Highly Sensitive Biological Detection Uisng Optical Microfluidic Sensor

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Lab-on-a-chip technology is attracting great interest because the miniaturization of reaction systems offers practical advantages over classical bench-top chemical systems. Rapid mixing of the fluids flowing through a microchannel is very important for various applications of microfluidic systems. In addition, highly sensitive on-chip detection techniques are essential for the in situ monitoring of chemical reactions because the detection volume in a channel is extremely small. Recently, confocal surface enhanced Raman spectroscopic (SERS) technique, for the highly sensitive biological analysis ina microfluidic sensor, has been developed in our research group. Here, a highly precise quantitative measurement can be obtained if continuous flow and homogeneous mixing condition between analytes and silver nano-colloids are maintained. In our research group, the SERS detection, in combination with lab-on-a-chip technology, has been applied to the trace analysis of cyanide ion, methyl parathion and duplex DNA mixtures. Compared with other methods for the trace analysis, the detection sensitivity was enhanced by several orders of magnitude. We expect this analytical technique to be successfully applied to highly sensitive bioanalysis as well as other trace analyses.[1]

We also reported a new analytical method of DNA hybridization involving a PDMS microfluidic sensor using fluorescence energy transfer (FRET).[2] This method overcomes many of the drawbacks of microarray chips, such as long hybridization times and inconvenient immobilization procedures. Hybridization analysis of DNA plays an important rolein the detection of genetic diseases and gene expression profiling. One of the most popular approaches to DNA hybridization analysis is the use of a microarray chip where probe DNA sequences are immobilized on a solid surface and incubated with a mixture of unknown target DNA. In microarray chip, however, a relatively long time is (about 1-2 h) is required for complete hybridization because of the diffusion-limited hybridization kinetics. DNA hybridization analysis using microfluidic technology overcomes many of the drawbacks of microarray chips, such as the long hybridization time and inconvenient immobilization procedures. In a microfluidic device, however, a new detection method is required, since nonhybridizing fluorescence oligonucleotides cannot be washed out inside the channel. In our work, the DNA hybridization detection using molecular beacon and FRET technology successfully resolved this problem. Compared to the previously reported work on DNA

analysis using microfluidic devices, both the detection sensitivity and the quantitative measurement capability have been greatly improved.(3)

Finally, a surface-enhanced Raman scattering (SERS)-based immunoassay for the sandwich complex using magnetic nanoparticles will be introduced. Glass-encapsulated Rhodamine 6G (R6G) silver nanotags and poly(3-thiolphenacetic acid (3TA))-tagged magnetic nanoparticles have been fabricated for this purpose. Surfaces of SERS nanotagsand magnetic nanoparticles have been conjugated with polyclonal and monoclonal anti-Rabbit immunoglobin G (IgG) antibodies, respectively. Then they were simply mixed with IgG antigens for the formation of sandwich-type immunocomplexes in a 1.5 mL microtube. Sandwich complexes were immobilized on the wall of microtube using a small bar. Quantitative analysis was performed bymeasuring the intensity of surface-enhanced Raman scattering (SERS) at 1630 cm^{-1} for the immunocomplexes immobilized on the glass wall. SERS-based immunoassays had a detection limit of 1 pg/mL for the IgG antigen. This is about 100 orders of magnitude more sensitive than conventional immunoassay techniques such as ELISA or SPR and the detection time is less than a few hours. The developed immunoassay method is suitable for the rapid and sensitive detection of specific antigens.(4)

In this presentation, our recent developments of the confocal Raman/fluorescence microscopic technology to a highly sensitive lab-on-a-chip detection for biological samples will be introduced.

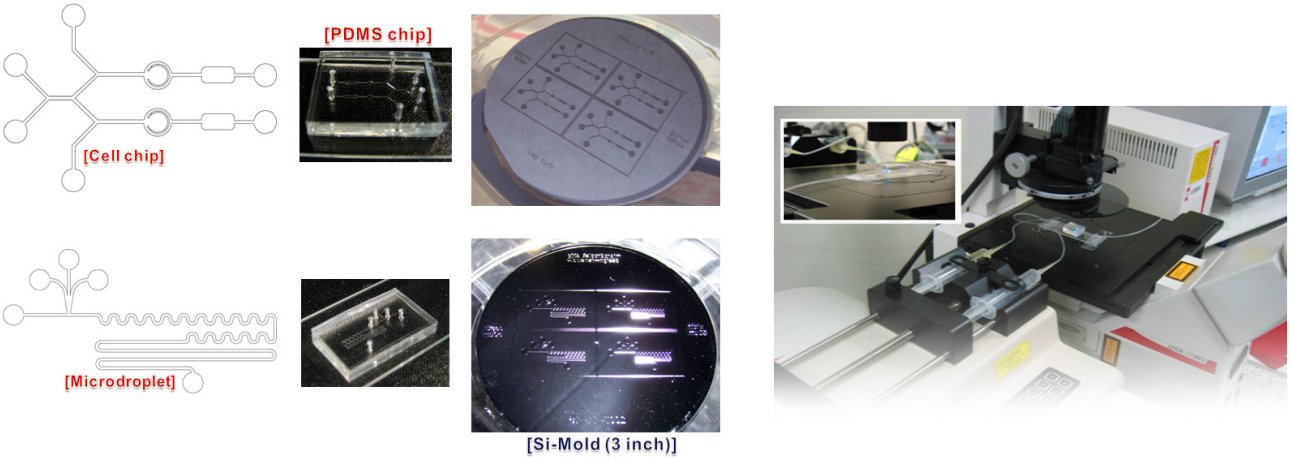

Figure 1. Fabrication of Lab-on-a-chip and Its Application to Optical Biosensors

References

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(3) S. Lee, J. Choo et al., Anal. Chem., 79, 916-922 (2007)
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