A method for redesigning molecular mechanics force field parameterization by use of a Bayesian statistical framework

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This document describes a collected set of best practices for computing various physical properties from molecular simulations of liquid mixtures.

Keywords: best practices; molecular dynamics simulation; physical property computation

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Todo list

I. Outline

A. Objectives $(0.5pages)$

- Molecular dynamics (MD) simulation is fast becoming a more useful tool in many scientific studies.
- However, some limitations remain in the ability of MD force fields to accurately and transferably describe molecular environments.
- Currently, force fields are parameterized heuristically and require the chemical intuition of experts to manually correct parameters, leading to a more suitable product. Additionally, the creation of a transferable method to update existing force fields based on new experimental data is limited due to lack of understanding and lack of consistency in how the original parameterization was done
- A possible solution to these problems is by recasting the force field parameterization process as a bayesian inference problem.
- The objective of this paper is introduce a framework for using high quality experimental data in order to parameterize molecular mechanics force fields
- In this paper I will describe the overall parameterization framework and my roles in the project, first, collecting and organizing large amounts of high quality thermochemical data and, currently, investigating use of the Multistate Bennett Acceptance Ratio (MBAR) as a means to improve throughput by reducing simulation requirements during the parameterization process.

B. Significance $(0.5pages)$

- A broad variety of research has been greatly impacted by the advent and improvement of MD simulation tools.
  - Observing physical phenomena at a molecular scale (phase changes, ligand docking, etc.)[1]
  - Drug discovery and deisgn of new molecules[2]
- The fundamental part of molecular simulation for describing the energetic interactions of a system is referred to as a force field, hence transferable and quantitatively accurate force fields are imperative for the use of molecular simulation tools to be validated.
  - Transferability of MD force fields and particularly sets of parameters is an extremely popular topic (and current limitation) in the molecular simulation field.[3–6] Transferability encourages use by providing convenience for scientists with wide arrays of research interests and simplifying the mystery that most observe force fields with.

- Inaccurate and poorly parameterized force fields have been shown to grossly misrepresent molecular systems[7,8]

C. Background and related literature $(1.5pages \pm 0.5pages)$

D. Methods $(1.5pages \pm 0.5pages)$

E. Progress $(1.5pages \pm 0.5pages)$

F. Research plan $(0.5pages)$

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