

## PREFACE

Modeling, simulations and theoretical studies of biological molecules have expanded tremendously in the last few years. Some of the growth was attributed to the rapid advances in computer technology. Faster and more economical computers made it possible to simulate larger systems for longer periods of time at lower costs. The impact on simulations of biological macromolecules such as proteins was thus profound.

However, this was only part of the story. Equally significant has been the explosion in the number of computational tools available today to investigators in the field. This is especially striking considering that the field was overwhelmed, just a few years ago, by essentially one methodology — the Molecular Dynamics (MD) approach. The strength of MD is its simplicity and generality. The prime weakness of the MD approach is the restriction on the time scale and the limited conformation space that one can sample.

A few recent uses of the MD approach are described by K. Kuczera. The studies of dynamics and thermodynamics of the globins are of special interest. This is due to the wealth of experimental data available, which makes detailed atomic studies worthwhile. Furthermore, since many processes in the globins occur rapidly (e.g. nitric oxide diffusion and recombination), the limited time scale of Molecular Dynamic simulations is less of a problem.

Due to the specificity of proteins and their complexity, it was difficult to come up with an analytical theory of proteins. It is desirable of course to have methods of sufficient generality to address more than one or a few special cases.

Difficulty is not impossibility. Motivated by a problem (protein folding) of utmost importance in biochemistry and biophysics, researchers from different fields entered the area of theoretical biophysics. Armed with a set of tools new to biophysics of proteins, researchers understood a number of beautiful and general principles of protein design. The “polymer physicists” approach to proteins is discussed by Garel, Orland, and Thirumalai.

The title of the chapter “Analytical theories of protein folding” clearly indicates that this is one contribution that is independent of the revolution in computational power.

Another development motivated by the protein folding problem is the work by Luthey-Schulten, Goldstein and Wolynes. This investigation aims at the design of an effective potential that will fold a protein to its correct structure at maximum speed. The principle of the design of such a potential came from the “physicists” approach to proteins and spin glass models. In fact, Peter Wolynes should be credited for many early studies and ideas on the relation between spin glasses and proteins.

Even if an exact potential energy surface is provided, the problem is not yet solved. It is still a non-trivial problem; how to find the global (free) energy minimum among all of the possible alternative conformations. Fortunately, a number of original algorithms appeared in the field of “global optimization”, suggesting that the problem previously believed to be too difficult to solve may be more tractable after all. Straub describes the philosophy and the applications of the new class of optimization techniques.

Low energy minima provide information on probable structures. However, they cannot tell us about kinetics. To bridge the gap between static information and dynamics it is necessary to compute properties related to transitions between alternative minima. Possible approaches to the problem are described in Chapter 2.

Finally we are concerned with electrostatic and ion channels. Ion channels belong to a specific type of proteins that transport ions through membranes. While electric field is important almost everywhere in molecular biology, its importance cannot be overemphasized in channel, in which a charged entity (the ion) is passed through a low dielectric medium (the membrane) using a special biological machinery (the channel). The discussion on electrostatic properties in channels and beyond, in dynamics and in statics of biomolecules, is provided in the last chapter by Eisenberg.

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