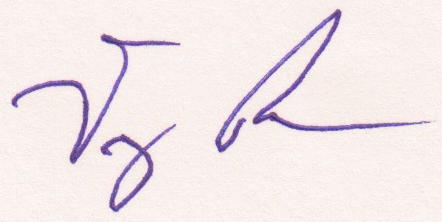
February 26, 2016

Dear Dr. Lester,

We are submitting the following report, entitled “Identification of simple reaction coordinates from complex dynamics,” for publication in the *Journal of Chemical Physics*.

The subject of this manuscript is the inference of reaction coordinates from molecular dynamics (MD) simulations. We first introduce a general definition of the reaction coordinate suitable for condensed phase and biomolecular systems, which we show is equivalent to a leading eigenfunction of an integral operator governing a system's ensemble dynamics. Subsequently, we develop a practical new estimator designed to find sparse, interpretable approximations to these reaction coordinates from MD simulations using a small number of structural order parameters. This work bridges recent developments in the fields of machine learning and optimization, such as sparsity-inducing regularizers and the alternating direction method of multipliers, with contemporary needs in biological and chemical physics arising out of the analysis of large-scale simulation data sets. We anticipate this report will be of interest to the broad readership of *JCP*.

Below, we provide a list of potential reviewers.

Sincerely,

Vijay Pande

Camille and Henry Dreyfus Distinguished Chair in Chemistry and (by courtesy) Professor of Structural Biology and of Computer Science

Director, Program in Biophysics

Director, Folding@home Distributed Computing Project

**List of suggested reviewers:**

1. Prof. Frank Noe  
   Department for Mathematics and Computer Science  
   Freie Universität Berlin

Email: [frank.noe@fu-berlin.de](mailto:frank.noe@fu-berlin.de)

1. Prof. Baron Peters

Department of Chemical Engineering and Department of Chemistry and Biochemistry

University of California at Santa Barbara

Email: [baronp@engineering.ucsb.edu](mailto:baronp@engineering.ucsb.edu)

1. Prof. Eric Vanden-Eijnden

Courant Institute of Mathematical Sciences

New York University

Email: [eve2@cims.nyu.edu](mailto:eve2@cims.nyu.edu)

1. Dr. Attila Szabo

Theoretical Biophysical Chemistry Section, Laboratory of Chemical Physics

National Institute of Diabetes and Digestive and Kidney Disease

Email: [attilas@mail.nih.gov](mailto:attilas@mail.nih.gov)