X-ray Scattering and Reflectivity Studies on the Absorption of DNA by Mixed Lipid/Diblockcopolymer Liposomes and Monolayers

Tsang-Lang Lin (林滄浪)[1], Po-Wei Yang (楊博偉)[1], I-Ting Liu (劉依婷)[1], U-ser Jeng (鄭有舜)[2], and Hsin-Yi Lee (李信義)[2]

[1]Department of Engineering and System Science, National Tsing Hua University, Hsinchu, Taiwan

[2]National Synchrotron Radiation Research Center, Hsinchu, Taiwan

Recently, many studies have been made on the cationic lipid-DNA complex due to the nonviral gene therapy. Other than using the lipids, cationic diblockcopolymers were also often used to form complex with DNA. Amphiphilic diblockcopolymers can form highly stable vesicles or micelles in solutions that can form complex with DNA through charge interactions. Highly stable polyplexes were formed due to the entropic gain of releasing the small ions from the DNA and the cationic brush. However, the detail structure of the DNA-cationic brush complexes is still not well studied. Cationic diblockcopolymers can also form stable monolayers at the air-water interface. The hydrophilic brush can extend into the water region and form a charged thick layer that could adsorb the DNA in the subphase. It is advantageous to investigate the interaction of the cationic brushes with the DNA using the Langmuir monolayer technique. It is easier to vary the brush density by compressing the monolayer at the air-water interface to a suitable area per molecule. At different brush density(number of molecules per unit area), the space between the brushes can be varied that would affect the adsorption of DNA due to volume constraint and ionic osmotic pressure changes. It would be difficult to investigate such effects using vesicles or micelles in solutions. There is very little or no studies so far on the structure and the interaction of mixed lipid/diblockcopolymer monolayers with DNA at the air-liquid interface although cationic lipids are widely used in forming lipid/DNA complex for gene therapy related studies. Using the lipid/diblockcopolymer system, it is possible to enhance the adsorption of DNA by constructing a thin layer of three-dimensional structure by the diblockcopolymer at the air-water interface.

The purpose of this study is to investigate the interaction of mixed lipid/diblockcopolymer liposomes and monolayers with DNA by SAXS and reflectivity. The cationic diblockcopolymer Poly(styrene-b-N-methyl-4-vinyl pyridinium iodide) (PS-P4VPQ), MW=19600 (PS)+12000 (P4VPQ)=31600, is used in this study. Figures 1 and 2 shows the SAXS profiles of the liposomes prepared with 10 mM DPPC and different amounts of PS-P4VPQ in aqueous solutions added with and without DNA (700 bp, MW 451500), respectively. The DNA to PS-P4VPQ molar ratio is kept at 0.0736 to keep the charge ratio equal to 1.

As shown in Fig. 1, the diffraction peaks of DPPC multilamellar disappears when sufficient amounts of PS-P4VPQ is added. The correlation between the bilayers is destroyed due to the incorporation of P4VPQ. The scattering is most likely from the form from of the DPPC bilayer incorporated with P4VPQ. When DNA is added, the scattering profiles remain similar but the scattering intensity is significantly increased. The X-ray reflectivity profiles from DNA/ P4VPQ monolayers in the presence of calcium ions are shown in Fig. 3. As the calcium ion concentration is increased, the adsorbed DNA layer thickness is increased. Detail modeling analysis will be carried out to reveal the detail structures.

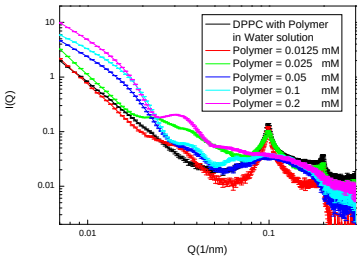

Figure 1. The SAXS profiles of the liposomes prepared with 10 mM DPPC and different amounts of PS-P4VPQ in aqueous solutions.

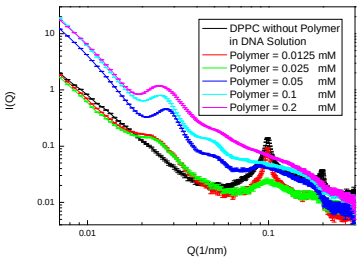

Figure 2. The SAXS profiles of the liposomes prepared with 10 mM DPPC and different amounts of PS-P4VPQ added with DNA.

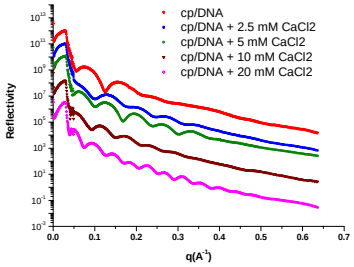

Figure 3. The X-ray reflectivity profiles from the DNA/PS-P4VPQ monolayers in the presence of different amounts of calcium ions.