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Master 2 project -2019

This project will take place in a highly interdisciplinary environment at IBCP, in the group of Luca Monticelli (molecular modeling) and in close collaboration with Sofia Caridade (experiments), who develops layer-by-layer (LbL) assemblies for drug delivery and other biomedical applications.
To apply, please send a CV and a motivation letter by e-mail to the two coordinators.

Understanding the polymer behaviour in Layer-by-Layer assemblies

The alternating dipping of a charged solid surface into a polyanion and then into a polycation solution usually leads to the progressive formation of films on the solid support, defined as polyelectrolyte multilayers [Decher 1997]. This electrostatic self-assembly method is called Layer-by-Layer (LbL) deposition technique and has been developed as a way for producing organic and hybrid organic-inorganic supramolecular assemblies without requiring extensive equipment. In particular, in the biomedical field, these multilayers constitute versatile tools for the design of synthetic membranes containing macromolecules such as proteins, nucleic acids, or polypeptides with targeted properties [Monge 2015]. However, explaining the behaviour of the polymers in the LbL assembly remains a challenge due to major difficulties in structural characterization of the materials. Understanding the molecular origin of the mechanical properties of the film and deciphering the interactions with the biomolecules they contain would lead to a greater control of the bioactivity of the final medical device.

Here we propose to characterize the self-assembly, the mechanical properties, and the interactions of LbL multilayers using molecular simulations. During the past decades, molecular simulations have become a powerful tool for interpreting experimental results in terms of nanometre-scale structures and interactions, particularly for biological systems such as proteins, nucleic acids, carbohydrates, and lipid membranes. In the first phase of the project we will build molecular models for two charged polysaccharides, chitosan and hyaluronic acid, experimentally used in LbL systems for drug delivery. We will start by building all-atom models, with the highest level of accuracy. These will be used as a basis for the parameterization of coarse-grained models, featuring higher computational efficiency, which is essential to reach the large time and length scales needed to characterize the properties of polyelectrolytes. Coarse-grained simulations will allow the characterization of dynamic and elastic properties of the polymers in solution, and will be carried out with the MARTINI model, one the most

widely used coarse-grained models. MARTINI has successfully been used for the description of a wide variety of biological and synthetic systems, including liposomes, models of complex biological membranes, polymers, and nanoparticles [Marrink 2007; Monticelli 2008; Marrink 2013]. Simulations will be validated by comparison with experimental data whenever possible.

Once the models of each polyelectrolyte will be built and characterized, in the second phase of the project we will perform self-assembly simulations, exposing a charged, solid surface alternatively to solutions of each polyelectrolyte – mimicking the experimental layer-by-layer deposition process. This will allow characterization of the multi-layer assembly in terms of internal structure (e.g., density profiles), dynamics (self-diffusion of the polymers), and elastic properties (e.g., Young modulus). Simulations of material swelling with aqueous solutions will also be possible, allowing changes in material properties and structural rearrangements upon modifications of pH and ionic strength, as well as exposition to other materials – allowing predictions on the interaction between LbL multilayers and proteins or nanoparticles. Such predictions will be used, in turn, to guide the experimental design of novel LbL materials with improved properties.

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