Final Report of the M³ Workshop at NYU, Oct. 12-14, 2000

Project title: International Workshop: Methods for Macromolecular Modeling

Principal Investigator: Tamar Schlick

Program Manager: Roland F. Hirsch

Period: 06/01/00 – 05/31/01

Organization:

New York University, Courant Institute of Mathematical Sciences

251 Mercer Street, New York, New York 10021

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DOE Patent Clearance Granted

Mark P. Dvorscak

(630) 252-2393

E-mail: mark.dvorscak@ch.doe.gov

Office of Intellectual Property Law

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Date

1. Abstract

Computational methods are increasingly being recognized as valuable tools for the study of biomolecular structure and function. Advances in simulation techniques, most notably in the areas of conformational sampling, fast evaluation of long-range electrostatic interactions, timestep integration for molecular dynamics, and quantum-mechanical calculations, have had significant impact on structural biology. New algorithmic approaches, hierarchical spatial representations, and improved computing platforms are continuing to enhance the reliability of macromolecular simulations and to increase their applicability and relevance to biomedical research.

The purpose of our multidisciplinary workshop on *Methods for Macromolecular Modeling* (M³) – the third in a series of meetings in Berlin (1994) and Kansas (1997) – was to bring together both the developers of computational tools for biomolecular simulations and those biological and chemical scientists who utilize modeling applications. The workshop was held at the Courant Institute of Mathematical Sciences in New York City on October 12-14. The Society for Industrial and Applied Mathematics (SIAM) co-sponsored the meeting as part of its new Activity Group on the Life Sciences.

The topics highlighted in M³ 2000 were: (1) new methods for long-term molecular dynamics simulations; (2) conformational sampling: equilibrium and nonequilibrium processes; (3) multiscale modeling; (4) quantum/classical mechanics; (5) fast electrostatics; and (6) applications to enzyme catalysis, DNA modeling, and DNA/protein systems.

The program provided unique opportunities for close interaction and scientific exchange among biomolecular researchers, computer scientists, and applied mathematicians. In the era of structural and functional genomics, it is more essential than ever to integrate concepts from disparate disciplines to generate new ideas and directions for this emerging field. The workshop was designed to serve this need. It also served to educate and inspire junior investigators interested in applying computational methods to problems of relevance to medicine, including the study of disease mechanisms and the improvement of drug design strategies.

The assessment of current progress and the identification of future directions was accomplished through a Perspectives session at the end of the workshop, a report of which is being prepared. Articles by invited speakers are being collected for Springer Verlag's *Lecture Notes series in Computational Science & Engi-*

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Abstract for Conference Proceedings: This special volume collects invited articles by participants of the Third International Workshop on Methods for Macromolecular Modeling, Courant Institute of Mathematical Sciences, October 12-14, 2000. Leading developers of methods for biomolecular simulations review advances in Monte Carlo and molecular dynamics methods, free energy computational methods, fast electrostatics (particle-mesh Ewald and fast multipole methods), mathematics and molecular neurobiology, nucleic acid simulations, enzyme reactions, and other essential applications in biomolecular simulations. A Perspectives article by the editors assesses the directions and impact of macromolecular modeling research, including genomics and proteomics. These reviews and original papers by applied mathematicians, theoretical chemists, biomedical researchers, and physicists are of interest to interdisciplinary research students, developers and users of biomolecular methods in academia and industry.

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2. Results:

A. Statistics of attendees

Total attendance: 187

Composition of attendees by region: US (148), Europe (31), Japan (3), Middle-East (3), South Africa (1), Mexico (1)

Number of speakers: 36

Number of posters: about 60

B. Participating organizations

Society for Industrial and Applied Mathematics (SIAM, co-sponsor)

Molecular Simulation Inc.

Silicon Graphics Inc.

C. Workshop proceedings

The M3 workshop proceedings will consist of 18 original and review articles by workshop speakers and participants, and an article by the editors (Tamar Schlick and Hin Hark Gan) assessing the progress made and future prospects for macromolecular modeling. As planned, the M3 Proceedings will be published in Springer Verlag's *Lecture Notes series in Computational Science & Engineering* (LNCSE). The volume is scheduled to be published sometime in the fall of 2001. The proceeding articles cover many of the main themes of the workshop, and we expect the book will be of interest to beginning and seasoned researchers, and funding agencies.

D. Responses to M3 workshop from attendees

Just a note to say how much I enjoyed the M3 symposium last week. You did a terrific job of mixing the latest efforts in numerical methods/development with a really good sampling of the most interesting recent applications! Thanks again for such a stimulating conference.

Ron Levy, speaker, Rutgers University

Thank you again for inviting me to the M3 workshop! I very much enjoyed my day there and I am very sorry I could not attend the whole conference....

Andrej Sali, speaker/organizer, Rockefeller University

I hope that you have availed yourself of some well deserved rest from the intense days of the meeting. I hope it helped you to know that the meeting was a success, and that your attention, care and talent were recognized by all to have made it such a success.

Harel Weinstein, organizer, Mount Sinai School of Medicine

Thanks Tamar, but I must say the congratulations are all for you! That was one of the most scientifically

informative, thought provoking, and well run conferences I can remember attending!

Don Gregory, participant/sponsor, Molecular Simulation Inc. (MSI)

It was fun, entertaining and educational.

Ron Elber, speaker, Cornell University

I very much enjoyed the meeting. Thanks for organizing such a wonderful event.

Achi Brandt, speaker, Weizmann Institute of Science

I enjoyed the conference and New York City very much!

Sebastian Reich, organizer, Imperial College, London

Thanks for a wonderful, albeit, short stay at your conference.

Peter Kollman, speaker, UCSF

Many thanks for your help and efforts with the M3 meeting. I was pleased to be able to come and present our work.

Stephen K. Burley, speaker, Rockefeller University

Best wishes and thank you for an interesting workshop.

Ulf Börjesson, student, ETH

I very much enjoyed the workshop and I could meet people from various backgrounds which was very interesting. Maybe some of the contacts will come to fruition. Particularly interesting were the researchers from more mathematical backgrounds. I was amazed by the number of applied mathematicians who work in macromolecular modeling.

Markus Meuwly, postdoc, Universite Louis Pasteur, Strasbourg

I congratulate you and your staff for a very interesting meeting.

Nina Pastor, speaker, UAEM, Mexico

Thank you for organizing such a great workshop.

Bo Durbeej, student, Uppsala University, Sweden

Thank you very much for the opportunity to attend this conference. It was enjoyable and intellectually stimulating.

Carol Parish, participant, Hobart and William Smith Colleges

The workshop was very interesting and stimulating, and I also had a very good time in New York.

Leonardo De Maria, researcher, Universite Libre de Bruxelles

Thank you for a wonderful conference.

Michel Kuttel, student, Cornell University/South Africa

I attended the Macromolecular Modeling Workshop and immensely enjoyed the talks and posters.

Pratul Agrawal, student, Penn. State U.

Thank you very much for the invitation to the meeting, it was very interesting!

David Baker, speaker, University of Washington

I thank you both for inviting me to participate in this exciting event.

Robert Krasny, speaker, University of Michigan

Thank you for the great organization.

Melih Sener, postdoc, Beckman Institute, UIUC

Thank you very much for organizing such a good conference.

Emmanuel Paci, postdoc, Universite Louis Pasteur, Strasbourg

I very much enjoyed the conference you organized.

Harold Scheraga, speaker, Cornell University

The meeting was excellent.

Eric Westhof, speaker, CNRS, France

Very well organized meeting.

Dusanka Janezic, speaker, Slovenia

Very good overall; extremely worthwhile trip.

Maggie Hurley, US Army Research Lab.

A good diverse range, with no field overdone, yet I was still interested in 80% of the talks.

Richard Henschman, postdoc., UCSD

E. M³ Workshop Program

Wednesday, Oct. 11 – Courant Institute, 251 Mercer Street

4:00–6:00 p.m. Registration (in the lobby)

Thursday, Oct. 12 – Hemmerdinger Hall, Main Building, 31 Washington Place

8:45–9:40 a.m. Registration and New York bagels

9:30–9:45 a.m. Welcome by Chair and Announcements

MOLECULAR DYNAMICS AND PROTEIN FOLDING

Chair: Tamar Schlick, New York University

9:45–10:30 a.m. **The use of molecular dynamics simulation methods in protein folding and design, ligand binding and enzyme catalysis.**
Peter Kollman, University of California, San Francisco

10:30–11:00 a.m. **Long time dynamics of proteins using the stochastic difference equation.**
Ron Elber, Cornell University

11:00–11:30 a.m. Break

11:30–12:00 **Combining bioinformatics and biophysics in the prediction of protein structure and function.**
Barry Honig, Columbia University

STRUCTURAL GENOMICS AND STRUCTURE PREDICTION

Chair: Andrej Šali, Rockefeller University

12:00–12:30 p.m. **Structural Genomics: An X-ray crystallographic approach.**
Stephen Burley, Rockefeller University

12:30–1:00 p.m. **Comparative protein structure modeling of genes and genomes.**
Andrej Šali, Rockefeller University
1:00–2:45 p.m.

2:45–3:15 p.m. **Prediction of protein structure and function on a genomic scale.**
Jeff Skolnick, Danforth Center

3:15–3:45 p.m. **Some developments in protein fold recognition: Scoring functions and more.**
Ronald Levy, Rutgers University

NUCLEIC ACID SIMULATIONS

Chair: Tamar Schlick, New York University

3:45–4:15 p.m. **DNA base sequence and three-dimensional structure.**
Wilma Olson, Rutgers University

4:15–4:45 p.m. **Molecular dynamics studies of DNA sequence effects and axis bending.**
David Beveridge, Wesleyan University

4:45–5:00 p.m. Break

PARALLEL SESSION I

Hemmerdinger Hall

Chair: Harel Weinstein, Mount Sinai School of Medicine

5:00–5:30 p.m. **Ab initio protein structure prediction.**
David Baker, University of Washington

5:30–6:00 p.m. **Protein-DNA interactions: Computational methods reveal the role of dynamics in sequence specific binding.**
Nina Pastor, UAEM, Mexico

PARALLEL SESSION II

Room 1003, 10th floor, Main Building

Chair: Hin Hark Gan, New York University

5:00–5:15 p.m. **The fast parallel algorithm TREMOLO for DNA and protein simulations.**
Attila Caglar, Universitaet Bonn

5:15–5:30 p.m. **A 'fast growth' method of computing free energy differences.**
Chris Jarzynski, LANL

5:30–5:45 p.m. **Integrating atomic-scale structural details into meso-scale biomolecular simulation: A model for the chromatin fiber.**
Daniel Beard* and Tamar Schlick, New York University

5:45-6:00 p.m. **The detection of correlated mutations in multiple alignments:
a new algorithm for protein modeling.**

Daniel Strahs*, Gary Benson, Tamar Schlick, and Harel Weinstein
New York University and Mount Sinai School of Medicine

6:00-7:30 p.m. **Social Hour** (Sponsored by Molecular Simulation, Inc.)
Silverstein Lounge

Friday, Oct. 13 – Courant Institute, 251 Mercer Street

8:45-9:30 a.m. New York bagels

GLOBAL OPTIMIZATION

Room 109

Chair: Jan Hermans, University of North Carolina at Chapel Hill

9:30-10:15 a.m. **Prediction of protein conformation by global optimization
of a potential function.**

Harold A. Scheraga, Cornell University

10:15-10:45 a.m. Break

NUCLEIC ACID STRUCTURES AND SIMULATIONS

Room 109

Chair: Tamar Schlick, New York University

10:45-11:15 a.m. **Multistranded DNA architectures and adaptive recognition.**

Dinshaw Patel, Memorial Sloan-Kettering Cancer Center

11:15-11:45 a.m. **MD simulations and phylogenetic analysis of RNA base pairs.**

Eric Westhof, IBMC-CNRS, France

MATHEMATICAL MODELING METHODS

Room 109

Chair: Peter Deufhard, ZIB, Berlin

11:45-12:15 p.m. **Climbing scales in molecular dynamics.**

Achi Brandt, Weizmann Institute of Science

12:15-12:45 p.m. **Car-Parrinello simulations of biological systems.**

Ursula Röthlisberger, ETH, Zurich

12:45-2:00 p.m.

QUANTUM METHODS AND FAST ELECTROSTATICS

Room 109

Chair: Robert Skeel, University of Illinois at Urbana Champaign

2:00-2:45 p.m. **How important are entropic effects in enzyme catalysis?**

Computer simulations of activation entropies in enzymatic reactions.

Arieh Warshel, University of Southern California

2:45-3:30 p.m. **Grid based approaches to fast electrostatics.**

Tom Darden, National Inst. of Environmental Health Sciences

3:30-3:45 p.m. Break

PARALLEL SESSION I: FAST ELECTROSTATICS

Room 109

Chair: Sebastian Reich, Imperial College, London

3:45-4:15 p.m. **Adaptive treecodes for computing nonbonded interactions.**

Robert Krasny* and Zhong-Hui Duan, University of Michigan

4:15-4:45 p.m. **Recent progress in fast multipole methods for molecular simulations.**

Leslie Greengard, Courant Institute Mathematical Sciences

PARALLEL SESSION II: QUANTUM DYNAMICS/ENZYMATIC REACTIONS

Room 101

Chair: Jan Hermans, University of North Carolina at Chapel Hill

3:45-4:15 p.m. **Mixed quantum/classical molecular dynamics simulation of
proton and hydride transfer reactions in enzymes.**

Sharon Hammes-Schiffer, Pennsylvania State University

4:15-4:45 p.m. **A combined ab initio QM/MM and free energy simulation
approach to enzyme mechanisms: Method and applications.**

Haiyan Liu, Duke/UNC-Chapel Hill

POSTER SESSION

Courant Lounge, 13th floor

4:45-7:00 p.m. Posters and Light Refreshments

SPECIAL EVENTS ON BROADWAY

8:00 p.m. "Copenhagen" by Michael Frayn, Royale Theater

8:00 p.m. "Proof" by David Auburn, Walter Kerr Theater

Saturday, Oct. 14 – Courant Institute, 251 Mercer Street

9:00-10:00 a.m. New York bagels

BIOMOLECULAR CONFORMATIONS

Room 109

Chair: Benedict Leimkuhler, University of Leicester, UK

10:00-10:45 a.m. **Dynamics of molecular recognition.**

J. Andrew McCammon, University of California, San Diego

10:45-11:15 a.m. **Direct identification of biomolecular conformations as metastable sets.**

Christof Schütte, Free University, Berlin

11:15-11:45 a.m. **Parallel simulated annealing for model and parameter determination in molecular biology.**

K. Chu, Y. Deng, James Glimm*, J. Reinitz, and D. H. Sharp, SUNY, Stony Brook

11:45-12:00 Break

PARALLEL SESSION I: MOLECULAR DYNAMICS APPLICATIONS

Room 109

Chair: Alan Mark, University of Groningen, The Netherlands

12:00-12:30 p.m. **Theoretical study of permeation through the KcsA potassium channel.**

Benoit Roux, Weill Medical College of Cornell

12:30-1:00 p.m. **Improving nerve agent destruction by phosphotriesterase.**

Rick Ornstein, Pacific Northwest National Laboratory

PARALLEL SESSION II: SHORT TALKS

Room 101

Chair: Paul Batcho, New York University

12:00-12:15 a.m. **Ewald summation and plane-wave based ab initio calculations in systems with 2-, 1-, or 0-dimensional periodicity.**

Mark E. Tuckerman, New York University

12:15-12:30 **Multiple timestep integration and the lattice sum for biomolecular simulation.**

Paul Batcho* and Tamar Schlick, New York University

12:30-12:45 p.m. **What can molecular dynamics tell us about nucleic acids: structure, dynamics, hydration, energetics?**

Thomas Cheatham, III, University of Utah

12:45-1:00 p.m. **Efficient long-time step symplectic method for macromolecular simulations.**

Dusanka Janezic, National Institute of Chemistry, Slovenia

1:00-1:15 p.m. **Metastable behavior of Markov processes induced by Langevin models.**

Wilhelm Huisinga, Free University, Berlin

PERSPECTIVES SESSION

Courant Lounge, 13th floor

1:15-2:30 p.m. Lunch and Discussion

END OF M³ WORKSHOP