Lateral diffusion and penetration of particles on a lipid bilayer membrane

Tsutomu Hamada Laboratory, 1440007, Kazuki Shigyou

General Introduction

Over the past several decades, nanoscience has attracted considerable attention to develop functional particles for the application to biological system. Nano/submicron particles can be modified with many kinds of unique properties. For example, gold and magnetic nanoparticles were used to kill cancer cells by near infrared light and magnetic field, and carbon particles delivered drug molecules into a cell. For the development of engineering to control cell function with particle, it is important that understand the physical mechanisms to govern the emergent behavior between particles and cellular interface system. Einstein-Storks model has described the diffusion of single particle in bulk solution. Helfrich free energy has explained membrane deformation. Each single system well understood. However, emergent behaviors between particle and cell membrane have been unclarified. In this paper, we experimentally investigated particle behaviors within artificial lipid bilayer membranes to clarify physical mechanism of a colloid-membrane system, i.e. composite soft matter. We focused on typical two motions of particles within the membrane, such as thermal diffusion and penetration. Particles exhibit a thermal motion under a drag force of membrane viscosity, once particles are applied to a cell and adhered on the membrane surface. We analyzed the particle movements and discussed the coupling between particle lateral diffusions and deformable membranes. Then, particles are expected to be introduced into a cell interior space by membrane dynamics, such as endocytosis. We demonstrated the particle penetration process and revealed that an intrinsic mechanical property of membranes determine the uptake of particles.

Lateral diffusion of submicron particle on a lipid bilayer membrane.

Cells use membrane proteins diffusing on the membrane surface to regulate the traffic of molecules between their interior and exterior through osmosis, ion channel, endocytosis, exocytosis and phagocytosis. Control of the motion of proteins diffusing on the membrane would lead to developing the regulation of physiological functions. There are two main methods by which the motion of objects on the membrane are controlled. First, molecules regulate membrane components, such as membrane lipids and cytoskeletal proteins that reinforce the membrane surface. Second, materials can be controlled using external stimuli. For example, the motion of self-propelled [10] particles can be controlled by light, which leads to a change in membrane fluidity and it motion. However, dynamical properties of such submicron particles on a lipid membrane still remain unclear.

In this study, we controlled the adsorption states of particles with a diameter of 200-800nm on cell-sized liposomes and investigated lateral diffusion of the adhered particles. We determined the particle-size-dependence of diffusion. We then studied two different adsorption states for particles: i) a fully wrapped state and ii) a partially wrapped state. Fully wrapped particles diffused more slowly than partially wrapped particles. An anomalous diffusion was observed when particles were adhered to a membrane with buds.

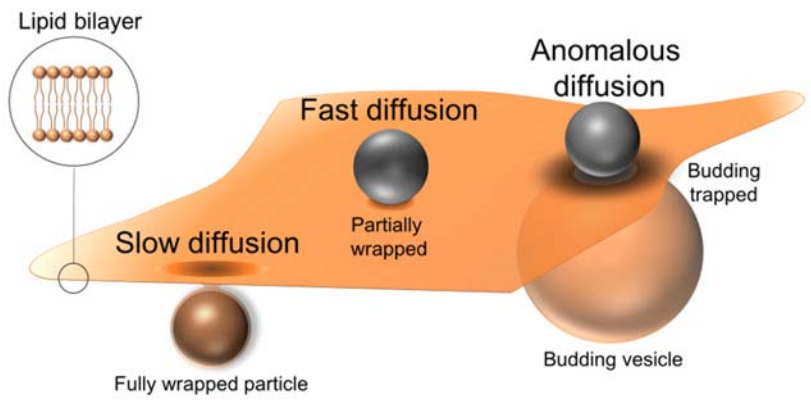

Fig. 1 The behavior of adhered particle on a lipid bilayer membrane.

Tension-induced penetration of particles into lipid bilayers

Nano/Submicron particles have important properties for controlling living cells, such as drug delivery, local heating and visualization of cell inside. To express these functions, the particles need to be transported into the cell. For transporting the particles, normally, cellular functions that are controlled by proteins are used. Recently, we reported a new particle penetration system without proteins. This indicated that membrane mechanical properties should play an important role on penetration behaviors. However, the physico-chemical mechanisms of penetration are unclear. It is useful that we used model membrane system for physical understand of phenomenon related with lipid membrane. Here, we had successed the expression of the self-penetration without any proteins using controlling lateral tension and adhesion state. In this study, we clarify that the mechanism of the penetration without the protein. This mechanism is that increasing the lateral tension creates a pore formation at the neck part of fully wrapped membrane using pore nucleation theory considering with additional curvature energy.

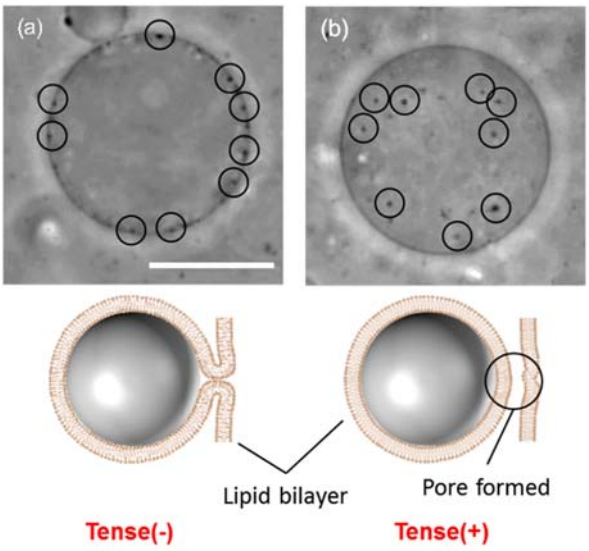

Fig.2 Lateral tension induced penetration of particle into the cell.

Table of contents

List of publication

1. **Shigyou, K**.; Nagai, K. H.; Hamada, T. Lateral Diffusion of a Submicrometer Particle on a Lipid Bilayer Membrane. Langmuir 2016, 32, 13771–13777.

2. Kawasaki, S.; Muraoka, T.; Hamada, T.; **Shigyou, K**.; Nagatsugi, F.; Kinbara, K. Synthesis and Thermal Responses of Polygonal Poly(ethylene Glycol) Analogues. *Chem Asian J* 2016, *11*, 1028–1035.

3. Seemork, J.; Sansureerungsikul, T.; Sathornsantikun, K.; Sinthusake, T.; **Shigyou, K.**; Tree-udom, T.; Jiangchareon, B.; Chiablaem, K.; Lirdprapamongkol, K.; Svasti, J.; *et al.*Penetration of Oxidized Carbon Nanospheres through Lipid Bilayer Membrane: Comparison to Graphene Oxide and Oxidized Carbon Nanotubes, and Effects of pH and Membrane Composition. *Acs Appl Mater Interfaces* 2016, 8(36):23549-57.

4. Tree-Udom, T.; Seemork, J.; **Shigyou, K**.; Hamada, T.; Sangphech, N.; Palaga, T.; Insin, N.; Pan-In, P.; Wanichwecharungruang, S. Shape Effect on Particle-Lipid Bilayer Membrane Association, Cellular Uptake, and Cytotoxicity.*Acs Appl Mater Interfaces* **2015**, *7*, 23993–4000.

5. Arayachukiat, S.; Seemork, J.; Pan-In, P.; Amornwachirabodee, K.; Sangphech, N.; Sansureerungsikul, T.; Sathornsantikun, K.; Vilaivan, C.; **Shigyou, K**.; Pienpinijtham, P.; *et al.* Bringing Macromolecules into Cells and Evading Endosomes by Oxidized Carbon Nanoparticles. *Nano Lett* **2015**, *15*, 3370–3376

Key words

Lipid membrane, lateral diffusion, colloidal particle, pore nucleation theory, lateral-tension, penetration.