**STRUCTURE AND SELF-ASSEMBLY OF DI-PEPTIDES THROUGH ATOMISTIC SIMULATIONS AND EXPERIMENTS**

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**ABSTRACT**

In the field of bio-inspired materials, the non-covalent self-assembly of relatively simple peptide based molecules has gained increasing attention for the formation of biologically functional materials, all with nanoscale order. Self-assembly is often associated with human medical disorders. Our work concerns the modeling of di-peptides, where the self-assembly propensity and the conformational properties, are studied through all-atom Molecular Dynamics simulations in explicit solvent and compared with experimental findings. Four dipeptides have been studied: diphenylalanine (FF), Alanine-Isoleucine (Ala-Ile), dialanine (Ala-Ala) and Isoleucine-Isoleucine (Ile-Ile) Of particular interest is FF peptide, the study of which reveals a strong self-assembling propensity in water in contrast to its behavior in an organic solvent, like methanol. These dipeptides belong to two different classes “Val-Ala” (Ala-Ile and Ile-Ile) and “Phe-Phe” (FF) and a systematic comparison in the self-assembly features among them has been performed.

We propose a consistent combination of complementary simulation and experimental methods, covering a broad range of length and time scales. The examined samples from both simulations and scanning electron microscopy experiments (SEM) cover a board range of concentrations as well, since these are usually in different concentration windows (i.e., high values in simulations vs low values in experiments). However, in the present study, there is an overlapping concentration regime and a qualitative agreement between simulation and experimental results is observed. The structural and conformational properties of all dipeptides is investigated in details in water and in methanol solvents. The effect of temperature on the formed structures is found to be small, from both simulation and experiments, when temperature varies from 278 to 300 K. Furthermore, the differences of Ala-Ile and Ile-Ile dipeptides from dialanine (Ala-Ala) and diphenylalanine (FF) dipeptides in similar conditions are highlighted. Based on various measures the strength of the self-assembly propensity of the four dipeptides in aqueous solutions attains the following order: FF > Ala-Ile > Ala-Ala > Ile-Ile.

**KEYWORDS:** Dipeptides, Molecular Simulations, Self-assembly

**REFERENCES**

 [1] Rissanou, A., Georgilis, E., Kasotakis, E., Mitraki, A., & Harmandaris, V. (2013) *J. Phys. Chem. B* **117** (15): 3962-75.

 [2] Rissanou, A., Simatos, G., Siachouli, P., Mitraki, A., & Harmandaris, V. (2020) *J. Phys. Chem. B*, **124** (33): 7102–7114.