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

DETAILS

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AUTHORS

Committee on Proposal Evaluation for Allocation of Supercomputing Time for the Study of Molecular Dynamics, Seventh Round; Board on Life Sciences; Board on Chemical Sciences and Technology; Division on Earth and Life Studies; National Academies of Sciences, Engineering, and Medicine

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Board on Life Sciences

Board on Chemical Sciences and Technology

Division on Earth and Life Studies

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October 27, 2016

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, Seventh Round.

The committee evaluated submissions received in response to a Request for Proposals (RFP) for Biomolecular Simulation Time on Anton, a supercomputer designed and built by D. E. Shaw Research (DESRES). Over the past five years, DESRES has made an Anton system housed at the Pittsburgh Supercomputing Center (PSC) available to the non-commercial research community, based on the advice of previous National Research Council committees. This year, DESERES made an Anton 2 system, also house at the Pittsburg Supercomputing Center (PSC) available to the non-commercial research community. As in prior rounds, the goal of the seventh RFP for simulation time on Anton 2 is 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 capabilities allow multi-microsecond simulation timescales. 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 success of the program has led DESRES to make the Anton 2 machine housed at PSC available for 15,800,000 molecular dynamic units (MDUs) over the period following November 2016, and DESRES asked the National Academies of Sciences, Engineering, and Medicine to once again facilitate the allocation of time to the non-commercial community. The work of the 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 Academies' Board on Life Sciences.

To undertake this task, the National Academies convened a committee of experts to evaluate the proposals submitted in response to the RFP. The committee of 19 was chaired by Dr. Robert Eisenberg, Bard Endowed Professor and Chairman Emeritus of the Department of Molecular Biophysics and Physiology at Rush University. The committee members were selected for their expertise in molecular dynamics simulations and experience in the subject areas represented in the 99 proposals that were considered. The members comprised a cross section of the biomolecular dynamics field in academia, industry, and government including both senior and junior investigators.

The Anton 2 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, which the committee drew on as supplemental material in its consideration of proposals. 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. Anton 2 time allocations of 460,000 MDUs were 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 19 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 proposals were not evaluated by reviewers from the applicant's same institution or who had close collaborative relationships with an applicant.

The committee held its meeting in Washington, D.C. on August 31, 2016. At the meeting, the two primary reviewers were asked to summarize their reviews 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 and key personnel. The committee considered the slate of proposals under consideration, 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 2. Detailed comments for each of the 99 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 2. Of these 52 proposals, 26 proposals were selected for a modified allocation (identified below with an *).

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

PSCA16005P Bykhovskaia, Wayne State University; **Protein Machinery Regulating Synaptic Vesicle Fusion** *[Returning user, identified for 230,000 MDUs]*

PSCA16006P Im, The University of Kansas; **Molecular dynamics simulation of the HIV-1 Env trimer** *[Returning user, identified for 306,667 MDUs]**

PSCA16007P Klauda, University of Maryland; **Ligand Effects on the Biological Function of the Serotonin Receptor in model Raft-forming Membranes** *[Returning user, identified for 460,000 MDUs]*

PSCA16008P Feigenson, Cornell University; **Leaflet Communication in Compositionally Asymmetric Lipid Membranes** *[New user, identified for 250,000 MDUs]*

PSCA16009P Lazaridis, City College of New York; **The mechanism of membrane pore formation by β-hairpin antimicrobial peptides** *[Returning user, identified for 460,000 MDUs]*

PSCA16010P Weinstein, Weill Cornell Medical College of Cornell University; **Molecular mechanisms of lipid scrambling by TMEM16 proteins** *[Returning user, identified for 450,000 MDUs]*

PSCA16012P Lyubchenko, University of Nebraska Medical Center; **MD Simulations of Interactions and Misfolding of Amyloid Beta (Aβ) Proteins** *[Returning user, identified for 230,000 MDUs]**

PSCA16013P Hwang, Texas A&M University; **Allosteric communication between dimeric motor heads in the processive motility of kinesin** *[Returning user, identified for* 460,000 *MDUs]*

PSCA16016P Bahar, School of Medicine, University of Pittsburgh; **Structural Plasticity of Eukaryotic TriC/CCT Chaperonins Resolved by Cryo-EM** *[Returning user, identified for 455,000 MDUs]*

PSCA16018P Wereszczynski, Illinois Institute of Technology; **Understanding the Role of LPS Modification on Bacterial Outer Membrane Permeability** *[New user, identified for 234,552 MDUs]*

PSCA16020P Feig, Michigan State University; **Microsecond Diffusion of Macromolecules in Realistic Cellular Environments** *[New user, identified for 460,000 MDUs]*

PSCA16021P Beratan, Duke University; **Simulating the Electron Transfer Mechanisms of Extremophiles** *[Returning user, identified for 224,888]**

PSCA16023P Evans, University of New Mexico; **All-atom molecular dynamics (MD) simulations to elucidate the interaction of curcumin with Amyloid-β (Aβ) and to determine its role in the disruption of cell membranes observed in Alzheimer's Disease** *[New user, identified for 100,000 MDUs]**

PSCA16024P Kaback, UCLA; **Identifying the molecular determinants of substrate specificity in sugar transport** *[Returning user, identified for 100,000 MDUs]**

PSCA16027P Cowburn, Albert Einstein College of Medicine; **FG repeat domain interactions of the Nuclear Pore by simulation and experiment** *[Returning user, identified for 460,000 MDUs]*

PSCA16030P Loverde, City University of New York, College of Staten Island; **Molecular Dynamics Simulation of the Melting of the Nucleosome Core Particle** *[New user, identified for 50,000 MDUs]**

PSCA16033P Roux, University of Chicago; **Selective ion binding and self-correcting occlusion in the sodium-potassium pump ATPase** *[Returning user, identified for 460,000 MDUs]*

PSCA16035P McCammon, University of California San Diego; **Investigatingthe mechanism of conformational activation of the CRISPR-Cas9 system via long-time scale molecular dynamics** *[Returning user, identified for 225,000 MDUs]**

PSCA16037P Houk, University of California, Los Angeles; **Understanding the Role of Mutations and Flexible Loops in the Directed Evolution of a Sitagliptinase** *[Returning user, identified for 200,000 MDUs]*

PSCA16038P Zhu, Georgia Institute of Technology; **Forced-induced pathways employed by viral epitopes to decrease immune recognition by the TCR** *[Returning user, identified for 115,000 MDUs]**

PSCA16039P Lyman, University of Delaware; **Toward Minimal Complexity Mixtures: Packing, Lateral Structure, and Nanoscale Dynamics in the Outer Leaflet of the Plasma Membrane** *[Returning user, identified for 230,000 MDUs]**

PSCA16043P Amaro, University of California, San Diego; **Exploring protein core plasticity and rapid ligand access to buried binding sites** *[Returning user, identified for 460,000 MDUs]*

PSCA16045P Phorille, UC San Francisco; **Toward rational design of antiviral drugs: computational electrophysiology for evaluating models of viral ion channels** *[Returning user, identified for 115,000 MDUs]**

PSCA16047P Shea, UC Santa Barbara; **Utilizing Underwater Mussels for Next-Generation Biological Adhesives and Lubricants** *[New user, identified for 250,000 MDUs]*

PSCA16049P Hoogerheide, National Institute of Standards and Technology; **Molecular Mechanisms of the Voltage-Dependent Anion Channel Regulation by Dimeric αβ-Tubulin** *[New user, identified for 360,000 MDUs]**

PSCA16050P Dror, Stanford University; **Structural basis for arrestin activation by G protein-coupled receptors** *[Returning user, identified for 345,000 MDUs]**

PSCA16051P Pastor, National Institutes of Health; **Characterization of ApoA-I and a Mimetic Peptide on Nascent High-Density Lipoproteins** *[Returning user, identified for 457,688 MDUs]*

PSCA16054P Polenova, University of Delaware; **Dynamic Characterization of the Spacer Peptide 1 in HIV-1 Capsid Protein Assemblies** *[Returning user, identified for 345,000 MDUs]**

PSCA16059P Best, National Institutes of Health, NIDDK; **Molecular dynamics simulations of amyloid elongation** *[New user, identified for 460,000 MDUs]*

PSCA16065P Madura, Duquesne University; **Determining Potassium Ion Transport Mechanism and Pathways in the Serotonin Transporter** *[New user, identified for 230,000 MDUs]**

PSCA16066P Thirumalai, The University of Texas at Austin; **Phosphate Release Mechanism From Myosin VI Nucleotide Binding Site** *[Returning user, identified for 460,000 MDUs]*

PSCA16067P Onuchic, Center for Theoretical Biological Physics, Rice University; **Quantitative study of Influenza Hemagglutinin in a Membrane-bound Environment** *[Returning user, identified for 416,022 MDUs]*

PSCA16069P Schulten, University of Illinois at Urbana Champaign; **A Computational Study on Dynamic Instability of Microtubules** *[Returning user, identified for 460,000 MDUs]*

PSCA16070P May, University of Connecticut; **Membrane Insertion and Oligomerization of Lytic Peptides from a Non-Enveloped Virus** *[Returning user, identified for 153,333 MDUs]**

PSCA16072P Gorfe, University of Texas Medical School at Houston; **Membrane re-orientation and assembly of K-Ras** *[New user, identified for 291,000 MDUs]**

PSCA16077P Axelsen, University of Pennsylvania; **Mechanisms of Amyloid Fibril Nucleation** *[Returning user, identified for 330,000 MDUs]**

PSCA16078P Ulmschneider, Johns Hopkins University; **Exploring the mechanism of lipid-mediated modulation of regulatory protein binding to the ammonia channel AmtB** *[Returning user, identified for 197,000 MDUs]**

PSCA16080P Yarov-Yarovoy, University of California, Davis; **Modeling of sodium channel state-dependent modulation by drugs and peptide toxins** *[Returning user, identified for 230,000 MDUs]**

PSCA16082P Tajkhorshid, University of Illinois at Urbana-Champaign; **Gating and ion permeation mechanism and pathway in a P2X receptor** *[Returning user, identified for 340,000 MDUs]**

PSCA16083P Tobias,University of California, Irvine; **Atomistic modeling of water permeation in the Aquaporin 0-Calmodulin complexes** *[Returning user, identified for 235,000 MDUs]*

PSCA16086P Freites,University of California, Irvine; **Molecular modeling studies of eye lens proteins at physiological concentrations** *[Returning user, identified for 230,000 MDUs]**

PSCA16091P Aksimentiev, University of Illinois at Urbana-Champaign; **Molecular mechanism of histone–DNA interactions** *[Returning user, identified for 230,000 MDUs]**

PSCA16098P Vashisth, University of New Hampshire; **Understanding the role of transmembrane helices in signaling via insulin receptor** *[New user, identified for 120,000 MDUs]**

PSCA16099P Buck, Case Western Reserve University; **The Signaling Mechanism of Plexin-B1--Computer Simulation of Plexin-B1 interacting with Small GTPase at the Membrane: Moving towards the full length Receptor** *[Returning user, identified for 120,000 MDUs]**

PSCA16100P Vukovic, University of Texas at El Paso; **RNA recognition by the exosome complex** *[New user, identified for 273,000 units]*

PSCA16101P Gruebele, University of Illinois at Urbana Champaign; **Testing the Mechanistic Convergence of Protein Folding Experiments and Simulations** *[Returning user, identified for 460,000 MDUs]*

PSCA16105P Lau, Johns Hopkins University School of Medicine; **Glutamate Receptor Activation** *[Returning user, identified for 460,000 MDUs]*

PSCA16106P Moradi, University of Arkansas; **Energetically Downhill Conformational Transition of a Bacterial Multidrug ABC Transporter** *[New user, identified for 460,000 MDUs]*

PSCA16107P Miller, California Institute of Technology; **Understanding the effect of membrane protein integration induced forces on restarting protein synthesis in SecM-stalled ribosomes** *[Returning user, identified for 200,000 MDUs]**

PSCA16108P Vorobyov, University of California, Davis; **Structural mechanisms of drug-induced cardiac toxicity** *[New user, identified* for 230,000 *MDUs*]*

PSCA16112P Kuriyan, University of California, Berkeley; **Membrane Effects on the Structure and Oligomerization of EGFR Kinase Domains** *[New user, identified for 340,000 MDUs]**

PSCA16115P Agard, University of California, San Francisco; **Conformational Dynamics of the Molecular Chaperone Heat Shock Protein 90 (HSP90)** *[Returning user, identified for 460,000 MDUs]*

The time allocations for the 52 proposals identified by the committee as best meeting the selection criteria for time allocations total approximately 15,879,150 MDUs. Approximately 29% MDUs were allocated to proposals whose principal investigator have not received time on Anton during the past five years (identified as "new users"). Approximately 71% of the MDUs are allocated to proposals from investigators who have 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. The total simulation time requested by the submitted proposals was over 37 million MDUs. As a result, a number of interesting proposals were not able to be recommended in this round, entailing difficult decisions.

The committee would like to thank D. E. Shaw Research, the Pittsburgh Supercomputing Center, and all of the 2016 Anton 2 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 2 and are looking forward to seeing the important new results from the Anton users.

Sincerely,

Robert Eisenberg
Chair

cc: Dr. Phillip Blood, Pittsburgh Supercomputing Center
Dr. Gregory Symmes, The National Academy of Sciences, Engineering, and Medicine
Dr. Frances Sharples, The National Academy of Sciences, Engineering, and Medicine

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.

APPENDIX C

PROPOSAL EVALUATION 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
2. 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, SEVENTH ROUND

Chair

ROBERT EISENBERG, Rush University

Members

JAMES BRIGGS, University of Houston
KAREN FLEMING, Johns Hopkins University
ANGEL GARCIA, Los Alamos National Laboratory
DONALD HAMELBERG, Georgia State University
FATEMEH KHALILI-ARAGHI, University of Illinois at Chicago
GLENN MARTYNA, IBM T.J. Watson Research Center
CLARE MCCABE, Vanderbilt University
BLAKE MERTZ, West Virginia University
SERGEI NOSKOV, University of Calgary
CHRISTOPHER ROWLEY, Memorial University
DAVID SEPT, University of Michigan
SADASIVAN (SADAS) SHANKAR, Harvard University
ERIKA TAYLOR, Wesleyan University
MARK TUCKERMAN, New York University
FENG WANG, University of Arkansas
CHUNG WONG, University of Missouri
YINGHAO WU, Albert Einstein College of Medicine
TROY W. WYMORE, University of Michigan

Project Staff

KEEGAN SAWYER, Project Director, Board on Life Sciences
LAURA DEFEO, Director, Program & Policy
ANNA SBEREGAEVA, Associate Program Officer, Board on Chemical Sciences and Technology
ANGELA KOLESNIKOVA, Sr. Program Assistant, Board on Life Sciences

BIOGRAPHICAL SKETCHES OF COMMITTEE MEMBERS

Chair

Robert Eisenberg is the Bard Endowed Professor and Chairman emeritus, Department of Molecular Biophysics & Physiology, Rush University. Eisenberg has been working at the interface of physics, physiology, and computation since he used Green's functions to solve and compute the linear electrical properties of nerve cells and has worked on multiple scales, from inside ion channels, to cell membranes, cells, and tissues. All of this work has used computation to allow theories to confront real experimental data taken on physiological scales. Eisenberg's recent work has concentrated on understanding the selectivity of calcium (e.g., L-type cardiac) and sodium channels, an area in which he has done extensive (about 30 papers) Monte Carlo simulations and a wide variety of multi-scale models. Dr. Eisenberg can bring to the Advisory Board a) knowledge of what needs to be computed to be useful for understanding natural function (e.g., the role of TRACE concentrations of calcium and messengers which are exceedingly difficult to simulate because of the immense number of water molecules needed to dilute the calcium and messenger ions); b) an appreciation of the necessity of calibration (validation and verification) in simulations as in experiments. In experiments, if things are not checked continually, results often have limited utility; and c) knowledge of the role of the electric field from tissues, to cells, to ions, and the various multi-scale treatments needed to meld with atomic scale simulations, so the simulations can reach biological length and time scales.

Members

James Briggs Ph.D., is an Associate Professor within the Biology and Biochemistry Department at the University of Houston. Dr. Briggs received his Ph.D. in Chemistry from Purdue University. His research focuses on computational studies of protein structure and function, inhibitor design, investigations of possible inhibitor resistance pathways, and development of methods for the above project areas. Targets for these studies include those important in the treatment of AIDS, cancer, bacterial infections, and other disease states. In addition, Dr. Briggs works on inhibitors to aid in biowarfare defense (botulinum neurotoxins, anthrax toxin, cholera toxin).

Karen Fleming is a tenured professor in T.C. Jenkins Department of Biophysics at Johns Hopkins University. Her research is motivated by the power a deep understanding of the physics/biology intersection can bring to disease, evolution and biological design. Her approaches are driven by the unique powers that biophysics can bring to solving complex cellular problems. For many years, Dr. Fleming studied the energetics of transmembrane helix-helix interactions. She has developed theory to describe their associations; defined conditions of "forced cohabitation" of helices in micelles and has discovered thermodynamic coupling in helix-helix dimerization reactions. Recently Dr. Fleming's work has targeted the protein-folding problem using transmembrane β-barrels. Her lab managed to quadruple the number of known membrane protein stabilities; we developed a novel water-to-bilayer side chain hydrophobicity scale and showed that aromatic side chain energies follow the polarity gradient inherent in a phospholipid bilayer. She received her B.A. in French and Pre-Medical Studies at the University of Notre Dame and her Ph.D. in Biochemistry and Molecular Biology from Georgetown University.

Angel Garcia is currently the Director of the Center for Nonlinear Studies at Los Alamos National Laboratory. Previously he was Department Head of the Physics, Applied Physics and Astronomy Department at Rensselaer Polytechnic Institute. He was also Professor of Physics and Senior Constellation Chaired Professor of Biocomputation and Bioinformatics. The Garcia Research Group focuses on the use of theoretical and computational methods to study aspects related to biomolecular dynamics and statistical mechanics. Their main research objectives are to understand the folding,

dynamics and stability of biomolecules. Research interests include the hydrophobic effect, enzyme catalysis, nucleic acid structure and dynamics, RNA folding, electrostatics, protein hydration, and peptide interactions with membranes. Dr. García received a Ph.D. in Theoretical Physics from Cornell University. He is a fellow of the American Physical Society and a member of the Biophysical Society, The Protein Society, the AAAS, and the American Chemical Society. He received the Edward Bouchard prize of the American Physical Society in 2006. Dr. García is an Associate Editor of Proteins, Structure, Function and Bioinformatics, a member of the editorial board of the Biophysical Journal, Molecular Simulations, and a member of the Faculty of 1000 for BioMed Central.

Donald Hamelberg is an Associate Professor in the Department of Chemistry at Georgia State University. Dr. Halmelberg's research focuses on he application and development of theoretical and computational methods with the intent of gaining an in-depth understanding of biological interactions and functions. In these endeavors, Dr. Hamelberg's laboratory uses simulation based approaches, related statistical mechanics, and classical and quantum mechanical methods. He also studies advanced simulation methods to study the dynamic fluctuations of biomolecules, as well as the hydration effects at binding sites and interfaces in biomolecular interactions.

Fatemeh Khalili-Araghi specializes in theoretical and computational studies of ion channels at the University of Illinois at Chicago as an Assistant Professor. She obtained her B.S. in Physics from Sharif University of Technology in 2001, and her PhD from University of Illinois at Urbana-Champaign in 2010. She has been a postdoctoral scholar at the University of Chicago from 2010 to 2013, where she has continued studies of membrane proteins with a focus on the NaK ATPase using computational modeling techniques, as well as molecular dynamics simulations. Her research at UIC will continue on theoretical and computational studies of membrane proteins.

Glenn Martyna received his Ph.D. from the Columbia University and subsequently became a NSF Postdoctoral Fellow in Computational Science and Engineering at the University of Pennsylvania. He was a tenured faculty member at Indiana University, Bloomington before joining IBM Research and was later named an Honorary Professor of Physics at The University of Edinburgh, UK. Dr. Martyna's research is focused on the atomistic modeling of soft condensed matter and materials systems as well as novel device physics, in addition to his interest in physics based computational methodology development. He is currently working to combine physical measurements with theory to study antimicrobial peptides and developing a new post-CMOS technology based on strain transductions that promises low power and high speed. He has co-authored approximately 125 papers, several of which are citations classics - papers with more than 1000 citations. Dr. Martyna has 12,000 citations total and a hindex>40.

Clare McCabe received her B.Sc. in Chemistry in 1995 and Ph.D. in 1999 from Sheffield University. Her PhD. was under the direction of George Jackson (now at Imperial College, UK) and focused on the statistical mechanics of chain molecules using the statistical associating fluid theory (SAFT) approach. After postdoctoral (1999-2000) and research faculty (2000-2001) appointments at the University of Tennessee, she joined the Colorado School of Mines faculty as an Assistant Professor of Chemical Engineering in January, 2002. In August of 2004 she moved to Vanderbilt University where she is now an Associate Professor of Chemical and Biomolecular Engineering and (since 2008) of Chemistry. McCabe has published over 100 papers in refereed journals and is a fellow of the Royal Society of Chemistry. Her research interests focus on the use of molecular modeling techniques, including molecular simulation, computational quantum chemistry and molecular-based equations of state, to understand and predict the thermodynamic and transport properties of chemical and biological systems.

Blake Mertz is an Assistant Professor in the Department of Chemistry at West Virginia University. Dr. Mertz's research focuses on using computational biophysics and experimental methods to investigate the structure-function relationships of membrane proteins, with an emphasis on the design of membrane

scaffolds for bacterial proton pumps; characterization and design of membrane insertion peptides; drug development; and optimization of bioelectronic circuits. The underlying theme of his research is to provide more detailed understanding and predictive capabilities of systems of interest to researchers in both medicine and alternative energy. Dr. Mertz received his PhD in Chemical Engineering from Iowa State University.

Sergei Noskov is an Associate Professor at the Institute of Biocomplexity and Informatics at the University of Calgary. His research interests include molecular modeling, membrane proteins (ion channels and ion-coupled transporters), quantum chemistry of biologically relevant molecules, free energy profiles, and protein structure/function prediction. Dr. Noskov's lab is comprised of a group of theoretical biologists and chemists interested in the understanding of molecular determinants of ligand transport across cellular membranes. Projects in his lab focus on studies of the family of fundamentally important ion-coupled neurotransmitter transporters implicated in diverse mechanisms of signal transduction in the brain. The studies of Dr. Noskov and his team resulted in a series of methods and software developed in close collaboration with other theoretical groups across the world. Dr. Noskov received his Ph.D. from the Russian Academy of Sciences and completed his postdoctoral studies within the Department of Biochemistry and Structural Biology at Weill Medical College of Cornell University. In Canada, Dr. Noskov is a recipient of the AHFMR Scholar, CIHR New Investigator, and AIF New Faculty awards. In the European Union, he is the recipient of the INTAS Young Scientist Award. Finally, in the U.S., he is the recipient of the Academia Sinica Research Fellowship and the American Epilepsy Foundation Post-Doctoral Fellowship awards.

Christopher Rowley is an Assistant Professor in the Department of chemistry at the Memorial University of Newfoundland. Dr. Rowley's research interests are in computational chemistry, statistical thermodynamics, medicinal chemistry, biophysical chemistry, protein folding, and multi-scale modeling. His research group uses application-driven method development to investigate issues irreversible enzyme inhibition, ion solvation, and environmental pollutants. Dr. Rowley received his Ph.D in Chemistry from the University of Ottawa.

David Sept is a Professor of Biomedical Engineering at the University of Michigan in Ann Arbor. Research in the Sept lab covers four primary areas. The first focus is on the molecular interactions underlying cell migration, a process central to many aspects of development, differentiation and the cellular response to diseases such as cancer. The second focus is work characterizing and developing drugs that target sub-cellular filaments to treat parasitic diseases like toxoplasmosis, leishmaniasis and malaria. The third area of research concerns channels that regulate the flow of ions in and out of the cell, how these channels are activated and how they malfunction in diseases such as epilepsy. The final research area is on nanoparticle based drug delivery and how these particle drug combinations are metabolized and distributed within the body.

Sadasivan (Sadas) Shankar Ph.D., is the first Margaret and Will Hearst Visiting Lecturer in Computational Science and Engineering at Harvard School of Engineering and Applied Sciences. In fall 2013, as the first Distinguished Scientist in Residence at the Institute of Applied Computational Sciences in Harvard, along with Dr. Tim Kaxiras, he developed and co-instructed with Dr. Brad Malone, a graduate-level class on Computational Materials Design, which covered fundamental atomic and quantum techniques and practical applications for new materials by design. Sadasivan earned his Ph.D. in Chemical Engineering and Materials Science from University of Minnesota, Minneapolis. Sadasivan has initiated and led multiple efforts in Intel, most recently the Materials Design Program. Over his tenure in research and development in the semiconductor industry, he and his team worked on several new initiatives: using modeling to optimize semiconductor processing and equipment for several technology generations; advanced process control using physics-based models; thermo-mechanical reliability of microprocessors; thermal modeling of 3D die stacking; and using thermodynamic principles to estimate

energy efficiency of ideal computing architectures. At Harvard, Dr. Shankar is involved in teaching and research in the areas of large-scale computational methods, chemistry, materials, and in translational ideas.

Erika Taylor has been investigating problems and finding solutions at the interface of chemistry and biology. During her undergraduate years she worked on the synthesis of natural product analogue inhibitors for a protein phosphatase that was important for the treatment of cancer. As a graduate student, she trained extensively in biochemistry, specializing in functional assignment to previously uncharacterized proteins, which gave her the tools to understand enzyme mechanisms and the impact of evolutionary context on the workings of proteins. During her postdoctoral training period, she applied all she learned while earning her earlier degrees to the discovery and characterization of inhibitors of nucleotide metabolism which are still being investigated as potential medicines to thwart malaria, a disease that still kills more than 500,000 people in the world each year. As a faculty member at Wesleyan, her projects have focused on the identification and characterization of enzymes that (1) are important for the development of antimicrobials for the treatment of Gram-Negative bacterial infections (with an emphasis on bacteria that cause food-bourne illnesses including E. coli, Salmonella, and V. cholerae); and (2) could improve the efficiency of biomass to biofuel conversion, in particular the breakdown and bacterial utilization of lignin. Erika earned an honors Chemistry undergraduate degree from the University of Michigan and her Ph.D. in Chemistry from the University of Illinois at Urbana-Champaign. After a Postdoctoral position at the Albert Einstein College of Medicine she began to teach and perform research at Wesleyan University.

Mark Tuckerman is professor of Chemistry at New York University. He earned his B.S. in Chemistry from the University of California at Berkeley and his Ph.D. from Columbia University. He served as a postdoctoral fellow at IBM Forschungs-laboratorium in Zurich, Switzerland. Dr. Tuckerman's research includes Modern theoretical methods combined with advanced scientific computing has transformed the ability to perform modeling and simulation studies of key processes in chemistry, nanoscience, and biology that generate realistic results with full atomic resolution. The research efforts in his group are focused on advancing this emerging capability and applying it to chemically important problems. Currently, Dr. Tuckerman and his team are investigating how protons are transported through various hydrogen-bonded media (water, liquid and solid acids, acid hydrates, and doped salt crystals) with an eye toward understanding and designing materials for proton-exchange membranes in fuel cells. These studies employ the method of ab initio molecular dynamics, in which the finite-temperature dynamics of a system is generated via electronic structure calculations performed "on the fly". Using this approach, they are also studying how organic molecules attach to semiconducting surfaces, and are developing new approaches for conformational sampling in complex systems such as biomolecules and crystalline polymorphs.

Feng Wang received his B.S. in Chemistry from Peking University (1998) and Ph.D. in Theoretical Chemistry from the University of Pittsburgh (2003) with Professor Kenneth D. Jordan. He did post-doctoral research in computational physical chemistry at the University of Utah with Professor Gregory A. Voth. He was an Assistant Professor in the Department of Chemistry at Boston University from 2005 to 2012. He currently holds an associate professor position in the department of chemistry and biochemistry at University of Arkansas. While at the University of Pittsburgh, Dr. Wang received an IBM graduate student award in 2001 and a Mellon Fellowship in 2002. He received a NSF CAREER Award in 2007 and an HP outstanding Junior Faculty Award in 2010. His research focuses on developing high quality force fields, free energy calculations, and enhanced sampling.

Chung Wong Ph.D., is a Professor within the Department of Chemistry and Biochemistry at the University of Missouri-St. Louis. He received his B.Sc. (Hons.) degree from the Chinese University of Hong Kong and his Ph.D. degree from the University of Chicago. He completed his postdoctoral work at

the University of Houston. His laboratory's research involves the development and applications of computational methods to study biomolecular structure, dynamics, and function and to aid the design of bioactive compounds. Dr. Wong has held academic and industrial positions at the University of Houston, Mount Sinai School of Medicine, SUGEN, Inc., University of California-San Diego, and the Howard Hughes Medical Institute before joining the faculty of University of Missouri-St. Louis in 2004.

Yinghao Wu is an Assistant Professor in the Department of Systems & Computational biology at Albert Einstein College of Medicine. By integrating computational analysis with experimental measurements, Dr. Wu's research focuses on developing multi-scale modeling frameworks to study the cross-talks between cell adhesion and cell signaling. He is particularly interested in why and how different cells form contacts, when and where these contacts are formed at specific locations of the human body, the functional impacts to the downstream signaling, and to human health.

Troy W. Wymore is an Assistant Research Scientist at the University of Michigan. He received his B.S. and PhD in Chemistry from the University of Missouri-Columbia. His current research focuses on applying hybrid QC/MM simulations to investigate the enzymatic mechanisms of DFPase, Xylose Isomerase, and 5-epi-aristolocholene synthase. The results of these studies provide insight into strategies for redesigning these enzymes to more effectively degrade nerve agents (DFPase) and improve the process of biofuel and pharmaceutical agent production.

APPENDIX E

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APPENDIX F

ACKNOWLEDGEMENT OF REPORT REVIEWER

This report has been reviewed in draft form by an individual chosen for his diverse perspectives and technical expertise. 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 process. We wish to thank the following individuals for his review of this report:

Robert L. Jernigan, Iowa State University

Although the reviewer listed above has provided many constructive comments and suggestions, he was not asked to endorse the report's conclusions. In addition, he was asked to ensure that an independent examination of the 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.