Doctoral Dissertation
Doctoral Program in Chemical Engineering ($XXXV$cycle)

Molecular Modeling of Supramolecular Systems with Controllable Stimuli-Responsive Properties

By

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Politecnico di Torino
2023

Abstract

Self-assembly allows obtaining materials with stimuli-responsive properties, offering a highly attractive alternative for new designing strategies and material engineering. However, the rational design of self-assembled materials with programmable properties requires a deep knowledge of the physical-chemical features controlling them. A detailed comprehension of the mechanism governing the material's response to a single stimulus or a combination of them may be particularly challenging solely through experimental results. In this view, molecular models and simulations may be useful to understand these mechanisms.

The aim of this thesis is to explore the internal dynamics of new self-assembled materials in relation to their responsiveness to various stimuli by using molecular dynamics (MD) simulations. In addition, molecular simulations are also used to support experimental evidences, enabling the observation of phenomena at the molecular level.

In the light of this perspective, this thesis starts presenting a first work exploring the dynamics of supramolecular self-assembled soft nanoparticles (NPs) scanning surfaces functionalized with chemical gradients of receptors. In particular, the utilization of coarse-grained (CG) molecular models give us the possibility to control the fate of the nanoparticle by adjusting the chemical and physical properties of the single assembling units. As a result, the combination of classical MD and enhanced sampling simulations provides valuable insights into the design of nanoparticles with controlled disassembly and cargo release.

Subsequently, we investigated the emergence of relevant physical behaviors in response to external stimuli, such as the addition of second components in self assembled micelles, or the application of electric fields on colloidal lattices by employing CG-MD simulations. The second part of the thesis highlights the effects of introducing second components, with different intermolecular interactions, on the

rearrangement and self-organization of surfactants in self-assembled micelles. While, in the third part of the thesis, the same model resolution enables us to explore the semiconductive properties of a lattice of positively charged nanoparticles that self-assemble in the presence of multivalent counterions, where the application of electric fields promotes ion conduction within the lattice. In both cases, the combination of MD simulations with machine learning approaches permits the observation of these phenomena with a local point of view.

The fourth part of the thesis presents a work where simulations are used to examine, from a submolecular perspective, thermo-responsive amphiphilic assemblies that undergo phase transition in correspondence to the lower critical solution temperature. In particular, CG molecular models allow for the observation of the monomer-monomer and monomer-solvent interactions at different temperatures. The final case study focuses on the realization of a tubulin-based nanocapsule stabilized by glue molecules. In this case, all-atom models lead to the quantification of the effects of the glue molecules adhering on the surface of the nanocapsule.

In conclusion, the results discussed in this thesis show how molecular dynamics simulations may provide a fundamental support for the development of new self-assembled stimuli-responsive materials, starting through a deeper understanding of the intermolecular interactions that characterize the macroscopic properties of the aggregate.