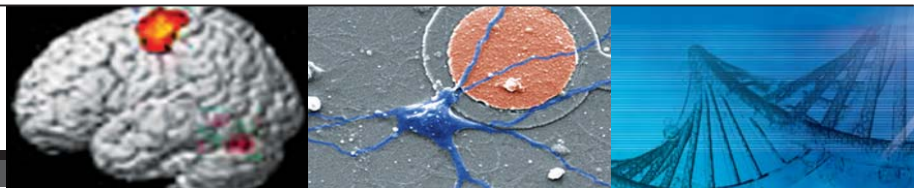
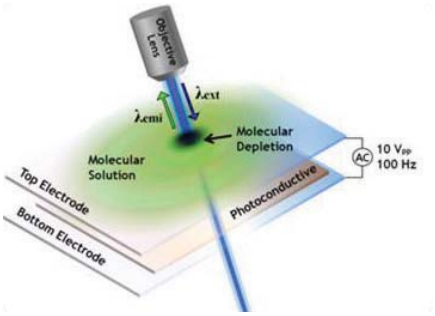


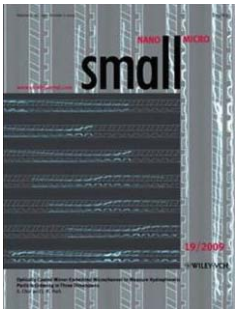
4.1.13. NanoBiotech Laboratory
(Prof. Je-Kyun Park, http://nanobio.kaist.ac.kr)

Micro/nano fluidics, one of the major nanobiotechnology fields, has been a key technology for the realization of micro total analysis systems (μTAS) or lab-on-a-chip and the next generation bio-tools for drug discovery. This research 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 nanobiotechnology and integrative bioengineering. During the last several years, his laboratory has been interested in developing novel microfluidic devices for biotechnology and bioengineering, based on the synergetic integration of miniaturization technology to biology, chemistry, and medicine. In particular, he is interested in developing a novel nanobiosensor, microfluidic device, and lab-on-a-chip as a new platform for biological sample processing and detection, including optoelectrofluidic manipulation, 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).

Optoelectrofluidic Manipulation Platform

Optoelectrofluidics refers to the motion of particles or molecules and their interactions with an optically induced electric field and surrounding fluid. Recently, we demonstrated the rapid and selective concentration of microparticles by combining several electrokinetic mechanisms and electrostatic interactions. The particle movements resulted from the frequency-dependent behavior according to the particle diameter. The dynamic control of local molecular concentration was also achieved by using several frequency-dependent optoelectrofluidic phenomena such as optically induced ac electroosmosis, dielectrophoresis and electrostatic dipole interactions [1a]. Optoelectrofluidic fluorescence microscopy, wherein an optoelectrofluidic device is integrated into a conventional fluorescence microscopy, made it possible both to modulate and to detect the molecular concentration in a localized area at the same time. In another application, we have demonstrated a sudden decay of molecular concentration in a localized area by optoelectrofluidics in a few hundred Hz frequency range. On the basis of this approach, the measurement of diffusion using different-sized biomolecules has been performed [1b]. This technique would be a useful tool for analyzing electrokinetic behavior of molecules as well as studying molecular diffusion kinetics. In addition, the sudden change of local molecular concentration can be applied for several biological and chemical applications such as cellular chemotaxis and optoelectrofluidic immunoassay.



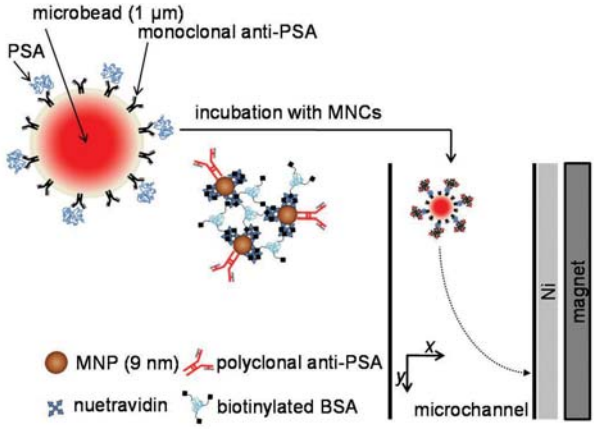


Hydrophoretic Separation Platform

We proposed a new microfluidic separation scheme, hydrophoresis, which uses slanted or anisotropic obstacles to induce hydrodynamic interaction between the obstacles and the particles subjected to rotational flows induced by the obstacles. By exploiting the slanted obstacles in a microchannel, we can eliminate the needs of sheath flows and complex channel networks. In addition, we can generate a lateral pressure gradient so that microparticles can

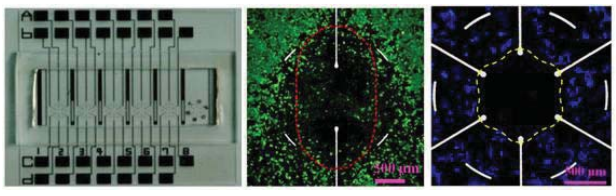
be deflected and arranged along the lateral flows induced by the gradient. The equilibrium positions of the particles by the hydrodynamic interactions depend on their size. The hydrophoretic principles were successfully applied to the particle sizing, sheathless particle focusing, isolation of white blood cells, and self-sorting of mammalian cells to achieve cell cycle synchrony [2a]. We recently reported the 3D measurement of hydrophoretic particle ordering for the exact characterization of hydrophoresis by using an optically coated mirror-embedded microchannel [2b]. The mirror, ideally at 45°, reflects the side view of the channel and enables 3D positional information to be obtained easily from two different orthogonal-axis images. With this method, it is shown that hydrophoresis is governed by convective vortices and steric hindrance. It is also observed that hydrophoresis enables 3D particle focusing without sheath flows and accurate flow-rate control.

Magnetophoretic Assay Platform

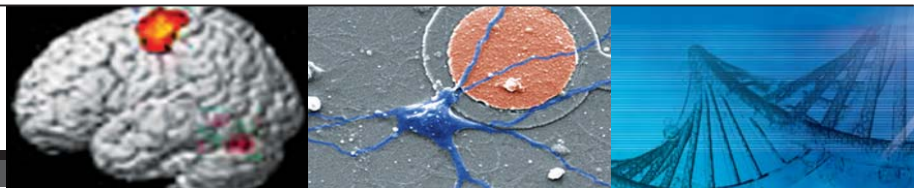


We developed a new immunoassay system based on the magnetophoretic mobility of a microbead, depending on the amount of associated superparamagnetic nanoparticles under magnetic field gradient in a microfluidic channel. By measuring the magnetophoretic deflection velocity of microbeads as the signal for the presence of analytes, the multiple analytes (such as allergen-specific IgEs in patient samples) in a microchannel are simultaneously quantified by conjugated nanoparticles as a label. Because magnetophoresis is also influenced by magnetic field gradient, the detection sensitivity of this assay system can be improved to the sub-femtomolar concentration range using an enhanced magnetic force from the ferromagnetic microstructures in a microfluidic device. This technology has been successfully applied to develop a magnetophoretic, continuous purification platform that rids single-walled carbon nanotubes (SWCNTs) of superparamagnetic iron-catalyst nanoparticles. We also demonstrated an ultrasensitive magnetophoretic assay for prostate-specific antigen (PSA) using magnetic nanoclusters (MNCs) as a signal amplifier [3]. The developed system enabled detection of PSA as low as 50 fg mL^{-1} with a detection limit of 45 fg mL^{-1}. It is expected to be effectively applied to the detection of a target analyte with low abundance.

Cell-based Assay Platform



A microfabricated cell-based electrochemotherapy (ECT) testing device which mimics a clinical electroporator of circular needle-array is demonstrated to study the electrochemotherapeutic effect on T47D human breast cancer cells. Until now, the performance between electroporators having two- and six-needle circular array electrodes, which are the general needle-type clinical electroporators for ECT, has not been evaluated systemically, although many studies have investigated the efficacy of ECT on cancer cells. In this study, the cell-based performance on the newly developed ECT testing device was analyzed in two and six-electrode modes using propidium iodide and bleomycin, and the electroporation characteristics were characterized [4a]. We also developed a microfabricated electroporator for the irreversible electroporation (IRE) of tissues by miniaturizing a clinical electroporator with a two-



needle array while keeping the same electric field strength distribution. With the developed microfabricated electroporator, the effect of IRE on rat liver tissues was analyzed with time by immunohistological stainings and electrical measurement, and the experimental results were compared with those operated with the corresponding real-scale clinical electroporator [4b].

■ References

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