17.X-7 *DIRECT METHODS OUTSIDE TRADITIONAL FIELD* *By Fan Hai-fu, Institute of Physics, Academia Sinica, Beijing, China.*

After 40 years of development, direct methods are entering into new fields of application. New procedures are under examination in the Institute of Physics in Beijing.
1. In protein crystallography, the combination of direct methods with isomorphous replacement or anomalous scattering data may play an important role in the near future. The method proposed in our group [Fan (1965) Acta Phys. Sin. 21, 1114; Fan, Han, Qian & Yao (1984) Acta Cryst. A 40, 489; Fan & Gu (1985) Acta Cryst. A41, 280.] has been tested with experimental protein data in the one-wavelength anomalous scattering case yielding a thousand of initial phases with average error of about 40 degrees.
2. In high resolution electron microscopy, direct methods may become a powerful tool of image processing. It has been proved by simulation that direct methods are useful in image deconvolution and resolution enhancement [Fan, Zhong, Zheng & Li (1985) Acta Cryst. A41, 163; Han, Fan & Li (1986) Acta Cryst. A42, 353; Liu, Fan & Zheng (1986) IUCr CSM Meeting, Beijing, China.].
3. Modulated structures are important in both solid state physics and structural chemistry. However there was no straightforward way to solve their structure. Recently a direct method has been proposed and used successfully to solve the phase problem of an incommensurate structure.This implies that direct methods will no longer be limited in solving 3-dimensional periodic structures. Hopefully, the method can be extended to solve the phase problem in the determination of quasicrystal structures.

17.X-8 FUTURE METHODOLOGY, SOME PROBABLES AND SOME POSSIBLES. By Jerome Karle, Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, D. C. 20375, U.S.A.

In the area of macromolecular structure determination, there are several developments which indicate the potential for enhanced analytical capability. In addition to the development of tunable, high-intensity sources (synchrotron radiation) and the continuing improvement of computing facilities, the results of theoretical studies of the isomorphous replacement and the anomalous dispersion techniques in recent years imply the potential for enhanced speed and facility in performing structure determinations. An algebraic analysis of multiple-wavelength anomalous dispersion, for example, has resulted in a set of simultaneous equations that are both exact and linear (J. Karle, Int. J. Quantum Chem. Symp., 1980, 7, 357-367). The exact algebraic analysis is valid for any number of anomalous scatterers and any variety of types of anomalous scatterer. The unknown quantities, which do not vary with wavelength, are composed of intensities, phase differences, or a combination of the two. The part that varies with wavelength occurs only as coefficients of the unknowns. The unknown phases and intensities are those that would be obtained from individual types of atoms as if each type were present in isolation from the rest. Knowledge of the intensities for the structure formed by a particular type of atom can facilitate the determination of the structure formed by this particular type of atom. Once the structure is known for any of the types of atom present, the entire structure can be readily determined. The determination of the structure of anomalous scatterers may not always be successful. In those cases, the structures of nonanomalously scattering atoms may, perhaps be obtainable from known values for triplet phase invariants of the type $\phi_h+\phi_k+\phi_{-h-k}$. Values for triplet phase invariants may be obtained from the exact algebraic analysis (J. Karle, Acta Cryst., 1984, A40, 526-531). Evaluations of triplet phase invariants have also been made from use of probability theory (H. Hauptman, Acta Cryst., 1982, A38, 289-294, 632-641; C. Giacovazzo, Acta Cryst., 1983, A39, 585-592; S. Fortier, N. J. Moore and M. E, Fraser, Acta Cryst., 1985, A41, 571-577) and alternative algebraic analyses that make use of special mathematical and physical properties of the isomorphous replacement and the anomalous dispersion phenomena (J. Karle, Acta Cryst., 1983, A39, 800-805; J. Karle, Acta Cryst., 1984 A40, 4-11, 366-373, 374-379; J. Karle, Acta Cryst., 1985, A41, 182-189). It has been further shown that by use of algebraic analysis essentially unique values can be obtained with one-wavelength anomalous dispersion data for the 2-phase invariant (J. Karle, Acta Cryst., 1985, A41, 387-394). This analysis was limited to the case of one predominant type of anomalous scatterer in a one-wavelength experiment. Another investigation has shown that with use of values obtained for 2-phase invariants in one-wavelength anomalous dispersion experiments and single isomorphous replacement experiments, knowledge of the structures of the anomalously scattering atoms or heavy atoms could afford a large number of phase values for initiation of a structure determination of a native or nonanomalously scattering structure (J. Karle, Acta Cryst., 1986, A42, 246-253). This could also provide a possible strategy for use of triplet phase invariants.

17.X-9 THE ROLE OF STATISTICS IN STRUCTURE REFINEMENT. E. Prince, Institute for Materials Science and Engineering, National Bureau of Standards, Gaithersburg, MD 20899, U. S. A.
Mathematical statistics provides some powerful tools for the extraction of information from experimental data. These tools are, however, frequently misused for purposes for which they were never intended, and for which they are ill suited, with the result that there is much confusion when a result is stated in statistical terms. In the context of crystallography, if structure factors, amplitude and phase, were known throughout reciprocal space, all possible information about the crystal would be known, but the only quantites that can be measured, with inevitably limited precision, are intensities at a finite number of lattice points within a bounded region of reciprocal space. The problem, then, is to estimate as precisely as possible the values of all structure factors given the finite set of measured intensities, or, mathematically, to find the means and variances of a set of conditional probability density functions (pdfs) of structure factors, given a set of intensities. Because crystals are composed of atoms, each structure factor can be expressed in terms of a model that is a function of a finite set of atom parameters, $F(\mathbf{h}) = M(\mathbf{h},\mathbf{x})$, so that if the elements of $\mathbf{x}$ can be estimated, the values of all $F(\mathbf{h})$ can be estimated.
An estimator is a function of observations that, under some conditions, approximates an unknown parameter of a population pdf. If the expected value of the estimate is equal to the parameter, the estimator is unbiased. If the expected values of a set of observations, $\mathbf{y}$, are linear functions of the parameters, so that $\langle\mathbf{y}\rangle = A\mathbf{x}$, where A is some matrix, and W is a positive definite weight matrix, usually, but not necessarily, diagonal, then the least squares estimate, $\hat{\mathbf{x}} = (A^TWA)^{-1}A^TW\mathbf{y}$ is an unbiased estimate of $\mathbf{x}$. If, in addition, $W = V^{-1}$, where V is the variance-covariance matrix for the elements of