Speed of Force Fields: Kinetic Comparison of Force Fields in Biological Systems

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The possibility to explore protein structures and dynamics via Molecular Dynamics (MD) simulations depends on how well the MD force fields capture the true energy landscape of the system under study. Continuous effort in the development of MD force fields is leading to more reliable descriptions of structural and conformational properties of biomolecular systems. In recent years, MD has increasingly been used to infer also kinetic properties of biological systems. One way of achieving this is by means of Markov State Models (MSM), which allows to identify the slowest kinetic processes and the associated time scales. Especially as force fields are usually parametrized only with respect to structural and equilibrium properties, a systematic characterization of force fields respect to kinetic properties has been carried out.

In this study, we performed extensive simulations of a small subset of amino acids and short peptides with four of the most commonly used force fields (AMBER ff99SB-ILDN, AMBER ff03, OPLS-AA and CHARMM27). Our results, in the MSM framework, highlight a force field dependence on the slowest implied timescales, which can vary up to an order of magnitude, even in the simple case of dipeptides; incongruity is also present in the identification of the slowest kinetic processes, especially in the case of small, very flexible, peptides . We suggest a necessity for the development of force fields that are also parametrized with respect to kinetic properties.