The IMA Volumes in Mathematics and its Applications

Volume 82

Series Editors
Avner Friedman Robert Gulliver

Springer
New York
Berlin
Heidelberg
Barcelona
Budapest
Hong Kong
London
Milan
Paris
Santa Clara
Singapore
Tokyo

Institute for Mathematics and its Applications
IMA

The **Institute for Mathematics and its Applications** was established by a grant from the National Science Foundation to the University of Minnesota in 1982. The IMA seeks to encourage the development and study of fresh mathematical concepts and questions of concern to the other sciences by bringing together mathematicians and scientists from diverse fields in an atmosphere that will stimulate discussion and collaboration.

The IMA Volumes are intended to involve the broader scientific community in this process.

Avner Friedman, Director

Robert Gulliver, Associate Director

* * * * * * * * * *

IMA ANNUAL PROGRAMS

1982–1983	Statistical and Continuum Approaches to Phase Transition
1983–1984	Mathematical Models for the Economics of Decentralized Resource Allocation
1984–1985	Continuum Physics and Partial Differential Equations
1985–1986	Stochastic Differential Equations and Their Applications
1986–1987	Scientific Computation
1987–1988	Applied Combinatorics
1988–1989	Nonlinear Waves
1989–1990	Dynamical Systems and Their Applications
1990–1991	Phase Transitions and Free Boundaries
1991–1992	Applied Linear Algebra
1992–1993	Control Theory and its Applications
1993–1994	Emerging Applications of Probability
1994–1995	Waves and Scattering
1995–1996	Mathematical Methods in Material Science
1996–1997	Mathematics of High Performance Computing
1997–1998	Emerging Applications of Dynamical Systems
1998–1999	Mathematics in Biology

Continued at the back

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

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

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

Mathematics Subject Classifications (1991): 92-06, 92C05, 92C40, 92E10, 92-04, 92-08, 82C21, 53A04, 57M25, 60J15, 82D60

Library of Congress Cataloging-in-Publication Data
Mathematical approaches to biomolecular structure and dynamics/ [edited by] Jill P. Mesirov, Klaus Schulten, De Witt Sumners
p. cm. — (The IMA volumes in mathematics and its applications; v. 82)
Includes bibliographical references.

ISBN-13: 978-1-4612-8485-7 e-ISBN-13: 978-1-4612-4066-2
DOI: 10.1007/978-1-4612-4066-2

1. Molecular dynamics—Mathematical models. 2. Biomolecules—Structure—Mathematical models. I. Mesirov, Jill P. II. Schulten, K. (Klaus) III. Sumners, De Witt L. IV. Series.
QP517.M65M38 1996
574.8'8—dc20 96-24164

Printed on acid-free paper.

Production managed by Hal Henglein; manufacturing supervised by Johanna Tschebull.
Camera-ready copy prepared by the IMA.

9 8 7 6 5 4 3 2 1

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

CONTENTS

III. Biomolecular Structure and Dynamics: Computation