STUDY ON HYDRATION OF BIOINSPIRED PHOSPHOLIPID POLYMERS FOR DESIGN OF BIOMATERIALS

（生体材料設計のためのバイオインスパイアードリン脂質ポリマーの水和に関する研究）

森作 俊紀

［Background］

According to the rapid advancement in biotechnologies, the importance of material surfaces that resist nonspecific protein adsorption has been stressed. Nonspecific protein adsorption on material surfaces is the first phenomenon in contact with blood or tissue and is followed by cell adhesion, thrombus formation, and immune response. Thus, protein-resistant surfaces are essential matrices for the molecular or cellular control of biologically-related processes, for example, drug release from nanometer-sized carriers administrated within human body, detection of trace amounts of biocomponents in blood, molecular recognition by surface-immobilized bioactive molecules（e.g., DNAs and antibodies）, and cell growth.

Many protein-resistant surfaces have been designed. Recently, some research groups achieved very low protein adsorption levels of < 10 ng/cm^2（“ng/cm^2” denotes mass of adsorbed protein per unit surface area）by controlling packing density and/or length of surface-tethered chains. On the other hand, the physico-chemical factors that determine the ability of surfaces to resist protein adsorption are still not elucidated. This is because of the complexity of the process caused by the interplay between surfaces, proteins, and water molecules. A satisfactory understanding of the factors allows not only the systematic design of protein-resistant surfaces

but also the elucidation of mechanism of protein adsorption resistance.

The present discussion on the factors that determine the outcome of protein adsorption resistance is centered on the relationship between hydration structures of material surfaces and protein adsorption. Of particular interest is the structures and properties of water molecules around poly(2-methacryloyloxyethyl phosphorylcholine) (poly(MPC)) and poly(ethyle glycol) (PEG) chains because they are the most effective synthetic materials for protein adsorption resistance. Hydration of PEG chains has been widely studied. Recently, the interactions of water with OEG-terminated SAMs, which highly resist protein adsorption, have been investigated by theoretical approaches and spectroscopic methods that can selectively prove aqueous interfaces. On the other hand, there is only a little information on the hydration of poly(MPC) chains. Thus, the understanding of the hydration of poly(MPC) chains is necessary to elucidate the relationship between hydration structures of material surfaces and protein adsorption. It is expected that the understanding provide a new design concept of protein-resistant surfaces.

[Research Scheme]

In this thesis, the properties of water in chemically cross-linked poly(MPC) hydrogels were investigated as a function of equilibrium water content (EWC). For the investigations, the following two experimental methods were used. One was differential scanning calorimetry (DSC), which allows the classification and quantification of different states of water contained in polymer-water systems. The other was relaxation time measurements by ^{1}H pulsed NMR, which have the potential to evaluate molecular mobility of water molecules contained in polymer-water systems. Water in the poly(MPC) hydrogels was compared with that in chemically cross-linked hydrogels composed of OEG-based polymer chains, poly(ω-methoxy tetra- or octa(ethylene

glycol) monomethacrylate (Me(EG)$_n$MA) (n = 4 or 8)) chains.

[Summary of each chapter]

In Chapter 1, the fundamental knowledge of water on material surfaces and poly(MPC) chains are explained in detail.

In Chapter 2, the preparation of the poly(MPC), poly(Me(EG)$_4$MA), and poly(Me(EG)$_8$MA), hydrogels is explained.

In Chapter 3, the water states of the poly(MPC), poly(Me(EG)$_4$MA), and poly(Me(EG)$_8$MA), hydrogels were investigated by DSC. It is found that the poly(MPC) hydrogels can keep a high level of hydration compared with poly(Me(EG)$_4$MA) and poly(Me(EG)$_8$MA), hydrogels.

In Chapter 4, the molecular mobility of the poly(MPC), poly(Me(EG)$_4$MA), and poly(Me(EG)$_8$MA), hydrogels were investigated by ^{1}H pulsed NMR relaxation time measurements. The hydration water in the poly(MPC) hydrogels has faster mobility compared with poly(Me(EG)$_4$MA) and poly(Me(EG)$_8$MA), hydrogels. In addition, the hydration water in the poly(MPC) hydrogels is thermodynamically stable.

In Chapter 5, on the basis of the result of the DSC and NMR, the hydration structures of polymers that determine protein adsorption are discussed.