04 Research Activities

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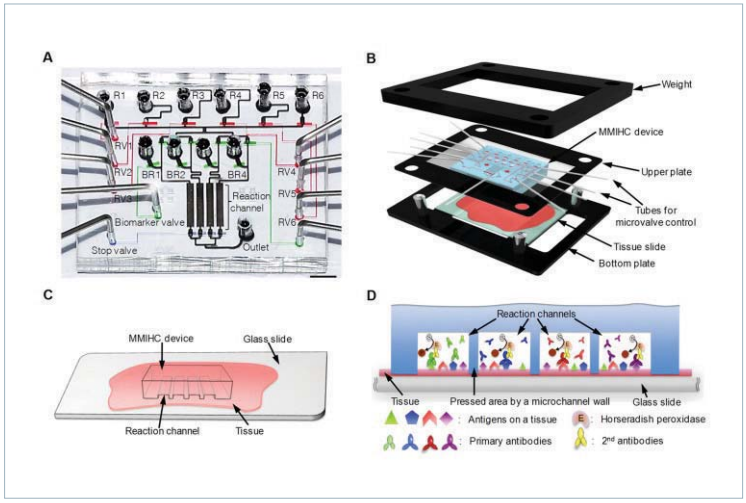
NanoBiotech Laboratory

(Prof. Je-Kyun Park, http://nanobio.kaist.ac.kr)

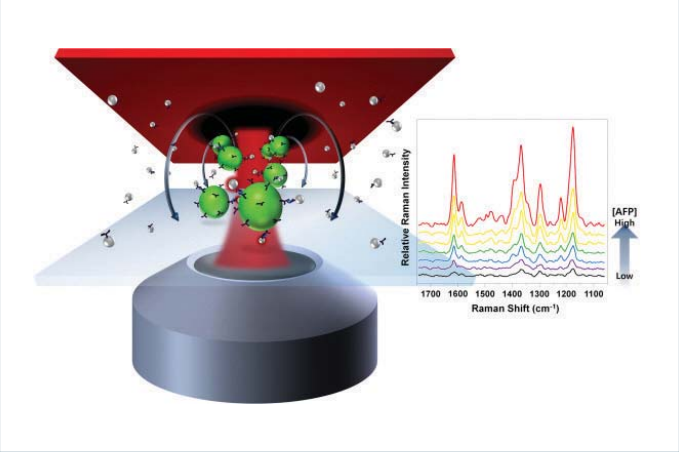
Recent progress of lab-on-a-chip technology is challenging for the development of nanobiotechnology and integrative bioengineering. Particularly, micro/nano fluidics has been a key technology for the realization of micro total analysis systems (μTAS) or lab-on-a-chip as well as the next generation bio-tools for drug discovery, diagnostics, and tissue engineering. This research area covers the design and development of miniaturized devices that manipulate liquid samples at nanoliter volumes, allowing biological assays to be integrated and accomplished on a small scale with minimum time and cost. Prof. Park's research focuses on the development of a nanobiosensor, microfluidic device and lab-on-a-chip as a new platform for biological sample processing, separation, and detection, including optoelectrofluidics, hydrophoretic separation, magnetophoretic assay, and cell-based assay. From June 2008, his laboratory has been selected to receive a National Research Laboratory (NRL) Program grant through the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology (MEST).

Microfluidic Multiplexed Immunohistochemistry Platform



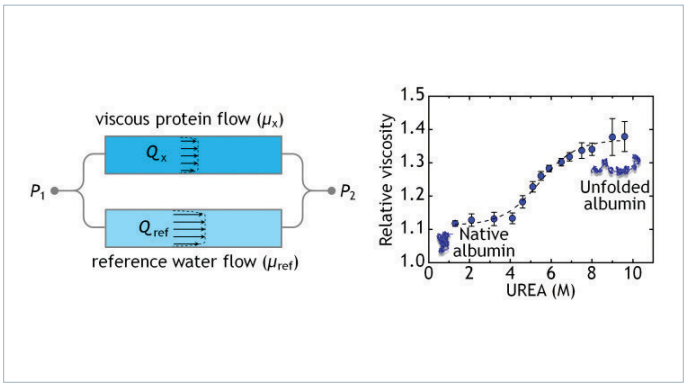
Breast cancer is a heterogeneous disease with many subtypes, and it is difficult to accurately monitor the treatment response of the disease, and to predict the clinical outcome of individual neoplasms. We recently succeeded in developing a microfluidic interface that enables multiplexed immunohistochemistry (IHC) measurements on breast tissue samples [1a]. The device consists of a PDMS microfludic layer with four parallel channels, which is simply pressed onto the tissue slide. Consequently, four biomarkers, estrogen receptor, human epidermal growth factor receptor 2, progesterone receptor and Ki-67, were examined simultaneously on human breast cancer tissues including needle biopsy. This new IHC platform has improved performance concerning assay time, consumption of tissue, antibodies and staining compounds, sensitivity, specificity and cost-effectiveness, and hence, it is a step towards the individualization of cancer therapy. The similar microfluidic platform has also been applied for quantitative proteomic profiling in breast cancer samples [1b]. Proteomic profiling via immunocytochemistry (ICC) was examined for four breast cancer cell lines. The device enabled 20 ICC assays on a biological specimen at the same time and could be used to quantitatively compare the expression level of each biomarker. This result indicates that the microfluidic IHC/ICC platform is useful for accurate histopathological diagnoses using numerous specific biomarkers simultaneously.

Optoelectrofluidics Platform



Optoelectrofluidic technology, which has been recently introduced as a new manipulation scheme, allows programmable manipulation of particles or fluids in microenvironments based on optically induced electrokinetics resulted from photochemical, photoconductive, and photothermal effects [2a]. Recently, we reported a new optoelectrofluidic immunoassay platform for simple, fast, and automated detection of human tumor marker based on surface-enhanced Raman scattering (SERS) [2b]. By using a conventional optoelectrofluidic device and a liquid crystal display module, simple and quantitative detection of human tumor marker, alpha-fetoprotein, in a 500nL sample droplet has been automatically conducted with lower detection limit of about 0.1 ng/mL within 5 min. This study depicts the first practical application, for protein detection, of the optoelectrofluidic manipulation technology. This image-driven immunoassay platform opens a new way for simple, fast, automated, and highly sensitive detection of antigens.

Microfluidic Rheometer for Characterization of Protein



Many of microfluidic applications require the precise transport of fluid along a channel network with complex patterns. Therefore, it is important to accurately characterize and measure the hydraulic resistance of each channel segment, and determines whether the device principle works well. However, there is no fluidic device that includes features, such as the ability to diagnose microfluidic problems by measuring the hydraulic resistance of a microfluidic component in microscales. To address the above need, we demonstrated a simple strategy to measure an unknown hydraulic resistance, by characterizing the hydraulic resistance of microchannels with different widths and defining an equivalent linear channel of a microchannel with repeated patterns of a sudden contraction and expansion [3a]. In addition, the balancing between a sample and reference flow with a common pressure drop enables simple and accurate measurement of fluid viscosity without standard pressure gauges and complicate theoretical calculations. On the basis of this principle, we also developed a simple microfluidic rheometer to characterize protein unfolding and aggregation in terms of a rheological aspect using a similar channel network of the microfluidic parallel circuit [3b].

Sol-Gel Transitional Hydrogel Free-Standing Microarchitectures

We developed a facile method to fabricate free-standing, 3D hydrogel microarchitectures of chemically sol-gel transitional hydrogels, which is based on the use of hydrophilic substrate and aerosol of gelling agent without molding (or sandwiching) process [4]. Using proposed methods, we fabricated hydrogel microarchitectures of sheets, meshes, or microunits without morphological distortions on the microscale. These hydrogel microarchitectures could be easily and stably exfoliated from the substrates and cultured (in the case of containing cells). These free-standing hydrogel microarchitectures in sheets, meshes, or microunits can be applied as a biofabrication unit to generate complex composites with controlled microscale structures for a variety of applications such as 3D cell culture systems, tissue morphogenesis study, and modular biofabrication of artificial tissues.

▶ References

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2. **a)** Hyundoo Hwang, Je-Kyun Park*, Optoelectrofluidic platforms for chemistry and biology, Lab Chip, 2011, 11(1): 33-47; **b)** Hyundoo Hwang, Hyangah Chon, Jaebum Choo, **Je-Kyun Park***, Optoelectrofluidic sandwich immunoassays for detection of human tumor marker using surface-enhanced Raman scattering, Anal. Chem., **2010**, 82(18):7603-7610
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4. Wonhye Lee, Jaejung Son, Seung-Schik Yoo, **Je-Kyun Park***, Facile and biocompatible fabrication of chemically sol-gel transitional hydrogel free-standing microarchitectures, Biomacromolecules, **2011**, 12(1): 14-18.