge of the day and often moved beyond that knowledge to provide new understanding of materials or electromagnetic effects that proved essential to his inventive work. Moreover, from 1874 until near the end of his career, Edison periodically undertook basic research designed to discover unknown natural forces; while these might ultimately be useful to the development of new technologies, the creation of new knowledge was the primary goal. The laboratory records that I draw on extensively show us a very different Edison from the commonly held image of a self-taught tinkerer.

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Response

It seems to me that it is a matter of tone that disturbs Israel. It is true that the phrases "overgrown workshop" and "tinkering" are mine, not his. But I did not omit to mention his attention to Edison's interest in and understanding of the basic science of his day. I certainly did not intend to denigrate Edison. I suggest that readers examine this very important biography for themselves and then decide if my review distorted or demeaned Edison's character or contributions.

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Journal Prices

As most of us know, the price of commercial scientific journals (R. Johnson, Letters, *Science*'s Compass, 1 Jan., p. 33; D. L. Roth, *ibid.*; P. T. Shepard, *ibid.*, 27 Nov., p. 1643; H. K. Lee, *ibid.*; D. Malakoff, News of the Week, 30 Oct., p. 853) has increased at about three to four times the consumer price index (CPI). Even allowing that the CPI is not the correct measure of costs in academia and even allowing for an increase in the number of journal pages published, this is an outlandish rate of increase. Most academic libraries cannot keep up with these price increases and, as a result, the number of subscribers for most commercial journals has decreased over the years. This "wastage" causes the commercial publishers to increase their subscription prices even faster to keep their revenues level. Because the users of these journals (the scientists who publish in them) are not the