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.

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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.

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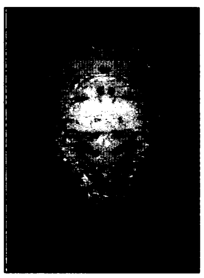
1. www.wardsystems.com

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.



THOMAS EISNER

Squash beetle pupae, master chemist

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.

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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.

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Melting, Maybe

In his article "Signs of past collapse beneath Antarctic ice" (News, 3 July, p. 17), Richard A. Kerr quotes Michael Oppenheimer's recent review of the status of understanding of the West Antarctic Ice Sheet (WAIS) and its stability (*1*). According to Kerr, "[Oppenheimer] concluded from the erratic behavior of late that its [the WAIS's] most likely fate is disintegration during the next 500 to 700 years, greatly accelerating sea-level rise beginning in the 22nd century." Kerr suggests that Oppenheimer provided one of several "alarming recent predictions." Oppenheimer discussed three possible future scenarios for the WAIS, and his assessment was that the scenario summarized by Kerr has the highest relative likelihood but, as noted by Oppenheimer, with low confidence. Oppenheimer started the discussion of possible future scenarios with the statement: "It is not possible to place high confidence in any specific prediction about the future of [the] WAIS."

Ross ice shelf: Stay awhile?

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1. M. Oppenheimer, *Nature* **393**, 325 (1998).

Learning from Others

In his article "U.S.–style universities for Germany?" (News & Comment, 19 June, p. 1826), Martin Enserink describes Germany's movement toward infusing private (partially public-supported) universities into its existing traditional higher education structure. This infusion may eventually result in institutions of higher education that operate more like those found in the United States. While the higher education system in Germany may learn from us, our system can also learn from some of Germany's present practices, especially related to teaching strategies emphasized in beginning college-level chemistry or other science courses.

For example, our recent study of teaching behaviors practiced by faculty and teaching assistants in beginning college chemistry education in the United States (*1*) concluded that more than 95% of laboratory instructional time is spent in instructors responding to students' procedural questions. Many students even believe that responding to these kinds of questions is the major role of the instructor. Thus, students spend little time reading and interpreting directions before, during, and after each 3- to 4-hour laboratory class per week. They also spend little time in drawing conclusions from the data collected and virtually no time in addressing the scientific and social significance of the laboratory findings.

We also observed and analyzed the teaching done by "overseers" during beginning college chemistry laboratories in Germany. Examples of effective practices were students spending from 20 to 25 hours per week engaged in laboratory settings planning for and carrying out real investigations. Overseers did not respond to procedural questions, and students met with them and the department chair for oral examinations on knowledge learned from the laboratory experience. On a voluntary basis, these students attended only three or four lectures each semester.

As an example of an ineffective practice, the laboratories were pretty much limited to classical qualitative analysis without the use of analytical instrumentation or computers. These "tools" are left for more advanced courses.

Our recommendation is for German institutions to not "throw out the baby with the bathwater"; that is, they should continue emphasizing active and extensive student participation in scientific investigations, but also adopt some of our more useful instructional laboratory practices.

At the same time, we in the United States need to place more emphasis on student inquiry and involvement in the instructional process. New curricula like MC2 and Modular Chemistry could take chemistry instruction in the United States in this more effective direction (*2*).

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References and Notes

1. A. Hilosky, F. Sutman, J. Schmuckler, *J. Chem. Educ.* **75**, 100 (1998).
2. These are two of the five major chemistry curriculum projects supported through the Division of Undergraduate Education of the U.S. National Science Foundation. The two projects joined efforts after initial development at the University of California, Berkeley, and Beloit College in Wisconsin.

A "Humouse" Project

In their commentary "Shotgun sequencing of the human genome" (*Science*'s Compass, 5 June, p. 1540), J. Craig Venter and his colleagues once more create a sensation by announcing that a new industrial entity is aiming to sequence the whole human genome in 3 years at a cost of $300 million, a small amount in comparison to those of other efforts.

There are two key elements to this project. First, a new generation of sequencers will be launched by Perkin-Elmer Corp., a partner in the project. Second, a global "shotgun" approach to sequencing will be attempted.