

Nano-Biodevice for Genomic Drug Discovery and Genomic Medicine

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Abstract

We have developed nano-biodevices to accelerate genomic drug discovery and post genome sequencing researches. The nanopillar chips, which has an array of nanometer-sized pillars inside a microchannel, were successfully fabricated on quartz substrate and applied for DNA separation. The nanopillar chips showed great potential to realize fast genome analysis and integration of whole lab procedures on a single chip.

1. Introduction

Micro Total Analysis Systems (μ TAS) for a size-based DNA separation have resolved a previous limiting factor, which is mainly Joule heating under applying a high voltage, owing to a high surface-to-volume ratio of a microchannel. However, it

still require of filling DNA sieving matrices into a microchannel. DNA sieving matrices, which is generally highly viscous, prevent a further integration of the other functions on a chip and also limit the application field. To defeat various limitations with the conventional DNA sieving matrices, alternative method such as an entropic trap [1, 2], a microfabricated array [3, 4] and a superparamagnetic particle [5] have been developed. Nanopillar chips are one of the possible resolution to realize higher efficient separation but their potentials as separation matrices are still unclear.

2. Experimental

Dense nanopillar array structures inside a microchannel were fabricated on quartz by dry etching process employing high selective Ni mask. This technique enabled to fabricate nano-structures, in the

range of 100 nm to 500 nm, with high aspect ratio on quartz.

A fluorescence videomicroscope was used for detection of DNA bands and for a direct observation of DNA electrophoretic behavior at a single DNA molecule level.

Numerical simulations of the electric field and DNA migration in nanopillar chips were performed using CoventorWare v2003.1 (Coventor Technology, Inc.).

3. Results and discussion

It was demonstrated that the nanopillars generate a molecular sieving effect as well as a conventional sieving matrices and can work as a DNA separation matrix. Moreover, long DNA fragments which requires pulsed-field technique for separation were separated in the nanopillar chip even under applying a DC field. A single DNA molecule imaging during electrophoresis in the nanopillars gave a qualitative explanation for the long DNA separation mechanism. [6]

In the nanopillar system, it is readily understood that considerable wide nanopillars against the width of microchannels might cause non-uniform electric field around the nanopillars and also their vast surface areas might generate complex electroosmotic flow (EOF). We should consider these non-uniform electric field and EOF to exploit the nanopillar chip because these factors would potentially degrade the DNA separation.

We studied the effect of an electric field and EOF from the viewpoints of both experimental results and numerical simulations. When a diluted buffer solution (0.5 x TBE) was applied for the DNA separation, the resolution gradually got worse according to an electric field strength. On the contrary, concentrated buffer solution (5 x TBE) gave a good separation even under a

higher electric field. The results of a numerical simulation and a direct observation suggested that suppressing the EOF is crucial to obtain a virtual molecular sieving effect and achieve high-resolved separation.

4. Conclusions

We demonstrated that the optimized nanopillar chip design to fractionate wide range of DNA molecules even under DC electric field. From both of the experimental results and the numerical simulation, suppressing the EOF is indispensable to realize high-performance DNA separation on quartz nanopillar chip. As we demonstrated here, nano-biodesives has a potential to replace the conventional laboratory instruments.

References

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