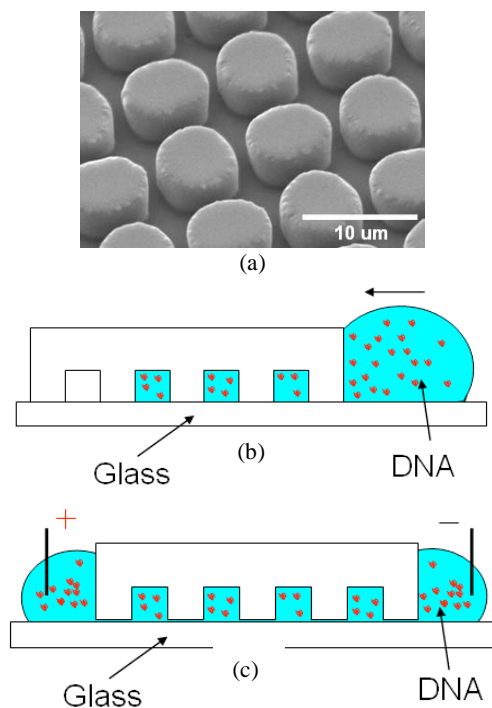


## Single DNA Dynamics in Micropillar Array

The commonly used technique to separate DNA, RNA, or protein molecules by size is gel electrophoresis with an applied electric current in the agarose gel matrix. This technique has achieved great success in many applications. An alternative approach, particularly useful for separating large DNA molecules is to use ordered micropillar arrays under either hydrodynamic or electrophoretic forces [1-2]. Huang, et. al. [3] have shown that large DNA molecules (with contour length from 61 to 209 kbps) can be well separated in seconds using a micropillar array device under two external electric fields (different strength and directions).

The efficiency of DNA separation in a micropillar array device is highly dependent on the pillar size, spacing (or gap) between two neighboring pillars, and local electric or flow field distribution (determined by the pattern of the micropillar array). To fabricate a micropillar array device, it is valuable to investigate the separation efficiency for different DNA molecules using computational methods, such as the coarse-grained Brownian dynamics simulation, which has successfully described single DNA dynamics in a single micropillar or a micropillar array [4-5].



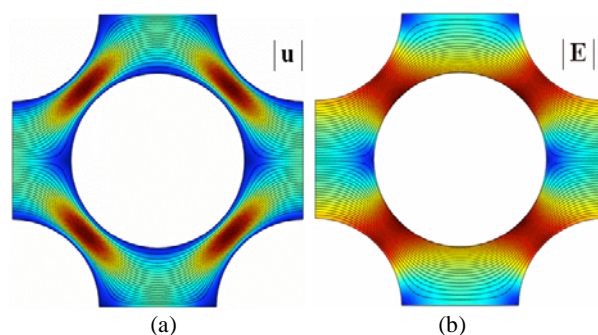
**Figure 1.** (a) PDMS stamp with micropillar array; Schematic of DNA migration in micropillar array by (b) a wetting flow; and (c) an imposed external electric field.

We have investigated hydrodynamic and electrophoretic behaviors of  $\lambda$ -DNA molecules (48 kbps, with a contour length around 21  $\mu\text{m}$ ) in a micropillar array device with both experiments and Brownian dynamics simulation.

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The device is composed of a PDMS stamp with micropillars, as shown in Figure 1(a), and a flat glass slit tightly pressed against the bottom of the PDMS stamp. Since glass is hydrophilic, a drop of DNA solution placed at one end of the device can be pulled into the device, producing a wetting flow (see Fig. 1(b)). We can also impose an external electric field across a device filled with DNA solution and study the migration of DNA molecules under the electric field (see Fig. 1(c)).

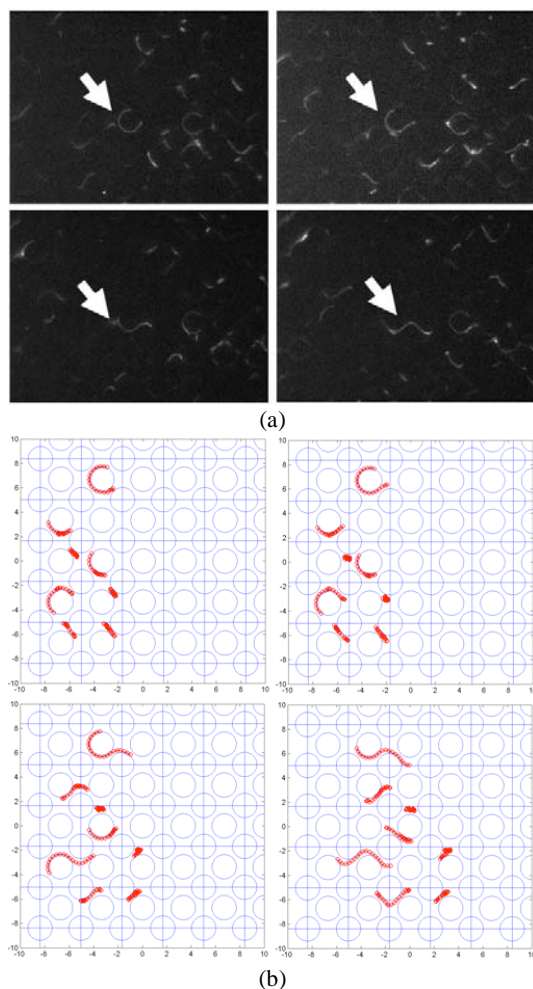
The local flow and electric fields play an important role in the behavior of DNA molecules in the micropillar array. The periodic field distribution in a single “cell” is shown in Figures 2(a) and 2(b), while the whole micropillar array is composed of thousands of such “cells”. These figures show that the maximum values of velocity and electric field (in dark red color) are located in the minimum gap area because of the incompressible condition satisfied by velocity and electric fields. The maximum gradients of velocity and electric fields also occur at the same location, indicating that DNA molecules experience the strongest stretching when passing through these areas.



**Figure 2.** (a) Streamline and magnitude of velocity profile; (b) electric field lines and magnitude of electric field.

In our Brownian dynamics simulation, we used the bead-spring worm-like chain model to depict a DNA molecule. To prevent the crossing of DNA molecules over micropillars, we added the wall-DNA repulsive force described by Deutsch [6]. A narrow Gaussian-excluded volume force was also considered to prevent the self-crossing of DNA chains [7]. A good agreement between experiments and simulation was achieved, and results are shown in Figures 3(a) and 3(b). In the experiments, once a YOYO-1 dyed DNA molecule got hooked by pillars, it was stretched by the local flow field to reach nearly its full length before one end slipped from the pillar. DNA molecules that were not hooked moved between pillars and were slightly stretched. Both behaviors were observed in the Brownian dynamics simulation, as shown in Figure 3(b).

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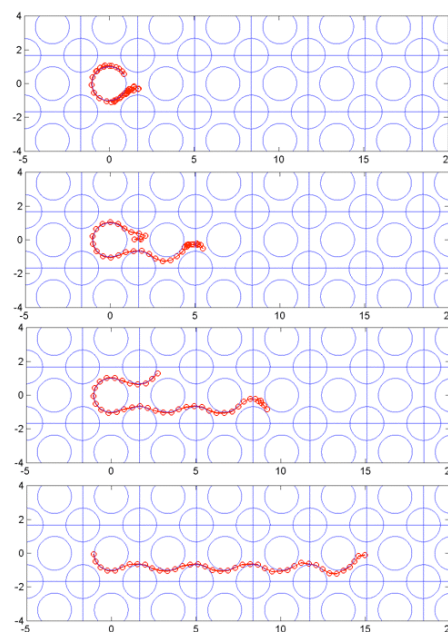
**Figure 3.** Different behaviors of DNA molecules in micropillar array shown in (a) experiments and (b) simulations.

To study the length effect of DNA molecules, we further considered the collision process of longer T2-DNA molecules (166 kbps, with contour length around 72  $\mu\text{m}$ ) with micropillars. Figure 4 shows the Brownian dynamics simulation results of a T2-DNA molecule in the same micropillar array at the same flow field as Figure 3(b). It was found that T2-DNA molecules are stretched longer once they are hooked with a micropillar [8]. This is because a T2-DNA is longer, and thus the probability of it slipping from one end within a same period of time is lower than a  $\lambda$ -DNA. Moreover, since T2-DNA is larger in its equilibrium size, the probability of it getting hooked is larger than the shorter  $\lambda$ -DNA. So we can observe that  $\lambda$ -DNA molecules move faster than T-2 DNA molecules in the micropillar array. Thus “separation by size” can be realized in this micropillar array.

We also considered the electrophoretic migration of DNA molecules in the micropillar array using the same method as described in [9-10]. But we did not find much difference, which might indicate that the velocity and electric fields have a similar effect to DNA dynamics in the micropillar array. Hydrodynamic interaction (HI) between DNA chains and pillars is neglected in our

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current study. This effect may be partially incorporated in the drag coefficient for such weak confinement. If the space between micropillars decreases to 1 micron or less, the HI effect may be too large to be hidden in the drag coefficient. We are now working on this issue by seeking collaboration with other groups inside our NSEC center.



**Figure 4.** Simulation of the collision process of a T2-DNA molecule with micropillars.

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