

U N I V E R S I T Y O F V I R G I N I A
Department of Chemical Engineering
Charlottesville, VA 22904-4741

June 13, 2011

Dear Editors:

We are submitting our manuscript: "Replica exchange and expanded ensemble simulations as Gibbs sampling: Simple improvements for enhanced mixing" by John D. Chodera and Michael R. Shirts for publication as an Article in the Journal of Chemical Physics.

We believe this work will be of significant interest and utility to readers of the journal who have interest in molecular or physical simulation, especially those who use replica exchange or expanded/generalized ensemble calculations.

In this paper, we demonstrate how both of these classes of algorithms can be considered a form of Gibbs sampling within a Markov chain Monte Carlo (MCMC) framework, which immediately inspires both a number of ways of analyzing and improving the sampling capabilities of these algorithms. We show how methods to update the state variables in common use for these methods lead to suboptimal mixing, and present some simple, inexpensive alternatives that can increase mixing of the overall Markov chain, reducing simulation times, often drastically, necessary to obtain estimates observables of the desired precision.

These improved schemes are demonstrated for several common applications, including an alchemical expanded ensemble simulation, parallel tempering, and multidimensional replica exchange umbrella sampling. Besides unifying many of these different methods under a single statistical framework, and proposing several novel efficient algorithms, this manuscript provides a rigorous statistical foundation for equations previously derived more heuristically.

We would suggest the following scientists as possible reviewers:

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Thanks very much for your time and consideration.

Sincerely,

A handwritten signature in black ink, appearing to read "Michael Shirts". The signature is fluid and cursive, with a prominent "M" and "S".

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