Self-induced back action actuated nanopore electrophoresis (SANE)

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Received 20 April 2018, revised 23 July 2018
Accepted for publication 3 August 2018
Published 21 August 2018

Abstract
We present a novel method to trap nanoparticles in double nanohole (DNH) nanoapertures integrated on top of solid-state nanopores (ssNP). The nanoparticles were propelled by an electrophoretic force from the cis towards the trans side of the nanopore but were trapped in the process when they reached the vicinity of the DNH-ssNP interface. The self-induced back action (SIBA) plasmonic force existing between the tips of the DNH opposed the electrophoretic force and enabled simultaneous optical and electrical sensing of a single nanoparticle for seconds. The novel SIBA actuated nanopore electrophoresis (SANE) sensor was fabricated using two-beam GFIS FIB. Firstly, Ne FIB milling was used to create the DNH features and was combined with end pointing to stop milling at the metal-dielectric interface. Subsequently, He FIB was used to drill a 25 nm nanopore through the center of the DNH. Proof of principle experiments to demonstrate the potential utility of the SANE sensor were performed with 20 nm silica and Au nanoparticles. The addition of optical trapping to electrical sensing extended translocation times by four orders of magnitude. The extended electrical measurement times revealed newly observed high frequency charge transients that were attributed to bobbing of the nanoparticle driven by the competing optical and electrical forces. Frequency analysis of this bobbing behavior hinted at the possibility of distinguishing single from multi-particle trapping events. We also discuss how SANE sensor measurement characteristics differ between silica and Au nanoparticles due to differences in their physical properties and how to estimate the charge around a nanoparticle. These measurements show promise for the SANE sensor as an enabling tool for selective detection of biomolecules and quantification of their interactions.

Keywords: solid-state nanopores, dual nanoholes, nanopore trapping, nanoparticles, nanopore sensing, dual modality nanoparticle sensing

(Some figures may appear in colour only in the online journal)

Introduction

Nanopore biosensors utilize resistive pulse sensing of ion currents to detect biological analytes. Translocation of the analyte through a nanometer aperture is driven by the applied bias [1–3]. This technique has been used to detect DNA [4–7], proteins [8–14], miRNA [15–18] and other bio-
analytes [19]. It has also been proposed as an affordable DNA sequencing tool [20, 21]. Although nanopores have been made from biological membranes [22, 23], solid state nanopores (ssNPs) have been widely used as a more robust alternative [24]. SsNPs are fabricated in silicon chips with suspended dielectric membranes in which the nanopores are etched or milled [25–28]. Over the past two decades, numerous enhancements in nanopore technology have been reported for biosensing, including surface attachment to nanopore walls [7, 16], nanopore arrays [29], optically enhanced nanopores [30] and embedded tunneling electrode nanopores [31]. These technologies were developed to address challenges relating to low throughput, high sensor noise, lack of self-referencing, and high pore translocation speeds [3, 32].

To enhance nanopore sensing further, attempts have been made to combine it with optical sensing. Optical enhancement of nanopore sensing has garnered much interest since Keyser et al [33, 34] used a tightly focused laser on a DNA-tethered micrometer bead translocating through an ssNP. Optical forces acted as a tweezer for controlling bead translocation thus enabling study of biomolecular interactions inside the nanopore by force spectroscopy. However, tweezeet cannot be extended to sub-diffraction limit nanoparticles directly due to the exponential reduction in optical trapping force with size. Surface charge control by optical excitation has also been used as an alternative approach employing electroosmotic flow to slow down the translocation of analytes through the nanopores [35]. Nevertheless, this technique only works in small nanopores due to Debye length restriction and requires fluorescent labeling for optical detection. Jonsson et al [36] used gold bowtie plasmonic nanoantennas to create optical field enhancement in the nanogap over the mouth of a TEM-milled silicon nitride nanopore. The plasmonic focusing led to increased ionic conductance due to localized heating but did not slow down translocation through the nanopore. They also reported photoresitive switching in plasmonic nanopores [37], which was attributed to plasmon-induced gaseous air bubble formation at the nanopore mouth. Recently, Meller et al [38] reported a plasmonic nanopore with a circular gold nanowell on the trans side of the nanopore. This resulted in dual-mode detection of nanopore current and plasmonically excited fluorescence from the labeled DNA, without any control on nanopore translocation speed.

Nanoperture-focused plasmons in metallic films are a potentially enabling technology for controlling analyte translocation through a nanopore, but this has been explored very little to date. Optical trapping at low laser powers can be attained in the immediate vicinity of metallic nanopapertures through a self-induced back action (SIBA) mechanism [39]. In SIBA, when a dielectric nanoparticle has a slightly different refractive index than its surrounding medium a photon-mediated feedback force is actuated due to conservation of momentum against diffusion forces near the nanoperture. The resulting coupling of light to the far field via the dielectric nanoparticle results in increased light transmission through the plasmonic nanoperture and therefore enables label-free detection [40]. Double nanopore (DNH) nanopaperes have been reported as SIBA-mediated optical traps by Gordon et al for high local field enhancement at the intersection of the nanoholes [41]. The Gordon group has reported a series of studies on the design characteristics of the DNH structure [42–44] and their use in many applications, including the trapping of nanoparticles [45–47] and single protein molecules [48–51].

Here we report nanofabrication and proof of principle studies for a DNH-ssNP sensor enabling simultaneous SIBA-mediated optical trapping by the DNH and electrophoresis through the ssNP. We name this a SIBA actuated nanopore electrophoresis (SANE) sensor. The nanopore is milled between the tips of the DNH where the highest plasmonic energy is focused, resulting in trapping of the nanoparticle due to dielectric loading at the mouth of the nanopore. The nanoparticle translocates through the nanopore after it escapes trapping and yields the characteristic drop in ionic current due to pore blockage. Two types of focused ion beam (FIB) milling enabled nanofabrication of the DNH structure in an Au layer deposited on top of a thin silicon nitride layer without damaging it. Furthermore, the DNH structure is known to dissipate heat very effectively with minimal temperature increases at optical trapping powers [52]. In proof of principle experiments, we show that the DNH-nanopore structure trapped 20 nm nanoparticles made of silica or Au for several seconds, while enabling their concurrent electrical sensing during the same time interval. The SANE sensor controlled the nanoparticle translocation through the nanopore, which extended the duration of electrical sensing by up to four orders of magnitude compared to nanopore sensing alone. The extended electrical measurement times revealed a newly observed high frequency charge transient phenomenon related to occupancy of the optical trap by one or more nanoparticles. Finally, we discuss how upon sensor calibration, these bimodal measurements could be used to estimate the total charge around a nanoparticle and how SANE sensor measurements characteristics differ between silica and Au nanoparticles due to differences in their physical properties.

Materials and methods

Dual nanohole—nanopore chip fabrication

The fabrication was done on double side polished, (100) orientation 4 inch silicon. Wet oxidation was done to grow 500 nm SiO$_2$ followed by a 60 nm LPCVD non-stoichiometric low stress silicon nitride (Si$_3$N$_x$). For each wafer, individual 15 mm × 15 mm square chips were created with one side patterned using S1813 photoresist with a dark field image and etched backside mask. The 786 μm size in the center. The 786 μm square etch windows were opened in Si$_3$N$_x$ using DRIE to etch through its entire 60 nm layer thickness and then a 6.1 buffer of hydrofluoric acid (BHF) solution was used to etch the SiO$_2$ to reveal the bare silicon (figure 1). The wafers were placed in 22% tetramethylammonium hydroxide (TMAH) solution at 90 °C to anisotropically etch the wafer all the way to the front side.
revealing the 100 μm square SiO2/SiN membranes at the other side, henceforth called the front side. The SiO2 was a sacrificial layer to protect the membrane during further processing and was etched away at the last step of the chip fabrication. The wafers were cleaned in Piranha solution and inspected under an optical microscope to confirm the design parameters of the anisotropic etch. E-beam evaporation was used to deposit 5 nm of Cr as the adhesion layer on which 100 nm of Au was subsequently deposited on the front side of the wafer on top of the suspended SiN membranes. The S1813 positive resist was used to coat the front side of the wafer to pattern four diagonal FIB alignment markers in Au. A backside aligner (EVG 620) was used to align the dark field second mask and to expose the front side while aligned to the backside patterns. Au and Cr were wet etched using commercially available wet etchants (Sigma Aldrich). The etched and cleaned wafers were inspected under an optical microscope for proper placement of FIB alignment markers on the suspended SiN membrane from the front side and the back side (figure 1(d)). The front side of the wafers was coated in thick S1813 photoresist and hard baked. The individual chips were diced and separated from each other. The sacrificial SiO2 layer beneath the SiN was then wet etched from the back side using 6:1 BHF for 8 min and the photoresist layer on the front side was removed in acetone. The individual chips were dried and inspected under an optical microscope to confirm the integrity of the membrane and of the alignment markers on it. The membrane area now consisted of a 50 nm thick SiN layer with a 5 nm Cr/100 nm Au metal stack (figure 1(c)). These 15 mm × 15 mm individual chips were now ready for FIB milling (figure 1(d)).

The FIB milling on these individual chips was done using a mix of Ne and He GFIS focused ion beams (Carl Zeiss, ORION NanoFab, Peabody, MA). The Ga FIB or TEM...
beam could not be used due to the complex requirements of the dual layer design (figure 1(c)). The dumbbell shape of the DNH was milled into the Au film (critical dimension = 25 nm) and the milling had to be stopped at the metal/dielectric interface. The DNH shape was designed to have 15%–20% tapered edges (figure 1(f)), in line with a prior feature optimization study [43], converging towards the metal/dielectric interface. A Ne ion beam was used to mill the DNH shape in the Au/Cr metal stack (500 mA beam current, 25 kV acceleration voltage, 10 μm aperture and 8.5 mm working distance). A beam dose of 0.2–0.225 nC μm⁻² was determined to be optimum to reach the Au/Cr–SiNₓ interface. The secondary electron current was used in the nanopatterning visualization engine to determine when the dielectric interface was reached to terminate the Ne FIB milling. At that point, the beam was switched to He ions and a 25 nm circle was drilled through the suspended SiNₓ membrane in the middle of the DNH shape (2 pA beam current, 30 kV acceleration voltage with 150 nC μm⁻² dose, 10 μm aperture and 8.5 mm working distance). He FIB nanopore drilling through the SiNₓ film was stopped when the secondary electron current suddenly decreased to almost zero (figure 1(e)).

### Experimental setup

The beam from an 820 nm laser diode (L820P200, Thorlabs) was collimated to a 2 mm diameter and circularly polarized through a QWP (WPQ05M, Thorlabs), followed by a Glan-Thompson linear polarizer (GTH10M, Thorlabs) for controlling the polarization of light incident on the chip. The light then passed through a tunable HWP (WPH05M, Thorlabs) to make the direction of polarization perpendicular to the DNH’s long axis to excite maximally wedge plasmons for trapping [46]. A downstream 4x beam expander (Newport) was used in combination with an 8 mm circular aperture (ID.1.0, Newport) to make the intensity profile of the cylindrical beam flatter. The beam then went through a periscope and into the back aperture of a 63x oil immersion objective lens and focused onto the front Au side of the SANE chip. The objective’s focal spot was aligned with the DNH center by adjusting the piezoelectric stage controls until polarized light transmission was maximized. Light transmission through the FIB alignment markers was used as a first coarse step to find the DNH on the chip. The light transmitted through the chip’s center and any leakage light scattering through alignment markers was collected by a condenser lens and focused onto a photodiode (PDA36A, Thorlabs).

Standard soft lithography techniques were used for fabrication of a flow cell that could house the SANE sensor chip with a cis and a trans chamber for the nanopore and to provide optical access to the DNH. The flow cell was made from polydimethylsiloxane (PDMS) mixed in a 10:1 ratio of polymer to initiator as prescribed by the manufacturer (Dow Corning). This mixture was degassed to remove air bubbles and subsequent fabrication was performed in three steps. In the first step, a flat PDMS slab of 2 mm thickness was created by adding the bubble-free mixture to a cavity created on a polished side of a silicon wafer and curing it on a hotplate at 100 °C for 10 min. After peeling this PDMS slab, a pattern was cut into it consisting of a 10 mm square opening at the center and a 2 mm wide rectangular channel connecting it to another 10 mm square opening towards the end of the slab (figure 2(a)). The PDMS slab was bonded onto a 3 in × 2 in glass slide using oxygen plasma (Electro-Technic). In the second step, the SANE sensor was placed over the central square opening using a double-sided tape (3M) sealing the square opening underneath and creating the trans chamber of
the nanopore. Another flat PDMS slab of 3 mm thickness was created using the same procedure and a hollow rectangle was cut and placed over the square opening at the end of the slab using double-sided tape (figure 2(b)). This secondary chamber acted as a reservoir holding enough ionic solution to keep the bottom of the nanopore always wet. The rectangular channel connecting these openings was also covered with the same double-sided tape to completely seal the flow path. In the third step, a 1 inch coverslip of 170 μm thickness (VWR) was plasma-bonded onto a very thin PDMS layer of 200 μm thickness, with a square opening of 10 mm cut through the center of this layer to form a cis chamber over the SANE sensor. An additional 1 mm wide gap was cut at the edge of this PDMS layer to allow introduction of analyte into the cis chamber along with the cis chamber electrode. Subsequently, the trans side was gently filled with ionic solution using Teflon tubing connected to a syringe up to the brim of the 3 mm PDMS reservoir wall. To complete the electrical path, the trans side electrode was introduced through the reservoir wall and pushed along the rectangular channel until its tip was located right below the sensor. Finally, the secondary reservoir was topped with a coverslip to confine the ionic solution within the flow cell. This flow cell was attached to a holder and the assembly was screwed onto a piezo-controlled translation stage (MDT6938, Thorlabs) immediately below the objective lens. The prepared PDMS flow cell with the SANE chip is shown in figure 2(b).

To implement electrical sensing the cis and trans chamber Ag/AgCl electrodes were attached to the Axon Headstage (CV 203BU) of the Axon Axopatch 200B patch clamp in voltage clamp mode. A custom-made Faraday cage using copper wire mesh (PSY405, Thorlabs) was installed to cover the entire optical assembly and shield the PDMS flow cell from low-frequency electromagnetic noise during highly sensitive patch clamp ionic current recordings. Subsequently, the nanopore was first tested for wetting. If the nanopore was blocked, an alternating ±5 volts square wave was applied to the two electrodes for 60 s to unblock the nanopore through electrophoretic pressure. After wetting, the trans side reservoir of the PDMS flow cell was filled with 7.4 pH 1 M KCl solution and the cis reservoir was filled with 200 pM solution of 20 ± 4 nm silica nanoparticles (MELO010, NanoComposix, zeta potential = −40 mV) suspended in the same solution. Au nanoparticles (C11-20-TM-DIH-50, Nanopartz, zeta potential = −15 mV) of the same size and concentration as silica were also used to fill the cis reservoir in separate experiments. A 2 mm thick methyl polymer coating on the Au nanoparticles helped maintain their stability in KCl solution. The PDMS flow cell was attached to the piezo-controlled stage using screws and the laser beam was aligned to the DNH center as described above. A 250 mV bias was applied through the patch clamp in voltage clamp mode. The photodiode and Axopatch 200B signals were both sent through an Axon Digidata 1440 ADC to a PC for recording and data analysis in Axon Clampfit 10.6 software. The complete experimental setup schematic is shown in figure 2(c). In subsequent data analyses the coefficient of variation was defined as the ratio of standard deviation to the signal mean value and the ionic current translocation time and signal to noise ratio (SNR) during translocation were defined as described previously [53, 54].

Results

Figure 3 shows the first proof of principle measurements with the SANE sensor that demonstrate multi-second trapping of a single 20 nm silica nanoparticle with concurrent electrophoretic measurements through the nanopore at the center of the DNH. When the 20 nm nanoparticle was trapped by the DNH, a step increase of 11% in optical transmission was seen due to dielectric loading of the trap (figure 3(a)). Concurrently, high frequency transients were seen in the raw ionic current (figure 3(b)), registering a positive charge peak of 38 nA which was 19 times higher than the baseline nanopore current. These ionic current oscillations were likely caused by axial nanoparticle oscillations, which we will henceforth refer to as ‘bobbing’, in the nanopore vicinity due to opposing optical and electrical forces. It is noteworthy that optical trapping enabled ionic current sensing of the nanoparticle for a few seconds, which is about four orders of magnitude longer than the typical current sensing times for nanoparticle translocation events through a nanopore alone.

The recorded raw ionic current was also filtered with a 20 Hz, low pass 8-pole Bessel filter in Axon Clampfit 10.6 to enable visualization of the nanoparticle movement effects on low frequency ionic current. A distinct positive peak of 26.2 ms was registered during charged nanoparticle entry in the DNH, when the trapping started (figure 3(a), Region A, green curve in third row). The nanoparticle was bobbing inside the DNH trap for about 2.15 s (figure 3(a), Region B) and the low-pass filtered ionic signal did not show any appreciable changes during that time. Towards the end of the trapping period, the amplitude of high frequency transients increased concurrently with a slight increase in optical transmission before the nanoparticle escaped and translocated through the nanopore (figure 3(a), Region C). When the nanoparticle translocated across the ssNP from the cis to the trans region, a characteristic negative ionic current pulse was seen (third row, green) due to nanopore blockage during translocation (1.79 nA, translocation time 22.3 ms) taking place concurrently with a drop in optical transmission back to the baseline (first row, blue).

In addition to single trapping events, more complex multiple nanoparticle trapping events were recorded and analyzed. Figure 4(a) provides a 1 min trace showing three such trapping events. The gray-shaded Region A in that figure highlights a two-nanoparticle trapping event, as deduced from the nearly doubled optical transmission amplitude compared to the trapping event in Region B (8.6 ± 0.8% versus 19.2 ± 0.5%). Frequency spectrum analysis of raw ionic current signals for Regions A and B is shown in figure 4(b). Interestingly, the peak of the frequency spectrum for Region A was found in the 850 Hz range whereas it was in the 1 kHz range for Region B. The latter had a remarkably similar power spectrum for the single nanoparticle trapping event for...
described in Figure 3 (frequency spectrum not shown for brevity). Furthermore, the frequency spectrum from a no-trapping (NT) period is included for comparison in Figure 4(b), demonstrating a plateau rather than a peak frequency and spectral amplitudes that were up to four orders of magnitude lower than those for trapping events. These spectral differences suggest the possibility of differentiating single versus double nanoparticle trapping events over background signals with the SANE sensor. A representative sequence of multiple nanoparticle trapping events is highlighted in Regions C and D of Figure 4(a). Figure 4(c) shows the power spectra of these Regions and compares them to the NT condition. The power spectrum of Region C with an amplitude peak at 850 Hz and a 22.2 ± 1.2% increase in optical transmission shows a two-nanoparticle trapping event. Optical transmission in region D was 8.7 ± 0.9% over baseline, indicating single nanoparticle trapping. However, the raw ionic current showed no high frequency transients in Region D, making its frequency spectrum indistinguishable from the NT condition, even though optical transmission indicated single nanoparticle trapping. We hypothesize that during this period the nanoparticle attained transient equilibrium in the DNH-ssNP trap and was not bobbing significantly. In Region E, another nanoparticle entered the trapping site, indicated by an increase in optical transmission to 15.6 ± 0.4% and shifted the ionic current fluctuation spectral peak from ~1 kHz to 850 Hz. These observations are interpreted as the entry of an additional nanoparticle instigating bobbing for both nanoparticles inside the trap before these translocated through the nanopore.

To further investigate the influence of charge of individually trapped nanoparticles on SANE sensor measurements, 20 nm methyl functionalized Au nanoparticles were also measured under identical experimental conditions to the silica ones, so as to make comparisons. Figure 5 shows the trapping event and electrophoretic movement of a single Au nanoparticle. When the nanoparticle was pushed towards the DNH center by the electrophoretic force, its optical trapping caused a rise in optical transmission of 6%. Simultaneously, the raw ionic current through the nanopore registered a positive peak of 8.5 nA for 27.7 ms, as the particle entered the trap (Figure 5, Region A). Unlike the silica nanoparticles, the electrical high frequency transients during particle trapping were attenuated to very low levels. At the same time, the coefficient of variation of optical fluctuations during Au nanoparticle trapping reduced to 0.02% compared to the
0.11% seen for the silica nanoparticle fluctuations (figure 3, Region B). Typical Au nanoparticle trapping durations were a few seconds, 3.28 s in figure 5, Region B. Subsequently they escaped trapping and translocated through the nanopore (figure 5, Region C). A negative ionic current pulse was measured during translocation, while the Au nanoparticle blocked the nanopore (2.64 nA, translocation time 19.1 ms). At the same time, optical transmission dropped back to baseline.

Comparisons of SANE sensor measurement characteristics for Au versus silica nanoparticles highlighted a number of differences:

1. Au nanoparticles had a lower optical step increase from baseline compared to silica by a factor of $2.9 \pm 0.4$.
2. The coefficient of variation for the optical signal during Au nanoparticle trapping was lower than silica by a factor of $148.3 \pm 2.4$.
3. After applying the same 20 Hz low pass 8-pole Bessel filtering to the ionic current during Au nanoparticle optical trapping, the coefficient of variation was lower than silica by a factor of $5.5 \pm 1.2$.
4. Translocation times were slower for Au nanoparticles by a factor of $0.87 \pm 0.05$.
5. The ionic current during Au nanoparticle translocation was higher than silica nanoparticles by a factor of $1.7 \pm 0.3$, resulting in an SNR of $\sim 72$ compared to $\sim 43$ for silica. These differences are considered in the Discussion section below.

**Discussion**

The dynamics of a nanoparticle in electrophoretic flow through a ssNP have been studied in detail [1]. In our study, the nanoparticle translocation dynamics changed drastically due the SIBA-actuated trapping of the nanoparticle in the DNH nanocavity. The trapping force acting on the nanoparticle remained balanced for several seconds, e.g. 2.15 s for the particle shown in figure 3(a). Furthermore, the characteristic negative peak due to ionic current blockage lasted 22.3 ms for the single 20 nm nanoparticle translocation event shown in figure 3(d), which is much longer than the $200 \pm 30 \mu s$ translocation times of similar nanoparticles in nanopores [55]. Therefore, optical trapping enabled ionic current recordings in the vicinity of the nanopore that were about four orders of magnitude longer than typical translocation times for similar nanoparticles and also slowed down their translocation through the nanopore.

The greatly extended ionic current recording times also revealed a newly observed high frequency charge transient phenomenon for silica nanoparticles. We hypothesize that this originates from bobbing of the nanoparticle through the mouth of the nanopore due to the competing electrophoretic and SIBA forces. These high frequency transients were seen both for single (figure 3(a)) and multiple (figure 4(a)) nanoparticle trapping. At the end of the single trapping event seen...
in figure 3(a) (Region D), the nanoparticle started bobbing, which resulted in larger amplitudes for both ionic current and optical transmission. These observations suggest that the electrophoretic force led the nanoparticle to translocate through the ssNP.

It was observed that the peak amplitude of high frequency transients for raw ionic current decreased as dielectric loading in the trap increased from one (∼1 kHz) to two (∼850 Hz) silica nanoparticles. Therefore, frequency spectrum analysis of the SANE sensor’s raw ionic current shows promise for distinguishing single nanoparticles from more complex trapping events. In addition to periods of high frequency ionic current transients, instances of trapping with relatively quiet ionic current signals were also observed. For example, the single nanoparticle trapping in figure 4(a) (Region D), with similar optical transmission amplitude as Region B did not show any high frequency transients. We hypothesize that this behavior was a result of transient equilibrium while the single nanoparticle was blocking the pore and temporarily stopped bobbing. However, when another nanoparticle entered the DNH trap this equilibrium was disturbed and the high frequency charge transients returned with a peak frequency of 850 Hz (Region E) in the raw ionic current trace (figure 4(c)). The latter behavior was consistent with two-nanoparticle trapping. The subsequent gradual decrease in optical transmission and low-amplitude spikes in the low-passed ionic current in Region E suggest that the two nanoparticles translocated through the nanopore sequentially and not as a single unit. These findings indicate that the SANE sensor can provide information on the dynamics of single and two-nanoparticle dynamics inside the optical trap.

Experiments were performed subsequently with Au nanoparticles of the same size under identical experimental conditions to silica to compare the effect of nanoparticle charge on SANE measurements. The lower change in optical transmission compared to silica when Au nanoparticles entered the optical trap could be attributed to differences in optical interaction cross-sections. Although the scattering cross-section of 20 nm Au nanoparticles in water is ∼59% higher than that of the silica ones at 820 nm, the absorption cross-section is about 4 times larger than scattering for the Au nanoparticles [56]. In contrast, silica nanoparticles have negligible absorption. The reduced coefficient of variation in optical signal during Au nanoparticle trapping is therefore expected to be at least in part due to increased absorption. In addition, Au is a conductor and the applied voltage bias across the sensor would exert an electric field force on the Au nanoparticles, which would push towards a preferential direction in nanoparticle displacement. Indirect evidence for the existence of an electric field force was seen in the shorter translocation times of Au nanoparticles even though they had a lower zeta potential relative to the silica nanoparticles. In addition to the reduced translocation time, the observed increase in ionic current amplitude during translocation for Au nanoparticles is consistent with a zeta potential based interpretation [57–59] and resulted in the observed increase in SNR compared to silica. Finally, it was evident that the raw ionic current during Au nanoparticle trapping (figure 5, bottom, red, Region B) had significantly reduced high frequency charge transients compared to silica. Although Au nanoparticles had reduced displacement amplitudes within the trap, as discussed above, it is hypothesized that charge fluctuations around the nanoparticle played a major role. Since Au is conducting, it is possible that charges within the nanoparticle would move around to cancel out charge fluctuations in its immediate vicinity.

Finally, it is worth pointing out the possibility of using calibrated SANE sensor measurements in future work to estimate the number of total surface charges around unknown analytes. The Grahame equation [60] can be used to calculate total surface charge using the experimentally determined zeta potential of the analytes by the SANE sensor. The zeta potential can be deduced from the electrophoretic mobility of the analytes, which entails measurement of their translocation time and knowledge of the applied bias and nanopore size [61]. Concurrent optical measurements of analyte radius can be used to determine which approximation of Smoluchowski’s theory is appropriate for deducing the zeta potential.
potential [62]. For experimental parameters relevant to this work the appropriate approximation is the Hückel equation, which would yield the zeta potential estimate for the analytes [63]. These considerations indicate the possibility of calibrating the SANE sensor’s optical and ionic current signals in future work to estimate the charge around unknown analytes by direct measurement of their radius and electrophoretic mobility.

Conclusions

We have demonstrated multi-second optical trapping of electrothermally translocating nanoparticles through a ssNP. The competing electrophoretic and SIBA forces induced bobbing inside the optical trap that led to high frequency ionic current oscillations sensed through the nanopore. Frequency analysis of these oscillations for silica nanoparticles demonstrated the possibility of distinguishing between one versus two nanoparticles inside the trap. Furthermore, the SANE chip’s bimodal sensing ability showcased the possibility of using it as a tool to estimate the charge around a nanoparticle. Different SANE sensors were used to collect the measurements for this work which demonstrated the repeatability of this approach. In future work, we plan to apply this sensor to study interactions between biological molecules. Our longer term vision is to scale up towards a multiplexed SANE array within a microfluidic channel to facilitate parallel detection of biomolecular interactions to help resolve their heterogeneity in solution.

Acknowledgments

We are grateful to Mr Soeren Eyhusen and Mr Chuong Huynh for allowing access and providing technical guidance on focused ion beam milling at the Zeiss ORION NanoFab facility in Peabody, MA. We are also grateful to Mr Huan (Mick) Nguyen, Mr Dennis Bueno and Mr Richard K Chambers for their invaluable technical guidance on fabrication at the Shimadzu Institute Nanotechnology Research Center, University of Texas at Arlington. Support for this work was provided through a Pilot Research Program for Interdisciplinary Collaboration funded by the Vice-President of Research Office of the University of Texas at Arlington.

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