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Controllable particle hopping in optofluidic lattice for antibody screening and binding efficiency measurement

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ABSTRACT

Particle patterning and hopping has attracted much attention owing to their extensive involvement in many physical and biological studies. Here, by configuring an intriguing Optofluidic, we are able to pattern 500 nm particles into a 2D array in the flow stream. We also achieve a 2D patterning of cryptosporidium in the microchannel. By investing particle-particle interactions, we studies the long ignored new particle hopping mechanisms, and used them to screen antibodies. Our observed particle hopping in the flow stream completes the family of particle kinetics in optofluidic potential wells and inspires new minds in the develop new light fields in the microchannel. The 2D patterning of particles facilites the parallel culture and study of multiple biological samples in the flow stream.

Keywords: Particle hopping, optical manipulation, antibody screening, optofluidics

1. INTRODUCTION

Patterning of nanoparticles and bacteria in the flow stream facilitates the quantification and bioanalysis of multiple bacteria [1−4]. Many methods using optical tweezers can trap nanoparticles into 2D arrays in the still water, including the conventional single beam optical tweezers, vector assembly, holographic optical tweezers and plasmonic optical tweezers. However, single beam optical tweezers require precise setup alignment and time-consuming manual work. Vector assembly technology needs multiple optical tweezers and information encoding for the patterning. For holographic optical tweezers, bulky optical system and appropriate algorithms for phase hologram calculation on a desired pattern are needed. While for the plasmonic optical tweezers, a carefully designed lithographic substrate is needed. The manufacturing process is also tedious and expensive. And the problem of substrate absorption and sample sticking also occur. Recently, Feldman and his co-workers uses the optical tweezers to trap the metallic nanoparticles at the resonance wavelength, guide them to the substrate, and bind the particles via van der Waals attraction to the substrate. Optoelectronic tweezers represent another milestone in extending the capability of optical tweezers. Based on the optically patterned virtual electrodes on a photosensitive substrate, optoelectronic tweezers can grab and immobilize colloidal particles on the surface of hydrogenated amorphous silicon. The bubble-pen lithography uses an optically controlled microbubble to capture and immobilize colloidal particles on the plasmonic substrates through the coordinated actions of Marangoni convection, surface tension, gas pressure, and substrate adhesion in the substrate−bubble−solution system. In the optical force stampinglithography (OFSL), the optical forces are used to push and accelerate along the directions of the light energy flux and fixed at desired positions on a substrate.

Particle hopping has many biological and chemical applications, such as cell and DNA stretching, protein folding, chemical reactions and biomolecule sorting [5−10]. Single particle random motion in a potential well has been well studes since the pioneering work of Kramer in the 1940s. Meanwhile, the process of particle transition between neighbouring potential wells in a system with multiple optical traps has been described as the particle hopping. The archetypal system used to study particle hopping experimentally is based on dual optical traps. Thermally activated particle hopping is studied in

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dual optical traps with symmetric or asymmetric potential distributions or in dual nanohole traps which complies closely with Kramer's theory. However, the rich flatland of the particle-particle interaction induced hopping remain unveiled.

Here, by developing an Optofluidic lattice in the microchannel, we are able to pattern nanoparticles and cells into a 2D array. The stable trapping is based on the balance of optical and fluidic forces. Meanwhile, with the precise control of forces, we investigate the particle hopping mechanisms, and even create a particle hopping loop in the microchannel. Our theoretical investigation shows that the particle residence time in the potential well can be largely reduced by the interaction of other particles. 2D patterning of cryptosporidium is also demonstrated using this optofluidic lattice, which has a great potential in the biological studies.

2. OPTOFLUIDIC CHIP AND MECHANISMS OF MANIPULATION

The optofluidic chip with hydrodynamic focusing and a quasi-Bessel beam is illustrated in Figure 1. Nanoparticles and biological samples were injected and confined to the core flow stream squeezed hydrodynamic focusing. The quasi-Bessel beam was coupled into the flow stream in the microchannel by irradiating a fiber (NA = 0.12) through the micro-quadrangular lens built integrated into the optofluidic chip. The micro-quadrangular lens can be regarded as the combination of two prisms with two open angles. The material of the lens is PDMS with refractive index of 1.41. The discrete interference pattern has isolated hotspots, which can exert optical forces on particles. The optical forces includes optical extinction force (F_{ext}) in the light propagating direction and the optical gradient force (F_{grad}) which attracts particles to the center of the hotspots. Meanwhile, the nanoparticle was affected by the drag force (F_{drag}) along the flow stream direction. The laser generates heat in the particles and induces the Brownian forces (F_{bro}), which plays an important role in the hopping and patterning of particles.

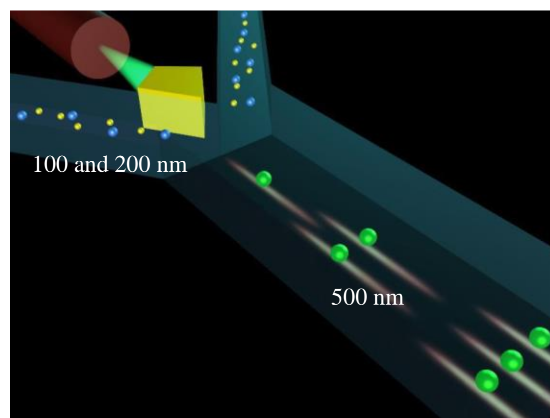

Figure 1. Illustration of particle patterning and looping in the optofluidic chip.

There exists two main and equivalent treatments of particle stochastic motion. One of them is based on the Langevin equation of motion with an added stochastic force. This method has been widely used for numerical simulations of various complex and even multidimensional problems, especially for overdamped systems (i.e. a microparticle moving in a viscous liquid), where the internal term in the equations are usually the omitted for the benefit of calculation. The other method uses the Fokker–Planck equation (FPE) simplified to the form of the so-called Smoluchowski equation that describes the development of the probability density function P(z, t) in time and space for an overdamped system. Practically, only some basic and 1D cases can be mathematically analized. Some complicated configurations also need approximate or numerical solutions. In this section, we focus on the problem of particle residence time in one potential well, investigating how long the particle takes to reach the potential boundaries located at points $z = a$ and $z = b$. Such a quantity, T (t), is frequently called the Mean first passage time (MFPT) as well as the escape or the residence time. It denotes the mean time needed for the particle originally (at $t = 0$) placed at ($a \leq z \leq b$) to leave the region between a and b. The general solution for an arbitrary 1D potential profile has been given by Gardiner. Only the key points of the MFPT derivation will be mentioned here, which will later be employed to compare with the experimental data. Let us assume that at time $t = 0$ the particle was located at z lying within the region of interval $\langle a, b \rangle$, i.e. $a \leq z \leq b$. This particle moves randomly in the potential energy

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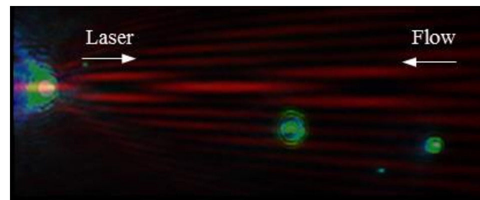
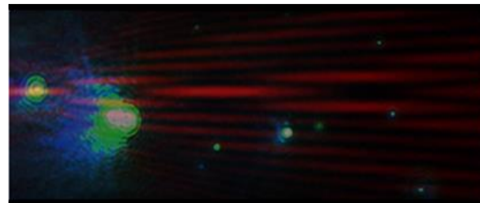
landscape described by a function U(z) until it reaches any of the two boundaries a or b at time t1 and, consequently, it escapes from the potential well. Considering a probability G(z, t) that the particle is still within the interval (a, b) at time t, we assume it was at z at t = 0. Such a probability is equivalent to the probability that the particle residence time t1 is bigger than t.The reason of the jumping lies in that the collision generates a particle wall and extrudes the red particle to the adjacent potential well.

3. EXPERIMENTAL RESULTS AND DISCUSSIONS

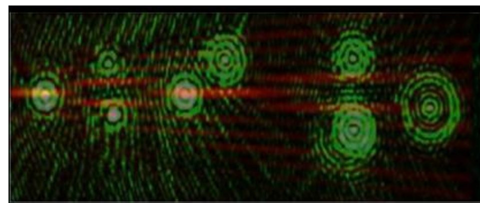
The Experimental demonstration of patterning of nanoparticles is shown in Figure 4-18. Only one 500 nm polystyrene nanoparticle was trapped when the laser power was 600 mW and the flow velocity was 150 μm/s. Optical forces in other two nanoparticles were trapped when the velocity was reduced to 100 μm/s. There were eight nanoparticles trapped when the laser power was 800 mW and flow velocity was 50 μm/s.



(a) Only one 500-nm polystyrene particle is trapping the discrete interference pattern when the laser power is 600 mW and flow rate is 150μm/s.



(b) More particles are trapped in two positions of the pattern when the flow rate is reduced to 100 um/s.



(c) 500-nm polystyrene particles are trapped into an array when the power is 800 mW and flow velocity is 50 um/s.

Figure 2. Patterning of polystyrene nanoparticles in the optofluidic lattice.

Experimental demonstrations of the selective binding and hopping of *S. flexneri* incubated with anti-*S. flexneri* antibodies was shown in Figures 3. The bacterial cells were trapped in the first hotspot when the laser power was 400 mW and the flow velocity was 50 μm/s. When the S. flexneri bacteria were stained with biotin-labeled anti-*S. flexneri* antibodies, the 1-μm silica microparticle captured a single bacterium, and the microparticle-bacterium complex hopped together to the adjacent hotspot where the potential well was deeper and stronger.

The binding happened when the *S. flexneri* incubated with anti-*S. flexneri* antibody in a very short time (< 100 ms) due to the specific binding. Once bound with bacteria, the particle hopped away with *S. flexneri*. While, when stained with non-specific antibodies, *S. flexneri* would remained trapped in the microchannel without binding to the particle. This was because of the non-specific binding. Therefore, there was no binding agents on the surface of bacteria. And the particle passed the cluster of *S. flexneri* and hopped away.

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4. CONCLUSIONS

In conclusion, we developed an Optofluidic lattice in the microchannel, which shows unprecedent potential on the patterning and hopping of particles and biological samples. 500 nm polystyrene nanoparticles can be patterned into a 2d array in the microchannel. Our demonstration inspires a burgeoning interest in the particle-particle interaction in the 2D even 3D optical lattice in either the still environment or the flow stream. In addition, our optofluidic chip may also facilitate the 2D untangled patterning of biological samples in the flow stream, which benefits the simultaneous investigation of their biological properties and chemical reactions. The hopping phenomenon enables the binding the screening of biological binding agents.

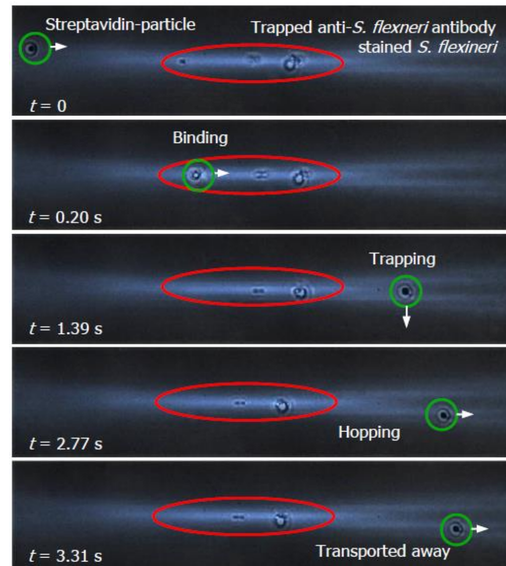

Figure 3. Antibody screening and binding using *S. flexneri* bacteria.

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