NOVEL MIGRATION PHENOMENA IN STRUCTURED MICROFLUIDIC DEVICES

J. Regtmeier[1], T. Duong[1], R. Eichhorn[2], D. Anselmetti[1], P. Reimann[2], A. Ros[1]

[1]Experimental Biophysics & Applied Nanosciences, Bielefeld University, GERMANY and [2]Condensed Matter Theory, Bielefeld University, GERMANY

ABSTRACT

Microfluidic and lab-on-a-chip devices have gained widespread attendance in separation sciences since they are characterized by advantageous properties like a gain in throughput, time, cost, performance and analyte amount. Beyond these advantages, microfluidic devices open access to completely new separation or particle sorting phenomena far from thermal equilibrium based on Brownian motion and non linear dynamics induced through microstructuring. Here, we demonstrate the migration phenomena of absolute negative mobility (ANM) for colloidal particles in structured microfluidic devices and discuss its application for separation of particles and biomolecules, such as DNA.

Keywords: structured microchannel, Brownian motion, non equilibrium, separation

1. INTRODUCTION

Novel migration phenomena have been investigated on the basis of thermal fluctuations in combination with asymmetric periodic potentials usually referred to as molecular ratchets [1]. Microstructuring allows for the design of ingenious microdevices serving as a basis for ratchet systems. Such ratchet devices have been employed for the separation of colloidal particles [2; 3] or biomolecules [4; 5].

Recently, we investigated a new migration phenomenon, which is different from the ratchet effect. Here, thermal fluctuations in a non-equilibrium environment can be utilized to generate a rather surprising and paradoxical migration behaviour termed absolute negative mobility (ANM), namely the average motion of a Brownian particle in the direction *opposite* to an applied static force. This phenomenon was originally predicted theoretically in simplified model systems [6]. We realized it experimentally in a structured microfluidic device with µm-sized latex particles in solution [7]. Conditions far from equilibrium are established by applying a symmetric AC electric field, which generates no net motion of the particles. However, additional application of a not too large static voltage results in a particle transport in the direction opposite to this static offset. We discuss potential adaptations of this concept to biomolecules, such as DNA.

2. EXPERIMENTAL

Microstructures were produced by soft lithography with poly(dimethylsiloxane). Corresponding master wafers were created by lithography of SU-8 photoresist on silicon wafers according to reference [8]. For ANM studies of colloidal particles, posts had a base of 3.1x6.1 μm^2 and a height of 9 µm and were periodically arranged in the microchannel as demonstrated in figure 1a. In each row, the gap sizes are alternately 1.7 and 3.1 µm. Microchannels were treated with Pluronic F108 to avoid adsorption of colloidal particles and subsequently filled with a suspension of 2 µm sized carboxylated polystyrene particles (IDC, USA) in 100 mM phosphate buffer (pH=8.2). For DNA dielectrophoresis, obstacle arrays were incorporated in the microchannels with a base of 3x10 μm^2, a period of 25 µm and a height of 9 µm. Microchannels walls were treated with a poly(oxyethylene) silane to

prevent DNA adsorption and reduce electroosmotic flow [9]. Lambda-DNA (48.5 kbp) was dissolved in 10 mM phosphate buffer (pH=8.3), containing fluorescent intercalator YOYO (1:10 ratio of bp to dye molecule), 2 % β-mercaptoethanol, 1 mM NaCl, 1 mM EDTA and 0.1 % POP-6 (Applied Biosystems, USA). The AC-drive was realized with a computer driven relays circuit and voltage supplies programmed by a labview programm according to ref. [8]. Microdevices were mounted on an inverted microscope and motion of analytes was recorded by real-time video fluorescence or bright field microscopy with a CCD-camera. Velocities were determined by particle tracking with ImageJ software.

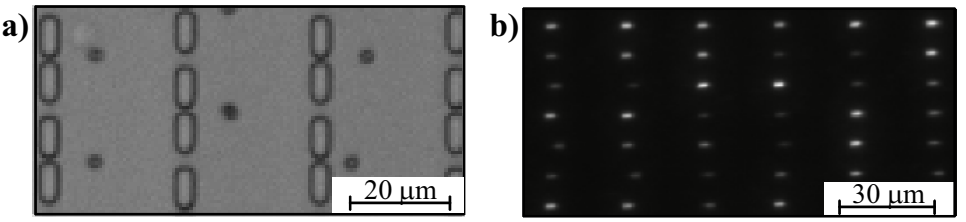

Figure 1: a) Bright field microscopy image of migrating latex particles (dark dots) in the structured ANM device with periodical obstacles (bright, rectangular) b) Fluorescence microscopy image of DNA molecules (bright spots) trapped by positive dielectrophoresis in a channel with an array of posts in an electric field of 150 V/cm of 100 Hz frequency. The non fluorescent posts are invisible in this image.

3. RESULTS AND DISCUSSION

The polystyrene particles were driven out of equilibrium by a symmetric AC voltage $U_{AC}(t)$. The migrational response to an additional offset generated by a static voltage U_{DC} was recorded, where the sign of the applied voltages has been defined in such a way that positive voltages correspond to positive forces acting on the microbeads, and accordingly for negative voltages. Figure 2a demonstrates that for not too large U_{DC}, the beads migrate in the direction opposite to the net acting force, independent of the sign of this force. This is the distinctive signature of ANM. For higher voltages U_{DC}, the motion in this direction slows down until a positive response in form of a motion in the "normal" direction, i.e. in the direction of the static force, is regained. The occurrence of ANM can be traced back to the presence of "traps" for the microbeads (note that the small gaps are smaller than the particles) and a diffusive (voltage-dependent) mechanism to avoid such traps.

The experimental data are – within the experimental uncertainty – in excellent agreement with numerical simulations adapted to the geometry of the microdevice, the actual diffusion coefficient and free mobility of the beads. Numerical simulations have also revealed that different bead sizes can exhibit different ANM characteristics, i.e. different maximal velocities and points of reversal. Beads of different sizes can even be steered into opposite directions with adequate choice of AC-drive and static offset U_{DC}, as theoretically predicted (figure 2b) and which could also be experimentally verified (manuscript in preparation). This result implies that ANM should be applicable for the separation or fractionation of colloidal particles or biological compounds of comparable size like cells or cell organelles.

ANM, as presented here for µm-sized particles, is a rather slow process limited by the slow diffusion of these objects. Our future interest is thus to speed up this migration mechanism with the use of smaller objects such as biomolecules (e.g. DNA or proteins). ANM for such molecules demands another mechanism of trapping, which is capable of trapping molecules with diameters in the nm-range. Energetic traps present a possible solution to this problem which can be realized by dielectrophoresis in obstacle arrays [10]. We have thus subjected

DNA to an alternating voltage of high frequency and could demonstrate that long DNA molecules, such as λ- and T2-DNA exhibit positive dielectrophoresis in an array of periodically arranged µm-sized posts (figure 1b). The DNA molecules are clearly trapped and focussed in the region of highest field gradient in between two adjacent posts in a row.

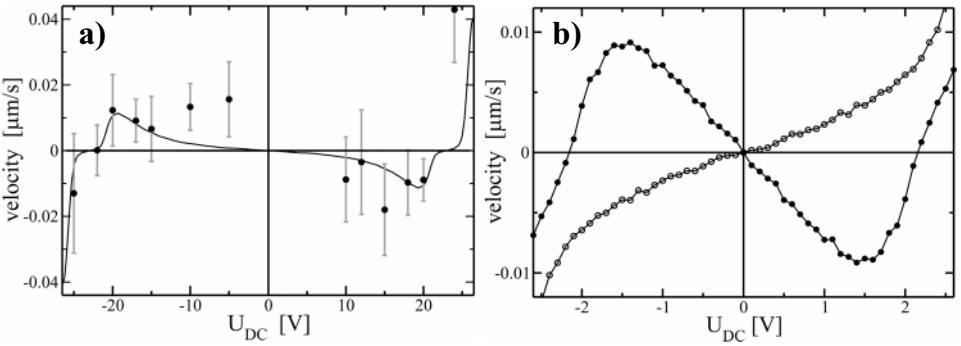

Figure 2: a) Absolute negative mobility in a microfluidic device: Dots: Experimentally obtained average velocities for 2 µm latex beads in a periodically arranged obstacle array subjected to a periodically switching voltage with static offset U_{DC}. Solid line: numerical simulation of particle velocities adapted to the experimental parameters. b) Numerical simulation of migration velocities as obtained for two different bead sizes. The beads with 2 µm diameter (dots) show ANM whereas the beads with 3 µm diameter (open circles) demonstrate "normal" response behaviour.

4. CONCLUSION

We could experimentally demonstrate the new migration mechanism of ANM in a tailored microdevice, and theoretically predicted a size dependent character of this new phenomenon for colloidal particles. Based on these results we will extend our studies for the separation or fractionation of biological compounds like cells or cell organelles and will exploit dielectrophoresis to generate ANM of small biomolecules such as DNA or proteins.

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