Extension of the stochastic CpHMD method to the CHARMM36m force field

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Constant-pH Molecular Dynamics (CpHMD) methods are nowadays essential to describe pH and the pH effects on the conformational space of biological systems [1]. The stochastic CpHMD method [2] has shown excellent performance over the years [1–3]. Until recently, our implementation of this method only supported the GROMOS 54A7, a force field compatible with the Generalized Reaction-Field (GRF) formalism to treat long-range electrostatic interactions, hence allowing for non-neutral systems [3]. Despite GROMOS popularity, one of the most used force fields is CHARMM36m, which is all-atom and particularly suited for protein, nucleic acids, and lipids simulations [4]. However, it uses mainly PME to treat the long-range electrostatics, which requires a system charge neutralization, a major limitation in its CpHMD implementation [3].

In this work, we present an extension to the stochastic CpHMD to include the CHARMM36m force field. In this preliminary benchmark study, we simulated two well-known proteins - lysozyme and thioredoxin - for which there is a significant amount of experimental data available [5]. These systems were thoroughly studied (pH range 1-12) and the final pK_a values were compared between force fields and with the experimental data [5]. Please visit our Poster to see the performance of both force fields, the details on how to circumvent the PME neutralization step, and the code efficiency (ns/day).

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