論文の内容の要旨

Abstract of Dissertation

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A study on separation method and analysis of mobility of long DNA molecules in nanofluidic device

(ナノ流体デバイスにおける長いDNA単分子の挙動分析及び分離法の開発に関する研究)

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The purpose of this thesis is to achieve the length-dependent mobility of 'long DNAs' in micro-fabricated fluidic devices. The 'long DNA' can be defined that 'a DNA cannot be separated by conventional gel-electrophoresis' under DC current and typically is the DNA with size above 20,000 base pairs (bps). In this thesis, we use the λ-DNA (48, 502 bps) and T4-DNA (166,000 bps) as the standard set of 'long DNA'.

With the devices fabricated with a novel process, the length-dependent mobility is observed. In the chamber-channel style device, the large T4-DNA's velocity is slower than the small λ-DNA and the gap is about ~3 μm /sec, which is caused by the DNA's deformation due to the confining environment of the device. However, the velocity difference disappears at high electric field (~ 30 V/cm).

Under the fluid drift caused by the imbalance of fluidic reservoirs, the length-dependent mobility is also observed. The longer T4-DNA moves faster than the shorter λ-DNA, and the velocity is T4-DNA ~ 132.41 ± 7.97 μm/sec, λ-DNA ~ 38.18 ± 9.98 μm/sec, respectively. This velocity difference is much higher than the previous observation.

Based on the single-molecule level observations, a new concept of 'electophoresis under hydrodynamic pressure gradient' is proposed. The simultaneous effect of electric and

hydrodynamic force induces the length-dependent mobility in the nanoslit device like in the nanochannel. And by adjusting the two forces, it is possible to manipulate the DNA to the different direction.

For achieving these results, this thesis presents the following 7 chapters.

First, the importance of long DNA separation technique and the present situation is reviewed in chapter I. Next, a brief background knowledge and DNA properties used in this thesis are introduced in chapter II. Based on this background, we consider the reasons why the long DNAs cannot be separated in the conventional methods, and propose a strategy in order to overcome the problems in chapter III.

As the first stage of the strategy, in chapter IV, two kinds of novel ('tube-like') nanochannel devices are fabricated with shadow evaporation and anisotropic etching of silicon substrate, which are the chamber-channel alternating style and the bottle-neck style by orientation-specific alignment of silicon substrate.

In chapter V, with these devices, the length-dependent mobility of λ & T4-DNA is observed. In the chamber-channel style, the deformation of DNA molecule can make the length-dependent mobility. And under a drift of buffer solution, which is one kind of hydrodynamic pressure gradient, the DNAs also show the length-dependent mobility.

With this single-molecule level observation, in chapter VI, the possibility of practical application for real separation process is tested in a nanoslit device. By proposing a concept of "the electrophoresis under pressure gradient in nanoslit device", the length-dependent mobility is also observed as well as the single molecule level. With the simultaneous action of electric field and hydrodynamic pressure, the DNA can be manipulated by adjusting the forces according to its size.