A lattice model of the protein diffusion in membranes

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Abstract. Diffusion of a protein in a biological membrane is studied by Monte Carlo computer simulations. The membrane is modeled as a two-dimensional lattice in which a protein and lipids diffuse under the action of Brownian motion. We calculate the diffusion coefficient of the protein as the concentration of lipids and the protein size are changed. These results are compared with our analytical calculation.

INTRODUCTION

Biological membranes consist of various lipid molecules and protein molecules, and their fundamental structure is a lipid bilayer including proteins. Since the "fluid mosaic model" was proposed by Singer and Nicolson in 1972, lipids in membranes have been considered that they are distributed uniformly, and can move almost freely. Later, dynamical domains which are organized by sphingolipids and cholesterol were observed in biological membranes. These domains are called "rafts".

Recently, new techniques of microscopy have made it possible to observe the motion of individual proteins or small clusters of lipids on the cell surface [1]. In these experiments, proteins or lipids are labeled with a highly fluorescent label or with colloidal gold microspheres. The shape of the trajectories implies various biologically important processes, such as binding to immobile species, free diffusion, hindered diffusion, directed transport, and trapping of particles in bounded microdomains.

In this paper, by using a lattice-model of a biological membranes, we investigate both numerically and analytically how the diffusion of a protein depends on its size and the concentration of lipids. The present study is the extension of Ref. [2] in which the concentration of lipids was fixed.

MODEL AND RESULTS

The key assumption embodied in the stochastic model is that the force exerted by the medium on the diffusing molecule consists of a stationary, rapidly fluctuating random force due to molecular bombardments which are independent of the velocity of the diffusing molecule.The drag force proportional to the velocity is supposed to be smeared out, because the water molecules immediately conduct away the momentum from the diffusing molecule.

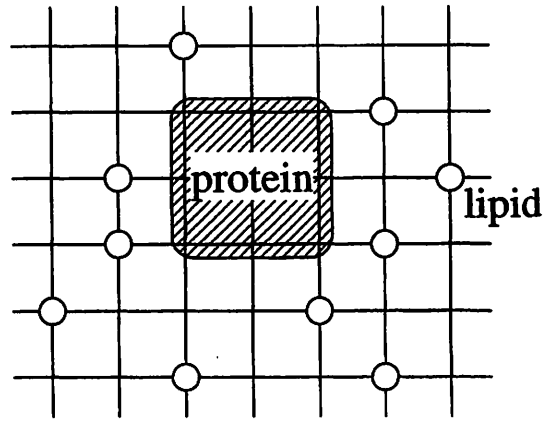

FIGURE 1. A two-dimensional square lattice model of a biomembrane. The square represents a protein, and white circles are lipids. The size of a protein is denoted by the number of sites occupied by it ($M^2 = 3 \times 3$ in this case).

We consider a two-dimensional square lattice model as shown in Fig. 1. A protein is represented by the square which covers $M \times M$ lattice sites, and lipids are represented by the small particles which occupy a single site. We have performed Monte Carlo (MC) computer simulations for the stochastic model with a 128×128 square lattice. Periodic boundary conditions are used in the simulations. The lipids, whose concentration is denoted by c, are initially distributed on the lattice so that they do not overlap with the $M \times M$ square (protein) or with each other.

In the computer simulation, a lattice site is randomly chosen initially. When there is a particle on the selected site, the particle is moved randomly into one of the four nearest neighbor lattice sites. The movement is executed

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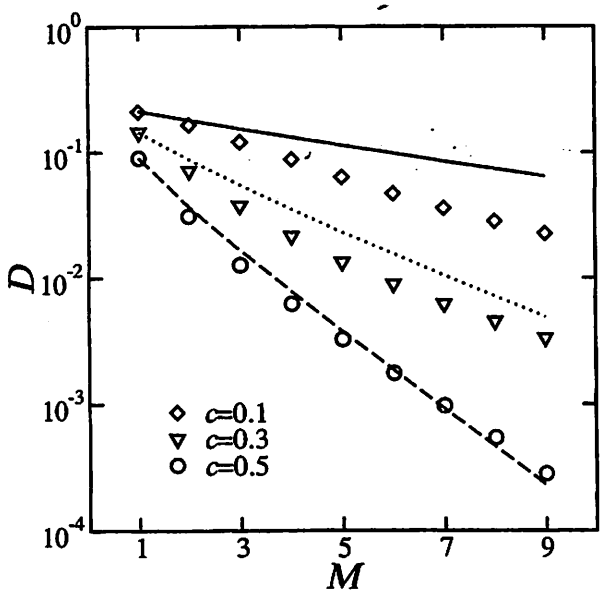

FIGURE 2. The protein diffusion coefficient D as a function of its size M. The symbols are MC results. The solid, dotted, and dashed curves represent Eq. (3) for $c = 0.1$, 0.3, and 0.5, respectively.

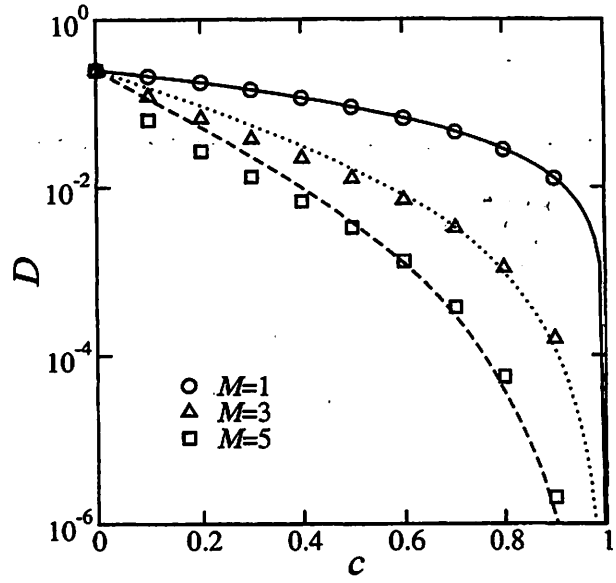

FIGURE 3. The protein diffusion coefficient D as a function of the lipid concentration c. The symbols are MC results. The solid, dotted, and dashed curves represent Eq. (3) for $M = 1$, 3, and 5, respectively.

if and only if it does not lead to any overlapping either among particles or between the square and the particles. A set of attempts which, on average, covers the entire lattice defines one Monte Carlo step (1 MCS).

The diffusion coefficient of a k MCS interval is calculated by

$$D(k) = \frac{1}{4}\frac{\langle r^2(k)\rangle}{k}, \tag{1}$$

where $r(k)$ is the absolute value of the displacement vector during an interval of k MCS's, and the average $\langle\cdots\rangle$ is taken for the displacement data over one simulation.

In the long-time limit ($k \to \infty$), $D(k)$ converges to a fixed value. Figure 2 shows the calculated diffusion coefficient D as a function of the protein size M, whereas Fig. 3 gives that as a function of the lipid concentration c. Note that the case of $M = 1$ is identical with self-diffusion of lipids. We see in Fig. 2 that the size dependence of the diffusion coefficient becomes more pronounced for larger c. On the other hand, the lipid concentration dependence of the diffusion coefficient is stronger for larger M as shown in Fig. 3.

As an analytical approach, we extend the Nakazato-Kitahara theory [3]. The number of sites is denoted by N, and the number of sites occupied by lipids is denoted by N_0. The average concentration of lipids is then defined as $c = N_0/(N - M^2)$. After some calculations, the diffusion coefficient is written in the form

$$D(M,c,k) = (1-c)^M f(M,c,k) D_0, \tag{2}$$

where D_0 is the diffusion coefficient in the case of $c = 0$, and $f(M,c,k)$ is called as the "correlation factor". The analytical approximate solution of D is obtained as

$$D(M,c,k) = \frac{1}{4}(1-c)^M\left(1 - \frac{A}{B}\right). \tag{3}$$

where

$$A = 2\alpha(k)\sum_{i=1}^{M}\binom{M}{i}c^i(1-c)^{M-i}, \tag{4}$$

$$B = 1 + (1-c)^M - \alpha(k)\Big[1 + (1-c)^M - 2\sum_{i=1}^{M}\binom{M}{i}c^i(1-c)^{M-i}\Big]. \tag{5}$$

Here, $\alpha(k)$ is the lattice Green's function. In the long-time limit ($k \to \infty$), $\alpha(k)$ approaches to 0.363. Equation (3) is plotted in Figs. 2 and 3 by various lines. When $M = 1$, the analytical result is in complete agreement with the MC simulation result as seen in Fig. 3. In Fig. 3, the size dependence is well described by Eq. (3) for larger c.

REFERENCES

1. Anderson, C. M., Georgiou, G. N., Morrison, I. E. G., Stevenson, G. V. W., and Cherry, R. J., *J. Cell. Sci.* **101**, 415-425 (1992).
2. Suzuki, Y. Y., and Izuyama, T., *J. Phys. Soc. Jpn.* **58**, 1104-1119 (1989).
3. Nakazato, K., and Kitahara, K., *Prog. Theor. Phys.* **64**, 2261-2264 (1980).