Temporal Size Distribution in Diffusion Limited Platelet Aggregation

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INTRODUCTION

Platelet deposition on artificial surfaces is a characteristic feature of platelet function in vivo and in vitro, and a vital component of a hemostatic plug [1]. Platelet aggregation and disaggregation are complex phenomena that involve various physiological and chemical reaction. The course of the aggregation process observed in vitro can be summarized as follows [2]. Following the introduction, diffusion an uptake of an aggregate-inducing agent, thrombocytes in plasma-rich plasma (PRP) begin to coalesce. Morphological changes occur, including swelling and the appearance of dendrites and pseudopodia. Aggregation includes platelet-platelet and platelet-aggregate adhesion, as well as aggregate-aggregate adhesion, in which smaller aggregates coalesce into large aggregates. As aggregation proceeds, there is a decrease in the total number of particles (platelet and aggregates) whereas the average particle size increases. Investigators have found that aggregation responses to low concentration of adenosine diphosphate (ADP) were rapidly reversible, whereas responses to higher concentrations of ADP were irreversible. Reversibility of aggregation, however, is not meant to imply reversibility of the underlying molecular processes. Dispersal of the platelet aggregates is accounted for by the breakdown of aggregating agent to other substances that do not cause aggregation but are potent inhibitors of the aggregation.

In this paper, we try to find the temporal size distribution of the platelet aggregators from computer simulation. We think that platelets move only by diffusion. During diffusion activated platelets form aggregator if they meet each other, whereas non-activated platelets do not. For the first trial, platelet-cluster interaction is only considered for simplicity. As time elapses, the size of aggregators becomes larger. Every number of various clusters at a given time is counted in order to plot the size distribution against time. Platelet diffusion is simulated by a 3 dimensional random walk model. Temporal size distributions from the simulation of diffusion limited platelet aggregation are compared experimental data of other investigators' [4].

MATERIALS AND METHODS

For the particle-cluster aggregation, we use the Meakin's diffusion limited aggregation (DLA) method [3]. Unlike other usual DLA, however, time information is so important in this case that it must be changed in details as follows;

First, if we are to get information at given time T1, every platelet's random walk steps must be T1 times.

Second, though the distribution of the distances between the core platelet and the other platelets is continuous, we assume that it is discrete. Then we make several circles, centered at core, on which a given number of platelets exist corresponding to the platelet concentration. In other words, R_1 radius circle has N_1 platelets, R_2 radius circle has N_2 platelets and so on. N_1, N_2, R_1, R_2 are chosen such that,

$$\text{concentration} = \frac{3N_1}{4\pi {R_1}^3} = \frac{3N_2}{4\pi {R_2}^3 - 4\pi {R_1}^3} = \cdots\cdots$$

where N_1, N_2, R_1, R_2 are chosen such that $R_1 \langle R_2 \langle \cdots, N_1 \langle N_2 \langle \cdots$. After DLA of all platelets on

the R_1 radius are finished, DLA of the platelets on the R_2 is tried because closer platelets are thought to contact the core cluster earlier. If the trial platelet aggregates to the core cluster before the T1 time steps, we try the other platelet. Following the usual DLA, if the trial platelet goes too far from the core, we think it goes the other cluster and remove it. The larger the radius of the starting circle, the more difficult to aggregate. If the trial platelets don't aggregate several times in succession within the T1 time steps, this DLA is terminated.

Now we get one cluster at time T1. Repeat this algorithm at time T1, then we have the histogram of the various cluster sizes. Likewise we can get the information at time T2, and so on.

In the detail of the interaction, we must consider the different features of this system because of its biological nature. The quantity of the activated platelets and sticking probability depend on the ADP concentration, and the activated platelet releases the ADP again. In the first place, ADP concentration is given and the activation probability Pa makes the trial platelet active or not. If the platelet is activated, it follows the algorithm, otherwise it is discarded. When the trial platelet contacts the core cluster, these aggregates with the sticking probability Ps. As making new cluster affects the ADP concentration, Pa and Ps are changed as soon as new cluster is formed.

Simulation is performed in IBM PC 386 compatible and program is written in c language.

RESULTS and DISCUSSION

Though there are large differences between our simulated and the real process of platelet aggregation, very similar results of temporal increase of platelet-cluster size are obtained from the simulation. The major discrepancy with the experiment is thought due to negligence of cluster-cluster interaction. The wall-obstacle of the foreign surface and fluid dynamic effects will be considered for the application of this simulation to blood-material interaction.

REFFERENCES

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