

## PP017

## 1,4-DHP-Lipid Forms a Tubular Micellae

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1,1'-[3,5-bis(dodecyloxycarbonyl)-4-phenyl-1,4-dihydropyridin-2,6-diyl]dimethylene} bispyridinium dibromide (1,4-DHP lipid) is a gene transfection agent [1, 2]. 1,4-DHP lipid structure was calculated with *ab initio* quantum mechanics to obtain the charges for molecular dynamics (MD) with AMBER 8.0 force field. 1,4-DHP-lipid molecules were subjected to MD from the initial structure of a periodic lipid bilayer-water box, with a small amount of excessive water on the lipid edges to ensure the mobility of lipid molecules. After 14 ns of MD simulation the lipid molecules with the fatty acid tails started to squeeze from one bilayer layer to another one. After 35 ns few lipid molecules turned with their charged heads to the side of the lipid bilayer and after 100 ns a profound tubular micelle structure began to form. The tubular micelle structure becomes more perfect during the course of simulation of 300 ns (Fig). The results of MD simulation were confirmed by electron microscopy, showing the interwinding tubular structures.

Conclusion is that the gene transfection agent 1,4-DHP lipid basic structure is a tubular micellae and that such the micellae are capable to form lipoplex for the DNA transfection.

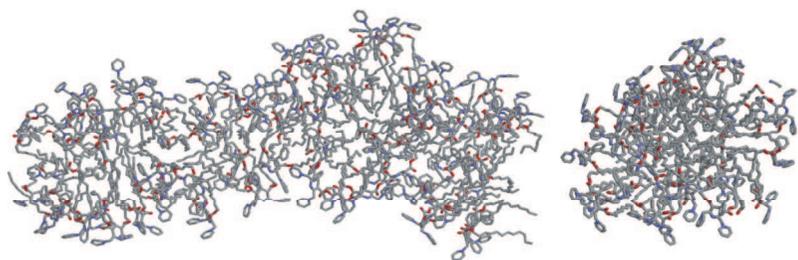


Fig. 1,4-DHP lipid tubomicellae side view and top view.

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[2]. Z. Hyvonen, S. Ronkko, M. -R. Toppinen, I. Jaaskelainen, A. Plotniece, A. Urtti Dioleoyl phosphatidylethanolamine and PEG-lipid conjugates modify DNA delivery mediated by 1,4-dihydropyridine amphiphiles. *Journal of Controlled Release*, **2004** 99, 177-190.

## PP018

## Hydration Structure and Dynamics of Lanthanides by Molecular Dynamics Simulations with a Polarizable Force Field

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Understanding hydration structure of heavy atoms – like transition metals, lanthanides or actinides – in aqueous solution is of fundamental importance to address their solvation properties and chemical reactivity. In the present work, based on MD simulations with a new reliable classical pair interaction potential plus explicit polarization [1,2], we have studied hydration properties of all the trications ( $\text{Ln}^{3+}$ ) in the lanthanide series.

We have performed classical MD of all the  $\text{Ln}^{3+}$  cations using the same Hamiltonian based on a polarizable force field previously developed by us for  $\text{La}^{3+}$  in water [1]. The original parameters for  $\text{La}^{3+}$  in water were extended to all the atoms in the series and modified taking into account available data on polarizability, and ionic radii through the series. This extrapolation method was first tested on  $\text{Lu}^{3+}$ -water interaction comparing model potential results with *ab initio* calculations [3]. Using this approach, we had to fit parameters only for the first atom in the series and then adapting them using atomic properties, thus obtaining a set of parameters able to treat the whole chemical series.

Our simulations produced the known change in coordination number (CN) from 9 to 8 water molecules across the  $\text{Ln}^{3+}$  series. The light  $\text{Ln}^{3+}$  atoms (in the beginning of the series) have CN = 9 with a Tricapped Trigonal Prism (TTP) structure: 6 prismatic water molecules and 3 capped water molecule forming a triangle in the medium of the prism. At the end of the series (heavy lanthanides), the CN is 8 and the structure is a Square Antiprism (SAP). In the middle of the series we do not observe a sudden change but the statistical coexistence of two stoichiometries (CN=9 and CN=8) with many interchanges [4].

Our microscopic data, in agreement with recent experimental results of Helm, Merbach and co-workers [5], suggest the following picture: moving across the series from lighter to heavier lanthanides we have a changing in statistical predominance of one first hydration shell structure containing 9 water molecules to 8 water molecules. This statistical picture is able to explain the hydration behaviour through the series.

Finally, we performed simulations as a function of the temperature ( $T = 277 - 624$  K) such that we can calculate thermodynamic parameters ( $\Delta_r H_{298}^0$  and  $\Delta_r S_{298}^0$ ) for the  $\text{Ln}(\text{H}_2\text{O})_8^{3+} / \text{Ln}(\text{H}_2\text{O})_9^{3+}$  hydration equilibrium. As expected,  $\Delta_r G_{298}^0$  varies linearly through the series, corresponding to the S shape observed for CN as a function of atomic number.

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