Structure and Self-Assembly of Biomolecules through Molecular Dynamics Simulations

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ABSTRACT

In the field of bio-inspired materials, the non-covalent self-assembly of relatively simple peptide based molecules and proteins has gained increasing attention for the formation of nanostructured, biologically functional materials, including nanofibers hydrogels and scaffolds, all with nanoscale order. Moreover, polypeptide self-assembly is often associated with human medical disorders[1,2]. Understanding the physicochemical determinants that underlie peptide self-assembly and protein folding are fundamental steps, in view of the rational design, or redesign of already existed nano-building blocks for biotechnological and biomedical applications.

Our work concerns the modeling of small biological molecules, such as peptides, and proteins (biopolymers), where the self-assembly propensity and the conformational properties, are studied through all-atom Molecular Dynamics simulations using an explicit solvent model.

The first part of our work concerns the study of a very common, but of particular interest, peptide, that is diphenylalanine, FF. Our findings reveal a strong self-assembling propensity of FF in water (inorganic solvent) in contrast to its behavior in methanol (organic solvent)[1]. We further quantify the interaction between two isolated peptides dissolved in water/methanol through the calculation of a potential of mean force. Pair radial distribution functions between FF peptides, as well as the number of hydrogen bonds are calculated, providing measures of the self-assembly of peptides in the aqueous solvent. Our results are in qualitative agreement with experimental observations.

The second part of our work concerns the modeling of two proteins in the native state, which studied through all-atom Molecular Dynamics simulations under specific (physiological) conditions, at room temperature. The homodimeric Rop protein, that is a paradigm of a canonical 4-a-helical bundle, and its loopless mutation (RM6) are studied in aqueous solution. Their structural, conformational properties, as well as their hydrogen bond network, are characterized in atomic detail.

Our findings reveal that both Rop and RM6 proteins have stable native states. According to the hydrogen bonding analysis the stability of the secondary conformation can be attributed to the formations of hydrogen bonds. On the other hand, for the stability of the native state, the electrostatic interactions play an important role. The calculation of the root mean square deviation (RMSD) verifies that the system in an equilibrated structure, evaluating at the same time, our model. Finally, the stereochemical quality of our protein models is demonstrated through the calculation of the Ramachandran plot.

Current work concerns studying the thermal stability of Rop protein, as well as studies of mutations of Rop, which are related with different topological structures.

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