Cation-induced changes to the structure of lipid membranes II

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Divalent metal cations (Ca^{2+}, Mg^{2+}, Zn^{2+}) play important role in cell's physiology and biochemistry. Their binding to the lipid bilayer of biological membranes depend not only on the property of the cation and the membrane lipid head-group, but also on the lipid tail chain [1]. In spite of many studies of cations adsorption on phosphatidylcholine membranes, the information concerning their influence on the lipid bilayer itself is rather scattered and often contradictive [2, 3, 4]. The molecular dynamics simulation results revealed a condensation of anionic lipid bilayer and a concomitant increase of the lipid ordering due to Ca^{2+} binding [5]. Recent small-angle neutron-scattering (SANS) measurements using DPPC vesicles and Ca^{2+} have revealed that cations at low concentration increase the order of lipid bilayers by increasing bilayer thickness (Fig. 1C) and decreasing area per lipid [6, 7].

We have studied the interactions of calcium with the biomimetic membrane, DPPC. The experiment was proposed with the aim to decouple effects due to electrostatics interactions from those of geometrical constraints found in curved vesicular bilayers [6]. The small-angle neutron-diffraction (SAND) experiment on oriented multilamellar samples has confirmed the changes of both the lipid bilayer thickness and the area per DPPC molecule due to Ca^{2+} binding [8]. Fig. 1 summarizes our results obtained from the extended study of this system.

DPPC oriented multilayers at selected molar ratios Ca^{2+}:DPPC were prepared by hydrating thin lipid films from vapors at defined humidity. Samples were hydrated with different D_2O/H_2O solutions (100%, 70%, 40%, and 8% D_2O) to vary the scattering contrast between the multilayers of lipid bilayers and water. A subtraction of such obtained data directly results in the water distribution profiles. In addition, contrast variation approach allows one to solve the phase problem necessary for the Fourier reconstruction of the one-dimensional scattering length density profiles [9, 10].

Results (summarized in Fig. 1A, B) show clearly that Ca^{2+} affects DPPC bilayer thickness (d_L). We found its increase due to Ca^{2+} binding, reaching $\Delta d_L = d_L - d_{L(DPPC)} = 4.2$ Å, where $d_{L(DPPC)}$ is the lipid bilayer thickness without any Ca^{2+}. However, the changes in DPPC bilayer structure depend strongly on the concentration of Ca^{2+}, showing a bilayer thinning at molar ratio exceeding ~ 0.15. Our observations agree well with previous SANS results [6,7] confirming that at very low concentrations, the Ca^{2+} induce structural changes to bilayer based on a prevailing effect of electrostatic interactions, rather than that of bilayer curvature.

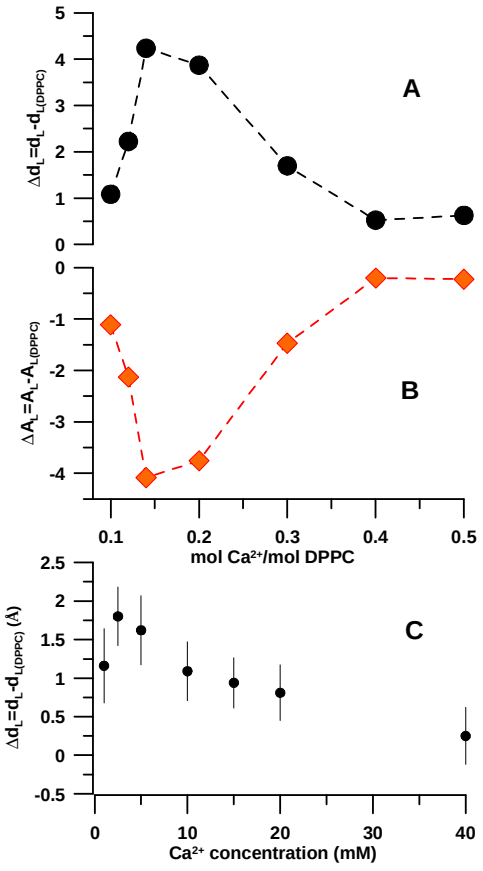

Fig. 1 The SAND results of change in the planar DPPC lipid bilayer thickness Δd_L (A), and the surface area per DPPC molecule ΔA_L (B) induced by Ca^{2+} binding. The effect of Ca^{2+} on the curved DPPC lipid bilayer thickness obtained by SANS (C).

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