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AUTHOR(S):
Ichikawa, M; Yoshikawa, K

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Optical transport of a single cell-sized liposome

Masatoshi Ichikawa and Kenichi Yoshikawa
Department of Physics, Graduate School of Science, Kyoto University & CREST, Kyoto 606-8502, Japan
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A closed phospholipid membrane vesicle, or giant liposome, with a diameter of ∼10 μm, constitutes a model of a living cell. Since the phospholipid membrane is about 5 nm thick, it is extremely difficult to trap an individual giant liposome with a laser. We report here the intact transport of an individual cell-sized liposome using an infrared laser. It is shown that the optical attractive potential on a liposome with an inner solution of higher refractivity is about one order of magnitude greater than that of a liposome with the same solution both inside and outside. Since this cell-sized liposome is rather stable, the optical manipulation of liposomes could be useful for the realization of a µm-scaled laboratory for use in biochemistry and molecular biology. © 2001 American Institute of Physics. [DOI: 10.1063/1.1430026]

All living organisms maintain their lives by making a µm-sized biosphere within a closed membrane several nm thick. The main constituent of this biological membrane is a phospholipid bilayer. A closed phospholipid bilayer membrane, or liposome, has been actively studied as a model of a living cell membrane. Most previous studies on liposomes have been devoted to rather small vesicles smaller than 0.1 μm in diameter. Experimental procedures to obtain such small vesicles from phospholipids are well established, including sonication and gel filtration. In contrast to the extensive studies on such small phospholipid vesicles, reports on cell-sized liposomes larger than 1 μm are rather limited. Surprisingly, there have been very few studies on the preparation of cell-sized liposomes with different chemical compositions inside and outside the membrane. In the present letter, we report a procedure for preparing cell-sized liposomes where the inner chemical composition is markedly different from that of the external environment. We show that such a cell-sized liposome containing a solution of higher refractivity can be efficiently trapped and transported by a focused laser.

Figure 1 shows an overview of the experimental system for optical trapping under microscopy. The infrared laser used for optical trapping was a Nd: yttrium–aluminum–garnet laser (SL902T, Spectron), TEM00 beam at a wavelength of 1064 nm. The laser was reflected by a dichroic mirror, and focused by an objective lens with a 1.3 numerical aperture. To transport the liposome, the stage was moved in a horizontal XY plane.
deformation effects in liposomes induced by a focused laser, such as pearling and fission, have been noticed in past studies.\textsuperscript{9–11} On the other hand, when the inner solution has a higher refractive index than the outer solution, the liposome is strongly trapped and safely transported without serious transformation, as in Fig. 2\textsuperscript{b}. During transport, the trapped position is shifted from the center of the spherical liposome, and this is attributed to competition between viscous dragging and the optical force.

To compare the efficiency of trapping in a quantitative manner, we measured the effective optical force by considering viscous drag.\textsuperscript{12} The results are summarized in Fig. 3.

Using unilamellar liposomes of 5–10 \( \mu \)m (\( \gg \lambda \); wavelength of light) in radius, we measured the dynamic responses of the position of the giant liposomes based on an analysis of video images (1/30 s). \( R/R_0 \) is the normalized radial distance from the center of the liposome, where \( R/R_0 = 1 \) corresponds to the position of the membrane. The terms \( n_{in} \) and \( n_{out} \) are the refractive indices of the inner and outer solutions. From the profile of optical force in experimental measurements on the \( XY \) plane, we evaluated the effective potential, as shown on the right side of Fig. 3. The effective attractive potential on a liposome with an inner solution of high refractivity [Fig. 3(b)] is about one order of magnitude greater than that of a liposome with the same solution both inside and outside [Fig. 3(a)]. When the refractivity of the inner solution is lower than that of the outer solution, the potential is always positive with respect to infinite distance [Fig. 3(c)]. This again indicates that the solution composition has a greater effect than direct trapping of the thin membrane. Let us briefly discuss the difference in trapping efficiency mentioned above. In the case of trapping with a thin membrane as in Figs. 2(a) and 3(a), we adapt the theory of a Rayleigh regime, since the thickness of the membrane is about 5 nm, which is two orders of magnitude smaller than the wavelength. The optical force acting on point \( \mathbf{r} \) of the liposome can be expressed as\textsuperscript{13,14}

\[
\mathbf{f}(\mathbf{r}) = \alpha(\mathbf{r}) \left( \frac{1}{2} \nabla \mathbf{E}(\mathbf{r})^2 + \frac{1}{c} \frac{\partial}{\partial t} [\mathbf{E}(\mathbf{r}) \times \mathbf{B}(\mathbf{r})] \right). 
\]
where \( E \) and \( B \) are electric and magnetic fields, \( c \) is the speed of light, \( \alpha = 3n_m^2(m^2 - 1)/(m^2 + 2) \) is the polarizability per unit volume under the dipole approximation, \( n_o \) and \( n_m \) are the refractivities of the object and the surrounding medium, and \( m = n_o/n_m \) is the relative index. The total force acting on the liposome is

\[
F = \int f(r)dr.
\]  

Equation (1) means that no optical force acts on the volume of the liposome under the condition \( m = 1 \), i.e., with the same solution inside and outside the liposome. Thus, the laser tends to cause deformation of the liposome rather than transportation. As for stable trapping of the liposome at \( n_o/n_m > 1 \), as in Figs. 2(b) and 3(b), the regime of geometrical optics in a dielectric sphere is applicable.\(^6\)\(^7\)\(^8\) Irradiated laser light is refracted and reflected at the membrane interface between the inside and outside solutions. The liposome undergoes counteractions from the refraction and reflection of light. In such a ray optics regime, the trapping force is expressed as \( F = (n_oP/c)Q \), where \( n_oP/c \) is light momentum per second, and \( Q \) is the trapping efficiency. The efficiency \( Q \) in Fig. 3(b) is about 0.01,\(^9\) whereas for the case in Fig. 3(a), \( Q \sim 0.001 \).

Up to now, optical manipulations of cell-sized liposomes have been carried out almost only for phospholipid membranes containing the same solutions as the bathing solutions. Under such experimental conditions, only the thin layer of the membrane can be effectively trapped by a laser. Thus, the trapping efficiency has been rather low,\(^10\) about 0.4 pN. In addition, serious effects of the focused laser have been noted when the laser power is made strong enough to “trap the membrane.” Due to this difficulty in optical trapping, liposomes have historically been manipulated mostly using tapered micropipettes,\(^11\) despite the advantages of laser trapping, handiness, simplicity of the system, and lack of adhesion. In contrast, laser force seems to have been merely used to deform the membrane, thus causing tension and fission,\(^12\) except for the trapping of smaller liposomes 1 or 2 \( \mu \)m in diameter.\(^13\)\(^14\)

In the present study, we have demonstrated the efficient optical trapping of cell-sized liposomes. Such cell-sized liposomes can carry various chemicals, including enzymes, DNA and RNA.\(^22\) Giant liposomes are also reasonably stable for up to several weeks, in contrast to smaller liposomes. In addition, the efficiency of trapping can be enhanced by using suitable inner and outer solutions. The application of this technique may be useful for the future construction of a \( \mu \)m-scale laboratory for use in biochemistry and molecular biology.

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17. The laser beam was reduced from 500 to about 100 mW by the dichroic mirror and objective lens in this experimental system.


