NANO-OPTOFLUIDICS FOR SINGLE MOLECULE DETECTION

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ABSTRACT

This paper reports a nano-optofluidic device with evanescent wave sensing for single molecule detection and sorting based on hydrodynamic focusing and total internal reflection (TIR). Nano-sized samples in a liquid can be detected although their size is smaller than the diffraction limit. We have demonstrated a successful imaging of 200-nm nanoparticles. In this nano-optofluidic TIR system, all samples focused in the liquids can be measured and counted rather than that detected only on the solid-liquid interface in conventional TIR microscope. It has wide range applications in single molecule detection, imaging and counting in near future.

KEYWORDS

Nanoparticles, evanescent wave, nano-optofluidics

INTRODUCTION

Single molecule/nanoparticle detection and sorting by optical means have great potential in biological and chemical sciences . Different from bulk collection of molecules, in which only average characteristic can be measured, single molecule detection technology is still a big challenge in conventional optics methods [1-3].

A total internal reflection (TIR) microscopy is based on the principle of the evanescent field illumination. Evanescent field is created by total internal reflection between two media with different refractive indices, such as glass and water. TIR microscopy has higher sensitive and signal-to-noise ratio as compared to conventional microscopy, making it one of the hottest technologies for single molecule detection. Although TIR microscopy has novel advantages for single molecule/nanoparticle detection and sorting, there still exists several problems that need improvement. First, the penetration depth is usually less than 200 nm from the solid-liquid interface into the sample medium. Samples that are further away cannot be detected. Second, compared to pure microfluidic system, TIR system with solid-liquid interface is not a suitable platform for complex chemical and biological processing and analysis. When a liquid dynamic technology [4-5] can be combined with traditional TIR microscopy, a more suitable and sophisticated platform can be designed for single molecule/nanoparticle detection and sorting.

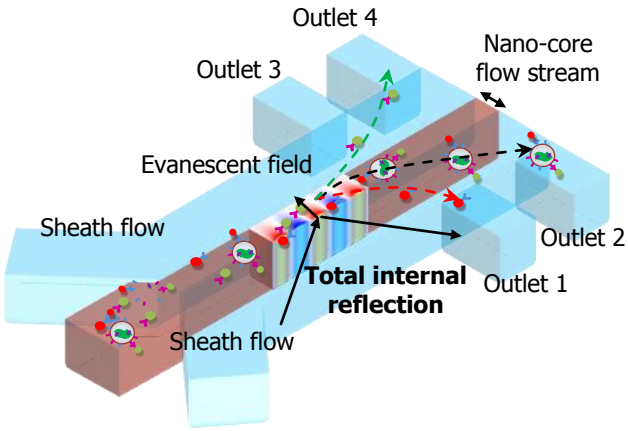

Figure 1: Schematic illustration of the nano optofluidic device for single molecule detection and sorting.

Hydrodynamic focusing is a pure microfluidic technology by building up the walls of the tunnel from liquids by using the effects of fluid dynamics. For example, sample can be injected into the extreme central flow stream, which can be experimentally controlled down to 50 nm in width [6]. When the sheath and central flow streams sufficiently differ in term of velocity and density, the three flow stream do not mix and a stable flow is achieved.

In this paper, we reports a nano-optofluidic device, which employs evanescent wave sensing for single molecule detection and sorting based on hydrodynamic focusing and TIR. Nano-sized samples in liquid can be measured and counted with their size smaller than the diffraction limit. 200-nm nanoparticles are used to demonstrate the working principle of the system for single molecule detection and sorting.

WORKING PRINCIPLE AND SIMULATION RESULTS

Figure 1 shows the schematic of the nano-optofluidic system. It consists of three flow streams in a microchannel, whereby the refractive index of the nano-core flow stream is lower than that of the two side sheath flow streams. Molecules/nanoparticles are injected and kept in the nano-core flow stream by the hydrodynamic focusing technology. An incident light with an incident angle larger than the critical angle is injected, such that TIR occurs at the interface between the cladding and core flow streams. Evanescent wave is propagated into the core flow stream. When the core flow stream is controlled with a width smaller than the penetration depth of the evanescent wave, all samples flowing in the core flow stream can be illuminated by the evanescent wave for detection and sorting.

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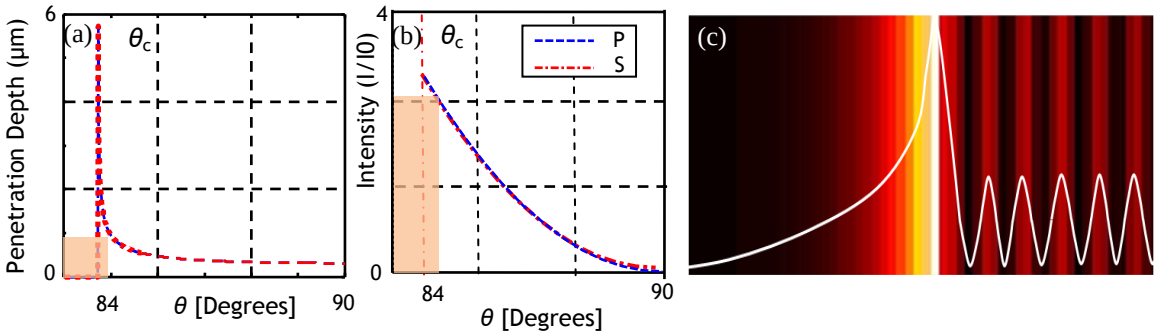

Figure 2: (a) Analytical solution of the penetration depth as a function of the incident angle. (b) Amplitude of the evanescent field for both parallel and perpendicular polarization. (c) Simulation result in microchannel.

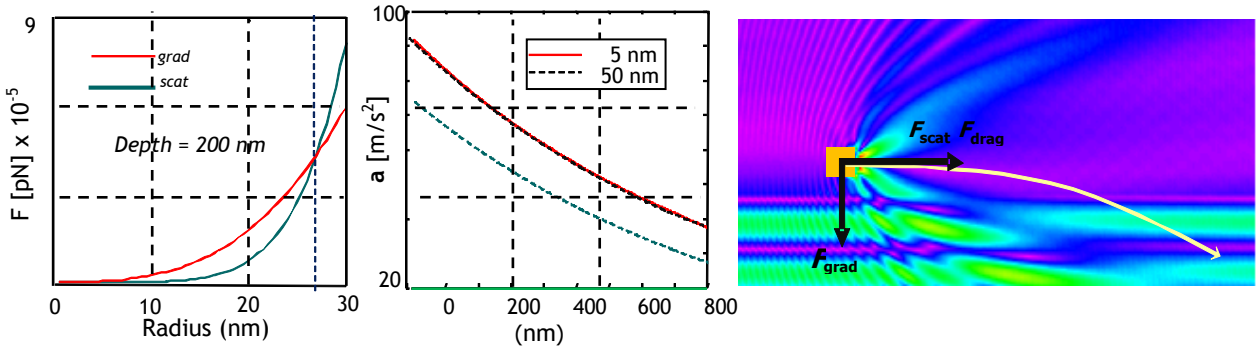

Figure 3: Analytical solution of (a) optical force for different sizes and (b) acceleration of the gradient. (c) Force diagram of forces acted on the particle in the microchannel.

The penetration depth decreases when the incident angle increases, and consequently, the optical forces decrease. When the incident angle is 85°, the penetration depth is nearly 1 μm as shown in Fig. 2(a). As a result, the samples are ensured to be illuminated by the evanescent field combined with hydrodynamic focusing technology. This condition is difficult to be achieved in solid TIR system. Fig. 2(b) shows the analytical solution of the evanescent wave intensity of the evanescent field for both parallel and perpendicular polarizations as a function of the incident angle in the condition where the refractive index contrast is fixed at 0.006. It is clearly shown that when the incident angle is 85°, the effect of the polarization can be ignored. Fig. 2(c) shows the simulation result of the optical field in the microchannel, whereby the evanescent field has a strong local confinement. The intensity in the interface between the two liquid media can be enhanced by approximately 3.3-fold with a sharp decay to form a gradient field. Fig. 3(a) and (b) show the analytical solution of the optical forces and the accelerations caused by them. Fig. 3(c) shows the simulated optical force acting on the 5-nm QDs.

EXPERIMENTAL RESULTS AND DISCUSSIONS

Figure 4 shows the fluorescent micro-image of TIR at the liquid-liquid interface between the sheath flow and the core flow streams. The refractive index of the sheath flow is same as the one of PDMS to avoid scattering by the relatively rough solid-liquid interface ($n_1 = n_{pdms} = 1.410$) while that of the core flow streams is $n_0 = 1.404$. The critical angle at the core-cladding interface is 84.7°, which is slightly smaller than incident angle of 85°. The low refractive index contrast between the core and sheath flow streams can reduce smearing and keep a smooth liquid-liquid interface.

Figure 5 shows the confocal image of the three flow streams, which revealS that the interface between the liquid-liquid is steady especially in the vertical direction. Figure 6 shows the microcopy images of the micro/nano particles by

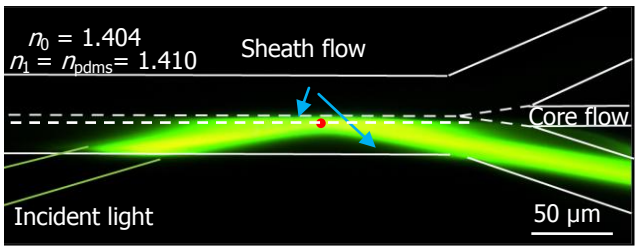

Figure 4: The fluorescent micrograph of total reflection by the liquid/liquid interface.

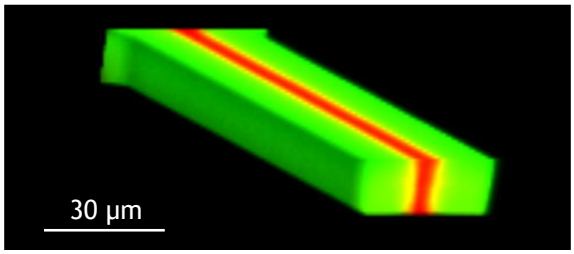

Figure 5: 3D confocal images of the three flow streams in the microchannel

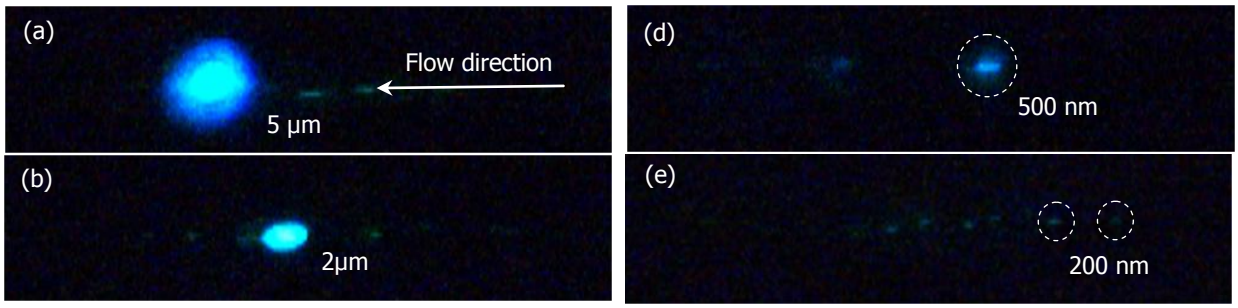

Figure 6: Evanescent microcopy of the TIRF illumination of Micro/nanoparticles in core flow streams from a Nd : YAG laser with the diameters: (a) G0500B, 5 µm;(b) R0200B, 2 µm;(c) F8813, 500 nm; (d) F8811, 200nm.

the evanescent wave illumination in the nano-core flow stream from a Nd:YAG laser with a wavelength of 488 nm. The samples diameters are ranging from 200 nm to 5 µm. All samples can be focused in the core flow streams by tuning the flow rate ratio between the core and sheath flow streams, and illuminated successfully by the evanescence wave propagating into the core flow stream. All the samples can be detected and measured in the central flow stream and not limited by the penetration depth of the evanescent wave, which ensures a more accurate analysis for biological and chemical sciences.

CONCLUSIONS

In conclusion, a nano optofluidic device for single molecule sorting by using an evanescent wave based on the hydrodynamic focusing is demonstrated. Nano-sized samples (as small as 200 nm) are detected and sorted by the evanescent wave and the optical forces, respectively. It has wide range of applications in single molecule detection, sorting and counting in the near future.

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