# Global Optimization and Protein Structure Prediction

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The protein folding problem, i.e., the problem of how to predict the folded (native, tertiary) structure of a protein, given its sequence of amino acids, is one of the most challenging problems in current biochemistry. It is a very rich source of interesting problems in mathematical modeling and numerical analysis, requiring an interplay of techniques in eigenvalue calculations, stiff differential equations, stochastic differential equations, local and global optimization, nonlinear least squares, multidimensional approximation of functions, design of experiment, and statistical classification of data.

A thorough review of the mathematics involved is given in my recent survey *Molecular modeling of proteins and mathematical prediction of protein structure*, SIAM Rev. 39 (1997), 407-460.

Here I shall discuss the mathematical formulation of the static protein folding problem only, ignoring the possible pathways of folding. The talk will have the form of a tutorial, with most things known for some time; but included is some new material on the statistical analysis of the data in the Brookhaven Protein Data Bank.

Topics discussed are

– background from physics and chemistry
– selection of an appropriate potential function
– global optimization techniques
– parameter identification by fitting to experimental data
– handling solvation effects
– recognizing misfolds
– experimental constraints to reduce the search region