TEMPLE UNIVERSITY
College of Science and Technology

ICMS
Institute for Computational Molecular Science

SERC (035-05)
1925 North 12th Street
Philadelphia, PA 19122-1801

Phone: 1-215-204-1327
Fax: 1-215-204-2257
www.temple.edu/cst/icms

May 9, 2017

Professor David Mobley
Department of Pharmaceutical Sciences
University of California at Irvine

Dear David,

I am writing to give my enthusiastic support for your application to the NIH for funding of the SAMPL series of blind prediction challenges. I am currently a professor at Temple University, my group works on a variety of problems in structural biology and computational biophysics. Among our diverse interests are techniques for calculating binding free energies, which we have employed on several of the recent SAMPL challenges; we have now participated in three or four of these challenges. I would like to share a brief explanation of how SAMPL has helped to drive progress in my group concerning statistical mechanical methods for estimating protein-ligand and host-guest binding affinities. The Binding Energy Distribution Analysis Method (BEDAM) is a method to estimate binding free energies based on a single decoupling alchemical thermodynamic path in implicit solvent. It occupies a niche between empirical docking methods on one hand, and absolute binding free energy, and FEP methods in explicit solvent, on the other. BEDAM captures entropic effects on binding in a more fundamental and physical way than empirical docking methods and its added value has been illustrated repeatedly in the SAMPL challenges. The availability of curated SAMPL datasets to test our methods has been extremely helpful in spurring our methods development, and I believe has had similar effects on many of the participating researchers and groups.

I have been informed that one of the main limitations of SAMPL so far has been the uncertainty concerning its future. Because of the lack of funding of the initiative, it has to rely entirely on donated data, and it has been uncertain if and when a new challenge will occur. Additionally, the lack of a clear roadmap has meant it is difficult to plan for participation in future challenges. This is certainly understandable for an initiative with no funding, but it also illustrates why funding is so vitally needed. I trust that having your proposal funded will allow you to remedy this.

Sincerely,

Ronald M. Levy

Ronald M. Levy
Laura H. Carnell Professor
Professor of Chemistry (primary appointment), Physics, and Biology
Director, Center for Biophysics & Computational Biology
Member, Institute for Computational Molecular Science
ronlevy@temple.edu https://ronlevygroup.cst.temple.edu