

COMPUTATIONAL MODELING OF DNA-CATIONIC LIPID COMPLEXATION

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Developments in gene therapy have led to a need for new and more efficient transfection vectors. So far, the use of viruses has received major attention. During the recent years, however, cationic liposomes have emerged as a potential rival for viruses and have several advantages, e.g. nonimmunogenicity, low toxicity and a capability to carry larger amounts of DNA. Yet, the properties of cationic liposomes and their interactions with DNA are not understood in detail [1-3].

One of the major difficulties in determining the properties of liposomes and their interactions with DNA is the presence of many time and length scales. Furthermore, the collective nature of complex formation makes the problem both theoretically and computationally challenging [3]. In particular, long-range electrostatic and dipolar interactions are crucial for the self-assembly process but they are very demanding from the theoretical and computational point of view. Current knowledge of DNA-cationic liposome complexes, also known as lipoplexes, is mainly based on experimental results, see e.g. Refs [1,4] and references therein.

We study the self-assembly and the nature of DNA-lipid interactions using molecular dynamics simulations. The system consists of strands of DNA, explicit salt (NaCl), and zwitterionic lipid (POPC) and cationic lipid (DHAB) confined to a monolayer (M. Karttunen, A. Pakkanen, P.K.J. Kinnunen, K. Kaski, in preparation). Non-bonded interactions were modeled by a Lennard-Jones potential and Ewald summation was used for electrostatic interactions. The Ewald summation was modified in order to study systems having a finite extension in one of the directions, i.e., systems having a slab geometry. The FENE-potential was used for bonded interactions.

Although the model is a coarse-grained one (at the level of Lennard-Jones interactions), it provides a good starting point to study systematically the processes relevant to self-assembly. Here, we compare structural properties, such as the re-orientation of the POPC dipoles, various pair correlation functions and the structure of the monolayer to experimental observations [4].

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Furthermore, we study the effect of salt and cationic lipid concentration on charge density. The results indicate a concentration dependent charge inversion. Finally, the application of novel coarse-grained methods (M. Karttunen, I. Vattulainen, A. Lyubartsev, A. Laaksonen, A hierarchical method for coarse-graining molecular systems: From molecular dynamics to mesoscopic simulations, submitted to Phys. Rev. Lett.) to lipid-DNA systems is discussed.

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