groups. Membrane thickness was measured by using energy transfer between the surface fluorescent probe 1-anilinonaphthalene-8-sulfonic acid(ANS) and hydrophobic fluorescent probe Py-3-Py. Lidocaine·HCl increased bulk lateral and rotational mobilities, and had a greater fluidizing effect on the inner than outer monolayer of liposome. Thickness of SPMVTL, SPMVPL lipid bilayer have been decreased by lidocaine·HCl, which means that membranes have been expanded. The sensitivities to increasing effect of lateral and rotational mobilities of liposomal lipid bilayer by local anesthetic differed depending on the native and model membranes in the descending order of SPMV, SPMVPL and SPMVTL. These effects are not only due to the influence of local anesthetic on lipids, but they are magnified by the interaction between lipids, proteins and water.

429-Pos

Drug Delivery Systems Featuring Withdrawn Fluoroquinolones

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With increasing menace of bacterial resistance, constant development of new drugs and strategies to increase their efficacy is of great importance. Quinolones are a very well know class of antibacterial agents, as well as one of the most prescribed drugs in medicine for treatment of various bacterial infections. This wide use seems to be the main cause for bacterial resistance and this class of antibacterial agents grew significantly in the past. Fluoroquinolones, which include newer generation quinolones, were developed by implementing structural changes to the basic drug structure. Although highly prescribed, these antibacterial drugs are known for their various side effects and toxicity, and some of the agents have been withdrawn or not approved for use.

Drug delivery systems have been the target, for the past few years, of intense research since they aim to achieve a greater efficacy in the site of action as well as to improve aspects such as pharmacokinetics and/or minimizing side effects, contributing to the development of these systems.

From the existing controlled drug delivery systems, liposomes are frequently used due to their high versatility and biocompatibility. Lipid vesicles are considered for drug delivery when therapeutic agents are toxic, have high potency and low blood circulation times. Encapsulation of drugs, such as antifungal agents, has been reported and even commercialized, but research, regarding quinolones and liposomes, consists, mainly, in membrane permeability and physicochemical studies.

Different lipid formulations for drug delivery of similar fluoroquinolones, withdrawn or not approved for use (due to side effects) were prepared, studied and optimized. Physicochemical characterization of the antibacterial drugs (free and encapsulated) and lipid interaction is also a target of this work.

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Membrane Active Peptides I

430-Pos

Multiscale Simulations of RNase E From E.coli: A Membrane Binding Protein

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RNase E is an essential endoribonuclease involved in RNA processing and mRNA degradation. The N-terminal half of the protein encompasses the catalytic domain; the C-terminal half is the scaffold for the assembly of the multienzyme RNA degradosome. Here we describe multiscale MD simulations of 'segment-A', an element in the beginning of the non-catalytic region of RNase E that is required for membrane binding. It has previously been demonstrated *in vitro*, that an oligopeptide corresponding to segment-A has the propensity to form an amphipathic α-helix and that it avidly binds to protein-free phospholipid vesicles. Disruption or mutation of segment-A *in vitro* and *in vivo* in full-length RNase E abolishes membrane binding.

We present a thorough multiscale MD simulation characterization of the behavior of RNase E in model membranes:

We have performed atomistic simulations of the wildtype segment-A and mutants in phospholipid bilayers to uncover the molecular-level details of membrane-binding. Furthermore, we have performed coarse-grained simulations of the same peptides in phospholipid vesicles of various sizes and lipid compositions to investigate the effect of membrane curvature, and lipid type on the membrane-binding, dynamics and potential aggregation of RNase E. The lipid compositions are designed to provide a realistic mimic of the *E.coli* inner membrane.

Not only are our simulations in good agreement with experimental work, but in addition, they provide molecular-level interpretations of the experimentally observed phenomena.

431-Pos

Poration of Lipid Vesicles By Antimicrobial Peptides: Simulation Studies With a Polarizable Coarse-Grain Model

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Antimicrobial peptides are a large family of peptides that include small cationic peptides that can permeabilize lipid membranes by disrupting the bilayer structure. Previous atomistic simulations of two specific antimicrobial peptides, magainin and melittin, show that they act by forming toroidal transmembrane pores in model bilayers. However, only systems of limited size and length scales have been studied and direct comparisons to experimental observations could not be made. Here, we study the poration propensity of these peptides with lipid vesicles using a coarse-grain description. A new version of the MARTINI force-field has been used which accounts for the polarizability of water. The explicit screening of the new MARTINI force-field provides for a more realistic description of membrane poration by antimicrobial peptides.

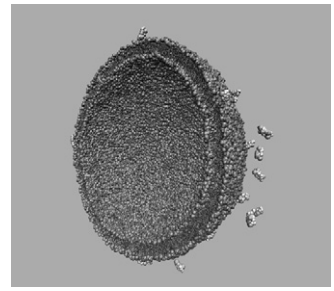

Figure: A snapshot of the starting structure of simulations of magainin-H2, an antimicrobial peptide, ''attacking'' a DPPC lipid vesicle. The vesicle is cut through to reveal its cross section. The head group beads are shown in purple and pink and the tails in gray. The antimicrobial peptides are shown in green (backbone beads) and yellow (side-chain beads). The water beads are not shown for clarity.

432-Pos

Binding of Antimicrobial Lipopeptides To Lipid Bilayers Characterized By Microsecond Molecular Dynamics Simulations

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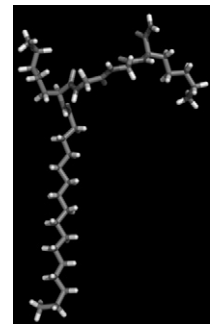

The emergence of antibiotic resistant pathogens is one of the major medical problems of the 21st century, prompting renewed interest in the development of novel antimicrobial compounds. Here we use microsecond-scale all-atom molecular dynamics simulations to characterize the structure, dynamics, and membrane-binding mechanism of a synthetic antimicrobial lipopeptide, C16-KGGK. The results of the simulations are validated by comparison with solid state NMR experiments, and yield new insights into the molecules' mechanism of action.

433-Pos

On the Roles of Anionic Lipids in Protein Localization and Permeability of Membranes

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Anionic lipids, such as phosphatidylglycerol and phosphatidylserine, play important structural and functional roles in cell membranes. In particular, they appear to provide strong interactions with positively charged protein side chains to promote membrane localization of lipid binding domains and antimicrobial peptides, as well as to modulate the function of many membrane proteins. All-atom molecular dynamics simulations were used to explore the strength of these interactions and the impact they have on the ability of charged protein residues to penetrate into membranes. Using an analog of arginine and bilayers of pure phosphatidylcholine or mixtures with phosphatidylglycerol, we have computed the thermodynamics of charged side chain translocation, as well as the binding affinity of each lipid within the membrane. We found that arginine deforms the bilayer in a similar fashion, regardless of composition, and that the free energy profile for translocation is relatively unaffected by anionic lipids: the ''neutralization'' of the protein side chain does not reduce the large ~20 kcal/mol barrier significantly. We decomposed these free energies to explain why anionic lipids do not play a significant role, with implications for the actions of many charged peptides and ion permeability. We also find