Development and production of Lab-on-Chip systems for DNA mapping

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During the last two decades, there has been a significant increase in the academic work in Lab on a Chip systems, while the number of commercial products has only increased a little. Many universities have research groups working within the field of Lab on a Chip and Micro Total Analysis Systems, and much funding has gone into the development of systems capable of performing a variety of different tasks. Meanwhile the industry has not seen the same potential in Lab on a Chip systems as the academic societies, resulting in knowledge being kept in the universities and not helping the population at large.

To try and overcome this situation, this thesis demonstrates a fabrication platform with the potential of producing thousands of identical polymer Lab on a Chip systems, containing structures in the length scale from 100nm to 50 μm on the same device and with a price that drops significantly as more devices are fabricated.

Such systems can be created, at the department, with a throughput of 25 devices per hour, and with a potential price as low as DKK 17.-

During the process, efforts were taken in developing a bonding scheme capable of giving a high yield on structures having aspect ratios as low as 1:200.

The developed polymer systems are tested by conducting two different experiments on DNA. Since such experiments are highly sensitive, efforts have been taken in order to lower the autofluorescence of the devices, resulting in a decrease of the background signal to roughly half the initial value.

The first experiment concerns mapping of short strands of λ-DNA and T4GT7-DNA against a theoretically obtained signal while stretched out in nanochannel confinements. The DNA is initially counterstained with a molecule that binds specifically to certain parts of the DNA. This counterstaining affects the staining with a fluorescent dye which, as a result of the first molecule, will distribute itself in a predictable, sequence specific, configuration along the DNA, thereby creating a fluorescent profile.

The nanochannels stretches the DNA to around 25% of their contour length and since several nanochannels can be placed parallel to each other, a large number of DNA molecules can be investigated.

In the second experiment, mapping is performed on human DNA in nanoslit devices. A fluorescent profile is created by heating the sample up to a temperature, where the DNA is partially denatured. The fluorescent dye will diffuse away from the denatured regions, and by analysing these black areas, the DNA molecule can be identified and potential mutations can be found.

In the nanoslits, the DNA is stretched out via a shear flow, resulting in a stretching of more than 95% of the contour length meaning a higher resolution compared to what was found when using the nanochannels.