Simulated Interactions between Structured Peptides and Biomaterials

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Introduction: The chemical and physical interactions between proteins and biomaterial surfaces govern the biocompatibility of those materials when introduced into living systems. Therefore, the possibility of controlling biocompatibility on a molecular level through strategic design of biomaterials begins with the study of these interactions at the atomic level. The lack of an accurate molecular description of the way in which proteins interact with biomaterials has often resulted in the implementation of ineffective biomaterial designs based on a trial-and-error approach. To facilitate this kind of study, we have begun the process of supplementing the molecular modeling community's range of computational approaches with methods designed specifically for the analysis of protein-surface interactions. Even the most advanced publicly-available molecular modeling force fields do not yet include parameterization options for molecular systems interacting with biomaterial surfaces, so we are working on a variety of studies to guide the development of methods for use in these types of simulations. Our studies include nanosecond-scale simulations of structured leucine-lysine (LK)-peptides interacting with charged and nonpolar self-assembled monolayer (SAM) surfaces within a physiological saline solution using three different protein force fields. The majority of this work is untaken using the replica-exchange molecular dynamics (REMD) technique to accelerate conformational sampling. Upon completion of these ongoing simulations, peptide structural data obtained from the simulations will be compared with experimental results in order to provide a means of evaluating the effectiveness of each of the tested force fields in simulating peptide-surface interactions.

Methods: Our model systems include a 14-mer alpha-helical or pair of 7-mer beta-sheet LK-peptides solvated in explicit TIP3P water, simulated under periodic boundary conditions in the presence of either a 50% deprotonated -COOH functionalized SAM or a -CH_3 functionalized nonpolar SAM. The CHARMM suite of simulation tools was used as a simulation engine for simulations conducted with the CHARMM, AMBER, and OPLS-AA force fields. We are also using the REMD approach (coordinated using the Multiscale Modeling Tools for Structural Biology (MMTSB) software) for optimizing conformational sampling with a temperature range of 298-520 K and 40 discrete replicas.

Results: Our simulations have resulted in a large pool of production-run structural data upon which we performed various analyses that would allow us to as closely as possible compare our results with experimental work completed by Prof. David Castner and coworkers at the University of Washington.

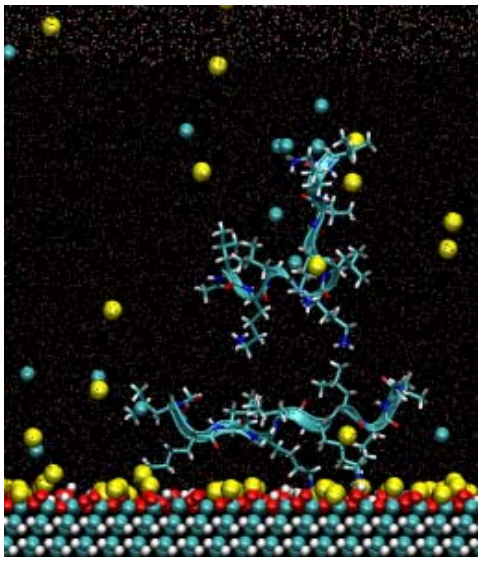

Figure 1. An example of one of the simulated systems. Here, two beta-sheet peptides are seen interacting with a charged COOH-SAM surface.

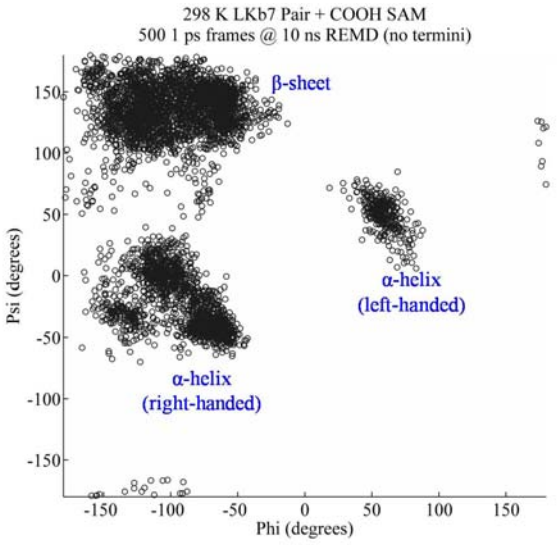

Figure 2. Ramachandran plot example of the structural characterization data (backbone dihedral angles) recorded for each system during the production stage of the REMD runs.

Conclusions: In the simulations of the alpha-helical LK-peptides, we have observed a strong tendency to adsorb to both surface chemistries in an irreversible manner, as well as conservation of the alpha-helical conformation when either free or adsorbed to a surface. In the simulations of the beta-sheet LK-peptides, we have noted a weaker tendency toward adsorption, as well as very little interaction between the individual peptides during the adsorption process.