Molecular Dynamics Simulations of Proteins using Reduced Point Charge Models

Laurence Leherte

Laboratoire de Physico-Chimie Informatique, Unité de Chimie Physique Théorique et Structurale, Department of Chemistry, Namur MEdicine & Drug Innovation Center (NAMEDIC), Namur Institute of Structured Matter (NISM), University of Namur, Rue de Bruxelles 61, B-5000 Namur, Belgium

Reduced point charge (RPC) descriptions of proteins are designed from local extrema in charge density (CD) distributions ρ_s obtained from the Poisson equation applied to smoothed molecular electrostatic potentials of the amino acids (AA). From the formalism given in references [1,2], the smoothed analytical CD distribution function of an atom $\rho_{a,s}(r)$ can be expressed as:

$$\rho_{a,s}(r) = \frac{q_a}{(4\pi s)^{3/2}} e^{-r^2/4s}$$

where s is the smoothing factor and q_a is, e.g., the Amber99 [3] atomic charge.

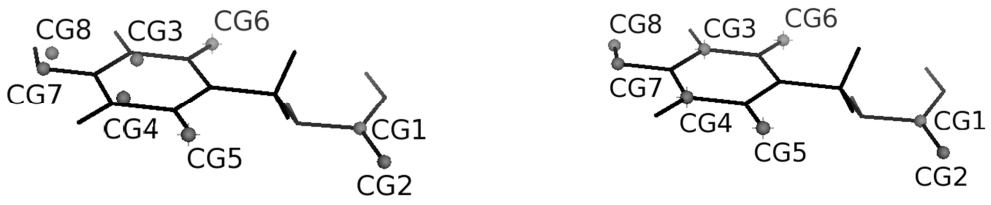

Figure 1. Reduced point charge model of Tyrosine as obtained from a smoothed Amber99-based CD distribution function. Point charges are located on (left) the smoothed CD extrema and on (right) atoms.

To generate charge values, various fitting conditions are selected, i.e., from either electrostatic Coulomb potential or forces, with a separate treatment of main and side chain charges. Full protein RPC descriptions are generated through a superposition algorithm of the AA templates (Figure 1) onto the protein structure.
The program GROMACS [4,5] is used to generate molecular dynamics trajectories of the proteins modelled using various RPC and solvent models. Point charges that are not located on atoms are considered as virtual sites with a null mass and radius. Applications are carried out on various protein complexes, especially Ubiquitin systems, to assess the RPC models [6-9].

1 Leherte L, Vercauteren DP. *J Chem Theory Comput* 2009, **5:**3279-3298.
2 Leherte L, Vercauteren DP. *J Comput-Aided Mol Des* 2011, **25** :913-930.
3 Wang J, Cieplak P, Kollman PA. *J Comput Chem 2000,* **21**:1049-1074.
4 Hess B, Kutzner C, van der Spoel D, Lindahl E. *J Chem Theory Comput* 2008, **4**:435-447.
5 Pronk S, Páll S, Schulz R, Larsson P, et al. *Bioinformatics* 2013, **29**:845-854.
6 Leherte L, Vercauteren DP. *J Molec Graphics Model* 2014, **47**:44-61.
7 Leherte L, Vercauteren DP. *Sci China Chem* 2014, **57**:1340-1354.
8 Leherte L. *Mol Simulat*, 2016, **42**:289-304.
9 Leherte L, Vercauteren DP. *J Phys Chem B* 2017, DOI: 10.1021/acs.jpcb.7b06355.