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Editorial

Introduction and Foreword to the Special Issue on Protein Flexibility and Folding

INTRODUCTION

The articles in this issue are from a workshop on Protein Flexibility and Folding organized by Dr. Leslie A. Kuhn and Dr. Michael F. Thorpe, professors at Michigan State University. The meeting, held at a lake shore town in northern Michigan, attracted leading experts in the field, including many chemists who have long been in the molecular modelling and computational chemistry community. We are delighted that many participants contributed papers to this issue. Authors were encouraged to include tutorial and review material to make the work accessible to a range of researchers with experimental, computational, and theoretical backgrounds. The manuscripts, which were refereed under the guidance of Professors Kuhn and Thorpe, went directly to Elsevier Science for production. In addition to the full articles here, the abstracts from this meeting were published in the journal's News and Views section last year (Vol. 18, Issue numbers 4/5).

Dr. Kuhn was educated at the University of Pennsylvania, first obtaining her B.A. in Computer Mathematics and then a Ph.D. in Biophysics. Her dissertation was on developing new methods for predicting transmembrane segments and their packing in proteins. Her postdoctoral research at The Scripps Research Institute focused on modeling the atomic structures of proteins and peptides, analyzing the interactions of ligands with proteins, and designing proteins that bind new ligands. As an Associate Professor in the Department of Biochemistry and an Adjunct Associate Professor of Physics, Dr. Kuhn directs the Protein Structural Analysis and Design Laboratory. Her group focuses on developing new computational techniques for modeling protein-ligand interactions, designing new ligands, and predicting the influence of hydration and flexibility in ligand binding. Their goal is to develop techniques that will be useful in applied research, as well as provide theoretical insights into how proteins bind other molecules so specifically. Dr. Kuhn is planning Michigan State University's Bioinformatics infrastructure to be supported under the new Life Sciences Corridor Initiative of the State of Michigan. She also directs MSU's Center for Biological Modeling and is a member of the editorial board of the *Journal of Computer-Aided Molecular Design*.

Prof. Thorpe is University Distinguished Professor of Physics and Astronomy at Michigan State University. He is a theoretical physicist who became interested in protein flexibility and folding, after developing graph theory methods for studying the rigid regions and flexible joints in network glasses and realizing that similar techniques could be applied to macromolecules and proteins to determine their flexibility. He obtained his B.Sc. degree in theoretical physics from Manchester University in 1965, followed by a D.Phil. degree from Oxford University in 1968. He was a post-doctoral associate at Brookhaven National Laboratory prior to joining the physics faculty at Yale University and then in 1976 moving to MSU. Dr. Thorpe maintains a dual citizenship in the United Kingdom and the United States. He was awarded the D.Sc. degree from Oxford University in 1993. A frequent visiting professor, he also serves as consultant to various companies and institutes. He is general editor of the book series *Fundamental Materials Research* and is co-editor of several books including *Rigidity Theory and Applications, Local Structure from Diffraction, Amorphous Insulators and Semiconductors*, and *Access in Nanoporous Materials*. He served a term as North American editor of the *Journal of Physics: Condensed Matter*.

It is my pleasure to welcome Professors Kuhn and Thorpe as Guest Editors of this issue.

Donald B. Boyd, Ph.D.
Editor, *Journal of Molecular Graphics and Modelling*

FOREWORD

The papers in this issue are from the workshop on Protein Flexibility and Folding held in Traverse City, Michigan, August 13–17, 2000. The purpose of the workshop was to bring together people interested in protein structure from theoretical, computational and experimental perspectives and to encourage discussion on new approaches and challenges in the field. The workshop was attended by 43 participants, including 24 invited speakers. The small size of the group made for easy exchanges, and many of the presentations by the invited speakers are collected here. There was also a very lively poster session.

The three-day workshop was organized so that the first day covered Flexibility and Dynamics, the second day Folding and Unfolding, and the third day Evolution and Design. We have used this same organization to present the articles. This area of science is particularly appealing because it spans a range of questions from very fundamental—how proteins fold in such

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short times with such reliability—to applications such as the role of flexibility in screening for new ligands to a protein. Protein flexibility and folding have attracted the attention of scientists from many disciplines, ranging from mathematics to molecular biology. The scientists at the workshop represented the breadth of challenges in theory and applications that keep this field so fascinating and dynamic.

We reproduce here a few comments that were made during talks at the workshop, without attribution. Scientists often feel that their work has cosmic significance. While one speaker said that "Protein folding is like a religion", modesty prevailed with another who defended himself by saying "I am not God". Many disciplines were represented, and some of the comments tried to put the present scientific progress in historical context: "It's old chemistry—as is most of chemistry" to a more inclusive "You're all biochemists", which gave everyone present a warm feeling. Near the end of the meeting, one speaker mused over the exciting prospects and caveats for the future with "You fold one protein, and you think you're going to Stockholm".

We thank David A. Case (Scripps Research Institute, La Jolla, California) and Gerald M. Maggiora (Pharmacia Corporation, Kalamazoo, Michigan) for help in selecting an insightful group of speakers, as well as Michigan State University and Pharmacia for their financial support. We acknowledge Ms. Lorie Neuman, who served as conference secretary, and Ms. Helen Geiger, who helped assemble the articles for this collection.

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