Optical transport of sub-micron lipid vesicles along a nanofiber: supplement

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Supplement DOI: https://doi.org/10.6084/m9.figshare.13237226

Parent Article DOI: https://doi.org/10.1364/OE.411124
Optical transport of sub-micron lipid vesicles along a nanofiber: supplemental document

Supporting information is presented for the article “Optical transport of sub-micron lipid vesicles along a nanofiber”.

1. RESEARCH METHODS

Fiber preparation and insertion into liposome solution
Tapered fibers were fabricated using a heat and pull process [1, 2] applied to commercial single mode optical fiber (780HP). The nanofiber was submerged in a ∼100 µL droplet of liposome solution (liposome density ∼ 12 × 10^9 mL^-1) by touching the droplet to the fiber from below and then “sinking” the nanofiber in the droplet by pipetting a small amount (∼10 µL) of pure water from above.

Optical measurement
We used a 50x objective (Nikon, Lu Plan Fluor 50x / NA 0.8) for observation of the nanofiber waist. The light from the lens was detected by a CMOS camera (Thorlabs DCC1545M). The liposome membrane was tagged with rhodamine dye whose optical absorption band exists near 550 nm, with a broad emission band centered near 600 nm. To excite the rhodamine and detect liposomes, we introduced a CW laser (wavelength 530 nm) into the nanofiber. To filter out the excitation light and any scattered light from the transport beam, we inserted two filters (600 nm long pass and 700 nm short pass) before the CMOS camera. For each optical power, we saved between 35 and 40 s of data as an avi format movie file.

Data processing
To process the data, we first extracted each frame from the raw movie data to separate image files. Secondly, we created one dimensional (1D) data from each image file by extracting pixel values along the line coinciding with the fiber position in the image. We then agglomerated the 1D data into a single 2D data set which allowed the visualization and analysis of trajectories taken by individual liposomes. We then identified the start and end point of each trajectory and calculated the associated velocity and lifetime. In rare cases where an apparent single trajectory has sections with varying velocity, we approximated the trajectory by straight line segments, so that Stokes law could be applied to each segment.

Liposome sample preparation
4 mg of 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC) (Avanti Polar Lipids, Inc.) and 0.006 mg of 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine-N-(lissamine rhodamine B sulfonyl) (RhodDOPE) (Avanti Polar Lipids, Inc.) were dissolved in chloroform in a glass vial. Chloroform was evaporated with a flow of nitrogen gas for 5 min and then evacuated in a vacuum desiccator for at least 6 h. The dried lipid films were rehydrated in 5 mL of pure water to give a lipid concentration of approximately 1 mM and vortexed for 1 h to prepare phospholipid multilamellar liposome suspensions. The liposome suspension was then repeatedly frozen and thawed five times with liquid nitrogen, and extruded five times through a polycarbonate membrane filter with a pore size of 400 nm (Merck Millipore Ltd.)[3, 4].

Liposome sample characterization
The size distribution of the prepared liposomes was measured using a nanoparticle characterization system equipped with a 405 nm wavelength laser (NanoSight LM10-HSBFT14, Quantum Design Japan). The radius \( r \) of liposomes, was derived using the Stokes-Einstein equation \( D_l = k_BT/6\pi\eta r \) where \( k_B \) is Boltzmann’s constant, \( T \) is the temperature, \( \eta \) is the viscosity of the liquid, and \( D_l \) is the diffusion coefficient. The value of \( D_l \) can be obtained based on the analysis of the Brownian motion of nanoparticles by the NTA technique. Measurements were carried out at room temperature in a cell installed in the NTA equipment.
2. FINITE DIFFERENCE TIME DOMAIN SIMULATIONS

Here, we provide more details regarding the numerical simulations of the light pressure force imposed by the fiber mode on the liposomes. This is the force which causes the liposomes to move along the nanofiber in the same direction as the mode propagation. The nature of the liposomes brings a number of challenges when performing simulations. In particular, we note the following: i) the low index contrast between the liposomes and the surrounding water means that the preferred (and memory efficient) method of calculation - the Maxwell stress tensor - is not suitable, ii) the lamellarity of individually trapped and transported liposomes is unknown and iii) the rhodamine introduced to the lipid layer causes an unknown increase in the liposome refractive index. We now consider these points in order:

We performed numerical evaluation of the optical forces on liposomes near the nanofiber surface by evaluating the Lorentz force throughout a 1 \( \mu m^3 \) volume which included the liposome but excluded the nanofiber. This “volumetric” method is more accurate than the usual Maxwell stress tensor method for particles which have small index contrast with the surrounding medium. Specifically, for particles of very small contrast with the surrounding medium, numerical calculation of the Maxwell stress tensor corresponds to finding a very small difference between two large numbers, and is therefore prone to numerical noise [5]. Second, we model the liposomes as

\[
\text{Fig. S1. (a) Numerically calculated terminal velocities as a function of unilamellar liposome diameter for various nanofiber diameters as indicated in the legend. (b) Same as (a) but for bilamellar liposomes. (c) Same as (a) but for trilamellar liposomes. (d) Average velocities over liposome diameter as a function of nanofiber diameter} \ 2a, \text{ for unilamellar (blue circles), bilamellar (red circles) and trilamellar (green circles) liposomes. Lines are included to guide the eye. The shaded region in each case indicates the range of } v_T \text{ values from minimum to maximum.}
\]

5 nm shells of dielectric material of index \( n_l = 1.5 \) [6] encasing pure water (\( n_{\text{water}} = 1.33 \)). Although the liposomes are predominantly unilamellar, it is expected that both bilamellar and trilamellar liposomes are present in the solution. Recently, using the same preparation method as that used here, Nele et al. reported percentages by number of 79, 14 and 6% for unilamellar, bilamellar (blue circles), bilamellar (red circles) and trilamellar (green circles) liposomes respectively [7], and a similar percentage composition is expected in our case.

Third, the liposomes are tagged with rhodamine-B dye to allow their detection by photoluminescence measurements. The addition of rhodamine dye is expected to cause an increase in refractive index of the lipid membrane. In particular, Alnayli et al. have reported values of
refractive index above 710 nm for Rhodamine B in solution of between 1.5 and 2.0 depending on concentration [8]. Although an exact measurement of the refractive index of the lipid membrane of the liposomes used in our experiment is beyond the scope of the present work, it is necessary to consider the possible range of refractive index when comparing experiment and simulations.

The numerical simulations of the light pressure force \( F_P \) on the liposomes were performed using the finite difference time domain method (Lumerical FDTD). We converted the force into a velocity by assuming that the light pressure force was balanced by the viscous force of the water, and using Stokes formula \( F_P = 3\pi \Phi_L \eta v_T \), where \( \Phi_L \) is the liposome diameter, \( \eta = 8.9 \times 10^{-4} \) Pa·s is the dynamic viscosity of water at room temperature and \( v_T \) is the liposome (terminal) velocity. (Note that in the main paper, we adjusted the velocities to allow for the 10 K increase in temperature expected at the fiber surface, which leads to a ~12% decrease in viscosity relative to room temperature, and an associated ~12% increase in the calculated velocity). The use of the unmodified Stokes formula may produce an overestimate of the liposome velocity given that the presence of the nanofiber should lead to additional resistance to the liposome motion. Corrections to Stokes law due to the presence of a plane surface which have been applied in experiments using microfibers are not obviously applicable here. More importantly, we find no experimental evidence to suggest that the true drag is significantly larger than that predicted by Stokes law. A more quantitative comparison of experiment and theory in this regard is beyond the scope of the present study.

The velocity is shown as a function of liposome diameter for unilamellar liposomes in Fig. S1(a) for various nanofiber diameters (NFDs) as indicated in the legend. We see that the mean velocity increases as the nanofiber diameter is decreased from 600 nm to 300 nm. The maximum velocity of \( \approx 0.6 \) µm s\(^{-1}\) is seen to occur when the fiber diameter is 350 nm, and the liposome diameter is 200 nm. In Fig. S1(b), the same results are shown for the case where the liposome is bilamellar (i.e. the lipid membrane is twice as thick). Roughly the same trend is seen with increasing velocity as the nanofiber diameter is decreased from 600 nm to 300 nm. However, the average value of the velocity is approximately three times that seen for unilamellar liposomes. The maximum value of about 2 µm s\(^{-1}\) occurs for a nanofiber diameter of 300 nm and a liposome diameter of 150 nm. Additionally, two broad peaks in the velocity are seen near values of \( \Phi_L = 200 \) nm and \( \Phi_L = 500 \) nm, suggesting weak resonant effects dependent on size (i.e. whispering gallery modes). In Fig. S1(c) shows the same calculations in the case of trilamellar liposomes. Here we see average velocities about 5 times higher than the unilamellar cases with a maximum velocity of about 2.7 µm s\(^{-1}\) seen for \( \Phi_L = 200 \) nm and 500 nm, and for a fiber diameter of 350 nm. Finally, In Fig. S1(d) We show a summary of the data in (a)-(c) by plotting mean velocities over liposome diameter as a function of the nanofiber diameter 2a.

3. ESTIMATION OF TEMPERATURE AT NANOFIBER SURFACE

![Fig. S2.](image)

We estimated the temperature at the nanofiber surface and the temperature gradient experienced by liposomes using a simplified model of a cylindrically symmetric heat source (light absorbed from the guided mode of the nanofiber) as shown in Fig. S2. Assuming an infinitely long nanofiber (in our case, since the nanofiber length is much longer than its radius, this is not a bad approximation), the Poisson equation for the temperature \( T \) is

\[
\nabla^2 T = \begin{cases} 
-\frac{\rho}{\lambda}, & r < a_{nf} \\
0, & r > a_{nf}
\end{cases}
\tag{S1}
\]
where \( \rho = 2.4 \text{ mW}/(\pi \times (200 \text{ nm})^2 \times 1 \text{ mm}) \) is the power density defined as the total absorbed power within the region of radius \( a_{nf} \) and over the 1 mm region where the nanofiber is at its thinnest, and \( \lambda = 0.592 \text{ W/m.K} \) is the thermal conductivity of water.

It is simplest to first use Gauss’ law to solve for the gradient of the temperature:

\[
\int_{\mathcal{V}} \nabla T \cdot d\mathbf{A} = - \int_{\mathcal{V}} \frac{\rho}{\lambda} dV
\]

\( \Rightarrow 2\pi rL(\nabla T)_r = -2\pi \frac{\rho a_{nf}^2 L}{\lambda} \)

\( \Rightarrow \frac{\partial}{\partial r} T = -\frac{\rho a_{nf}^2}{\lambda r} \)  \hspace{1cm} (S2)

Integrating Eq. S2 gives a general solution for \( T \):

\[
T(r) = -\frac{\rho a_{nf}^2}{\lambda} \log(r) + C. \hspace{1cm} (S3)
\]

The constant \( C \) can be determined by imposing an appropriate boundary condition. Here, we will assume that at the surface of the water droplet, a radial distance \( R \) from the fiber center, the water is at room temperature \( T_0 \). This leads to the equation

\[
C = T_0 + \frac{\rho a_{nf}^2}{\lambda} \log(R). \hspace{1cm} (S4)
\]

Finally, we find that the temperature difference \( \Delta T \) between the fiber surface and room temperature can be written

\[
\Delta T(r) = \frac{\rho a_{nf}^2}{\lambda} \log \left( \frac{R}{r} \right). \hspace{1cm} (S5)
\]

Taking \( a_{nf} \) to be 200 nm, and \( R \) to be 1 mm, we find that \( \Delta T \approx 10 \text{ K} \). This value is insensitive to the exact values of \( a_{nf} \) and \( R \), being sensitive instead to the difference in their orders of magnitude due to the logarithmic dependence.

The temperature gradient in the radial direction can now be calculated. As a representative example, we set the nanofiber radius to \( a_{nf} = 200 \text{ nm} \), and choose a liposome diameter \( \Phi_1 = 300 \text{ nm} \). Then, using Eq. S2, the temperature gradient at the center of the liposome is found to be about \( 3 \times 10^6 \text{ K/m} \).

The gradient along the nanofiber is more difficult to model accurately. As an upper bound, we can assume the the entire temperature gradient \( \Delta T \) occurs along the ~1 mm length of the nanofiber. Then, in a one dimensional approximation, the temperature gradient is \( 10\text{K}/1 \text{ mm} = 10^4 \text{ K/m} \).

4. NANOFIBER DIAMETER MEASUREMENTS

Here, we show typical results for diameter measurements of optical nanofibers. The measurements were made after the experiment was finished and the nanofibers had been removed from the liposome solution.

Fig. S3(a) shows a scanning electron microscope image taken of the nanofiber within the region of smallest diameter (the “waist” region). By taking such images along the length of the nanofiber, we can measure its diameter profile. Such a profile over a ~1 mm range is shown in Fig. S3(b). The nanofiber diameter is sub-micron over this range, and liposome transport along with heating of the water due to absorbance from the fiber mode can in principle happen anywhere along this region. Fig. S3(c) shows the same data as Fig. S3(b), but zoomed in to the region near the nanofiber waist.

5. LIPOSOME SIZE MEASUREMENTS

Here we display extra diameter characterization data for liposomes extruded through a 100 nm polycarbonate membrane filter. We first show the data presented in the main paper (Fig. 2(a)) to allow easy comparison. Note that the size of the liposomes after filtering can be larger than the filter pore size due to the elasticity of liposomes, whose shape can deform sufficiently to pass through gaps smaller than the nominal liposome diameter.
Fig. S4(a) shows the diameter characterization data for liposomes filtered through a 400 nm polycarbonate membrane as used in the experiments whose results are given in the main paper. We also attempted experiments with liposomes filtered through a 100 nm polycarbonate membrane (diameter characterization shown in Fig. S4(b)) but for that liposome sample, no transport behavior was observed, suggesting that transport occurs predominantly for liposomes with diameter greater than 100 nm.

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Fig. S3. (a) Scanning electron microscope of nanofiber used in experiments in its waist region (i.e. smallest diameter region). (b) Diameter measurements of the nanofiber over a ∼1 mm range. (c) Diameter measurements over the nanofiber waist region.
Fig. S4. (a) Diameter characterization of liposomes used in our experiments. (b) Diameter characterization of liposomes filtered with a 100 nm polycarbonate membrane.