A FAST METHOD OF COMPARING THREE DIMENSIONAL STRUCTURE OF PROTEINS.

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Comparative studies on protein structures form an integral part of protein crystallography. They provide important information regarding the patterns of protein folding, evolutionary relationships and similarities of active site geometries. The methods currently available for the quantitative comparison of chain folds require considerable computing time. Hence, a new method has been developed by representing protein structures as a set of secondary structural elements. This method is a three dimensional extension of Levitt and Chotia's (Nature, 261, 552 (1976)) diagrammatic representation of helices and sheets. Equivalence between secondary structural elements of two proteins are determined based on their relative orientation using a procedure developed by Needleman and Wunch (J. Mol. Biol., 48, 443 (1970)).

The method provides information regarding statistical significance of similarities, insertions and deletions and preferred packing arrangements. The latter information is not easily obtained by earlier methods. The present method can be used to compare any newly determined structure with all the previously known structures without demanding excessive computing time. However, in contrast to the earlier methods, the present one can be used only for proteins with some secondary structure. The usefulness of the method will be illustrated with examples from globin folds, cytochromes and dehydrogenases.

THE THREE-DIMENSIONAL STRUCTURE OF A 'SALT-LOVING' FERREDOXIN FROM HALOBACTERIUM OF THE DEAD SEA.


Extreme 'halophilic' bacteria are unique in the realm of living organisms since their cellular interiors are approximately 4 M in ECl (Werber et al. in "Energetics & Structure of Halophilic Microorganisms" (1978) Cappel Books, Washington, D.C., pp. 1-654) Bax & Arg, 427, Biochim. Biophys. Acta (1981) 20, 653-664). The survival of these microorganisms depended upon the ability of their proteins to have adapted to their extreme environment; moreover, most of these proteins require high salt for their stability, in contrast to most 'nonhalophilic' proteins which are inactive under such conditions.

A 2Fe-ferredoxin has been isolated and purified from Halobacterium of the Dead Sea. Large red-colored hexagonal plate crystals were grown of it in 4 M phosphate buffer (Sussman et al., J. Mol. Biol. (1979) 124, 375-377). A partially-refined model of a 'nonhalophilic' 2Fe-ferredoxin from a blue green alga, S. platensis, was recently published (Yokoyama et al., Nature (1980) 286, 552-554). Although these two proteins are acid sequence similarity between these two ferredoxins, the 'halophilic' ferredoxin is about 25% larger and has a significantly higher net negative charge at neutral pH than its 'nonhalophilic' counterpart. Therefore the S. platensis structure can at most serve as a possible model for part of the halophilic structure.

The crystal structure of T state met-haemoglobin.

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The aim of our work is to define the structural perturbations produced by ligation of T state haemoglobin. This has been achieved by studying the molecule in a crystal lattice which inhibits the switch to the R conformation.

The structure of a partially oxygenated crystal has been described (Brzozowski et al., Nature, 307, 74-76) and the study has now been extended to the T state met-haemoglobin crystal. Diffraction data have been collected to 2.1A spacing on these crystals (in which all four haems are oxidised). With the coordinates of partially oxygenated haemoglobin as the starting model, the R factor was 46. This has been reduced to .29 by automatic refinement, using Agarwal's FPT routines in conjunction with the simultaneous application of geometrical restraints (Konnerth-Hendrickson). Rebuilding of this structure is now in progress. Preliminary results indicate that all four haems are ligated. Comparison with the structure of deoxyhaemoglobin reveals that the haem geometry has responded to the change in Fe's co-ordination, and that these effects have been transmitted to the surrounding globin and extend to the subunit interfaces. The magnitude of these movements (+1A) is greater than that observed in the partially oxygenated structure. We believe that these structural comparisons will shed new light on the mechanism of haem-haem interaction in haemoglobin.