Introduction to molecular dynamics simulations: from liquid water to proteins.

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Molecular dynamics simulations are one of the most adopted computational methods to study structural, dynamic, and thermodynamic properties of molecular systems in condensed phases. The reliability of the simulations is related to the accuracy of the force field (FF) in describing the interactions in the studied system [1]. The importance of the FF is discussed by presenting the results of molecular dynamics simulations for three different systems: liquid water, imidazole in aqueous solutions and zinc proteins.

Liquid water has a primary role in ruling most of the biological, chemical, physical, geological, and environmental processes occurring in nature. Water molecules are associated through hydrogen bonds, which determine the tetrahedral arrangement of the first coordination shell and characterize the tridimensional extended network in condensed phase. The relation between structure and dynamics of the hydrogen bond network of liquid water in different thermodynamic conditions has been investigated by means of molecular dynamics simulations [2, 3, 4, 5].

A FF for the imidazole molecule with improved modeling of the electrostatic interactions has been developed, reparametrizing the charge distribution on the heterocyclic ring and introducing an extra site accounting for the lone pair on the deprotonated nitrogen. The FF has been applied to simulate aqueous solutions at various imidazole concentrations to obtain information on both imidazole-water and imidazole-imidazole interactions, providing a description of the different molecular arrangements in solution [6].

A series of FF parameters for metalloproteins have been optimized through a computational procedure, which relies on *ab initio* calculations in the framework of density functional theory (DFT). Molecular dynamics simulations with the new FF have been performed on a series of zinc proteins, providing structural and thermodynamic properties in agreement with experiments [7, 8].

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