The head of a European genome program says that the "shotgun sequencing of the human genome" proposed by "J. Craig Venter and his colleagues" deserves "a demarche" that includes sequencing the "mouse genome." Studies finding an "association of the *DRD2 A1* allele with alcoholism" are defended. And might German and American chemistry instructors benefit from swapping some "teaching strategies"?

Retro-Laser

In his article, "Engineers dream of practical star flight" (News of the Week, 7 Aug., p. 765), James Glanz did not mention the 1991 science fiction novel *The Mote in God's Eye* by Larry Niven and Jerry Pournelle, in which laser-launching cannons and a light sail used for interstellar travel are imagined. One possibility described in the book, but not in Glanz's article, is the use of the light sail for military purposes. Maybe the U.S. Department of Defense is working on it.

Ann Schaeffer
LEDA Systems, Inc., 14785 Preston Road, Suite 550, Dallas, TX 75240, USA. E-mail: annsch@ledasys.com.

Neural Net Wizard

I would like to clarify some features of the program NeuroShell Easy described in "Neural nets for novices" by John Wass (*Science*'s Compass, 7 Aug., p. 789). First, our Turboprop2 paradigm is not based on the General Regression Neural Network (GRNN), although GRNN is also in the package. Second, the software is not just for novices. It is true that users of older algorithms are accustomed to fine-tuning controls. Our Web site (*1*), however, has many testimonials by neural net professionals praising our newer algorithms that do not require "tweaking" to make them classify and predict accurately. Finally, Wass emphasizes what he perceives is an absence of cutting and pasting ability. Although the software does not edit the raw data (most raw data is kept in spreadsheets or other editors, anyway), it has full facilities for cutting and pasting graphs and predictions to other programs. One can use the standard right mouse click, as documented in the Instructor wizard.

Steven A. Ward,
President, Ward Systems Group, Inc., Executive Park West, 5 Hillcrest Drive, Frederick, MD 21703, USA. E-mail: wardsystems@msn.com

References

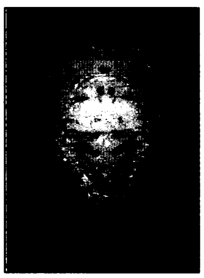
1. www.wardsystems.com

Beetle Juice

Frank C. Schröder *et al.* do well to recognize a natural combinatorial library in beetle pupal secretions ("Combinatorial chemistry in insects: A library of defensive macrocyclic polyamines," Reports, 17 July, p. 428). But contrary to enthusiastic remarks in the accompanying News article by Luis Campos ("Building a better bug repellent," p. 321), other natural libraries exist, although they may not have been titled as such. Combinatorial arrays include polyphenolics [for example, poly(tannin)s and lignin] and polyisoprenoids (for example, terpenes). These arrays are often involved in plant defenses (*1, 2*) and so are comparable in role to the newly discovered cyclopolyesteramine library for pupal self-defense.

One reason the phytochemicals have eluded apprehension as libraries may be the nature of linking bonds, which are variable as to type, site, and number of such links on each "mer" in an oligomer or polymer. (*1, 2*) To date, the complexity of combinatorial phytopolymer arrays has frequently been viewed as evidence of startlingly crude or unaudited synthetic pathways. As one might expect, pupal secretions were also conceded to be possibly the result of a "sloppy" pathway, as mentioned by Campos.

Biological defense is evidently served well by loosely ordered chemistry: "Random" chemical arrays have eluded development of resistance by natural foes for unknown ages. The use of defensive arrays not only by disparate phytochemical pathways suggests that human medicinal formulations could benefit from this strategy, too. Moreover, where many randomly linked products are needed, "sloppy" pathways are economical: Lignin biosynthesis (which has a reasonably well-understood mechanism) (*2*) uses few enzymes.



Squash beetle pupae, master chemist

THOMAS EISNER

What other functions rely on libraries? Given the olfactory qualities of terpenes, it seems possible that combinatorial arrays also contribute to reproduction-related messages such as pheromones, scents to allure pollinating insects, and the like. One wonders how many mysteries of physiology would be solved simply by recognizing that a combinatorial library is present.

Frank R. Denton III
Senior Staff Scientist, Motorola Energy Systems Group, 1750 Belle Meade Court, Lawrenceville, GA 30043, USA. E-mail: erd006@email. mot.com

Response

We are basically in agreement with the points expressed in the thoughtful letter by Denton. What struck us as special about the squash beetle defensive secretion is the simplicity of the chemistry leading to the formation of the polyazamacrolide library. With the use of only three homologous precursors and a single reaction (esterification) to join the monomeric units, the entire array of large-ring defensive compounds is generated. It is conceivable that no more than a single enzyme is responsible for the indiscriminate assembly of the entire set of macrocycles. In addition, we see no evidence for any post-assembly enzymatic transformations. These insects, therefore, practice combinatorial synthesis in what might be its most elementary form.

Of course, in a sense, many natural product mixtures can be viewed as having been assembled combinatorially. The mixture of isoprenoids found in a typical plant essential oil would be a good example. Such plant "libraries," produced from a single building block, gain most of their chemical diversity from the subsequent enzymatic modification of the primary combinatorial products (geranyl pyrophosphate, farnesyl pyrophosphate, and so forth). An essential oil—which contains only a small subset of the almost unlimited number of terpenoid compounds possible—is, therefore, not entirely analogous to the insect-produced secretion which we have described.

We are confident that other examples of randomly assembled mixtures derived from a single precursor or from a small set of closely related precursors will be encountered in nature. Our suggestion is that only such collections of compounds be designated as natural combinatorial libraries.

Jerrold Meinwald
Department of Chemistry, Cornell University, Ithaca, NY, 14853–1301, USA. E-mail: fs31@cornell.edu

Thomas Eisner
Section of Neurobiology and Behavior, Cornell University

Frank Schröder
Department of Chemistry, Cornell University. E-mail: fs31@cornell.edu

Melting, Maybe

In his article "Signs of past collapse beneath Antarctic ice" (News, 3 July, p. 17), Richard A. Kerr quotes Michael Oppen-