bond in the non-polar interior of a globular protein is not known with accuracy, and even the planarity of the amide group may not be as invariant as is often assumed.

The resolution normally available from X-ray crystallographic studies of globular proteins is such that electron-density maps do not reveal the positions of individual atoms and can only be interpreted in detail by the use of molecular models incorporating geometrical constraints in the atomic arrangement (such as the planarity of the amide group). In one or two cases there is hope that conventional crystallographic methods of refinement, used with high-resolution X-ray results, may allow these constraints to be dispensed with, leading to atomic arrangements that have not been prejudiced by models used in interpretation. It should then be possible to see how much variation actually occurs in the geometries that are normally assumed to be constant and thus to learn whether the assumptions are valid.

Numerical Methods for Fitting Parameters to Data

By M. J. D. POWELL. (*Building 8.9, Atomic Energy Research Establishment, Harwell, Didcot, Berks., U.K.*)

Theory or a model of a physical system may predict the value $\phi_t(x_1, x_2, \dots, x_n)$ of a measurement y_t , where the x_i ($i = 1, 2, \dots, n$) are parameters of the theory or model. Given a number of measurements, say $y_1, y_2, \dots, y_m$, one may wish to determine the values of the parameters by solving the equations:

$$\phi_t(x_1, x_2, \dots, x_n) = y_t, \quad t = 1, 2, \dots, m \quad (1)$$

In the usual case when $m > n$, it hardly ever happens that one can satisfy all the equations simultaneously, owing to approximations in the theory or model, and owing to errors in the measurements. Indeed one prefers to have m much larger than n , for then one can use methods for calculating $(x_1, x_2, \dots, x_n)$ that tend to smooth out random experimental errors. In this talk we survey the methods that are available for solving the overdetermined system of eqns. (1).

The usual way of allowing for the fact that $m > n$ is to calculate the parameters $(x_1, x_2, \dots, x_n)$ to minimize the sum of squares of residuals:

$$\sum_t \{\phi_t(x_1, x_2, \dots, x_n) - y_t\}^2 = F(x_1, x_2, \dots, x_n) \quad (2)$$

say. The general numerical methods for this calculation are iterative, and a typical iteration improves an estimate, $(\xi_1, \xi_2, \dots, \xi_n)$ say, of the required vector of parameters. Most of the iterative

methods obtain a correction $(\delta_1, \delta_2, \dots, \delta_n)$ to make to $(\xi_1, \xi_2, \dots, \xi_n)$ by using the approximation:

$$F(\xi_1 + \delta_1, \xi_2 + \delta_2, \dots, \xi_n + \delta_n) \approx \sum_t \{\phi_t(\xi_1, \xi_2, \dots, \xi_n) + \sum_j J_{tj}(\xi) \delta_j - y_t\}^2 \quad (3)$$

where $J_{tj}(\xi)$ is the first derivative:

$$J_{tj}(\xi) = [\partial \phi_t(x_1, x_2, \dots, x_n) / \partial x_j]_{(\xi_1, \xi_2, \dots, \xi_n)} \quad (4)$$

The approximation (3) is used because it is a quadratic function of $(\delta_1, \delta_2, \dots, \delta_n)$, and therefore it can be analysed by the methods of linear algebra.

If $(\delta_1, \delta_2, \dots, \delta_n)$ is calculated to minimize the right-hand side of expression (3), then the replacement of ξ_i by $\xi_i + \delta_i$ ($i = 1, 2, \dots, n$) is called the Gauss-Newton iteration. Sometimes it works well, but sometimes it fails to converge, so it has been modified by Levenberg and Marquardt. This modification is described. Also, we mention some methods, based on the approximation (3), that avoid the calculation of first derivatives.

Another approach to solving the overdetermined system (1) is to minimize either the function:

$$F_1(x_1, x_2, \dots, x_n) = \sum_t |\phi_t(x_1, x_2, \dots, x_n) - y_t| \quad (5)$$

or the function:

$$F_\infty(x_1, x_2, \dots, x_n) = \max_t |\phi_t(x_1, x_2, \dots, x_n) - y_t| \quad (6)$$

In these cases if we make the approximation:

$$\phi_t(\xi_1 + \delta_1, \xi_2 + \delta_2, \dots, \xi_n + \delta_n) \approx \phi_t(\xi_1, \xi_2, \dots, \xi_n) + \sum_j J_{tj}(\xi) \delta_j \quad (7)$$

then we find that the iterative methods for calculating the parameters $(x_1, x_2, \dots, x_n)$ are based on linear programming. There are good reasons for occasionally preferring to minimize expression (6) or (7) instead of expression (2), and they are discussed in this paper.

The Conformation of Polynucleotides with Particular Reference to Transfer Ribonucleic Acids

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Structural parameters of RNA. The structural features of double-helical RNA species and their monomer units have been established mainly by X-ray-diffraction studies (Sundaralingam, 1969; Arnott, 1970) and have been supplemented by optical-rotatory-dispersion, circular-dichroism and n.m.r. spectroscopic data.

In RNA the conformation about the glycosidic C-1'-N bond that defines the position of the base relative to the sugar moiety is *anti* with O-2 in pyrimidine and C-4 in purine nucleosides, pointing away from the sugar residue. The five-membered