

LETTERS

Soundings

An invertebrate's inner spark provides inspiration for a musical composition (right, leech neuron). Carl Djerassi writes that "the features of a truly novel contraceptive . . . are precisely the economic disincentives" that keep companies from developing such a drug. Another author questions whether new developments in the x-ray analysis of atoms can accurately be described as holography. Clinical trials of "natural" substances to test whether they might prevent cancer are discussed.



DAVID VAN ESSEN

Hirudo medicinalis Unplugged

In August 1994, Ken Muller, chair of the neuroscience program at the University of Miami Medical School, asked if I would compose a musical tribute (1) to neuroscientist John G. Nicholls (2, 3) for his 65th birthday, as I am a scientist (4), a composer, and a former student of Nicholls'.

The "Nichollsfest" was planned for November; I was at the Marine Biological Lab at Woods Hole and had little free time for music until the squid stopped running in September.

Knowing Nicholls' love of Beethoven (whom he often compared to his own mentor, Nobel Laureate Bernard Katz), I based the first movement on Beethoven's music, using thematic gestures and the sonata-allegro form. Nicholls' passion for Peru inspired the rhythms and melodies of the second movement, while the third movement was based on a 15th-century Nahuatl-Aztec poem he translated and sent as a greeting card to all his colleagues in 1993. This movement also uses gestures from a song cycle by Berlioz, "Les Nuits d'Été."

The thematic material for the final movement was borrowed from the electrical firing patterns of neurons in the central nervous system of the leech *Hirudo medicinalis*, a biological model system (3) developed by Nicholls before his current work on the opossum, in which he made significant discoveries about the role of glia and neurons in electrical signalling (2, 5) and about fundamental principles of axonal regeneration (6). As an undergraduate student in Nicholls' lab at Stanford in the late 1970s, I was surrounded by these neuronal rhythms, even in my dreams.

To alleviate possible boredom to the noninitiate, I added a Swiss yodel, intended to symbolize Nicholls' position as chair of

pharmacology at the BioCenter in Basel, Switzerland.

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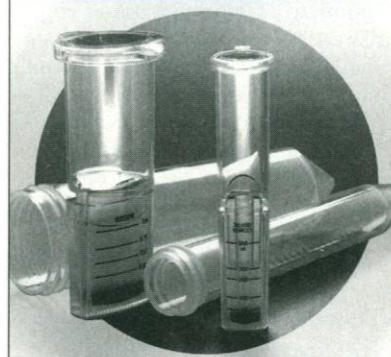
References and Notes

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7. I thank K. Muller and many other colleagues of J. G. Nicholls for support in producing the CD.

Striving for Creativity

My joy in seeing the title of Eliot Marshall's article "NIH panel urges overhaul of the rating system for grants" (News & Comment, 31 May, p. 1257) turned to dismay when I read that members of the National Institutes of Health (NIH) panel evaluating the peer-review system "left innovation out," according to Hugh Stampfer (extramural research director at the National Institute of Mental Health), "because it seemed a bad idea to suggest that every grant should strive for creativity." The current very low proportion of funded grants coupled with a rating system subject to a ceiling effect effectively results in a blackball system: Even one disgruntled

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evaluator can knock a proposal out of the competition. Many scientists have deplored an evaluative system that they have seen as implicitly rewarding grant proposals that are not objectionable to anyone passing judgment, rather than proposals that are highly creative and therefore likely to offend at least some vested interest (1). The recommendation of the panel makes explicit what before had been implicit—the institutionalized view that scientific creativity is not a necessary condition for a grant's being reviewed favorably. Yet, the research that has mattered in science has always been that which is creative and thus often defies existing conventions. There is a problem with the rating system at NIH, but fixing the rating system won't fix the larger problem of priorities that fly in the face of the history and philosophy of science.

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The Economics of Contraceptives R&D

A recent report by an Institute of Medicine (IOM) committee on contraceptive research and development (R&D) (Robert F. Service, *News & Comment*, 31 May, p. 1258) clearly defines the global unmet need for contraception. It decries the withdrawal of the pharmaceutical industry from the contraceptive field and considers it important "to show drug companies the massive need and potential market for new contraceptives." That massive need may well exist, but not the potential market. Of the eight largest pharmaceutical companies in the world, not one is active in contraceptive R&D; not one seems to sell contraceptive drugs or devices. The pharmaceutical market, which has changed dramatically during the past decade, has spoken. It now focuses on blockbuster drugs dealing with diseases of aging or deterioration in the increasingly geriatric populations of affluent Japan, North America, and Europe, not the needs of the poor pediatric societies of Latin America, Asia, and Africa.

An item in the same issue (*Random Samples*, 31 May, p. 1269) features the ominous trends for infectious diseases, list-

ing the four biggest global killers: acute respiratory infections, diarrheal diseases, tuberculosis, and malaria. If we again consider the minute fraction of the huge R&D budgets of the top eight pharmaceutical companies dedicated to these fields, we see that unmet burning societal needs do not necessarily equal financial returns.

The most important point missed by the IOM committee is that the features of a truly novel contraceptive (say, a contraceptive vaccine or a once-a-month anti-implantation or menses-inducer pill) associated with major societal advantages (for example, low cost and long duration for a vaccine; short action and minimal pill consumption involving 13 pills per year for a menses-inducer versus 250 or more pills per year for current oral contraceptives) are precisely the economic disincentives keeping companies, which search for billion-dollar drugs used daily, from reentering the contraceptive field. The proposal "that commitments [by international aid agencies] to buy large volumes of contraceptives would induce companies to develop low-cost products" is a pipe dream. The only reason why some of the current oral contraceptive manufacturers will sell monthly pill regimens at 20 cents a pack-

Even Carl von Linné
would have difficulty
classifying us

