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Molecular dynamics simulations of large gas-phase proteins with the fast multipole method

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Classical all-atom molecular dynamics (MD) simulations are a powerful tool for investigating the structures and interactions of biomolecules in the gas phase. Until recently, these simulations were limited to systems containing only a few thousand atoms, due to the quadratic scaling of computational cost with system size. However, the recent integration of a linearly-scaling algorithm for computing the long-range electrostatic forces—the fast multipole method (FMM)—into the MD engine GROMACS has significantly enhanced performance for large biomolecular systems. With this advancement, MD simulations can now be performed efficiently on systems in the megadalton (MDa) range, aligning more closely with the sizes of biomolecules investigated in XFEL experiments.

Here, we demonstrate how to effectively use FMM to achieve high accuracy and performance, and present insights from its initial application to several multimeric protein complexes. Extending the simulation time up to one microsecond, we have gained new insights about the behavior of large proteins in vacuum. Simulations were also performed at multiple temperatures to mimic the effects of thermal activation via collisions with inert gas. These collisions range from low-energy impacts commonly used during electrospray ionization to higher-energy impacts used in techniques like ion mobility spectrometry to probe structural rearrangements and conformational stability. Overall, we demonstrate that FMM-accelerated MD is a powerful tool for investigating large gas-phase biomolecules, yielding results directly relevant to a wide range of gas-phase experimental techniques.

Scholarship elegibility

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