

The work by Milton *et al.* on the synthesis of mirror-image enzymes reporting experimental proofs of enzymology on the other side of the mirror is causing a stir in the biomolecular community. Molecular chirality (handedness) presents a unique form of chemical isomerism (enantiomerism) where the physical and chemical relationship between enantiomers (mirror images) is determined only by the properties of either enantiomer and the constraints of symmetry, independent of chemical bonding or structural size. The ramifications of these constraints razor through the palaver about the mirror-image worlds now pervading the community.

With regard to "mirror-image" syntheses, it follows from first principles that within the stereoselective total synthesis of an enantiopure natural product like amphotericin lies the precise synthetic methodology for "mirror-image" amphotericin (1). Even for a stereoselective reaction brew for which the exact structure of the active species is unclear [for example, Sharpless epoxidation (2)], determination of the stereoselective characteristics of the *d*-brew unequivocally determines the characteristics of the *l*-brew. Thus, the characterization of a naturally occurring enzyme must dictate irrefutably the properties of the enantiomeric enzyme; independent synthesis is unnecessary.

As for structural mandates, the statement that "two enzyme molecules are mirror images in every respect" contradicts the idea that the structural elucidation of the mirror-image protease is "a *fundamental* demonstration that the final folded 3-D structure and . . . biological activities of this . . . enzyme molecule are completely determined by the amino acid sequence" (emphasis added). Symmetry mandates both the structure and properties of the mirror-image protease, and nothing new about protein folding or properties could come from this experiment without the discovery of a major violation of parity. The experiment has no option but to fall into register, and any rigorous scientist must refute the statement that "We can now state, based on experimental evidence, that protein enantiomers should display reciprocal chiral specificity in their biochemical interactions."

Without loss of generality, these principles apply even when speaking of life forms. Therefore, it is a mistake to assume that only after the experiment by Milton *et al.* need we consider the possibility of enantiomeric life forms and their incompatibility with our own. The possibility of enantiomeric life forms has been known and cogently discussed since the time of Louis Pasteur (3).

Important questions that can be addressed by the synthesis of mirror-related natural products deal with chiral diastereomeric interactions, that is, the differential effects associated with a right- or left-handed molecule interacting with an independent chiral molecule. Evaluation of these diastereomeric interactions requires that only one of the reactants be available in *both*-handed forms; symmetry determines the missing combinations. For example, the finding of a difference in binding constants between lambda and delta forms of an octahedral coordination complex with right-handed DNA determines that there must be a difference in the binding of right-handed and left-handed DNA to the lambda isomer; the synthesis of both pairs of enantiomers is redundant.

When Milton *et al.* state that "To date only L-enzymes have been described . . ." and conclude that "this leaves the presumed properties of D-enzymes . . . as unexplored questions," they must be referring to properties resulting from diastereomeric interactions. In such cases, it would be judicious first to decide if the mirror-image substrate would be an easier synthetic target than the enzyme, given that it provides the same information.

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REFERENCES

1. K. C. Nicolaou and W. Oglevie, *Chem. Tracts* 3, 327 (1990).
2. K. B. Sharpless, *Chem. Br.* 22, 38 (1986).
3. L. Pasteur, "Researches on molecular asymmetry" (Alembic Club Reprint no. 14, Univ. of Chicago Press, Chicago, IL, 1860).

Response: The experiment described in our paper was not intended as a test of the principle of parity or of the principles of chirality in chemistry. It was, rather, a vivid demonstration of the basis of the protein folding process that gives rise to the active tertiary and quaternary structure of an enzyme. This is clearly evident from the paper. Due credit was given to Fischer and Pasteur.

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Several readers of my Perspective "On the other hand . . ." (5 June, p. 1403) have pointed out that molecules possessing an axis of symmetry can be chiral; a molecule need only have more than one chiral center (for example, DNA or tartaric

acid). I meant in my definition to speak of a center within a molecule rather than the molecule as a whole and should have made this point clearer. It is probably most useful to regard chirality as a property of arbitrary figures and achirality, the property of being superimposable on one's mirror image, as something special. Here is what I should have said: Molecules, or three-dimensional objects in general, are achiral if they have a center or a plane of symmetry.

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Amber Trees

Virginia Morell's intriguing report on extraction of DNA from insect inclusions in amber (Research News, 25 Sept., p. 1860) gives as the origin of Dominican Republic amber "the now-extinct tropical *Hymenaea* tree. . . ." In fact, *Hymenaea courbaril*, the species most closely linked with amber from South and Central America, is still found in these regions (1). Several years ago in the Dominican Republic, I photographed clear sap oozing from the trunk of a living *H. courbaril* and encapsulating ants in precisely the same fashion as the ants in my amber collection were encapsulated eons ago.

Some scientists, in the quest for ancient DNA, have purchased or otherwise acquired large collections of amber containing specific insect inclusions. They should be aware of possible regulations in the United States and the country of origin concerning the disposition and intentional destruction of fossils removed from museum collections and from other countries. If such destruction is permitted, it is to be hoped that the investigators will carefully document and photograph the specimens before they are destroyed.

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REFERENCES

1. J. H. Langenheim, *Science* 163, 1157 (1969); D. H. Janzen, Ed., *Costa Rican Natural History* (Univ. of Chicago Press, Chicago, IL, 1983), pp. 253-256.

Response: My article incorrectly stated that the resin came from "the now-extinct tropical *Hymenaea* tree." It should have read, "an extinct species (*H. protera*) of the tropical *Hymenaea* tree." A related species, *H. courbaril*, thrives today in

the Dominican Republic, as well as in Mexico and Central and South America, yet this is not the closest living relative to *H. protera*. According to Jean Langeheim, a paleobotanist at the University of California, Santa Cruz, the extinct tree's closest ancestor (*H. verrucosa*) is actually found in East Africa and Madagascar.

—Virginia Morell

A Career in Industry

It was most refreshing to see the discussion of industrial careers in the Careers '92 section of *Science* (18 Sept.). It caused me to remember the climate I experienced while at the University of California, Berkeley (1965–1970). My fellow graduate students and most professors felt that industrial careers were for those who could not do real science or could not get an academic position, or both. They could not understand why I might want a career in industry. But since I had industrial experience gained between receiving my baccalaureate degree and entering graduate school, I knew there were very good scientists and engineers doing real science in industrial positions and that their work was enhancing the quality of life for society at large. Moreover, I knew that truly competent scientists and engineers could use the problem-solving skills gained in their university experience to address problems of great breadth and complexity having technical, financial, and social dimensions.

I have greatly enjoyed working in industry. I highly recommend it to young scientists and engineers who want good opportunities to develop depth and breadth of knowledge and experience.

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Corrections and Clarifications

In Joe Alper's 25 September article "Everglades rebound from Andrew" (News & Comment, p. 1852), the species name of *Melaleuca quinquenervia* was misspelled and the tree was described incorrectly as "an Australian eucalypt." The *Melaleuca* are a distinct genus and are commonly referred to as paperbarks.

The article about the viral hybrid SHIV by Joseph Sidroski and his colleagues that was reported in Jon Cohen's News & Comment article "Monkey-human viral hybrid is new weapon in AIDS fight" (24 July, p. 478), appeared in the July issue of the *Journal of Acquired Immune Deficiency Syndrome*, not the June issue, as stated.

REQUEST FOR PROPOSALS

In 1981–82, Heptachlor epoxide contaminated a considerable part of Hawaii's milk supply. This has led to concern that adverse health effects might result from consumption of contaminated dairy products, particularly among children. Studies to identify potential disease problems, and to develop measures to prevent or ameliorate them are sought and will be supported.

Research Areas of Interest

Although a wide range will be considered, primary focus will be devoted to six research areas likely to lead to practical applications in public health and clinical care.

1. Follow-up of those persons tested for heptachlor epoxide in Hawaii.
2. Case control studies of conditions that might be caused by heptachlor, with residue analyses of cases and controls, such as heptachlor epoxide, fat levels and breast cancer.
3. Baseline studies of child development, behavior, school function and socialization.
4. Preclinical studies of agents that might assist the removal of heptachlor.
5. Studies on the clinical management of persons exposed to heptachlor, both medical and psycho-social.
6. Metabolism of heptachlor and related substances. Biological effects of heptachlor and related substances in model systems (subcellular, tissue culture or experimental animals).

Coordination among different research projects will be encouraged where possible to avoid duplication of effort and to facilitate access to material and populations. Projects up to two years duration will be considered for funding.

Applications: Submit a letter of intent of less than 500 words to the Foundation for review by the Scientific Advisory Council. The Scientific Advisory Council of the Hawaii Heptachlor Health Effects Research Program is chaired by Dr. David P. Rall. Letters of intent received by January 10, 1993 will be reviewed. Submitters will be notified by March 20, 1993 on whether or not to submit full applications. Send all letters of intent to the address below. Copies of the Foundation's research policies are available upon request to the Foundation office.

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