

Study of the Structure of Solutions of Organic Compounds Using Computational Methods

Carlos E. S. Bernardes¹

¹ Centro de Química Estrutural, Institute of Molecular Sciences, Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade de Lisboa, 1749-016 Lisboa, Portugal.

*cebernardes@ciencias.ulisboa.pt

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Understanding the structure of solutions of organic materials is an important topic, as it can be used to rationalize the properties of a substance, such as its solubility or how the molecules join to form a crystal structure. Quite often, when referring to a solution, the first image that comes to mind is the view of ideal mixtures, where solute molecules are solvated and isolated from each other. Still, molecular aggregation is widely discussed, like in the case of crystal nucleation studies. Thus, to what extent do solute molecules aggregate in solution, particularly close to or at the solubility limit of a substance? How does this process affect the solution/substance properties? The answer to the earlier questions may be difficult experimentally but easily addressed using computational methods, which can provide a unique microscopic view of the structure of solutions under different conditions (e.g., concentration, temperature, and pressure). This requires, however, proper tools to interpret the simulation data.

In this work, the program AGGREGATES [1], specifically developed to investigate the structure of solutions, will be presented and used to analyze molecular dynamics simulation data for solutions of simvastatin and 4'-hydroxyacetophenone (HAP). It will be shown that solubility can depend on the ability of the solvent to solvate large aggregates of solute instead of individual molecules. The study of simvastatin solutions in acetone, where the solute activity coefficient is approximately unitary, $\gamma = 1$, reveals the formation of mixtures in which the interplay between solvent and the aggregates is optimal [2]. In turn, by investigating HAP aqueous solutions, it will be shown that the solvent–aggregates interplay is a thermally activated process where high temperatures stabilize the formation of these structures, increasing the compound solubility.

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