Excitement over X-ray lasers is excessive

Structural biology is a rich field in which existing techniques are providing many advances.

Sir — It is not the case, as your News Feature[1] states, that free-electron lasers (FELs) will have their "biggest impact" in biology. Such a prediction could normally be left to live or die peacefully, but the very high cost of X-ray FELs might make it an expensive funeral, and biological scientists should not have to pay the costs.

In structural biology, the fundamental limitation is radiation damage. This puts a ceiling on the dose of X-rays that can pass through a molecule before it is destroyed[2]. A small advantage might be gained from the use of pulsed X-ray sources such as the FEL promises to deliver, but this advantage will not be obtained in the first generation of X-ray FELs[3] because the pulse lengths will be too long. A much bigger advantage has already been obtained during the 1990s by freezing protein crystals to liquid-nitrogen temperature and below. Together with improvements in the technology from expression and purification of proteins and brighter sources (third-generation synchrotrons), it has produced the current flood of new structures and has turned structural biology into the superbly productive field it is at present.

Sample freezing has also revolutionized electron microscopy, which can produce more structural information from a single protein molecule than can X-ray diffraction — before radiation damage terminates data collection. Electron cryomicroscopy already delivers many of the advantages hoped for from the X-ray FEL and has two further advantages. First, the cross-section for electron scattering is higher than for X-ray scattering, so working with single molecules is simpler. Second, by using lenses to focus the electrons, the diffracted beams can be collected and used to form an image which gives the phases of the Fourier components of the structure directly. X-ray diffraction gives only amplitudes.

The use of X-ray FELs in biology, as reported in your feature, is being hyped. Those who wish to build X-ray FELs should think of some good uses in another field and put aside for the moment the idea that they will have a big impact in biology. Your feature also suggests that there are relatively few good structural data on membrane proteins. While there is always more to be done, there are now excellent membrane protein structures for several members of at least 20 different membrane-protein families, obtained either by X-ray crystallography of three-dimensional crystals (mostly frozen) or by electron microscopy of frozen two-dimensional crystals. Progress towards atomic structures of membrane proteins without crystals will come from electron microscopy[4], and nuclear magnetic resonance is also beginning to succeed with small membrane proteins[5]. I would not bet on getting any help from X-ray FELs.

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1. Patel, N. *Nature* **415,** 110–111 (2002).
2. Henderson, R. *Q. Rev. Biophys.* **28,** 171–193 (1995).
3. Neutze, R., Wouts, R., van der Spoel, D., Weckert, E. & Hajdu, J. *Nature* **406,** 752–757 (2000).
4. Orlova, E. V., Serysheva, I. I., van Heel, M., Hamilton, S. L. & Chiu, W. *Nature Struct. Biol.* **3,** 547–552 (1996).
5. Fernandez, C., Adeishvili, K. & Wuthrich, K. *Proc. Natl Acad. Sci. USA* **98,** 2358–2363 (2001).

Sklyarov: big business vs academic freedom

Sir — Your News in Brief "US drops case against Russian programmer" (*Nature* **415,** 6; 2002), reports that the US Department of Justice dropped its charges against the computer scientist Dmitry Sklyarov in return for his cooperation with its case against his employer, Elcomsoft. You did not report, however, that Sklyarov is also free to testify for Elcomsoft (see www.oreillynet.com/cs/weblog/view/wlg/983).

The Department of Justice issued misleading statements about the case (including the untruth that Sklyarov is no longer employed by Elcomsoft) to try to save face despite the controversy surrounding the Digital Millennium Copyright Act (DMCA). In fact, charges against Sklyarov were not dismissed as part of a plea bargain. Sklyarov still maintains that he and Elcomsoft are not guilty of misconduct, and has offered to tell the truth whether called as a witness by the prosecution or the defence.

To many scientists, the freedom to publish one's findings is taken for granted. Under the DMCA, technologists have no such guarantee, as demonstrated by the threatened lawsuit against professor Edward Felten of Princeton University for publishing a discussion of security vulnerabilities in an incipient digital watermark technology (see *Nature* **412,** 756; 2001). In cases such as this, the Department of Justice has used the DMCA to pursue the financial interests of large corporations at the expense of freedom of information.

Sklyarov's release was a tentative first step away from the draconian enforcement of the dangerously vague DMCA. Yet in releasing him, the Department of Justice incorrectly attempted to imply that Sklyarov was a hacker who saw the error of his ways and decided to incriminate his own employer to avoid jail. The Elcomsoft case may yet bring to light flaws in the DMCA, and cause the public to think twice about its worth. It is to be hoped that the Department of Justice will acknowledge problems as they arise, rather than undertaking a 'spin' campaign and accepting free speech only when it does not hinder big business.

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More light on pioneers of electrochemistry

Sir — Your interesting 2002 annual scientific anniversary Commentary "1902 and all that" by J. L. Heilbron and W. F. Bynum (*Nature* **415,** 15–18; 2002), credits Stanley Lloyd Miller and Harold Urey as the first to find amino acids in the silent electrical discharge, in 1953. But in 1913, Walther Löb had found glycine in the silent electrical discharge in a reducing atmosphere.

Löb had been looking for the formation of amino acids, especially glycine, at least as early as 1909. Oskar Baudisch (1913) also showed that amino acids are generated by ultraviolet light only in a reducing atmosphere. J. S. Haldane (1929) referred to the work of Edward Baly *et al.* (1922), who found glycine using ultraviolet light.

Urey and colleagues had published at least three papers on the chemical effects of electrical discharges in gas in 1928 and 1929, so the field of electrochemistry of gases was well known to him and others at the University of Chicago in the 1950s. Miller's contribution was to repeat the experiments of Löb, Baudisch and Baly *et al.* with more sophisticated modern techniques which were not available to previous authors, such as two-dimensional paper chromatography and elution from Dowex 50.

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