ESRF	**Experiment title:** High-resolution structural study of self-assembled Liposome-DNA-Metal Complexes	**Experiment number:** SC-1139
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Report:

The association between liposomes and DNA has been object of several studies over the last two decades. In particular, cationic liposomes (CLs) complexed with DNA have been shown to be promising nonviral delivery systems for gene applications therapy. Within the general scope of providing new biological materials of potential interest for gene delivery systems we have recently carried out a systematic study of interaction among neutral liposome (Ls), DNA (from calf thymus) and metal cations (Mn^{2+}, Mg^2, Fe^{2+}, Co^{2+}). We have performed a detailed study on the structures of the triple complex dioleoylphosphatidylcholine (DOPC)-DNA-Mn^{2+} by synchrotron x-ray diffraction [1, 2]. This self assembled complex exhibits the lamellar symmetry of the liquid crystaline phase L_α^C: the structure consists of an order multilamellar assembly, where the hydrated DNA helices are sandwiched between the lipid bilayers. The condensation of DNA into the interstitial water space is promoted by positively charged metal ions that act as a bridge among two-negatively charged phosphate groups of DNA and the DOPC headgroups. In order to develop DNA delivery systems, in this experiment we have studied new complexes differing in the nature of the neutral lipid and the DNA chain length. In particular we have studied the triple complex dioleoylphosphatidylethanolamine (DOPE), divalent cations (Me^{2+}) common in biological cells and DNA molecules which form a two dimensional hexagonal inverse structure (H_{II}). This complex consistent of a 2D columnar inverted hexagonal phase where the water space inside the lipid cylindric elements are filled by DNA. The metal ions play the same *binding* role discussed for DOPC-DNA-Me^{2+} (L_α^C) complex [1].

Fig.(1) shows the SAXS pattern of DOPE-DNA-Fe^{2+} complex at 3:4:12 molar ratio. At room temperature, the x-ray data show the coexistence of the pure DOPE, H_{II}, with unit cell a=74.1 Å and the DOPE in the inverse hexagonal phase with the DNA strands and metal ions intercalated within its water tubes, H_{II}^C, with a a=68.7 Å [3]. In the Fig.1 the arrows indicate the peaks relative to hexagonal complex H_{II}^C, the remaining peaks refer to hexagonal phase associated to pure DOPE. From electron density profile we have calculated the structural parameters for H_{II}^C and H_{II} phases. Moreover we have studied this system with different Me^{2+} cations such as Co^{2+}, Mg^{2+} and Mn^{2+} at the same molar ratio DOPE:DNA:Me^{2+} (3:4:12). We have found that the mixture of DOPE and DNA with different metals form the same hexagonal arrangement seen for DOPE-DNA-Fe^{2+}. We have also carried out a study on DLPC:DNA_{SS}:Me^{2+}, where the DNA_{SS} is a salmon sperm DNA at low molecular weight. Fig.2 shows diffraction pattern for DLPC:DNA_{SS}:Mg^{2+} at 3:4:12 molar ratio. From x-ray data it can observed the coexistence of two different lamellar phases one with the unit cell $d_1 = 74$ Å associated to the presence of the L_α^C lamellar phase of the triple complex, the other one with the $d_2 = 57$ Å spacing, associated to L_α phase of DLPC. The data indicate a structure similar to that observed for the DOPC:DNA:Me^{2+}. However, in this case a broad peak at $q_{DNA_{SS}}$=0.12 $Å^{-1}$, ($d_{DNA_{SS}}$=51 Å) is observed due to the DNA interaxial spacing. In the next experiment we will propose a structural study of triple complexes using high XRD resolution in order to evaluate the elastic properties of the membranes.

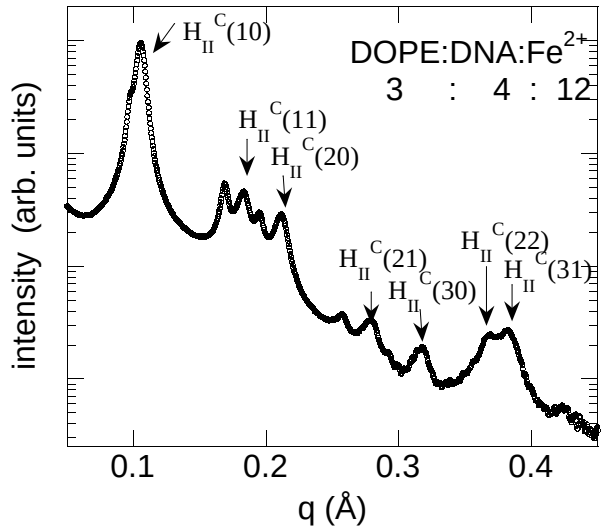

Fig.1. SAXS pattern of the DOPE:DNA:Fe^{2+}.

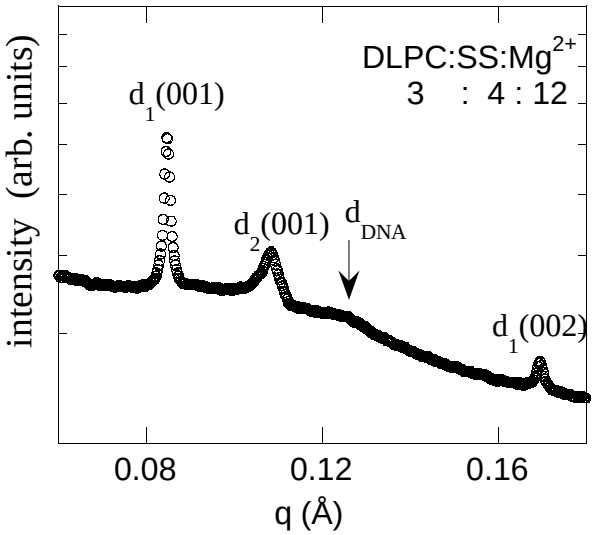

Fig.2. SAXS pattern of the DOLPC:DNA_{SS}:Mg^{2+}.

References

[1] Francescangeli O., Stanic V., Gobbi L., Bruni P., Iacussi M., Tosi G. and Bernstorff S. Phys. Rev. E. **67** 2003 011904.

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[3] Francescangeli O., Pisani M., Stanic V., Bruni P., Giorgini E., Conti C. and Weiss T., to be submitted to Europhysics Letters