Cation-induced changes to the structure of lipid membranes III

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It is well known that divalent metal cations play important role in cell's physiology and biochemistry. In addition to calcium and magnesium, metals such as iron, manganese, copper, zinc, nickel and cobalt are essential at the appropriate concentration, yet toxic beyond normal levels. Among the first-row transition metals, zinc is second only to iron in terms of abundance and importance in biological systems. Zn^{2+} plays a fundamental role in several critical cellular functions such as protein metabolism, gene expression, structural and functional integrity of biomembranes, and in metabolic processes [1]. Compared to other micronutrients, zinc exists in biological systems in high concentrations, particularly in biomembranes. Concentration of zinc in animal organels ranges from $<10^{-9}$ M in cytoplasm to $>10^{-3}$ M in some membrane vesicles [2].

In spite of many studies of divalent cations (Me^{2+}) adsorption on phosphatidylcholine membranes, the information concerning their influence on the lipid bilayer itself is rather scattered and often contradictive [3-5]. We have studied the interactions of calcium with the biomimetic membrane made of dipalmitoyl-phosphatidylcholine (DPPC) previously [CNBC-2012-SM-3]. The experiment was proposed with the aim to decouple effects due to electrostatic interactions from those of geometrical constraints found in curved vesicular bilayers [6,7]. 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 (Fig. 1A,B empty symbols) [8]. Recently, the study was extended to Zn^{2+}. The electronic structure of zinc is different from that of divalent alkaline earth metal ions. Zinc cation possesses a higher affinity to electronegative groups [9], and therefore, also other electronegative moieties such as ester oxygens and/or carbonyl groups of the lipid headgroup can be directly involved in complex formation. Fig. 1A,B (full symbols) summarizes our results obtained from the extended study of DPPC-Zn^{2+} system.

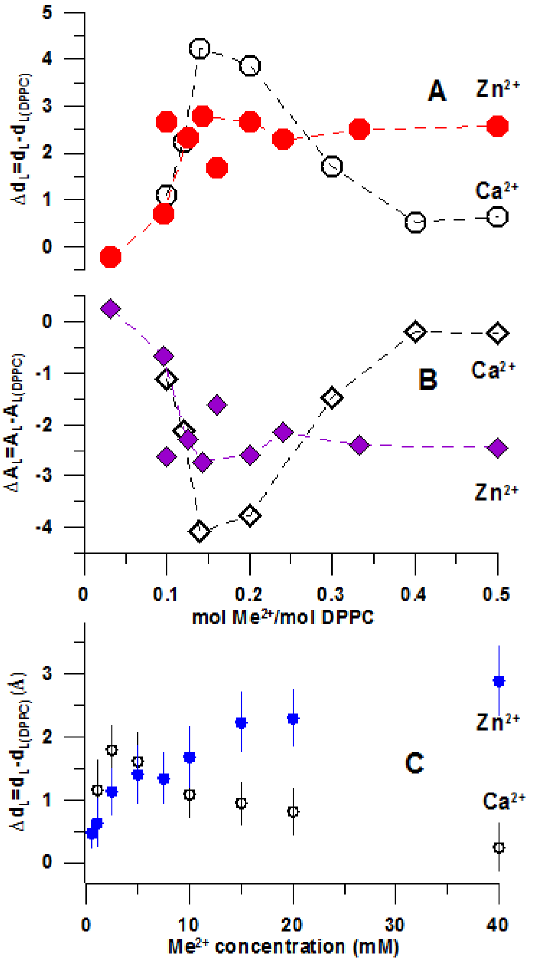

Fig. 1 The SAND results of change in the planar DPPC lipid bilayer thickness Δd_L (A), and the surface area per DPPC molecule ΔA_L (B) induced by Me^{2+} binding (Ca^{2+}, Zn^{2+}). The effect of Me^{2+} on the curved DPPC lipid bilayer thickness obtained by SANS (C).

DPPC oriented multilayers at selected molar ratios Zn^{2+}:DPPC were prepared by hydrating thin lipid films from vapors at defined humidity. Samples were hydrated with different D2O/H2O solutions (100%, 70%, 40%, and 8% D2O) 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 [10, 11].

The effects of Ca^{2+} and Zn^{2+} on the DPPC bilayer are different, as shown in changes of the lipid bilayer thickness (d_L) and the area per lipid molecule (A_L) in Fig. 1A, B. For both cations, d_L increased due to Me^{2+} binding, reaching the maximum in $\Delta d_L = d_L - d_{L(DPPC)}$ at stoichiometry Me^{2+}:DPPC~1:7 mol/mol, where $d_{L(DPPC)}$ is the lipid bilayer thickness without any Me^{2+}. However, while the further increase in Ca^{2+} results in a bilayer thinning down to the level of pure DPPC ($d_{L(DPPC)}$), the Zn^{2+}binding indicates the behavior of a typical isotherm, reaching a level of saturation.

Our observations agree well with previous SANS results [6,7] shown in Fig. 1 C, in which curved bilayers in form of unilamellar vesicles dispersed in water were utilized. Comparison of the data suggests that the effect observed can most likely be rationalized in terms of electrostatic interactions, rather than that of geometrical constraints due to bilayer curvature, and thus reinforcing the notion of special importance of these cations.

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