Quantum noise in optical tweezers

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Abstract. Quantum enhanced sensitivity in optical tweezers based particle tracking was recently demonstrated. This has provided the necessary tool for quantum metrology to play an important role in biological measurements. Here we introduce the basic theory relevant to such optical tweezers experiments, and overview the significance of sub-shot noise limited sensitivity to practical experiments. In particular, biophysical experiments are subject to optical power constraints, which therefore limits the absolute sensitivity which is classically achievable. Quantum enhanced particle tracking can overcome this limit, and is therefore likely to play an important role in such biophysical experiments in the near future.

1. Introduction

The development of optical tweezers made it possible to manipulate and measure the motion of single microscopic particles [1]. This revolutionized the field of biophysics by allowing the study of single-molecule kinetics, without need for ensemble averaging [2, 3]. For instance, this advance enabled observation of steps in the motion of the protein motor kinesin [4] and the muscle protein myosin [5]. It also allows direct measurement of the stretching and folding properties of DNA and RNA [3, 6, 7], the strain on an enzyme during catalysis [6], and the dynamics of virus-host coupling [8].

After decades of research, optical tweezers continue to advance technologically, which allows observation of an ever-increasing range of biophysical phenomena [9]. With these advances, leading experiments are approaching the quantum limit on sensitivity, such that further improvements will soon require integration of quantum correlated light [10]. Recently, the first optical tweezers experiment with sensitivity beyond the quantum shot noise limit was demonstrated [11]. Here we briefly overview the significance and outlook of such quantum techniques in optical tweezers.

2. Benefit of quantum enhanced sensitivity

In any optical measurement, quantum noise sets a fundamental limit on the achievable sensitivity [12, 13]. This limit can only be surpassed if quantum correlations between photons are used to suppress the quantum noise, such that more more information is extracted per photon [14, 15]. Hence, quantum metrology allows high sensitivity measurements to proceed with a lower light intensity than classically possible [16, 17], and in the presence of optical power constraints, allows sensitivity which can outperform any classical competitor. Of the quantum technologies available, squeezed light is the most promising technology for practical measurements, as it is compatible with high photon flux and offers the best possible performance in the presence of optical losses [15]. In most experiments, however, it is easier to simply increase the power than to integrate quantum correlated light. The only practical application of quantum metrology so far has been the use of squeezed light in gravity wave observatories, where the optical power already operates near the damage threshold of the mirrors [18]. Another frontier where

quantum metrology could be important is in biological measurements [16, 17, 19], where observation of nanoscale features classically requires a high photon flux that also introduces disruptive photochemical interactions [20, 21].

In biological measurements, any incident light interacts strongly with living cells. Laser heating increases the temperature and induces temperature gradients, which can cause vast changes to the cellular respiration and division, and can also destroy the cell [20, 22]. This heating effect is minimized by using light in the visible spectrum, where water is highly transparent. However, the light also directly writes chemical changes into living cells by producing reactive oxygen species [23]. It is known that the cell division rate is substantially changed by illumination [24], as is enzyme activity [25] and many other processes. Photochemical interactions are particularly well studied in nerve cells, where they allow controlled neural stimulation [26]. When too much light is used, these photochemical effects are fatal for the cells [21]. The damaging chemical effects are dramatically reduced by using infra-red laser beams [2]. For optical tweezers experiments, 1064 nm lasers are a very common choice, as these lasers are low-noise and this wavelength approximately minimizes the collective photochemical and photothermal cellular damage [22, 2]. However, while minimizing the damage can make the light non-fatal to the cell, it still perturbs a wide range of cell functions, which can influence the biological parameter under study.

3. Shot-noise in optical tweezers

In many optical tweezers experiments, a biological molecule exerts a force on a trapped particle, and the particle position is measured to determine the biomolecular force. Since such experiments are performed in an aqueous environment at room temperature, the desired force competes with the stochastic thermal force on the particle. Force resolution is therefore limited by both the absolute sensitivity of the apparatus and the background of thermal forces. These experiments are typically limited by detection drifts at sub-Hz frequencies, thermal noise over the bulk of the detection range, and are shot-noise limited only above a few tens of kHz [27]. While providing additional measurement bandwidth, sub-shot noise sensitivity would not generally improve the signal-to-noise ratio at biologically relevant frequencies in the Hz range. Additionally, such experiments rely on optical forces which scale with the light intensity, such that quantum enhanced sensitivity alone does not necessarily allow the use of lower photon flux.

Although thermal fluctuations can limit the resolution of non-thermal forces, they also provide a method to probe the mechanical nature of the fluid surrounding the particle. The thermal motion of a particle is determined both by the thermal force and the mechanical properties of its surrounding medium. Hence, particle tracking allows characterization of the viscosity and elasticity of the surrounding fluid [28, 29], as well as the hydrodynamic properties of the system which can couple the particle motion to surrounding walls [30, 31] and other particles [32], and also introduces non-Markovian memory to the viscous damping [33, 34, 35]. These characteristics are all extremely important in cellular systems, since they influence all chemical processes which are mediated by thermal motion. The sensitivity of such experiments is limited by detection noise at all frequencies, so quantum enhanced sensitivity allows characterization of such effects with improved bandwidth and precision. Furthermore, optical forces are not typically required in such experiments, so enhanced sensitivity allows reduced photon flux and a corresponding reduction in photochemical interactions.

4. Optical trapping theory

Optical manipulation in optical tweezers is based on the interaction between a tightly focused laser beam and a small particle (see Fig. 1a). The momentum of the optical field changes as the particle scatters light, which thus imparts a force on the particle. The resulting force is simple to evaluate if the trapped particle is approximated as a point dipole [36]. In this case, the optical field $\mathbf{E}$ induces an oscillating dipole with polarization $\mathbf{p} = \alpha \mathbf{E}$, where α is the polarizability. Neglecting components at optical frequencies, the optical gradient force on the dipole is given by

$$\mathbf{F}_{\text{grad}} = (\mathbf{p} \cdot \triangledown)\, \mathbf{E} = \frac{1}{2}\alpha \triangledown E^2, \tag{1}$$
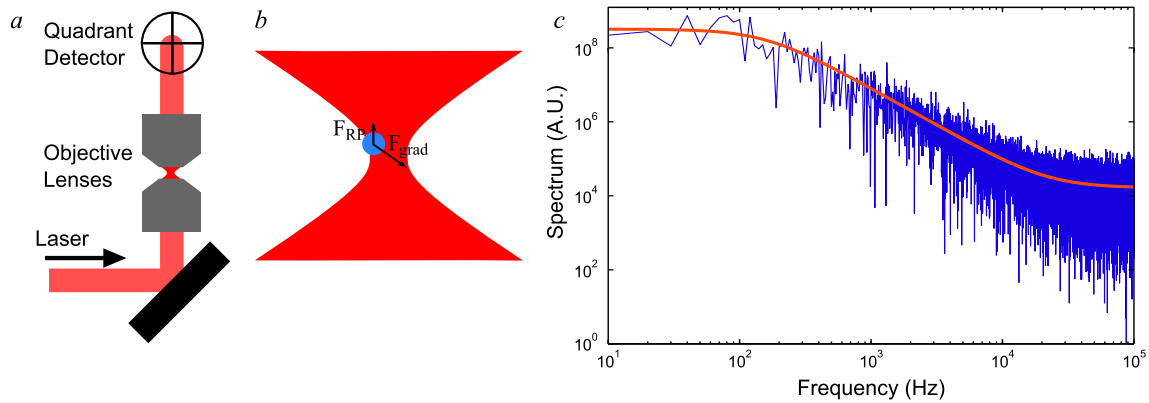
Figure 1. (*a*) The most basic elements of an optical tweezers experiment. Laser light is focused to a point to trap particles, and then collected for measurement. In most cases, this measurement occurs on a quadrant detector as shown here. (*b*) The particle is trapped near the focus of the beam, and is subject to two forces; a gradient force F_{grad}, which points toward the intensity maxima (see Eq. 1), and radiation pressure F_{RP} which pushes in the direction of light propagation (see Eq. 2). (*c*) A spectra as is typical for trapped Brownian motion. The expectation value is given by a Lorentzian mechanical profile (Eq. 5) along with a noise floor.

where the vector identity $\nabla E^2 = 2\left(\mathbf{E}\cdot\nabla\right)\mathbf{E} + 2\mathbf{E}\times(\nabla\times\mathbf{E})$ has been used, along with $\nabla\times\mathbf{E} = 0$ from Maxwell's equations [36]. The force described in Eq. 1 points toward maxima in intensity for particles with positive polarizability, or equivalently, a higher refractive index than the surrounding medium. In addition to this force, the radiation pressure of the trapping laser also pushes the particle along the optical axis $\hat{z}$, which tends to destabilize the trap (see Fig. 1*b*). This force is given by

$$\mathbf{F}_{RP} = \frac{k^4\alpha^2}{12\pi n^2\epsilon_0}E^2\hat{z}, \tag{2}$$

where k is the wavenumber, n the refractive index of the surrounding medium, and ϵ_0 the vacuum permittivity [36]. To enable stable trapping, the trapping force must dominate the radiation pressure. To achieve this, the intensity gradient is maximized by focusing the laser to the smallest spot possible. Additionally, the scattering rate is important because the gradient force scales as α while the radiation pressure scales as α^2. The scattering rate therefore should not be vanishingly small, as this produces minimal optical forces, but it also cannot be very large, as this produces large radiation pressure forces which destabilize the optical trap. Both the gradient and radiation pressure optical forces scale linearly with the light intensity, so there is no upper limit on the optical power which can be used to trap particles.

When an optical force is exerted on the particle, the momentum of the light changes such that the laser beam is deflected. Thus, measurement of the direction of the transmitted light provides a simple and effective method to measure the particle position. This measurement is typically performed by collecting the transmitted light with an objective lens and directing it onto a quadrant detector [37].

5. Trapped Brownian motion spectra
Here we derive the expected thermal trajectory $x(t)$ of a trapped particle in the simple case of a purely viscous medium with no elasticity or hydrodynamic interactions. In this case, the equation of motion along one dimension is given by

$$m\ddot{x}(t) = -\gamma\dot{x}(t) - k_{opt}x(t) + F_T, \tag{3}$$

for a particle mass m, friction coefficient γ, a harmonic optical force $-k_{\text{opt}}x(t)$, and a fluctuating thermal force $F_T = (2k_BT\gamma)^{1/2}\xi(t)$, with T the temperature and k_B Boltzmann's constant [38]. The fluctuating function has the properties $\langle\xi(t)\rangle = 0$ and $\langle\xi(t)\xi(t')\rangle = \delta(t - t')$. By taking the Fourier transform of Eq. 3 and rearranging, we find that

$$x(\omega) = \frac{(2k_BT\gamma)^{1/2}}{-m\omega^2 + i\omega\gamma + k_{\text{opt}}}\xi(\omega). \tag{4}$$

From this we can see that the inertial term $m\ddot{x}(t)$ is negligible at frequencies far below the rate at which the kinetic energy is lost through friction, $\omega \ll \gamma/m$. The friction is given by Stokes' law as $\gamma = 6\pi\eta R$, where R is the particle radius and η is the fluid viscosity. The inertial contribution is measurable only at very short timescales [39, 40]; for instance, a 1 μm diameter silica microsphere in water has $m/\gamma = 120$ ns. This term is therefore typically neglected [38], with the resulting power spectra of trapped Brownian motion given by

$$\langle|x(\omega)|^2\rangle = \frac{2k_BT/\gamma}{\omega^2 + \omega_c^2}, \tag{5}$$

where we have used $\langle|\xi(\omega)^2|\rangle = 1$ and introduced the corner frequency $\omega_c \equiv k_{\text{opt}}/\gamma$. Measurements of this mechanical spectra will also include a detection noise floor, as shown in Fig. 1c. This Lorentzian spectral shape is characteristic of trapped Brownian motion. In many regimes, particularly in biological systems, the spectral shape is altered by fluid elasticity or hydrodynamic interactions. These effects can be characterized by determining the profile of the thermal motion. If squeezed light is used, the minimum resolvable displacement is smaller and the profile of thermal motion can be characterized more precisely and over a wider bandwidth. Alternatively, equivalent sensitivity is achievable with reduced light intensity, which therefore reduces damage to the specimen.

6. Status of the field

In Ref. [11], the quantum shot noise limit was overcome in optical tweezers based particle tracking, and then quantum enhanced sensitivity applied in measurements of living systems. In that work, a microparticle tracking technique was developed which is both compatible with non-classical light and immune to low frequency optical and electronic noise which would otherwise dominate shot-noise at the Hz–kHz frequencies of interest [41]. For the first time, this provided the tools necessary to perform a broad range of quantum enhanced measurements in biology.

This apparatus was then applied to tracking the thermal motion of naturally occurring lipid granules within *Saccharomyces cerevisiae* yeast cells, with amplitude squeezed light yielding a 2.4 dB enhancement in displacement sensitivity. Since the cellular cytoplasm is crowded with large molecules, polymer networks, and various other organelles, the thermal motion of embedded particles differs from the Brownian motion described above. This thermal motion was characterized with quantum enhanced sensitivity, thus allowing enhanced characterization of the mechanical properties of the cellular cytoplasm, and allowing dynamic changes in these properties to be measured with enhanced temporal resolution.

Following this demonstration, the biological experiment was extended to spatially resolved sub-diffraction limited quantum imaging of the cytoplasmic structure [42]. Spatial variations in the local mechanical properties of the cellular cytoplasm were sampled by lipid granules as they diffused thermally through the cells. These spatial structures were resolved at length scales down to 10 nm, far below the diffraction limit. In this case the use of quantum correlated light enhanced the spatial resolution by 14%. If combined with state-of-the-art squeezed light with over 10 dB of measured squeezing [43], this technique is predicted to allow up to an order of magnitude improvement in resolution over similar classical imaging techniques.

These experiments firmly demonstrated that sub-shot noise limited biological measurements are possible in optical tweezers. However, this was demonstrated in an apparatus which used microscope objectives with a relatively low numerical aperture (NA) of 0.4, such that the collection angle was

smaller than is typically used in similar classical experiments. Although the absolute sensitivity was comparable to that achieved in similar classical experiments [44], the experiment was not classically optimal, and could be improved substantially by integrating higher NA objectives. However, microscope objectives are generally designed for operation in the visible, while the optical tweezers experiment were performed at 1064 nm. At this wavelength, most commercially available objectives have around 50% loss [2], which would vastly degrade the squeezed states of light. To improve upon the initial experiments, microscope objectives are required which combine high transmission with high NA. Also, the initial experiments also only provided one-dimensional particle tracking, while many applications require tracking in three dimensions. Future experiments would benefit from combining standard 3D particle tracking techniques [45] with multimode squeezed states [16].

Given the improvements mentioned above, quantum enhanced particle tracking can be expected to perform far better in the near future. Classical particle tracking techniques, however, have limited room for improvement as they are already approaching quantum limited sensitivity [10]. It is reasonable to expect that optical tweezers using squeezed light will soon outperform classical experiments, and lead the field. Considering the rapid rate of technological progress, one may even consider it implausible that in decades to come, particle tracking microscopy should remain confined by the shot-noise limit.

7. Conclusion

Optical tweezers are a powerful tool for biophysical studies which are approaching the limits of classical technology. The quantum technology of squeezed light provides a route to further improved sensitivity. Initial demonstrations have proven that quantum enhanced particle tracking is possible and practical. With further development, quantum enhanced particle tracking is likely to lead the field and enable unprecedented levels of precision in practical biological experiments.

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