

Multipoint viscosity measurements in microfluidic channels using optical tweezers

Stephen Keen,^a Alison Yao,^a Jonathan Leach,^a Roberto Di Leonardo,^b Chris Saunter,^c Gordon Love,^c Jonathan Cooper^d and Miles Padgett^{*a}

Received 15th January 2009, Accepted 9th April 2009

First published as an Advance Article on the web 20th April 2009

DOI: 10.1039/b900934e

We demonstrate the technique of multipoint viscosity measurements incorporating the accurate calibration of micron sized particles. We describe the use of a high-speed camera to measure the residual motion of particles trapped in holographic optical tweezers, enabling us to calculate the fluid viscosity at multiple points across the field-of-view of the microscope within a microfluidic system.

Introduction

The emerging fields of microfluidics and lab-on-chip technology promise many advantages over conventional methods for biological and chemical measurement. The miniaturisation of micro-analytical devices results not only in a low fabrication cost and a reduction in the volume of (potentially expensive) reagents used, but also in an increased speed of analysis and the ability to run multiple analytical processes in parallel.

In recent years there have been a number of applications using optical tweezers with microfluidics, for example, to sort cells,^{1,2} or to manipulate and measure fluids within microdevices.^{3–5} Techniques used in microrheology⁶ often involve introducing micron-sized particles to the fluid and tracking their thermal motion (passive microrheology),⁷ providing information about rheology at the micron-scale. A variant of this method involves actively applying a force to the particles (active microrheology) to gain more information about the dynamic properties of the fluid. Active microrheology has been attempted by several means including atomic force microscopes,⁸ magnetic tweezers^{9,10} and optical tweezers.^{11–13} Fluid viscosity has been measured successfully by various methods with optical tweezers, using a single micron sized particle as a probe.^{14–18} Most of these approaches have inferred the surrounding viscosity by using a quadrant photodiode (QPD) to track the motion of the particle.

Alternatively, it is also possible to infer the viscosity from the rotational velocity of a particle subject to a known torque.¹⁹ There are many scenarios across the physical and life sciences where it would be useful to measure changes in the viscosity at many positions simultaneously.²⁰ However, this requires specialist particles and its extension to multiple particles is, as

yet, unproven. Moreover, although a QPD has been used for tracking two particles^{21,22} extension to many particles is cumbersome.

Recent advances in camera technology have, however, enabled a high-speed camera to be used as an alternative to a QPD to measure the positions of particles in optical tweezers.^{23,24} Cameras have the advantage of allowing the tracking of many particles simultaneously at high frame rates.²⁵

In this paper we demonstrate the technique of using micron sized silica beads trapped using holographic optical tweezers to measure the viscosity at multiple points and then to probe local (effective) changes in viscosity due to the presence of walls within a microfluidic channel. We use a CMOS camera²⁶ to measure the x ; y positions of multiple particles in two axes. Note that the integration of the center-of-mass processing means that only the particle positions are transferred to the hard drive, rather than the whole image, which allows indefinite monitoring of up to 16 particles at several kHz without data management problems. Typically we collect positional data at a frame rate of 2 kHz.

In both cases we use our results to accurately calibrate the diameter of the beads (which are stated by the supplier, Bangs Laboratories, to have a standard deviation of $\sim 10\%$). Once calibrated, this offers the possibility for the precise knowledge of spatially and temporally varying viscosity distributions which allow controlling processes in colloidal systems and biological samples. In addition, the technique has the potential to create a new method for mapping microfluidic device structures/micro-landscapes.

Materials and methods

Experimental set-up

Fig. 1 shows the configuration of our optical tweezers which are based upon an inverted microscope. The objective lens, 100×1.3 NA (Zeiss, Plan-Neofluor) was mounted on a piezo-controller and used to both focus the trapping beam and to image the particles. A 50 W tungsten-halogen lamp and condenser was used to illuminate the sample. Trapping was achieved using a CW Ti:sapphire laser system (M2, SolsTiS). The laser was expanded to slightly overfill the aperture of a spatial light modulator, SLM (Hamamatsu, LCOS X1046802), and then

^aSUPA, Department of Physics and Astronomy, University of Glasgow, Glasgow, UK. E-mail: m.padgett@physics.gla.ac.uk; Fax: +44 (0)141 330 2893; Tel: +44 (0)141 330 6432

^bINFN-CRS SOFT, Dipartimento di Fisica, Roma, Italy. E-mail: roberto.dileonardo@phys.uniroma1.it; Fax: +39 06 4463158; Tel: +39 06 49913548

^cDurham University, Department of Physics, Durham, DH1 3LE, UK. E-mail: g.d.love@durham.ac.uk; Fax: +44 (0)191 334 5823; Tel: +44 (0)191 334 3696

^dElectronics and Electrical Engineering, University of Glasgow, Glasgow, UK. E-mail: j.cooper@elec.gla.ac.uk; Fax: +44 (0) 141 330 6010; Tel: +44 (0) 141 330 4931

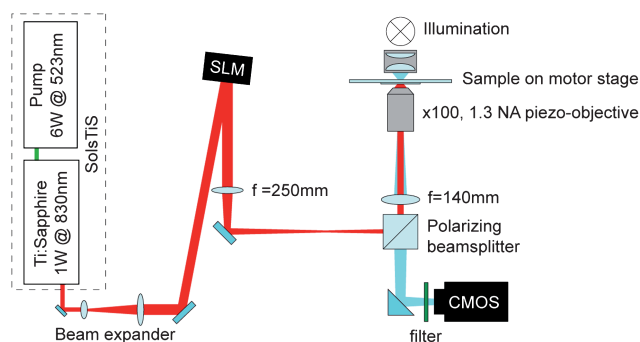


Fig. 1 Experimental setup.

coupled into the tweezers system by imaging the SLM on to the back aperture of the microscope objective lens. By appropriate hologram design, this allows multiple optical traps to be created in the sample plane. The microscope slide and cover slip, forming the sample cell, were mounted on a motorized microscope stage (ASI, MS-2000) above the objective.

Deriving the fluid viscosity from residual motion of the trapped particles

The viscosity of the fluid around each particle can be calculated by analysis of the thermal motion of the particles. Assuming a particle of radius a is held in optical tweezers, tens of radii from any surfaces, the drag coefficient γ is $6\pi\eta a$, where η is the viscosity of the surrounding fluid. The translational drag coefficient can be calculated using two nominally equivalent methods in the time and frequency domains. In the time domain, the autocorrelation function of the position data x over time t has the form:

$$\langle x(0)x(t) \rangle = \langle x^2 \rangle \exp\left(-\frac{t}{\tau}\right) \quad (1)$$

where $\langle x^2 \rangle$ is the mean square displacement of the particle from the trap centre and $\tau = \gamma/\kappa$ is the decay time. By the equipartition theorem, the trap stiffness is given by $\kappa = k_B T / \langle x^2 \rangle$, where k_B and T are the Boltzmann constant and the temperature respectively. The viscosity η can then be calculated from:²⁷

$$\eta = \frac{\tau k_B T}{6\pi a \langle x^2 \rangle} \quad (2)$$

In the frequency domain, a power spectrum analysis²⁸ can be used to calculate viscosity.¹⁴ In the usual case, where the motion of the particle is massively over-damped, the power spectral density, $S(\omega)$, is a Lorentzian of the form:

$$S(\omega) = \frac{k_B T}{3\pi\eta a(\omega^2 + \omega_0^2)} \quad (3)$$

where $\omega_0 = \kappa/\gamma$ is the corner frequency.

In principle both approaches should give the same answer. However, in practice, a number of parameters need to be set, ranging from the degree of thresholding of images from which the centre of mass of the trapped particle is determined, to the length of time over which data should be taken and subsequently windowed or averaged.²⁸ These parameters affect the viscosity

calculated from the two approaches in different ways. For example, the duration of the data and how one subdivides this into shorter lengths is important due to low-frequency drift in the apparent particle position (most likely due to thermal drift in the camera mounting and laser pointing stability).²⁴ We use the two approaches simultaneously in “real time” as a way of increasing our confidence in the fitting routines and the validity of our data.

In both cases, the uncertainty in the radii of the trapped particles (which typically have a 10% standard deviation) limits the accuracy to which the viscosity can be calculated. By trapping multiple particles at fixed points in a bulk fluid of known viscosity we can calculate the particle sizes and hence calibrate the viscosity measurements.

Faxén's correction

In microfluidic devices it is not possible for particles to be tens of radii away from any surfaces and changes in viscosity due to the presence of walls must also be taken into account. Strictly, the viscosity of the fluid is unchanged, but the modified drag coefficient does change the dynamics of the particle motion in an equivalent fashion. The change in viscosity due to walls can be precisely predicted by Faxén's correction^{29,30} and a particle moving perpendicular to the wall will experience a drag coefficient, γ^\perp , which is related to its unbounded drag coefficient, γ , by:

$$\frac{\gamma^\perp}{\gamma} = \frac{\eta^\perp}{\eta} = \left[1 - \frac{9}{8} \frac{a}{s} + \frac{1}{2} \left(\frac{a}{s} \right)^3 \right]^{-1} \quad (4)$$

where s is the distance from the wall to the mid-point of the particle. By trapping multiple particles at different distances from a microfluidic wall (see Fig. 3(a)), which can then be moved towards them, we can measure the viscosity at different positions in the channel and then use Faxén's correction to calibrate the size of the particles.

Note that when trapping particles close to a microfluidic wall some disruption of the illumination occurs which may affect the particle tracking accuracy. In order that the particles could be brought to within a radius of the wall without illumination problems larger, 5 μm , diameter particles were trapped (instead of 2 μm). Camera field-of-view constraints then meant that only three particles could be trapped in a line in order that the inter-particle distance would be large enough to have little effect on the measured viscosity.

Results and discussion

Multi-point viscosity measurements and particle calibration

In the initial experiment nine 2 μm silica particles were trapped in water at 27 °C. The particles were arranged in a rectangular grid 10 μm above the coverslip (see Fig. 2(a)) and far from any other boundaries. Particle positions were measured for 60 seconds and the viscosity for each particle was calculated from 5 second intervals of data using eqn (2) and assuming that each particle had a radius, a , of 1 μm .

As shown in Fig. 2(a), the measured viscosities are distributed around the predicted viscosity of 0.85×10^{-3} Pa.s. These variations are due to the expected deviations in particle size. For

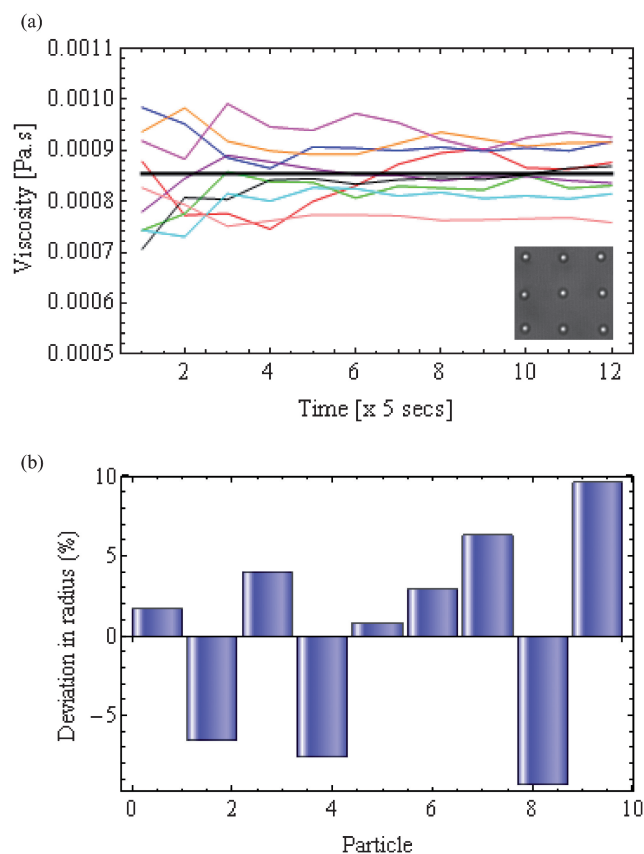


Fig. 2 (a) Viscosity calculated from the thermal motion of nine 2 μm silica particles in optical tweezers, trapped as shown in inset. Particle positions were measured for 60 seconds and the viscosity calculated from 5 second intervals of data. The black line shows the predicted viscosity for water at 27 °C. (b) Percentage deviation in particle size from $a = 1$ μm, calculated using the predicted viscosity.

a known viscosity, we can rearrange eqn (2) to calculate the actual radii of the particles. The percentage change from the expected value of $a = 1$ μm for each particle is shown in Fig. 2(b). As expected, all lie within the 10% standard deviation.

Particle calibration in microfluidic devices using Faxén's correction

To calibrate particle size in microfluidic devices, three 5 μm diameter silica particles were trapped in a sample of water within a polydimethylsiloxane (PDMS) microfluidic channel (25 μm deep) sealed with a cover slip (150 μm thick). The particles were initially trapped at different distances from a microfluidic wall (see Fig. 3(a) inset) which was then moved towards them, allowing the viscosity to be measured at different positions in the channel. Note that, as before, there may be small deviations in the sizes of the particles.

Fig. 3(a) shows the change in effective viscosity, $\Delta\eta^\perp/\eta$, for each of the particles and the predicted variation (solid line), calculated using Faxén's correction eqn (4), assuming the particles are all 5 μm in diameter. The general agreement between measured and predicted values is good. However, the agreement is improved, as shown in Fig. 3(b), if we take into account

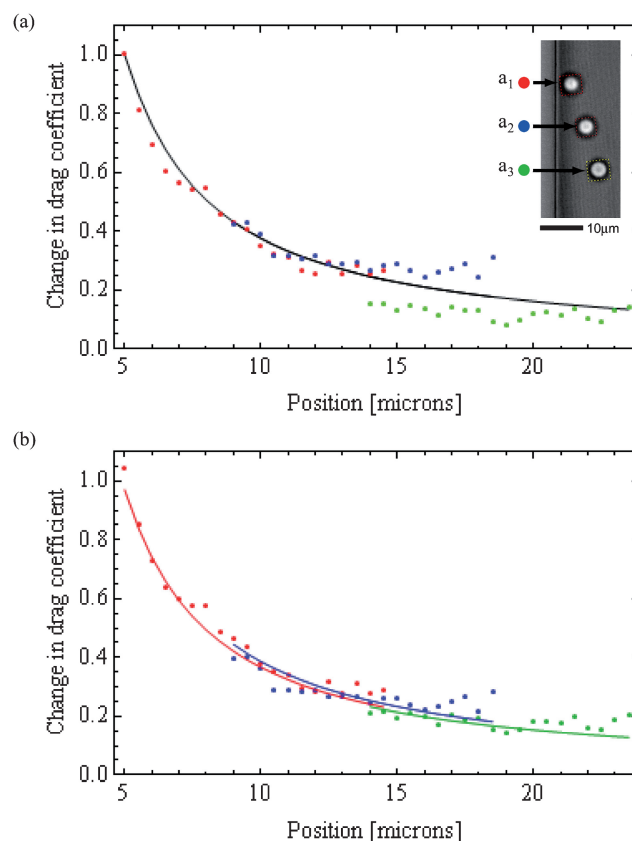


Fig. 3 (a) Measured fractional change in viscosity for three particles at different distances from the microfluidic wall (inset) assuming $a = 5$ μm. Solid line shows corresponding Faxén's correction. (b) Fractional change in viscosity and corresponding Faxén's correction for particles of radii $a_1 = 2.45$ μm, $a_2 = 2.55$ μm and $a_3 = 2.375$ μm.

deviations in particle size. In this case we find the radii of the particles to be: $a_1 = 2.45$ μm, $a_2 = 2.55$ μm and $a_3 = 2.375$ μm.

This method allows us to calibrate the size of particles within microfluidic devices. Once calibrated, we can then accurately measure viscosity as a function of position since we know that any further variations are due entirely to the geometry of the device.

Note that the drag force for a particle moving in the direction *parallel* to the wall will also increase as the particle-wall separation decreases. In this case, however, the results are significantly more affected by the hydrodynamic interactions between the particles. This was confirmed by calculating the parallel and perpendicular autocorrelation functions for an individual particle, first without any other particles nearby and then when another particle was trapped 4 radii away. For the direction perpendicular to the interparticle axis the change in the decay time due to the introduction of the second particle was less than 1%. For the direction parallel to the interparticle axis, however, the change was around 8%.

Conclusions

We have demonstrated that high-speed video imaging of the thermal motion of optically trapped beads results in a micro-probe which allows the measurement of the viscosity of a fluid at

multiple points within a microfluidic device. The capability of holographic optical tweezers to manipulate the spheres enables the probe to be positioned accurately within a microfluidic channel, thus allowing spatial and temporal variations in viscosity to be investigated.

As an example of the potential of the technique, arrays of particles were trapped and tracked. The simultaneous tracking of multiple particles at fixed positions in bulk fluid allowed small variations in particle size to be calculated and the viscosity measurements calibrated. In microfluidic devices, where there are always effects due to boundaries, we used the well-known Faxén's correction to again calibrate the particles. We propose that the calibrated microprobe could be used in colloidal systems or biological samples to allow multi-point rheology measurements. This opens the potential for monitoring the change in viscosity under different conditions: for example, change in temperature, chemical reactions, cell diffusion. Alternatively, the effective change in viscosity due to the presence of boundaries could be used as a means to map the structure of microfluidic devices.

References

- 1 M. P. MacDonald, G. C. Spalding and K. Dholakia, *Nature*, 2003, **425**, 421.
- 2 R. W. Applegate, Jr., J. Squier, T. Vested, J. Oakey and D. W. M. Marr, *Opt. Express*, 2004, **12**, 4390.
- 3 J. Leach, H. Mushfique, R. di Leonardo, M. Padgett and J. Cooper, *Lab Chip*, 2006, **6**, 735.
- 4 H. Mushfique, J. Leach, H. Yin, R. Di Leonardo, M. J. Padgett and J. M. Cooper, *Anal. Chem.*, 2008, **80**, 4237.
- 5 H. Mushfique, J. Leach, R. Di Leonardo, M. J. Padgett and J. M. Cooper, *Proc. IMechE Vol. 222 Part C: J. Mechanical Engineering Science*, 2008, **829**, 37.
- 6 P. Cicuta and A. M. Donald, *Soft Matter*, 2007, **3**, 1449.
- 7 M. A. K. Williams, R. R. Vincent, D. N. Pinder and Y. Hemar, *J. Non-Newton. Fluid Mech.*, 2008, **149**, 63.
- 8 T. Okajima and H. Tokumoto, *Nihon Reorogi Gakkaishi*, 2008, **36**, 81.
- 9 C. Wilhelm, *Phys. Rev. Lett.*, 2008, **101**, 028101.
- 10 A. R. Bausch, W. Moller and E. Sackmann, *Biophys. J.*, 1999, **76**, 573.
- 11 R. R. Brau, J. M. Ferrer, H. Lee, C. E. Castro, B. K. Tam, P. B. Tarsa, P. Matsudaira, M. C. Boyce, R. D. Kamm and M. J. Lang, *J. Opt. A: Pure Appl. Opt.*, 2007, **9**, S103.
- 12 M. Fischer and K. Berg-Sorensen, *J. Opt. A: Pure Appl. Opt.*, 2007, **9**, S239.
- 13 M. Atakhorrami, J. I. Sulkowska, K. M. Addas, G. H. Koenderink, J. X. Tang, A. J. Levine, F. C. MacKintosh and C. F. Schmidt, *Phys. Rev. E*, 2006, **73**, 061501.
- 14 G. Pesce, A. Sasso and S. Fusco, *Rev. Sci. Instrum.*, 2005, **76**, 115105.
- 15 A. Buosciolo, G. Pesce and A. Sasso, *Opt. Commun.*, 2004, **230**, 357.
- 16 A. Rohrbach, C. Tischer, D. Neumayer, E.-L. Florin and E. H. K. Stelzer, *Rev. Sci. Instrum.*, 2004, **75**, 2197.
- 17 B. A. Nemet, Y. Shabtai and M. Cronin-Golomb, *Opt. Lett.*, 2002, **27**, 264.
- 18 R. Lugowski, B. Kolodziejczyk and Y. Kawata, *Opt. Commun.*, 2002, **202**, 1.
- 19 S. J. Parkin, G. Knoner, T. A. Nieminen, N. R. Heckenberg and H. Rubinsztein-Dunlop, *Phys. Rev. E*, 2007, **76**, 041507.
- 20 D. Weihs, T. G. Mason and M. A. Teitell, *Biophys. J.*, 2006, **91**, 4296.
- 21 J. S. Meiners and S. Quake, *Phys. Rev. Lett.*, 1999, **82**, 2211.
- 22 K. Visscher, S. P. Gross and S. M. Block, *IEEE J. Sel. Top. Quantum Electron.*, 1996, **2**, 1066.
- 23 S. Keen, J. Leach, G. Gibson and M. J. Padgett, *J. Opt. A: Pure Appl. Opt.*, 2007, **9**, 264.
- 24 G. M. Gibson, J. Leach, S. Keen, A. J. Wright and M. J. Padgett, *Opt. Express*, 2008, **16**, 14561.
- 25 R. Di Leonardo, S. Keen, J. Leach, C. D. Saunter, G. D. Love, G. Ruocco and M. J. Padgett, *Phys. Rev. E*, 2007, **76**, 061402.
- 26 C. D. Saunter, G. D. Love, M. Johns and J. Holmes, *Proc. SPIE*, 2005, **6018**, 429.
- 27 A. Pralle, E. L. Florin, E. H. K. Stelzer and J. K. H. Horber, *Appl. Phys. A: Mater*, 1998, **66**, S71.
- 28 K. Berg-Sørensen and H. Flyvbjerg, *Rev. Sci. Instrum.*, 2004, **75**, 594.
- 29 H. Faxen, *Annalen der Physik*, 1922, **4**, 89.
- 30 J. Happel and H. Brenner, *Low Reynolds number hydrodynamics*, Kluwer Academic Publishers, 1983.