LETTERS

Ilya Glezer's Struggle

The actions of diplomats tend to overshadow the countless individual struggles upon which they are based. One such struggle which should not be ignored or forgotten by the scientific community is that of the Soviet investigative neuropathologist, Ilya Glezer. He is coauthor, with Samuel Blinkov, of *The Human Brain in Figures and Tables* (Plenum, New York, 1968). On 7 February 1972, Glezer was arrested and convicted of anti-Soviet activity. His crime was the possession of Zionist literature. He was given a sentence of 3 years at hard labor to be followed by 3 years of banishment to Siberia. The hard labor portion of his sentence terminated on 8 February 1975, and it has been learned that, immediately thereafter, he was transferred to Krasnoyarsk for the banishment portion of his sentence.

Glezer, now 43, was in poor health when he began his sentence. He suffers from severe myopia with night blindness. Conditions at the camp have resulted in swelling of his legs with resulting physical disability. Some medical treatment that was previously available to him has now been withdrawn, and he has been denied contact with fellow prisoners of conscience. Thus, at a time when détente is preached at government levels, the treatment of Glezer and other political prisoners appears to be as bad or worse than ever.

Despite Soviet protestations about interference in its internal affairs, external pressure can bring relief to individual sufferers. Valery and Galina Panov, who are now free in the West, would still be detained if such pressure had not been applied. Now is the time to mount a campaign to relieve Glezer of the further torture of the prison camp and of three additional years of banishment to Siberia. We urge all readers to wire or write Leonid I. Brezhnev, General Secretary, Communist Party of the Soviet Union, The Kremlin, Moscow, U.S.S.R., asking him to grant a pardon to Ilya Glezer, to suspend the remainder of his sentence, and to permit him to join his mother who now lives in Israel. Copies should be sent to His Excellency Ambassador Anatoly F. Dobrynin, Ambassador of the U.S.S.R., 1125 16th Street, NW, Washington, D.C., and to your local senators and representatives urging further action by them. We also suggest that resolutions demanding Glezer's release be proposed at all international scientific meetings. Inquiries about further details of the Glezer case are welcome and should be directed to the first signer.

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X-ray Crystallography Techniques

We would like to reply to the article by Thomas H. Maugh II, "X-ray crystallography: A refinement of technique" (Research News, 6 Dec. 1974, p. 913), because we believe it is likely to cause some misconceptions. The technological developments discussed may indeed prove useful, but they need to be put in the perspective of the whole process of obtaining a protein structure.

Briefly, the process of determining a protein structure consists of the following steps: (i) crystallization of the native protein and collection of diffraction data; (ii) obtaining and collecting diffraction data from heavy atom derivatives; (iii) obtaining phases for the native data; (iv) computing an electron density map from the data of steps (i), (ii), and (iii); (v) interpreting the electron density map; (vi) checking the structural model against the observed data and possibly refining the model to improve the fit to the data.

The misconceptions stem in part from minimizing the last two steps. Essentially, methods exist [MIR (multiple isomorphous replacement) phasing] for obtaining the phases necessary in step (iii). The techniques described in Maugh's article can be used primarily in a place between steps (iii) and (v): that is, it is apparently possible to take a poorly phased map or a map with limited resolution and improve it by extending the set of phases and by improving those on hand without imposing any interpretation on the electron density map. Inasmuch as protein crystallographic work in the past has been based only on interpretation of MIR-phased maps without

going on to step (vi), any improvements in these maps will be welcome. However, it has become clear in our own laboratory and in others that substantial improvement can be made in a trial model by refinement in the classic crystallographic sense: that is, once approximate atomic positions have been deduced from an electron density map, more accurate positions can be determined by minimizing the difference between the observed and calculated diffraction amplitudes.

We believe that, in an effort to make some complex material understandable to the general reader, Maugh has made some misstatements. Several examples follow. Maugh refers to refining the data, but this is by no means the case. Trial models are refined so that calculated amplitudes better fit the observed values; in the case of Sayre's technique, phases are refined to give a better fit for the equations he derived which constrain them.

It is true that substitution of heavy atoms may make the derivative crystals less isomorphous (that is, less like the native crystal), which may in turn result in both limited resolution and poorer phases for the data on hand. A loss of information occurs and maps may be less interpretable, but the native structures are not distorted. The techniques of Sayre and Collins may serve to add information, thereby improving interpretability of the maps, but in fact, since both their techniques and classical methods need a set of phases initially, they all start with the same distortions, and it is not yet clear how free of error the extended sets of phases really are.

Two statements in Maugh's article concerning our work at the University of Washington are erroneous, First, the assertion that Sayre's map correctly identified five amino acids that were obscure in our map is incorrect. The situation is essentially as stated in Sayre's paper (*1*). Second, Maugh states that our map could not have been obtained using 2.5-Å phase angles. All these methods of refinement, including classical methods, can be regarded as extending phases. In the *Cold Spring Harbor Symposium* (*2*) we state: "In retrospect, it is clear that the refinement [of rubredoxin] could almost equally well have been initiated with atomic coordinates from the 2.5-Å map rather than with those from the 2-Å map. Probably no more than one or two additional ΔF refinement cycles would have been re-

quired." Our refinement of the ferredoxin model amply justifies this statement (*3*).

The point is not to quibble over techniques, but to judge which ones are useful at what stage of the game, and to be aware of the power and limitations of each. The techniques of Sayre and Collins are a welcome addition to the repertoire of possible approaches to obtaining reliable protein structures. The new methods contribute to improving the interpretability of the electron density maps while classical refinement results both in improved interpretability and in a set of atomic coordinates.

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Ethiopian Revolution

The article "Ethiopia: Did aid speed an inevitable upheaval?" by Constance Holden (News and Comment, 27 Dec. 1974, p. 1192) contains some absurdities and contradictions.

It is contradictory to call Ethiopia an "American client state," while at the same time pointing to Haile Selassie's "posture of nonalignment" which "welcomed aid from any and all foreigners" but "sought to prevent them from becoming too influential."

It is proposed in Holden's article that the United States may have helped shape the foundation for the events now being played out. Unfortunately, military dictatorships are frequent occurrences in many "less developed" countries, regardless of which country has been assisting with foreign aid. As for the Ethiopians themselves, the shock of the massacre of 23 November 1974, ordered by junior officers, will surely remind them of their own proverb:

> A village ruled by young men,
> in one year it will become a desert.

What Ethiopian peasant sharecroppers desire most of all is ownership of