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Jill P. Mesirov Klaus Schulten
De Witt Sumners
Editors

Mathematical Approaches to Biomolecular Structure and Dynamics

With 52 Illustrations



Springer

Jill P. Mesirov
Computer Science Department
Boston University
111 Cummington Street
Boston, MA 02215 USA

Klaus Schulten
Beckman Institute
Theoretical Biophysics Group
University of Illinois
405 N. Mathews Avenue
Urbana, IL 61801 USA

De Witt Sumners
Department of Mathematics
Florida State University
Tallahassee, FL 32306-3027 USA

Series Editors:
Avner Friedman
Robert Gulliver
Institute for Mathematics and its
Applications
University of Minnesota
Minneapolis, MN 55455 USA

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FOREWORD

This IMA Volume in Mathematics and its Applications

MATHEMATICAL APPROACHES TO BIOMOLECULAR STRUCTURE AND DYNAMICS

is one of the two volumes based on the proceedings of the 1994 IMA Summer Program on “Molecular Biology” and comprises Weeks 3 and 4 of the four-week program. Weeks 1 and 2 appeared as Volume 81: *Genetic Mapping and DNA Sequencing*. We thank Jill P. Mesirov, Klaus Schulten, and De Witt Sumners for organizing Weeks 3 and 4 of the workshop and for editing the proceedings. We also take this opportunity to thank the National Institutes of Health (NIH) (National Center for Human Genome Research), the National Science Foundation (NSF) (Biological Instrumentation and Resources), and the Department of Energy (DOE), whose financial support made the summer program possible.

Avner Friedman
Robert Gulliver

PREFACE

The revolutionary progress in molecular biology within the last 30 years opens the way to full understanding of the molecular structures and mechanisms of living organisms. Interdisciplinary research in mathematics and molecular biology is driven by ever growing experimental, theoretical and computational power. The mathematical sciences accompany and support much of the progress achieved by experiment and computation as well as provide insight into geometric and topological properties of biomolecular structure and processes.

This volume consists of a representative sample of the papers presented during the last two weeks of the month-long Institute for Mathematics and Its Applications Summer 1994 Program in Molecular Biology. The papers in this volume cover the spectrum from experiment to computation to simulation to theory. Week 3 (July 18–22, 1994) of the Program was Protein Structure and Dynamics, organized by Jill P. Mesirov and Klaus Schulten. Week 4 (July 25–29, 1994) was Topology and Geometry of DNA and RNA, organized by De Witt Sumners.

Protein structure and dynamics is a broad field with a large array of interesting topics. It is of key importance in answering basic scientific questions about the nature of all living organisms and has practical biomedical applications. The major subareas of structure prediction and classification, techniques and heuristics for the simulation of protein folding, and molecular dynamics provide a rich problem domain where mathematics can be helpful in analysis, modeling, and simulation. One would like to infer information about the gross geometric conformation of a protein from its primary amino acid sequence (secondary structure prediction); a robust and biologically significant geometric classification scheme is required to do this. The *ab initio* simulation of protein folding is beyond current technology. However, groups are experimenting with different techniques and heuristics for simulating folding, for example using lattice models and searching conformational space, or exploring certain “folding pathways”. Molecular dynamics is an area where recent progress in *n*-body algorithms has already had a direct beneficial effect.

Experimental scientists have become increasingly aware that the powerful analytical techniques of geometry and topology can be used in the interpretation and design of experiments. Chemists have long been interested in developing techniques that will allow them to synthesize molecules with interesting three-dimensional structure. Polymer scientists continue to study the chemical and physical ramifications of random topological entanglement in large molecules. One of the important problems in molecular biology is the three-dimensional structure of proteins, DNA and RNA in

the cell, and the relationship between structure and function. We need to develop greater understanding of the topology of cellular DNA, RNA and proteins and the various life-sustaining mechanisms used by the cell which modify this molecular topology. Models for molecular structure and metabolic mechanism must be built and understood; simulation, computation and proof of molecular spatial structure and metabolically induced change in structure must be produced. The mathematical tools used in this analysis include statistical and continuum mechanics, partial differential equations, differential geometry, geometric topology, and Monte Carlo simulation, both on lattices and in the continuum.

Jill P. Mesirov

Klaus Schulten

De Witt Sumners

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