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Molecular Modeling of Amphiphilic Invertible Polymers Self-Assembly in Solvents of Different Polarity

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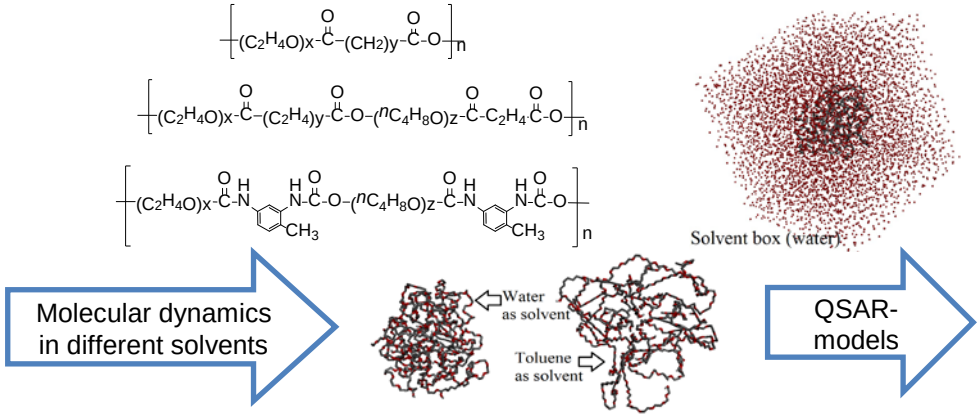
Recently, a lot of attention has been devoted to development of drug delivery agents to target specific biomolecules or cells in living organism. A series of amphiphilic invertible polymers (AIPs) that are capable of self-assembling into invertible micellar assemblies (IMAs) and changing macromolecular conformation in response to changes in polarity of environment (solvent) were designed by this group.[1] The IMAs are capable of solubilizing poorly water-soluble drugs as well releasing the cargo molecules by conformational inversion of AIPs macromolecules. The latter was demonstrated by loading IMAs with a phytochemical drug, curcumin, insoluble in water, and further experiments on micellar curcumin bioavailability and cancerous cells treatment.[2]



The aim of this study is to investigate the formation of IMAs in solvents of different polarity by computational approaches, namely, molecular dynamics (MD), in order to demonstrate IMAs inversion and identify factors (particularly, chemical structure) that improve their performance as drug carriers.
In current computational study a preliminary optimization was done in HyperChem 8.[2] It was found that the AIPs formed a well-packed, folded micelle in polar solvent (water), while in non-polar solvent (toluene) the AIPs were forming an unfolded micelle, able to release a drug (Figure). The computational results are corresponded to the experimental data.[3] Next steps in this study will be to make more accurate calculations using large systems with hundreds of thousands solvent molecules in NAMD software environment.[4] The obtained data on IMAs will be used to build a QSAR model, to predict polymers' ability for conformational inversion in response to different environmental changes for further development as an effective drug-delivery system.

References

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