Computer Simulation of Shear Rate Effect on Protein Adsorption

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Introduction

Protein adsorption is known to be the first stage of blood-material interaction. Many researchers have tried to find the basic mechanism of protein adsorption on the polymeric surface. Since fibrinogen is one of the adhesive proteins to activate platelet, it has been mostly focused in thrombosis researches. Relationships between the adsorbed proteins and platelet adhesion on them have been considered as one of the key factors for thrombus formation in blood-material interaction.

Polymeric surfaces also have various complex characteristics according to their composition and fabrication methods. Various techniques of surface modification are tried to improve the antithrombogenicity of biomedical polymers. Therefore, the characteristics of protein adsorption which is, in turn, related to platelet aggregation or thrombus formation as shown in complex patterns according to the characteristics of polymer surface.

In this paper, simulations of protein adsorption on polymeric surface were performed by considering one of major factors in fibrinogen-polymeric surface. In order for this simulation, the conventional random sequential adsorption model was modified. Effect of fluid dynamical characteristics on protein adsorption was modelled.

Polymeric Surface and Protein Adsorption

Polyurethane elastomers are generally two-phase systems consisting of alternating hard and soft segments which phase separate into microdomains. At the relatively low hard segment levels that are common in such biomedical polyurethanes as Biomer and Pellethane, the hard domains are distributed in a soft segment matrix. The hard segment microdomains, which have a size on the order of 50 - 100 A, may be primarily isolated or interconnecting, depending on the relative hard to soft segment composition.

The adsorption of proteins onto polymeric surfaces will generally involve hydrophobic, electrostatic and hydrogen bonding interactions. These multiple binding possibilities may result in denaturation of the adsorbed protein which is the major reason for the thermodynamic irreversibility of the adsorption process. The major driving force for folding a polypeptide into a compact protein structure is the dehydration of hydrophobic side groups, which is almost completely due to the entropy increase in water that is released from their contact with hydrophobic components. Consequently, hydrophobic and hydrophilic interactions between the foreign surface and plasma proteins can be considered as one of the most important factors in protein adsorption since about 90% of blood is composed of water.

In consideration of interaction between fibrinogen and polyurethane in aqueous environment, hydrophobic interaction between hydrophobic domains composed of hard segments and fibrinogen will be modelled in the modified RSA.

Modified RSA Process

According to the chemical composition of polyurethane, its surface was modelled as two segments; hydrophobic (H-) and hydrophilic (H+) domains. The length of the monomer chain of hard segment which is hydrophobic in aqueous environment is about 100 A. Any point in the NxN lattice represents H+ or H-, which was determined randomly. The ratio of H+/H- can be adjusted by weighted random sampling. In order to reduce the finite size effect, periodic boundary condition was adopted. The shape of fibrinogen is fibrous whose length of long side is about 400 A and that of short side is about 70 A. Therefore, fibrinogen can be modelled as a small box which is composed of m x m lattice. The adsorption of proteins and latexes on flat uniform surfaces can often be described by a random sequential adsorption (RSA) process. In this paper, the hydrophobic surface in the conventional RSA process was modified by the randomly mixed surface of hydrophobic and hydrophilic domains. This mixed surface is represented the the hard and soft segments of the polyurethane surface. This modified random sequential protein adsorption process was performed as follows ;

1. Select a random position in N x N lattice which is made of randomly mixed hydrophobic and hydrophilic points at given ratio.
2. Count the number of hydrophobic points in a m x m lattice which centered at the position selected by above procedure.
3. Determine adsorption according the counted hydrophobic number in second procedure.
4. Steady state of protein adsorption was checked by unabsorbed trials of three procedures.

The protein box was modelled as a square of m x m, but the shape of fibrinogen is more similar to a rectangle. Therefore, the shape dependency of the protein adsorption was also tested. The threshold of protein adsorption was 5 of 9 points in the protein box, which means that the hydrophobic interaction is strong enough to adsorb on the polyurethane surface. Under the flow condition, this threshold must be changed due to different shear stress. With various thresholds of the protein adsorption, several simulations were performed in order to find the appropriate value of the threshold. Steady state of the protein adsorption is one of the important parameters in this simulation. So we tried to find the appropriate steady condition by changing the steady state threshold in the simulation.

Fluid dynamic effect was also modelled. In high shear rate condition, more hydrophobic points are needed for adsorption. So the adsorbing threshold is different from that in low shear rate.

Simulation was performed on IBM PC 386 with Borland C++ version 2.0 language.

Results and Discussion

Simulations were performed for several ratios of area of the hydrophobic and hydrophilic domains and these results are shown graphically in Figure 1. Amount of adsorbed fibrinogen under different shear rate is shown in Figure 2. If the polyurethane surface is fully hydrophilic, the amount of the adsorbed fibrinogen is not changed by different shear rate as shown in Figure 2.

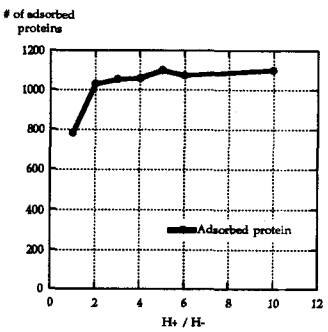

Figure 1 Protein Adsorption Test on the Different Hydrophobic and Hydrophilic Ratio

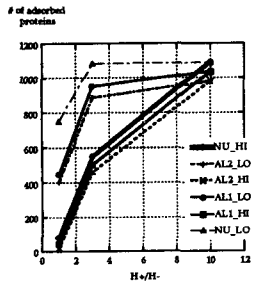

Figure 2 Protein Adsorption Test on the Different Shear Rates