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Coarse grain approaches to study drug delivery systems

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Abstract:

Computer simulations, such as Molecular Dynamics simulations, are a very powerfull tool to understand biomolecular processes. In this direction, Coarse Grain (CG) models - where atoms are grouped in specific sites - allow simulation time and length scales of the systems beyond what is achievable with traditional atomistic models [1]. In this work, we go over different application of this methodology to Drug delivery systems (DDS) carried out in the group.

DDS - a formulation or a device that enables the introduction of a therapeutic substance in the body and improves its efficacy and safety by controlling the rate, time, and place of release of drugs - are an important component of drug development and therapeutics [2]. Biocompatible nanoparticles are materials in the nanoscale emerged as important players in this direction, improving efficacy of aproved drugs, for example. In this direction, the molecular understanding of the encapsulation process could be very helpful to guide the nanocarrier for a specific system.

Here we discuss different aplications of drug delivery carriers, such as liposomes, polymeric micelles and polymersomes using CG molecular dynamics simulations, based on Martini forcefield [3]. In particular we investigate [4]:

- The encapsulation of sumatriptan – an antimigraine drug - with polymeric micelles. We based the drug parametrization on atomistic simulations. We found that the drug escentially partition between the hydrophilic crown and water phase.
- The interaction of Prilocaine, a local anesthetic, in liposomes and poly(ethylene oxide)-poly(butadiene) di-block copolymer polymersomes. For the di-block copolymers, we also run bilayer systems under different ensembles. In this consition, we were are to reproduce key structural and mechanical experimental for different length chains with a similar weight fraction.
- The differential interaction of amphiphilic antimicrobial peptides with 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) lipid structures. We simulated the peptide/lipid system from different initial configurations. The peptides used for our simulations are aurein 1.2 and maculatin 1.1, two well-known AMPs from the Australian tree frog, molecules that present different membrane-perturbing behaviors. Our results showed for each peptide a different

pathway for the peptide-induced membrane leakage and in good agreement with experimental observations.

Key-words: Molecular Dynamics, Coarse grain, Drug delivery systems, MARTINI forcefield

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