Report of the Committee on Proposal Evaluation for Allocation of Supercomputing Time for the Study of Molecular Dynamics: Fourth Round

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Board on Life Sciences

Division on Earth and Life Studies

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September 18, 2013

Jodi Swidzinski Hezky, Ph.D.
D. E. Shaw Research
120 West 45th Street, 39th Floor
New York, NY 10036

Dear Dr. Hezky:

This letter describes the work and transmits the final report of the Committee on Proposal Evaluation for Allocation of Supercomputing Time for the Study of Molecular Dynamics, Fourth Round.

The committee evaluated submissions received in response to a Request for Proposals (RFP) for Biomolecular Simulation Time on Anton, a supercomputer specially designed and built by D.E. Shaw Research (DESRES) that allows for dramatically increased molecular dynamics simulations compared to other currently available resources. Over the past three years (October 1, 2010 – September 30, 2013), DESRES has made available to the non-commercial research community node-hours on an Anton system housed at the Pittsburgh Supercomputing Center (PSC), based on the advice of previous National Research Council committees convened in 2010, 2011, and 2012.

The success of the program has led DESRES to make the Anton machine housed at PSC available for an additional 3,700,000 node-hours over the period following October 2013, and DESRES has asked the National Research Council to once again facilitate the allocation of time to the non-commercial research community. The work of the National Research Council committee to evaluate proposals for time allocations was supported by a contract between D.E. Shaw Research and the National Academy of Sciences and was performed under the auspices of the National Research Council's Board on Life Sciences.

To undertake this task, the National Research Council convened a committee of experts to evaluate the proposals submitted in response to the RFP. The committee of 15 was chaired by Dr. Michael Levitt (NAS), Professor and Chair, Department of Structural Biology, Stanford University School of Medicine. The committee members were selected for their expertise in molecular dynamics simulations and their experience in the subject areas represented in the 65 proposals that were considered by the committee. They comprised a cross section of the biomolecular dynamics field in academia, industry, and government including an array of both senior and junior investigators.

The goal of the fourth RFP for Biomolecular Simulation Time on Anton has been to continue to facilitate breakthrough research in the study of biomolecular systems by providing a massively parallel system specially designed for molecular dynamics simulations. These special capabilities allow multi-microsecond simulation timescales, which previously had been unobtainable. The program seeks to continue to support research that addresses important and high impact questions demonstrating a clear need for Anton's special capabilities.

The Anton RFP described the three criteria against which the committee was asked to evaluate proposals:

- **Scientific Merit**, including the potential to advance understanding on an important problem or question in the field; potential for breakthrough science resulting in new discoveries and understanding; the impact that successful completion of the proposed research would have on knowledge, methods, and current barriers in the field; and a scientifically and technologically feasible project with clear, well-developed, and appropriate goals, objectives, and approach to the proposed studies.

- **Justification for Requested Time Allocation**, including a clear and well-justified need for multi-microsecond simulation timescales and a clear and convincing justification that the length and number of proposed simulation runs and node-hours requested are necessary and sufficient to achieve the scientific objectives.

- **Investigator Qualifications and Past Accomplishments**, including the appropriate experience and training to successfully conduct the proposed studies, evidence of knowledge and prior experience in molecular simulations, and past publications.

Proposals from investigators who had previously received an allocation of time on Anton were required to include progress reports. Following guidance provided by DESRES and PSC, the committee drew on these progress reports as supplemental material in its consideration of proposals. The committee also received information from PSC on the number of node-hours of simulation time remaining on 2012 Anton allocations (as of July 17, 2013), as further supplemental information. As explained in the RFP, staff at PSC conducted an initial assessment of all proposal submissions for completeness and to determine whether they were technically feasible for simulation on Anton. A member of the PSC staff was present as an observer throughout the review committee's discussions to address any additional questions that arose on Anton's technical capabilities or on how the computer will be made available to researchers during the period of the project.

The committee was asked to identify proposals that best met the selection criteria defined above. As in the previous rounds of Anton time allocations, 100,000 node-hours was the maximum amount of time available to a proposal. Principal investigators could also request a lesser time allocation. The committee was further asked to allocate at least 25% of the time to principal investigators who had not previously received an Anton allocation. The judgments of the committee are based on which proposals best met the selection criteria described above and on the estimates of required simulation time provided by the applicants. The committee was permitted to consider a modified time allocation if it concluded that the proposed research required a greater or lesser number of node-hours than initially requested by an applicant.

Initial reviews of the proposals were provided by the 15 committee members. Each proposal was assigned a minimum of two primary reviewers who were asked to evaluate the proposal based on the RFP and guidelines described above. Review assignments were made so that no proposal was

evaluated by a reviewer from the applicant's same institution or who had a collaborative relationship with an applicant.

The committee held its meeting in Washington, D.C. on August 5, 2013. At the meeting, members undertook a detailed discussion of the proposals. The two primary reviewers were asked to summarize their review for the committee, which was followed by discussion of the proposed research. As described in detail above, committee members considered the scientific merit, justification of the requested time, and the qualifications of the principal investigator. The committee then considered the slate of proposals, came to a consensus on which proposals it judged best met the selection criteria, and, in some cases, decided to suggest a modified allocation of time on Anton. Detailed comments for each of the 65 proposals are included in Appendix B.

The committee concluded that the proposals listed below best met the selection criteria set forth in the RFP for Biomolecular Simulation Time on Anton. Of these 48 proposals, 15 proposals were selected for a modified allocation (identified below with an *). For investigators who received an Anton allocation in 2012 that had over 50% of the simulation time remaining (based on the data provided to the committee by Pittsburgh Supercomputing Center), the committee automatically reduced the 2013 allocation request by 10%.

In numerical order by proposal submission number, the proposals judged by the committee as best meeting the selection criteria of the RFP are:

PSCA13003P **The calcium dependent regulation of thin filament protein troponin – molecular dynamics insights of troponin relaxation and activation pathways**; PI: Lu, University of Illinois at Chicago *[New user, identified for 25,000 node-hours]**

PSCA13005P **Microsecond scale simulations to characterize skeletal muscle Ca2+-binding proteins**; PI: McCammon, University of California San Diego *[Returning user, identified for 45,000 node-hours]**

PSCA13006P **Exploring Roles of Glycans in Interactions between HIV-1 gp120 and Broadly Neutralizing Antibodies**; PI: Im, University of Kansas *[Returning user, identified for 100,000 node-hours]*

PSCA13007P **Alternating access dynamics in lactose permease (LacY)**; PI: Kaback, University of California Los Angeles *[New user, identified for 50,000 node-hours]**

PSCA13008P **Ensemble Modeling of Intrinsically Disordered Proteins: DNA Binding by Pdx1**; PI: Showalter, Pennsylvania State University *[Returning user, identified for 100,000 node-hours]*

PSCA13009P **Molecular Machinery Controlling the Activation and Clamping of Synaptic Vesicle Fusion**; PI: Bykhovskaia, Universidad Central del Caribe *[New user, identified for 100,000 node-hours]*

PSCA13011P **Investigating the atomic detail mechanisms of mutagenesis modulated cation selectivity of bacterial voltage-gated sodium channels**; PI: Clapham, HHMI/Cardiology Boston Children's Hospital *[New user, identified for 40,000 node-hours]**

PSCA13012P **Visualizing dynamic movements in heme proteins**; PI: Poulos, University of California, Irvine *[New user, identified for 50,000 node-hours]**

PSCA13013P **Molecular details of the activation of the μ opioid receptor**; PI: MacKerell, University of Maryland School of Pharmacy *[Returning user, identified for 100,000 node-hours]*

PSCA13014P **Atomistic mechanism for the microtubule-activated kinesin ATPase**; PI: Hwang, Texas A&M University *[Returning user, identified for 100,000 node-hours]*

PSCA13015P **Microsecond simulation studies of mechanochemical coupling in the molecular motor myosin**; PI: Cui, University of Wisconsin-Madison *[New user, identified for 99,533 node-hours]*

PSCA13017P **Calculating Conductance of Ion Channels**; PI: Pohorille, University of California San Francisco *[Returning user, identified for 50,000 node-hours]*

PSCA13018P **Using Microsecond Simulations to Characterize Cholesterol Interactions with Chemokine Receptors**; PI: Handel, University of California San Diego *[New user, identified for 50,000 node-hours]**

PSCA13019P **Peptide-induced Pore Formation in Lipid Membranes**; PI: Lazaridis, City College of New York *[New user, identified for 99,533 node-hours]*

PSCA13023P **Long Time Scale Molecular Dynamics Simulation of Protein Folding**; PI: Gruebele, University of Illinois at Urbana-Champaign *[Returning user, identified for 90,000 node-hours]**

PSCA13024P **Gold-Standard Conformational Transitions of Adenylate Kinase**; PI: Beckstein, Arizona State University *[New user, identified for 50,412 node-hours]*

PSCA13025P **The Correlated Dynamics of the Tandem Cyclic Nucleotide Binding Domains in the Regulatory Subunit of Protein Kinase A**; PI: Amaro, University of California, San Diego *[Returning user, identified for 100,000 node-hours]*

PSCA13029P **Dynamics of Bacterial Transcription Initiation**; PI: Thirumalai, University of Maryland *[Returning user, identified for 100,000 node-hours]*

PSCA13031P **Evolutionary Pathways of Engineered Sitagliptinases through Microsecond Molecular Dynamics**; PI: Houk, University of California, Los Angeles *[Returning user, identified for 100,000 node-hours]*

PSCA13032P **Determining the mechanisms of protein folding in membranes**; PI: Gumbart, Georgia Institute of Technology *[Returning user, identified for 100,000 node-hours]*

PSCA13033P **The molecular determinants of selective ion binding in the sodium-potassium pump ATPase**; PI: Roux, University of Chicago *[Returning user, identified for 90,000 node-hours]**

PSCA13034P **Resolving specific structural implications of functional mechanisms of the Leucine Transporter with long MD simulations**; PI: Weinstein, Weill Cornell Medical College of Cornell University *[New user, identified for 25,000 node-hours]**

PSCA13035P **Pathway and mechanism of drug binding to HIV-1 protease**; PI: Chang, University of California, Riverside *[New user, identified for 73,396 node-hours]*

PSCA13036P **Investigation of long time protein dynamics under physiological conditions**; PI: Cheng, University of Tennessee, Knoxville *[New user, identified for 100,000 node-hours]*

PSCA13037P **Simulations of the HER2-HER3 heterodimeric kinase complex: Understanding the activation mechanism and its role in cancer therapy**; PI: Sept, University of Michigan *[New user, identified for 100,000 node-hours]*

PSCA13038P **Dynamics of the Early Translational Machinery**; PI: Luthey-Schulten, University of Illinois at Urbana-Champaign *[Returning user, identified for 100,000 node-hours]*

PSCA13039P **Ligand-Binding Mechanics in a Glutamate Receptor**; PI: Lau, Johns Hopkins University School of Medicine *[New user, identified for 100,000 node-hours]*

PSCA13040P **A novel approach for simulating the complete transport cycle of neurotransmitter:sodium symporters**; PI: Bahar, University of Pittsburgh School of Medicine *[Returning user, identified for 100,000 node-hours]*

PSCA13041P **Anomalous transport and lateral structure in physiological, nanodomain forming lipid mixtures**; PI: Lyman, University of Delaware *[Returning user, identified for 100,000 node-hours]*

PSCA13043P **An unconventional approach to rhodopsin activation using detergent micelles**; PI: Mertz, West Virginia University *[New user, identified for 50,000 node-hours]*

PSCA13044P **Kinetic studies of heterogenous folding pathways in a hyper-stable RNA motif**; PI: Garcia, Rensselaer Polytechnic Institute *[New user, identified for 100,000 node-hours]*

PSCA13046P **Computing the Thermodynamics of HIV-1 gp41-Mediated Viral Membrane Poration using Microsecond MD Simulation**; PI: Abrams, Drexel University *[Returning user, identified for 35,000 node-hours]**

PSCA13048P **Simulations of a Peripheral Membrane Protein Binding Mechanism to Yeast Organelle Membranes and Forming Membrane Contact Sites**; PI: Klauda, University of Maryland *[Returning user, identified for 90,000 node-hours]**

PSCA13050P **Modeling the Antibody-Eliciting Conformation of the HIV gp41 MPER**; PI: DeGrado, University of California San Francisco *[New user, identified for 98,835 node-hours]*

PSCA13051P **20 μs simulation of bc1 complex of mitochondrial respiratory chain**; PI: Matyushov, Arizona State University *[Returning user, identified for 55,000 node-hours]**

PSCA13052P **Molecular mechanisms of geometry-based intracellular organization**; PI: Huang, Stanford University *[New user, identified for 25,000 node-hours]**

PSCA13053P **Understanding the pathway of integrin headpiece opening**; PI: Springer, Harvard Medical School and Children's Hospital Boston *[Returning user, identified for 100,000 node-hours]*

PSCA13056P **Characterizing the disordered FG repeat domains of Nuclear Pore Complexes by simulation and experiment**; PI: Cowburn, Albert Einstein College of Medicine, Yeshiva University *[New user, identified for 100,000 node-hours]*

PSCA13062P **Membrane Insertion and the Equilibrium Configurational Ensemble of Histidine Kinase Receptors**; PI: White, University of California, Irvine *[Returning user, identified for 95,581 node-hours]*

PSCA13063P **Co-translational folding of nascent protein on the ribosome**; PI: Schulten, University of Illinois at Urbana-Champaign *[Returning user, identified for 100,000 node-hours]*

PSCA13065P **Detailed characterization of the structure and conformational dynamics of full-length HIV-1 gp120 in the unliganded form**; PI: Langmead, Carnegie Mellon University *[Returning user, identified for 50,000 node-hours]*

PSCA13066P **Molecular modeling studies of drug binding to human P-glycoprotein**; PI: Freites, University of California-Irvine *[Returning user, identified for 100,000 node-hours]*

PSCA13068P **An investigation into intramolecular diffusion of a disordered protein**; PI: Stultz, Massachusetts Institute of Technology *[New user, identified for 50,000 node-hours]*

PSCA13069P **Microsecond Dynamics of HIV-1 Stem Loop1 RNA for computation of NMR order parameters and comparison with HIV-1 TAR RNA**; PI: Andricioaei, University Of California at Irvine *[Returning user, identified for 50,000 node-hours]*

PSCA13070P **Dynamics of the Resting State of the Ci-VSP Voltage Sensor Under Applied Transmembrane Potentials**; PI: Perozo, University of Chicago *[New user, identified for 100,000 node-hours]*

PSCA13072P **Polycyclic Natural Products and Analogues through Computational Enzyme Engineering: Upstream Design for New Polyketide Building Blocks**; PI: Pande, Stanford University *[Returning user, identified for 45,000 node-hours]**

PSCA13074P **Sequencing DNA Using MspA**; PI: Aksimentiev, University of Illinois at Urbana-Champaign *[Returning user, identified for 90,000 node-hours]**

PSCA13077P **Characterizing Ion-coupled Structural Transitions in Secondary Active Membrane Transporters**; PI: Tajkhorshid, University of Illinois at Urbana-Champaign *[Returning user, identified for 25,000 node-hours]**

The time allocations for the 48 proposals identified by the committee as best meeting the selection criteria for time allocations total approximately 3,698,000 node-hours. Of the 48 proposals identified, 30 were identified at the approximately 100,000 node-hour level and 18 at the 25,000-50,000 node-hour level.[1] A total of approximately 1,488,000 node-hours were allocated to 21 proposals whose principal investigator did not receive time on Anton during the past three years (identified as "new users"). Approximately 40% of the available simulation time thus was allocated to new users of Anton. The remaining 2,211,000 node-hours are allocated to 27 proposals from investigators who had received allocations of time on Anton in previous rounds (identified as "returning users").

In carrying out its task, the committee identified as many promising proposals as possible given the constraints on the total available simulation time.

[1] The 100,000 node-hour level is defined as proposals that were identified for 70,000 node-hours or greater. The 50,000 node-hour level is defined as proposals that were identified for less than 70,000 node-hours.

The committee would like to thank D.E. Shaw Research, the Pittsburgh Supercomputing Center, and all of the 2013 Anton applicants for the opportunity to assist in identifying the proposals best meeting the selection criteria for time allocations on the Anton machine. The committee members were universally enthusiastic about the potential advances in the field that are facilitated by Anton and are looking forward to seeing the important new results from the Anton users.

Sincerely,

Michael Levitt
Chair

cc: Dr. Markus Dittrich, Pittsburgh Supercomputing Center
Dr. Gregory Symmes, National Research Council
Dr. Frances Sharples, National Research Council

Appendices:

APPENDIX A

TABLE 1: PROPOSALS REVIEWED BY THE COMMITTEE

This appendix is not available to the public.

APPENDIX B

INDIVIDUAL PROPOSAL SUMMARY EVALUATIONS

This appendix is not available to the public.

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APPENDIX C

PROPOSAL REVIEW CRITERIA

The committee used the points below to help guide its review of the proposals. The reviewers were asked to comment on the strengths and weaknesses of the proposals by considering the following:

Level of scientific merit

1. Potential to advance understanding of an important problem or question in the field; potential for breakthrough science resulting in new discoveries and understanding
2. Impact that successful completion of the proposed research would have on the knowledge, methods, and current barriers in the field
3. Project is scientifically and technologically feasible with clear, well-developed, and appropriate goals, objectives, and approach to the proposed studies

Justification for requested time allocation

1. Clear and well-justified need for multi-microsecond simulation time
   Clear and convincing justification that the length and number of proposed simulation runs and node-hours requested are necessary and sufficient to achieve the scientific objectives

Investigator qualifications and past accomplishments

1. Appropriate experience and training to successfully conduct the proposed studies
2. Evidence of knowledge and prior experience with molecular simulations
3. Past publications

APPENDIX D

COMMITTEE ON PROPOSAL EVALUATION FOR ALLOCATION OF SUPERCOMPUTING TIME FOR THE STUDY OF MOLECULAR DYNAMICS, FOURTH ROUND

MICHAEL LEVITT *(Chair)*, Professor and Chair, Department of Structural Biology, Stanford University School of Medicine
L. MARIO AMZEL, Professor and Director, Department of Biophysics and Biophysical Chemistry, Johns Hopkins University School of Medicine
NILESH BANAVALI, Research Scientist, Wadsworth Center, New York State Department of Health, and Assistant Professor, School of Public Health, State University of New York, Albany
JAMES BRIGGS, Associate Professor and Interim Chair, Department of Biology and Biochemistry, University of Houston
CHARLES L. BROOKS III, Warner-Lambert/Parke-Davis Professor of Chemistry and Professor of Biophysics, Department of Chemistry and Biophysics, University of Michigan
THOMAS CHEATHAM III, Associate Professor, Department of Medicinal Chemistry, University of Utah
SCOTT FELLER, Howell Professor of Chemistry and Chair, Division of Natural Sciences and Mathematics, Wabash College
TOSHIKO ICHIYE, Professor and William G. McGowan Chair in Chemistry, Department of Chemistry, Georgetown University
JEFFRY D. MADURA, Professor, Department of Chemistry and Biochemistry, Duquesne University
GLENN MARTYNA, Research Staff Member, Physical Sciences Division, IBM T. J. Watson Lab
RUTH NUSSINOV, Senior Investigator, Center for Cancer Research**,** National Cancer Institute**,** National Institutes of Health
LOUKAS PETRIDIS, Research Staff Scientist, Center for Molecular Biophysics, Oak Ridge National Laboratory
JEFFERY SKOLNICK, Georgia Research Alliance Eminent Scholar in Computational Systems Biology**,** Center for the Study of Systems Biology**,** Georgia Institute of Technology
CHUNG WONG, Professor, Department of Chemistry and Biochemistry, University of Missouri-St. Louis

NATIONAL RESEARCH COUNCIL STAFF

KATHERINE BOWMAN, Senior Program Officer, Board on Life Sciences
KATHRYN HUGHES, Senior Program Officer, Board on Chemical Sciences and Technology
CARL G. ANDERSON, Program Associate, Board on Life Sciences

BIOGRAPHICAL SKETCHES OF COMMITTEE MEMBERS

CHAIR

Michael Levitt, Ph.D. (NAS), is Professor and Chair of the Department of Structural Biology at Stanford University School of Medicine. He is known for his pioneering work in computational biology, especially protein folding. He co-discovered the four protein-fold classes and explained how these segments pack. He was also the first to automate secondary structure identification and pioneered simulation of protein unfolding in solution, emphasizing qualitative aspects and using film to show protein motion. His early use of restraints and annealing in folding forms the basis for current methods of NMR structure determination. Primarily focused on proteins, he has also contributed to the computational structural biology of DNA and RNA. Starting with his model for tRNA, which captured many features of the subsequently determined x-ray structure, he went on to correctly predict that DNA would have 10.5 not 10 base-pairs per turn in solution. He also ran the first molecular dynamics simulations of DNA in vacuo and in solution and has developed methods to combine distant homology searches of genomic sequences with automated modeling. These results have been combined in the BioSpace database. Dr. Levitt received his Ph.D. in Biophysics from the University of Cambridge in 1971.

MEMBERS

L. Mario Amzel, Ph.D., is Professor and Director of the Department of Biophysics and Biophysical Chemistry at the Johns Hopkins University School of Medicine. Dr. Amzel's research interests include structural enzymology of redox and phosphoryl-transfer enzymes, particularly the enzymes MICAL, VP14, PI3K, and Nudix hydrolases, and selected areas of structural thermodynamics. He received his Ph.D. in Physical Chemistry in 1968 from the Universidad de Buenos Aires, Argentina and completed his postdoctoral research in the structure of proteins from 1969-1970 at the Johns Hopkins University School of Medicine.

Nilesh Banavali, Ph.D, is a Research Scientist at the Wadsworth Center of the New York State Department of Public Health and an Assistant Professor in the School of Public Health at the State University of New York, Albany. The primary goal of his research is to use computational calculations and refined analysis techniques to optimally extract free energy landscapes describing biologically relevant macromolecular conformational change. Dr. Banavali also develops techniques to facilitate validation of computational predictions with structural and biochemical data. He received his Ph.D. from the University of Maryland in 2001 for studies on nucleic acid force fields and base flipping with Alexander MacKerell Jr. He pursued postdoctoral training at Weill Medical College of Cornell University and the University of Chicago with Benoît Roux on implicit and implicit/explicit solvent models and free energy characterization of conformational change and allostery in macromolecules.

James Briggs, Ph.D., is Associate Professor and Interim Chair of Biology and Biochemistry at the University of Houston. He studies the kinetic and thermodynamic properties of enzymes and receptors utilizing molecular mechanics, molecular and Brownian dynamics, electrostatics, quantum mechanics, and quantitative structure-activity relationship methods. Application areas include the search for inhibitors of e.g., HIV-1 integrase (anti-AIDS), Rho Kinase 1, PTen, STAT3, identification of the function of proteins of known structure but unknown function, inhibition of biofilm formation, and more. Dr. Briggs received his Ph.D. in Theoretical Organic Chemistry from Purdue University in 1990.

Charles L. Brooks, Ph.D., is the Warner-Lambert/Parke-Davis Professor of Chemistry and Professor of Biophysics at the University of Michigan. His research includes multi-scale modeling of the dynamics and assembly of complex biological assemblies, protein folding, unfolding and aggregation, and free energy approximations. He received a B.S. from Alma College in 1978 and his Ph.D. in Physical Chemistry from Purdue University in 1982. Dr. Brooks was the recipient of an NIH Postdoctoral Fellowship and engaged in postgraduate work at Harvard University with Professor Martin Karplus, focusing on theoretical and computational biophysics. In 1985, Professor Brooks joined the Chemistry Faculty of Carnegie Mellon University and was promoted to Professor of Chemistry in 1992. He received an Alfred P. Sloan Research Fellowship in 1992 and during this period, 1992-1993, spent a sabbatical year working at the Karolinska Institute in Stockholm Sweden and The Scripps Research Institute in La Jolla California.

Thomas E. Cheatham III, Ph.D., is an Associate Professor in the Department of Medicinal Chemistry and an Adjunct Associate Professor in the Department of Bioengineering at the University of Utah. He is also a member of the Henry Eyring Center for Theoretical Chemistry, a senior fellow of the Center for High Performance Computing, a member of the NSF Teragrid Scientific Advisory Board, and a member of the University of Utah Information Technology Council and the University of Utah Cyberinfrastructure Council. He serves as a member of the board of editors of the *Journal of Biomolecular Structure & Dynamics*. Dr. Cheatham's research focuses on the development of molecular dynamics, free energy simulation, and trajectory analysis methodologies in applications aimed at better understanding biomolecular structure, dynamics and interactions including the representation of nucleic acid systems in solution. He received his Ph.D. in pharmaceutical chemistry from the University of California, San Francisco, and B.A. degrees in chemistry and in mathematics and computer science from Middlebury College. He was subsequently an NRC postdoctoral fellow in the Computational Biophysics Section of the Laboratory of Biophysical Chemistry at the National Heart, Lung and Blood Institute, National Institutes of Health.

Scott Feller, Ph.D., is the Lloyd B. Howell Professor of Chemistry and Chair of the Division of Natural Sciences and Mathematics at Wabash College. His research focuses on simulations of lipid bilayers and on membrane biophysics. Dr. Feller was named the College's McLain-McTurnan-Arnold Excellence in Teaching Award Winner for 2009 and often conducts his research with the students he teaches, many of who have gone on to pursue advanced degrees in the chemical sciences. Dr. Feller is a graduate of Willamette University in Oregon and holds his Ph.D. in Physical Chemistry from the University of California, Davis.

Toshiko Ichiye, Ph.D., is Professor and William G. McGowan Chair in Chemistry at Georgetown University. She is a leader in the field of molecular dynamics simulations, an area of computational chemistry that enables pharmaceutical companies, biotechnology firms, and bioengineering firms to design and perfect their products. Dr. Ichiye's research interests include theoretical biophysical and physical chemistry, structure and function of proteins, statistical mechanics of macromolecules and liquids, and molecular dynamics simulations of biological macromolecules. She received her B.A. in Physics from Rice University in 1978 and her Ph.D. in Biophysics in 1985 from Harvard University.

Jeffry D. Madura, Ph.D., is a Professor in the Department of Chemistry and Biochemistry at Duquesne University. He served as Department Chair from 2000-2010. Dr. Madura earned a B.A. from Thiel College in 1980 and a Ph.D. in Physical Chemistry from Purdue University in 1985, followed by a postdoctoral fellowship in computational biophysics with Professor J. Andrew McCammon at the University of Houston. His research focuses on the computational biophysics of neurotransmitter transporters. He has published more than 100 papers in physical chemistry

and chemical physics and is co-author of the textbook *General Chemistry: Principles and Modern Applications*. He was the recipient of the 1997-1998 Dreyfus Teacher-Scholar Award, the Bayer School of Natural and Environmental Sciences Award for Excellence in Service in 2004, the Bayer School of Natural and Environmental Sciences and the Duquesne University Presidential Award for Excellence in Scholarship in 2007, was inducted into the Duquesne University Office of Research Hall of Fame in 2008, and was elected as an ACS Fellow in 2011.

Glenn J Martyna, Ph.D., is a Research Scientist at IBM's T.J. Watson Research Lab in Yorktown Heights, NY. Dr. Martyna received his Ph.D. in chemical physics from Columbia University in 1989 and was an NSF postdoctoral fellow in computational science and engineering at the University of Pennsylvania. Dr. Martyna was appointed to the faculty of Indiana University, Bloomington in 1993 and was awarded tenure in 2000. In 2001, he joined IBM's TJ Watson Research Lab in Yorktown Heights, NY. Dr. Martyna was awarded an honorary Professorship of Physics at the University of Edinburgh, UK in 2008. His research focuses on the use of novel methodology, parallel algorithms, and computer simulation to probe biophysical, materials and chemical systems including studies of aqueous solutions, complex heterogeneous interfaces, phase change materials, and nanomaterials.

Ruth Nussinov, Ph.D., is a Professor in the Department of Human Genetics, School of Medicine, Tel Aviv University and a Senior Principal Scientist and Principal Investigator at the National Cancer Institute (NCI) of the National Institutes of Health. She maintains a research group in Tel Aviv in collaboration with Prof. H. Wolfson from the School of Computer Science as well as a research group at NCI, and is the author of over 440 scientific papers. Dr. Nussinov was a pioneer in studying DNA sequence and structure and nucleic acid-protein interactions. Currently her research focuses on computational studies of protein folding, binding and protein function. She received her B.Sc. in Microbiology from the University of Washington and her Ph.D. in Biochemistry from Rutgers University. Dr. Nussinov serves as Editor-in-Chief of *PLoS Computational Biology* and as an Editor of the *Journal of Biological Chemistry*, *Physical Biology*, *Proteins*, *Biophysical Journal*, and *BMC Bioinformatics*. She also serves as a long term member on the NIH Study Section Macromolecular Structure and Function D.

Loukas Petridis, Ph.D., is a Research Staff Scientist in the Center for Molecular Biophysics at Oak Ridge National Laboratory. His research focuses on high-performance computer simulation of biological macromolecules, neutron scattering in bioenergy research and polymer physics. In particular, he investigates the origins of biomass recalcitrance via the integration of computer simulation with neutron scattering experiments, undertakes computer simulations of lignocelluloses, and investigates molecular-scale mechanisms stabilizing soil organic carbon by application of molecular dynamics simulation and neutron reflectometry. He also studies scaling of molecular dynamics simulation on supercomputers and physics of biopolymers. He obtained his Ph.D. in theoretical physics from Cambridge University in 2006 and was a postdoctoral fellow at Oak Ridge National Laboratory from 2007 to 2009.

Jeffrey Skolnick, Ph.D., is Professor and Director of the Center for the Study of Systems Biology and Georgia Research Alliance Eminent Scholar in Computation Systems Biology at Georgia Institute of Technology. He received his B.A. in Chemistry from Washington University, St. Louis in 1975, his M.Phil. in Chemistry from Yale University in 1977, and his Ph.D. in Chemistry from Yale University in 1978 with Professor Marshall Fixman. His research focuses on computational systems biology and bioinformatics including the development of algorithms and their application to proteomes for the prediction of protein structure and function, the prediction of small molecule ligand-protein interactions with applications to drug discovery and the prediction of off-target uses of existing drugs, fundamental studies on the nature and completeness of protein structure space and the exploration of the interplay between protein

physics and evolution in determining protein structure and function, prediction of protein-protein and protein-DNA interactions, cancer metabolomics and molecular simulations of cellular processes. He is a member of the editorial boards of *PeerJ*, *Journal of Metabonomics & Metabolites*, *Current Bioinformatics*, *Biology Direct*, and *Protein Science*.

Riina Tehver, Ph.D., is an Assistant Professor in the Department of Physics and Astronomy at Denison University. She received her Ph.D. in Physics from Pennsylvania State University and B.S. in Physics from Tartu University, Estonia. She was subsequently a postdoctoral research fellow at the Institute for Physical Science and Technology at the University of Maryland. Dr. Tehver's research seeks to understand how biomolecules, particularly motor proteins, perform their cellular functions, using numerical analysis and computational modeling to connect protein structures to their operations. Dr. Tehver serves as a reviewer for the journals *Bioinformatics* and *Physical Review Letters*, and was the Chair of the Protein Folding Dynamics Gordon Research Seminar in 2010.

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APPENDIX E

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APPENDIX F

ACKNOWLEDGMENT OF REPORT REVIEWER

This report has been reviewed in draft form by an individual chosen for his perspective and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individual for his review of this report:

Sean Eddy, Howard Hughes Medical Institute, Janelia Farm Research Campus

Although the reviewer listed above has provided many constructive comments and suggestions, he was not asked to endorse the conclusions. In addition, he was asked to ensure that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.