Center for Scientific Review

National Institutes of Health

6701 Rockledge Drive

Bethesda, MD 20892-7710

To Whom It May Concern:

Attached please find my R01 proposal, “Advancing predictive physical modeling through focused development of model systems to drive new modeling innovations”, in response to PA-16-160. This proposal seeks funding to continue and extend the Statistical Assessment of Modeling of Proteins and Ligands (SAMPL) series of blind challenges. We will collect a series of data sets carefully tailored to drive improvements of physical modeling relating to drug discovery, then, via blind challenges, facilitating exactly that improvement. While SAMPL has had a great deal of success in the past (as evidenced by nearly 100 publications resulting from the effort), so far it has been driven by availability of donated data, so we have been unable to focus the effort specifically on driving progress in modeling. With the possibility of collecting our own data, we will do exactly that.

This effort will interface with the NIH-funded Drug Design Data Resource (D3R) at UCSD, which focuses on blind challenges on protein-ligand interactions using pharmaceutical datasets. This effort provides a foundation for the D3R work, collecting tailored datasets spanning a spectrum of difficulty up to that of the D3R effort. There is a real risk that the D3R data sets will be so challenging that they fail to drive improvements in models because the origin of failures is unclear. The targeted data sets collected here focus on specific challenges, allowing sources of failure to be isolated and resolved separately, improving the likelihood of success on D3R data sets.

**Please assign this application to the following:**

Institutes/Centers:

National Institute of General Medical Sciences – NIGMS

Scientific Review Groups:

Macromolecular Structure & Function D Study Section – MSFD

I am comfortable having anyone in this general area review my proposal. This proposal is at the interface of computational chemistry, thermodynamics and physical chemistry, medicinal chemistry, and supramolecular chemistry.

Thank you very much for your help, and please don’t hesitate to contact me if there are any questions or problems.

Sincerely,

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