Optical stretching of giant unilamellar vesicles with an integrated dual-beam optical trap

Mehmet E. Solmaz,1,* Roshni Biswas,1 Shalene Sankhagowit,2 James R. Thompson,2 Camilo A. Mejia,1 Noah Malmstadt,2 and Michelle L. Povinelli1

1Ming Hsieh Department of Electrical Engineering, University of Southern California, Los Angeles, CA 90089, USA
2Mork Family Department of Chemical Engineering and Materials Science, University of Southern California, Los Angeles, CA 90089, USA
*solmaz@usc.edu

Abstract: We have integrated a dual-beam optical trap into a microfluidic platform and used it to study membrane mechanics in giant unilamellar vesicles (GUVs). We demonstrate the trapping and stretching of GUVs and characterize the membrane response to a step stress. We then measure area strain as a function of applied stress to extract the bending modulus of the lipid bilayer in the low-tension regime.

© 2012 Optical Society of America

OCIS codes: (000.1430) Biology and medicine; (350.4855) Optical tweezers or optical manipulation.

References and links

1. M. Ozkan, M. Wang, C. Ozkan, R. Flynn, and S. Esener, “Optical manipulation of objects and biological cells in microfluidic devices,” Biomed. Microdevices 5(1), 61–67 (2003).
2. C.-W. Lai, S.-K. Hsiung, C.-L. Yeh, A. Chiou, and G.-B. Lee, “A cell delivery and pre-positioning system utilizing microfluidic devices for dual-beam optical trap-and-stretch,” Sens. Actuators B Chem. 138(1), 388–397 (2008).
3. N. Bellini, K. C. Vishnubhatla, F. Bragheri, L. Ferrara, P. Minzioni, R. Ramponi, I. Cristiani, and R. Osellame, “Femtosecond laser fabricated monolithic chip for optical trapping and stretching of single cells,” Opt. Express 18(5), 4679–4688 (2010).
4. J. Guck, R. Ananthakrishnan, H. Mahmood, T. J. Moon, C. C. Cunningham, and J. Käs, “The optical stretcher: a novel laser tool to micromanipulate cells,” Biophys. J. 81(2), 767–784 (2001).
5. J. Guck, S. Schinkinger, B. Lincoln, F. Wottawah, S. Ebert, M. Romeyke, D. Lenz, H. M. Erickson, R. Ananthakrishnan, D. Mitchell, J. Käs, S. Ulvick, and C. Bilby, “Optical deformability as an inherent cell marker for testing malignant transformation and metastatic competence,” Biophys. J. 88(5), 3689–3698 (2005).
6. M. Martin, K. Mueller, F. Wottawah, S. Schinkinger, B. Lincoln, M. Romeyke, and J. A. Kas, “Feeling with light for cancer,” Proc. SPIE 6080, 60800P (2006).
7. R. Phillips, T. Ursell, P. Wiggins, and P. Sens, “Emerging roles for lipids in shaping membrane-protein function,” Nature 459(7245), 379–385 (2009).
8. D. Marsh, “Protein modulation of lipids, and vice-versa, in membranes,” Biochim. Biophys. Acta 1778(7-8), 1545–1575 (2008).
9. D. Marsh, “Elastic curvature constants of lipid monolayers and bilayers,” Chem. Phys. Lipids 144(2), 146–159 (2006).
10. L. V. Chernomordik and M. M. Kozlov, “Mechanics of membrane fusion,” Nat. Struct. Mol. Biol. 15(7), 675–683 (2008).
11. E. A. Evans, “New membrane concept applied to the analysis of fluid shear- and micropipette-deformed red blood cells,” Biophys. J. 13(9), 941–954 (1973).
12. E. Evans and D. Needham, “Physical properties of surfactant bilayer membranes: thermal transitions, elasticity, rigidity, cohesion and colloidal interactions,” J. Phys. Chem. 91(16), 4219–4228 (1987).
13. D. Cuvelier, I. Derényi, P. Bassereau, and P. Nassoy, “Coalescence of membrane tethers: experiments, theory, and applications,” Biophys. J. 88(4), 2714–2726 (2005).
14. V. Heinrich and R. E. Waugh, “A piconewton force transducer and its application to measurement of the bending stiffness of phospholipid membranes,” Ann. Biomed. Eng. 24(5), 595–605 (1996).
15. R. Dimova, K. A. Riske, S. Aranda, N. Bezlevkina, R. L. Knorr, and R. Lipowsky, “Giant vesicles in electric fields,” Soft Matter 3(7), 817–827 (2007).
16. M. Kummrow and W. Helfrich, “Deformation of giant lipid vesicles by electric fields,” Phys. Rev. A 44(12), 8356–8360 (1991).
17. R. S. Graciá, N. Bezlyepkina, R. L. Knorr, R. Lipowsky, and R. Dimova, “Effect of cholesterol on the rigidity of saturated and unsaturated membranes: fluctuation and electrodeformation analysis of giant vesicles,” Soft Matter 6(7), 1472–1482 (2010).
18. T. M. Pinon, L. S. Hirst, and J. E. Sharping, “Fiber-based dual-beam optical trapping system for studying lipid vesicle mechanics,” in Optical Trapping Applications, OSA Technical Digest (CD) (Optical Society of America, 2011), paper OTTuB2.
19. T. M. Pinon, L. S. Hirst, and J. E. Sharping, “Optical trapping and stretching of lipid vesicles,” in CLEO: Applications and Technology, OSA Technical Digest (online) (Optical Society of America, 2012), paper ATThM4.
20. S. Ebert, K. Travis, B. Lincoln, and J. Guck, “Fluorescence ratio thermometry in a microfluidic dual-beam laser trap,” Opt. Express 15(23), 15493–15499 (2007).
21. F. Wetzel, S. Rönkinke, K. Müller, M. Gyger, D. Rose, M. Zink, and J. Käs, “Single cell viability and impact of heating by laser absorption,” Eur. Biophys. J. 40(9), 1109–1114 (2011).
22. M. Yamazaki and T. Ito, “Deformation and instability in membrane structure of phospholipid vesicles caused by osmophobic association: mechanical stress model for the mechanism of poly(ethylene glycol)-induced membrane fusion,” Biochemistry 29(5), 1309–1314 (1990).
23. W. Helfrich, “Lipid bilayer spheres - Deformation and birefringence in magnetic-fields,” Phys. Lett. A 43(5), 409–410 (1973).
24. A. Ashkin, “Acceleration and trapping of particles by radiation pressure,” Phys. Rev. 24, 156 (1970).
25. G. Roosen, “A theoretical and experimental study of the stable equilibrium positions of spheres levitated by two horizontal laser beams,” Opt. Commun. 21(1), 189–194 (1977).
26. L. Kou, D. Labrie, and P. Chylek, “Refractive indices of water and ice in the 0.65- to 2.5-µm spectral range,” Appl. Opt. 32(19), 3531–3540 (1993).
27. M. Angelova, S. Soléau, P. Méléard, F. Faucon, and P. Bothorel, “Preparation of giant vesicles by external AC electric fields. Kinetics and applications,” Prog. Colloid Polym. Sci. 89, 127–131 (1992).
28. E. Evans and W. Rawicz, “Entropy-driven tension and bending elasticity in condensed-fluid membranes,” Phys. Rev. Lett. 64(17), 2094–2097 (1990).
29. P. M. Vlahovska, R. S. Graciá, S. Aranda-Espinoza, and R. Dimova, “Electrohydrodynamic model of vesicle deformation in alternating electric fields,” Biophys. J. 96(12), 4789–4803 (2009).
30. E. Sidick, S. D. Collins, and A. Knoesen, “Trapping forces in a multiple-beam fiber-optic trap,” Appl. Opt. 36(25), 6423–6433 (1997).
31. H. Sosa-Martínez and J. C. Gutierrez-Vega, “Optical forces on a Mie spheroidal particle arbitrarily oriented in a counterpropagating trap,” J. Opt. Soc. Am. B 26(11), 2109–2116 (2009).
32. J. R. Henriksen and J. H. Ipsen, “Measurement of membrane elasticity by micro-pipette aspiration,” Eur Phys J E Soft Matter 14(2), 149–167 (2004).
33. H. Bouvrais, T. Pott, L. A. Bagatolli, J. H. Ipsen, and P. Méléard, “Impact of membrane-anchored fluorescent probes on the mechanical properties of lipid bilayers,” Biochim. Biophys. Acta 1798(7), 1333–1337 (2010).
34. J. Henriksen, A. C. Rowat, and J. H. Ipsen, “Vesicle fluctuation analysis of the effects of sterols on membrane bending rigidity,” Eur. Biophys. J. 33(8), 732–741 (2004).
35. M. Kocun and A. Janshoff, “Pulling tethers from pore-spanning bilayers: towards simultaneous determination of local bending modulus and lateral tension of membranes,” Small 8(6), 847–851 (2012).
36. G. Niggemann, M. Kummrow, and W. Helfrich, “The bending rigidity of phosphatidylcholine bilayers: dependences on experimental method, sample cell sealing and temperature,” J. Phys. 5, 413–425 (1995).
37. L. Miao, U. Seifert, M. Wortis, and H.-G. Döberreiner, “Budding transitions of fluid-bilayer vesicles: The effect of area-difference elasticity,” Phys. Rev. E Stat. Phys. Plasmas Fluids Relat. Interdiscip. Topics 49(6), 5389–5407 (1994).

1. Introduction

In recent years, there has been growing interest in the integration of optical traps with microfluidics for manipulation of biological systems such as cells [1–4]. The dual-beam optical trap (DBOT) [4] is a biophotonic device that can create stress on the surface of trapped objects without physical contact or electrical charging. The DBOT has previously been used to characterize the mechanical properties of cells [5,6]. In this work, we demonstrate that the DBOT can be used to characterize the mechanical properties of the lipid bilayer of the plasma membrane, as modeled by the membrane of giant unilamellar vesicles (GUVs).

GUVs are synthetic, spheroidal, lipid-bilayer systems ideal for studying membrane mechanics. Membrane bending and stretching control key aspects of cellular function, and the mechanical properties of a membrane are altered as its chemical composition changes [7–10]. While there have been several approaches to measuring membrane mechanics in GUVs, existing techniques are not well suited for rapid analysis of the mechanical behavior of a
membrane as it is exposed to physicochemical stimuli. An ideal approach should be minimally invasive, analyzing the membrane in a biologically relevant, free-solution environment. Moreover, since the time course of physiological processes at the membrane can vary widely, it is important to be able to apply precisely-controlled patterns of forces in time, and to be able to take measurements quickly.

Micropipette aspiration is a well-developed technique for studying the mechanical properties of GUVs [11,12]. However, this method requires direct contact with the GUV. Another method for applying mechanical force to a GUV is to use magnetic or optical tweezers [13,14]. The tweezers are used to pull on a bead in contact with the GUV, resulting in the extrusion of a narrow bilayer (tether) from the membrane. A third method used to study basic mechanical properties of GUVs is deformation induced by an electric field, or electrodeformation [15–17]. This method may produce pores, due to electroporation, introducing error into the measurement of mechanical moduli. Moreover, electrodeformation is not suitable for charged lipids, which are critical for a number of biological processes and are ubiquitous in nature.

The DBOT provides a method for non-invasive application of time-dependent forces in a device suitable to rapid, high-throughput measurements. However, because GUVs typically contain the same solution on the interior and exterior of the spherical, lipid bilayer, the refractive index difference required for trapping is not present. Here, we present a method for fabrication of GUVs with different, osmotically-balanced solutions on the interior and exterior of the bilayer. We construct a DBOT based on optical fibers integrated with a capillary flow channel and demonstrated trapping and stretching of a GUV. We characterize the response of the GUV to a step increase in stress. We further conduct experiments in which the area strain of the GUV is measured as a function of applied stress and develop a method to extract the bending modulus of the membrane from the data. This method incorporates three-dimensional ray-tracing methods to calculate the applied stress in the DBOT. The value we obtain for bending modulus agrees well with literature values. Unlike previous results in the literature [18,19], we use a laser-wavelength selected to minimize heating effects [20,21], avoid the use of polyethylene glycol, which is known to destabilize membranes [22], and model the mechanical properties of the GUV as a lipid bilayer, according to the accepted approach developed by Helfrich [23]. Our results demonstrate the potential of the DBOT for rapid, flow-through measurements of membrane response to changing physicochemical environments, opening a path for a wide range of biological experiments.

2. Methods

Dual-beam optical trap

A schematic view of a dual-beam optical trap is shown in Fig. 1. Light emitted from each of the two optical fibers (OF) has the form of a Gaussian beam. The optical fiber used is HI780 (Corning, USA) with ~2.4µm mode-field radius. The beam size at the center of the flow channel \( (w_0 = 11.5 \pm 0.2\mu m) \) was calculated from the size of the optical fiber mode using the ABCD matrix method. Radiation pressure pulls the GUV into the center of the two beams, creating a stable trap [24,25]. In this position, the light, due to change in momentum resulting from reflection and refraction, also creates a surface stress [4,5] that can deform the GUV along the beam axis, as shown.

We constructed a dual-beam optical trap, shown in Fig. 1. A square capillary with 100 µm inner diameter (Vitrocom, USA) and wall thickness of 100 µm was used as a flow channel to transport GUVs to the trapping site [5] and is placed perpendicular to the optical fibers. The optical fibers and channel are aligned using a custom holder, which is fabricated by creating alignment grooves in a silicon chip via photolithography and reactive ion etching. The distance between the fibers was 300 µm. The capillary-to-fiber union was coated with index-matching liquid, and the capillary is coupled to a peristaltic pump (Instech, USA) using
microfluidic adapters (Upchurch, USA). A modified upright microscope in reflection mode with digital camera attachment was used to image the observation area. Shut-off valves (Upchurch, USA) were used on both the input and output side of the flow channel, in order to isolate the capillary from back flow during stretching experiments.

Fig. 1. The setup used to stretch GUVs using optical radiation pressure. (a) Schematic of the stretching of a GUV using dual Gaussian beams launched by optical fibers. (b) Optical setup that incorporates a silicon chip for fiber-to-capillary alignment and microfluidic adapters to couple the flow channel to a peristaltic pump, all located under a customized microscope.

Two high power fiber coupled semiconductor diode lasers at a wavelength of 808 nm (Lumics GmbH, Germany) were used as light sources. These lasers are compact, versatile, and responsive to current modulation. The maximum power out of each fiber was measured to be 250 mW. The wavelength was selected to minimize water absorption [26] in the infrared, in order to avoid heating effects [20,21]. For a wavelength of 808 nm, we have simulated the heating of our flow channel in COMSOL and found that the temperature increases less than 1 K for 250 mW of laser power.

In trapping and stretching experiments, the lasers were simultaneously driven by two laser diode controllers (Thorlabs, USA). The microscope was used to observe the experiment, and video was recorded at 61 fps by a GiGe camera with CCD image sensor (Basler AG, Germany). Both the laser controllers and the camera were controlled by a Labview code (National Instruments).

Experiments were performed on GUVs with diameter smaller than the height of the flow channel. The optical fiber axis was vertically aligned so the trapping region was in the center of the flow channel, and trapped GUVs were not in physical contact with capillary walls.

Fabrication of GUVs

To facilitate trapping, it is necessary to create a refractive index difference between the interior and exterior of the GUV. To achieve this, we fabricated GUVs with a sucrose solution inside and transferred them to an osmotically-balanced glucose solution. The density difference between sucrose and glucose results in a refractive index difference.

GUVs with sucrose inside were fabricated by electroformation from pure dioleoylphosphatidylcholine (DOPC), using a modification of the technique in Ref. [27]. The synthetic lipid, 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), was purchased from Avanti Polar Lipids (Alabaster, AL). The lipids were dissolved in chloroform and deposited onto an indium-tin oxide (ITO) coated glass slide from Delta Technologies (Loveland, CO). The electroformation chamber was formed with two ITO slides, with the conducting sides facing inwards and separated by a 2.5 mm thick silicone spacer. A 500 mM sucrose solution in 4 mM HEPES titrated to pH 7.0 with sodium hydroxide was added to the overnight vacuum-dried lipid film on the slides giving a final lipid concentration of 0.25
A 2.65 V AC electric field, generated at 100 Hz by a function generator, was applied to the chamber at room temperature for two hours in order to grow the GUVs.

Transfer to a glucose solution was achieved by performing three two-fold serial dilutions on the GUV suspension using an identical buffer solution, but with the sucrose swapped for an equimolar quantity of glucose.

Refractive indices were measured for the pure sucrose and glucose solutions using a refractometer (PAL-RI Refractometer - Atago, Bellevue, WA). Values were obtained for the pure glucose solution (RI = 1.3455 ± 0.0003) and sucrose solution (GUV interior RI = 1.3575 ± 0.0003), and the dilution used in the experiment yielded a final refractive index difference of 0.0105 ± 0.0003, slightly less than the difference between the two pure solutions. The prepared mixture was then left to sit for ten minutes in order to allow GUVs to sediment to the bottom of the tube, after which time half of the total liquid volume was carefully removed at the surface. This suspension was then directly pumped into our microfluidic device.

The electroformation process also yields multilamellar vesicles, which are stiffer than unilamellar vesicles. In experiments, vesicles were inspected visually for evidence of membrane fluctuation. Experiments were only performed on vesicles that were clearly fluctuating.

3. Results

Trapping and stretching of GUVs

GUVs were captured using minimal power (total power of 100 mW; 50 mW from each fiber) while ensuring the flow was stopped and the GUV was resting at the bottom of the channel. As a GUV is pulled up to the optical axis, its initial circular shape is drawn into a slightly prolate elliptical shape due to the stress profile created by the optical force. A characteristic example is shown in Fig. 2(a). The total power was then increased to 500 mW, and the deformed shape at maximum power is shown in Fig. 2(b).

Matlab was used to process each image frame extracted from the recorded video. Our algorithm finds the edge contour of the trapped GUV as well as its geometric center. Contours were inspected visually after processing to ensure accurate edge detection. Figure 2(c) shows the contours at minimum and maximum power. Stretching of the GUV along the beam axis can be clearly observed.

![Fig. 2. Axial deformation of a giant unilamellar vesicle made of POPC lipid. Sucrose and glucose solutions are used inside and outside to create a refractive index gradient. The major axis is increased from (a) \(d = 11.53 ± 0.05\mu m\) to (b) \(d = 11.94 ± 0.05\mu m\) along the beam axis, while the minor axis decreased from \(10.29 ± 0.05\mu m\) to \(10.05 ± 0.05\mu m\). (c) A plot of the contours fitted to both stretching powers (blue = low power / low tension, green = high power / high tension). The scale bar is 10 \(\mu m\).](image)

Instantaneous response to applied stress

We measured the response of the GUV to a step increase in applied stress. The total laser power was increased from 100 mW to 500 mW, as shown in Fig. 3(a) (blue line; right axis).
The power was held at its maximum value for 5 seconds and then decreased to the initial value. The major axis strain is shown on the left axis (red dots). The major axis strain was calculated by assuming that the shape of the GUV at maximum power is a prolate spheroid. We take the diameter of a sphere with the same volume as the zero-power value of the major axis. The major axis strain is the percent change in major axis compared to the zero-power value. From Fig. 3A, it can be seen that the major axis strain increases nearly instantaneously with the step increase in power. The initial strain of $8.2 \pm 0.4\%$ increases by $4.1 \pm 0.25\%$. Based on our frame rate of 61 fps, we are able to capture 2-3 data points in the transition region between power levels.

![Fig. 3. Step-stress experiment. (a) The optical power (blue line; right axis) is suddenly increased from 100 mW to 500 mW. The major axis strain is shown by the red dots (left axis). (b) Video micrograph (Media 1) of deforming GUV. The scale bar is 10 μm.](image)

**Measurement of lipid bilayer bending modulus**

The bending modulus $\kappa_B$ of the GUV membrane can be obtained by calculating area strain as a function of lateral tension. In the low-stress regime [28],

$$\frac{A - A_0}{A_0} = \frac{kT}{8\pi\kappa_B} \ln \left( \frac{\sigma}{\sigma_0} \right),$$

where $(A - A_0)/A_0$ is the vesicle area strain, $k$ is Boltzmann’s constant, $T$ is temperature, $\sigma$ is the lateral tension on the membrane, and $\sigma_0$ is the lateral tension at zero laser power [28].

In our experiment, we gradually ramped the laser power from 100 mW to 500 mW as shown in Fig. 4(a). The power was increased in 11 steps, with a holding time of 1 s at each step. As the power increased, we observed axial deformation of the GUV and a clear dampening of membrane fluctuations. We calculated the area at each power level by expanding the vesicle contours in terms of spherical harmonics. Writing the contour as the radius of an equivalent-volume sphere plus a sum of Legendre polynomials, the area strain is obtained from the second mode of the expansion, averaged over all contours at a given power level [17,29]. The area deformation of the GUV obtained from this expansion is plotted as a function of time in Fig. 4(b). The plot corresponds to first half of the contour where the angles of $0$ and $\pi$ radians are the elongated values of the major axis; an angle of $\pi/2$ corresponds to the minor axis value. A steady increase in the vesicle major axis length and corresponding decrease in minor axis length are observed as the total power increases. The area strain result as a percentage is shown in Fig. 4(c). As expected, we observe an increase in area strain with increasing laser power.
In order to determine the lateral tension on the membrane at each power level [16], it is necessary to calculate the surface stress on the GUV. Ray optics approaches have previously been used to calculate the force on spherical [30] and spheroidal [31] objects. We assume a spheroidal shape for the GUV, as in Ref. [31], and calculate the total force on the front and back surfaces. For each power level, we calculated the force on a spheroid with major and minor axes equal to the average values over all image frames. We included the effect of multiple reflections, up to 5 bounces. For each incident ray and each bounce, we determine whether the bounce occurs on the front or back surface and store the vector force. For each surface, we then add the force contributions vectorially to determine the total force on the surface. The stress is calculated by dividing the total force by the surface area.

The calculated average stress is shown in Fig. 4(d). We present the results as a function of eccentricity ($e$) and base radius ($R$). The parameters $e$ and $R$ are related to the major axis ($a$) and minor axis ($b$) of a spheroid by

$$e = \sqrt{1 - \frac{b^2}{a^2}}, \quad R = \sqrt[3]{ab^2}.$$  

For a sphere, $R = a = b$. For a spheroid, $R$ is equal to the radius of the sphere with the same volume as the spheroid. The optical power from each beam was taken to be 250 mW and the refractive index difference ($\Delta n$) to be 0.0105. While the average stress decreases slightly with eccentricity, it substantially decreases with increasing base radius ($R$), in the 8 – 14 μm range.

The average stress is then translated to a lateral tension $\sigma_t$ as described in the literature [16,17]. We calculate an initial tension ($\sigma_0$) of $5.76 \pm 0.25 \times 10^{-5}$ mN/m and plot area strain as...
a function of the log of scaled lateral tension in Fig. 4(e). The error bars on both axes are equal to the standard deviation of the corresponding quantity, taken over all images recorded at a fixed laser power. The slope is proportional to the bending modulus, which is found to be $7.95 \pm 0.45$ kT. The log-linear relationship indicates that we are in the low stress regime and that area expansion of the membrane comes from damping bending fluctuations, as opposed to direct stretching (i.e. area dilation) of the membrane, as observed at higher stresses [32].

We note that the experimental data shown in Figs. 4(a), 4(b), 4(c), and 4(e) is obtained from a single GUV. Moreover, we note that since the stress is not uniform over the GUV surface, a more sophisticated model of vesicle deformation would include the effects of stress non-uniformity on final shape. This is an interesting area for further research.

Comparison with literature values

Other investigators have measured the bending modulus of POPC membranes using a range of methods [16,33–36]. Values are summarized in the Table 1. Our measured value is within the range of reported values. The variation in literature values suggests the need for a high-throughput technique capable of generating ensemble statistics.

4. Conclusions

In conclusion, we have demonstrated the trapping and stretching of GUVs in an integrated dual-beam optical trap. Different, equimolar sugar solutions were used in the interior and exterior of the GUV to create the required refractive index gradient. The response of the GUV to a step stress was measured and found to be nearly instantaneous, on the time scale corresponding to the frame rate of the camera (~0.02 s). We then used our device to measure the area strain of the GUV as a function of increasing stress. Analysis of the data allowed us to determine the bending modulus of the membrane in the low-tension regime, and the value obtained was consistent with the literature.

In the low-tension regime of membrane deformation, the expansion of membrane area comes primarily from smoothing of thermal fluctuations of the membrane. In the high-tension regime, area strain comes from direct dilation of the membrane in two dimensions [28]. In future work, we plan to upgrade our setup to achieve higher laser power, allowing measurement of both bending and area dilation moduli [23,37].

Improvements to the imaging system, for example through the use of phase-contrast optics, should provide higher contrast images of the GUV edges. Moreover, use of a high-speed camera will allow finer time resolution for studies of dynamic membrane response.

The high-throughput, flow-through nature of our setup will allow the convenient collection of data on large numbers of GUVs, e.g. with varying size, composition, and/or biochemical environment. In this manner, the platform provides a method for the quantitative response of membrane mechanical properties to small molecules, drugs, nanoparticles, and other agents.

Acknowledgments

Optical device development (M. L. P., M. E. S.) was funded by NCI/NIH Award No. 5U54CA143907. Optical force calculations (M. L. P., R. B.) were funded by an NSF
CAREER award under Grant No. 0846143. RB was also funded by a USC Viterbi Fellowship. GUV fabrication, contour tracing, and mechanical analysis (N. M., S. S., J. R. T.) were funded by NIH/GMS Award No. 1R01GM093279. SS was also funded by a USC Provost’s Fellowship. The authors acknowledge Parag Mallick, Maryann Vogelsang, Shannon Mumenthaler, and Ningfeng Huang for helpful discussions.