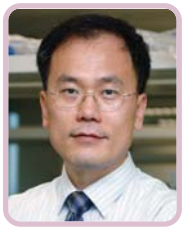
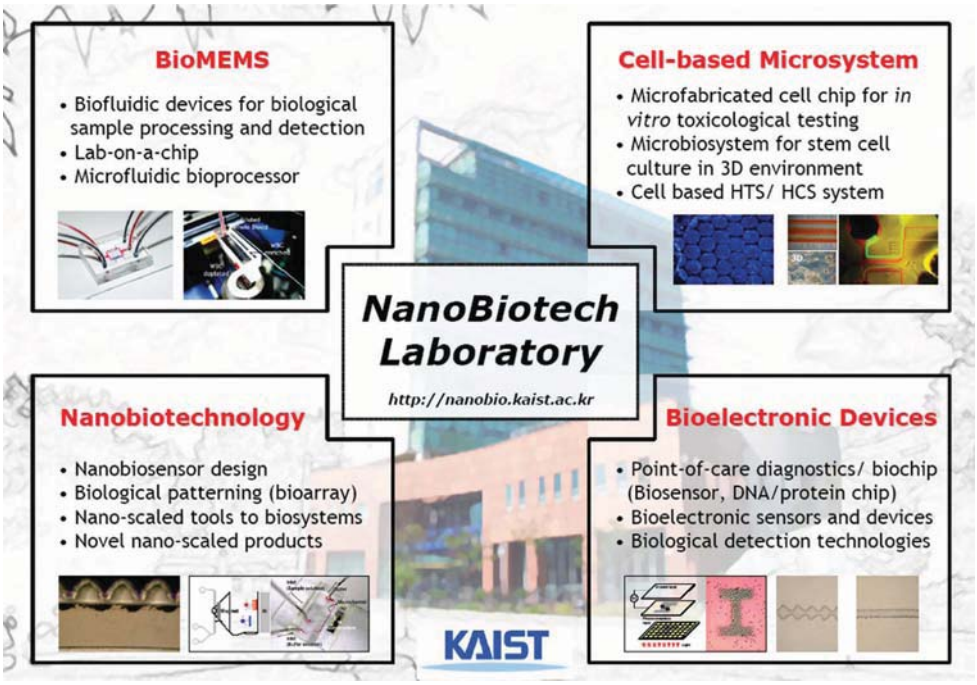


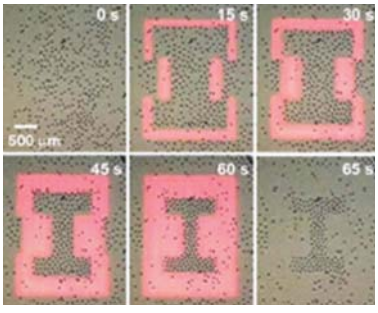
3.1.3. NanoBiotech Laboratory
(Prof. Je-Kyun Park, http://nanobio.kaist.ac.kr)

The aim of NanoBiotech Laboratory (NBL) lies in conducting research and development on the nanobiotechnology as well as microsystems technology. During the last 4 years, NBL has interested in developing a novel biomicrofluidic devices for biotechnology and bioengineering, based on the synergetic integration of miniaturization technology to biology, chemistry, and medicine. Currently, NBL focuses on the development of a nanobiosensor, microfluidic device and lab-on-a-chip as a new platform for biological sample processing and detection. The main application areas include biomolecular diagnostics, micro total analysis system (μTAS), cell-based high-throughput screening, and nanobio device.



Dielectrophoretic Separation Platform

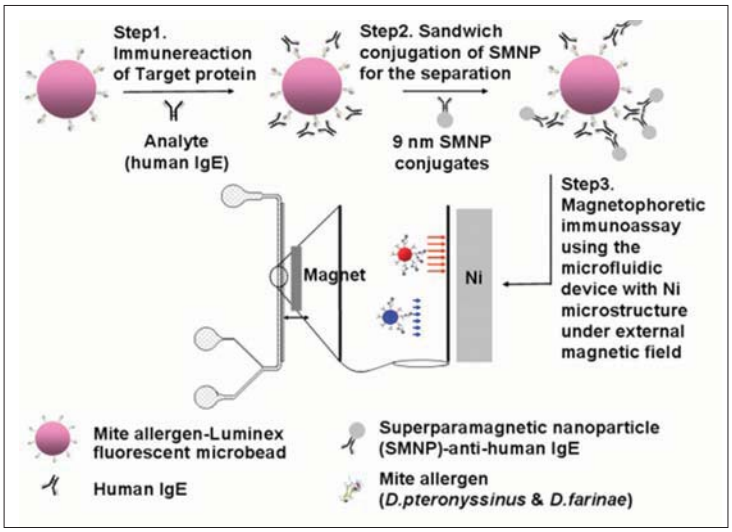
We recently report a new portable microfluidic platform, "lab-on-a-display", that microparticles are manipulated by dielectrophoretic force generated from the optoelectronic tweezers (OET) on a liquid crystal display (LCD). It was successfully applied to the programmable manipulation of 45μm polystyrene beads; more than 100 particles were transported with an optical image-driven control, following the moving edge of the image at every moment. Due to the portability and compatibility for disposable applications, this new platform has potential for programmable particle manipulation or chip-based bioprocessing including cell separation and bead-based analysis [1].



LCD driven optical manipulation of microbeads with a diameter of 45μm

Magnetophoretic Assay Platform

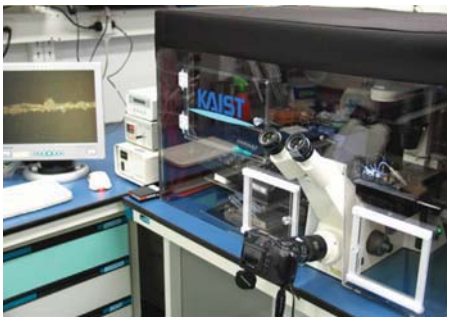
A new detection system based on the magnetophoretic mobility of a microbead, depending on the amount of associated superparamagnetic nanoparticles under magnetic field gradient in a microfluidic channel, was developed [2]. By measuring the magnetophoretic deflection velocity of microbeads as the signal for the presence of analytes, the multiple analytes (rabbit IgG and mouse IgG) in a microchannel were simultaneously quantified by conjugated nanoparticles as a label. Because the magnetophoretic deflection velocity was also decided by the magnetic field gradient, the detection sensitivity of this assay system can be improved to the femtomolar concentration range. Currently, we are applying this technology to detect allergen-specific IgE in patient samples [3] and to purify single-walled carbon nanotubes (SWCNTs) from the superparamagnetic iron impurities in a microfluidic device without any influence on inherent SWCNT properties.



Magnetophoretic immunoassays

Microfluidic Cell-based Assay Platform

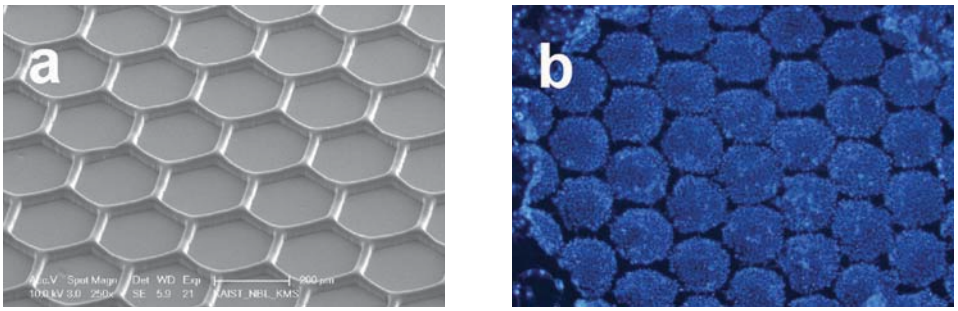
We report a novel cell culture platform for 3D cell immobilization as well as a dose-dependant cell-based assay by forming linear concentration gradient inside a peptide scaffold of a microchannel. A sol-gel transition peptide hydrogel, Puramatrix™, was first adopted in microfluidics. As the mixture of the peptide hydrogel and human hepatocellular carcinoma cells (HepG2) was flowed and gelled in the middle of a main channel by diffusion of media, we could simply fabricate a stripe-shaped peptide scaffold. Encapsulated HepG2 were cultivated in the 3D microenvironment and applied to cytotoxicity assays using Triton X-100. This platform also could be applied to co-cultures, angiological research, cytotoxicity tests, cell viability monitoring, and continuous dose-response assays as well as drug-drug interaction studies [4].



Microfluidic 3D cell culture system for in-vitro cell-based assays

Microfabricated Embryonic Stem Cell Divider (ESCD)

Microtechnology has supported innovative tools enabling micro-scale control so that a variety of tools have been applied for biological and medical applications. Recently, microwell-based human ESC culture has been used to control cluster size and cell differentiation. However, applications of microtechnology have rarely been studied for a large expansion of undifferentiated human ESCs and precise control of ESC clump size under intact culture



(a) SEM image of the PDMS replica (b) DAPI-stained image of a human ESC colony after pressing with ESCD with a hexagonal pattern (×100)

conditions. We propose a simple cell dissociation method using an embryonic stem cell divider (ESCD) to support large-scale expansion with high efficiency and minimization of damage to human ESCs. The ESCD was constructed from a poly(dimethylsiloxane) (PDMS) replica with a square or hexagonal pattern. Using the ESCD, human ESC colonies can be easily and efficiently dissociated into regular-sized ESC clumps without enzymatic treatment. Its quality and reliability were confirmed by maintaining undifferentiated ESCs up to the 15th passage. The ESCD will contribute to the advance quality control of in vitro ESC cultures and allow large-scale production of qualified ESCs with tremendous time- and work-saving [5].

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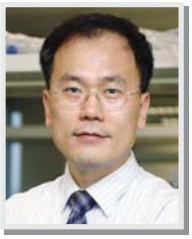
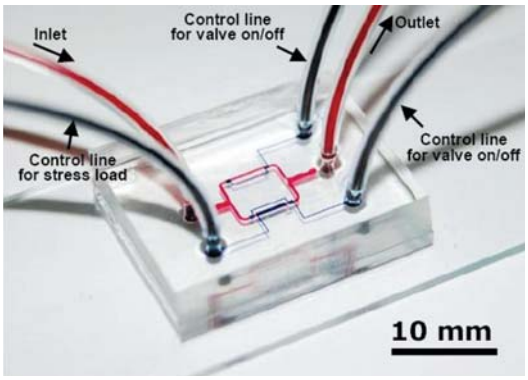
4.1.8. NanoBiotech Laboratory
(Prof. Je-Kyun Park, http://nanobio.kaist.ac.kr)



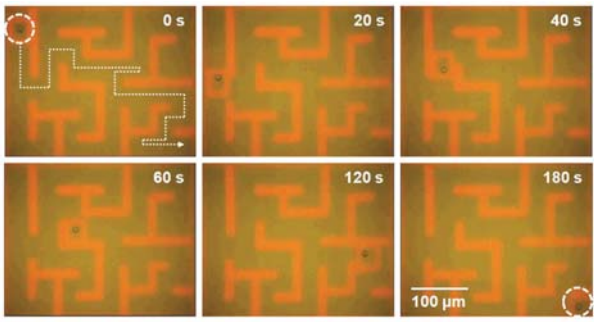
The aim of NanoBiotech Laboratory (NBL) lies in conducting research and development on nanobiotechnology as well as microsystems technology. During the last five years, NBL has interested in developing a novel biomicrofluidic devices for biotechnology and bioengineering, based on the synergetic integration of miniaturization technology to biology, chemistry, and medicine. Currently, NBL focuses on the development of a nanobiosensor, microfluidic device and lab-on-a-chip as a new platform for biological sample processing and detection. The main application areas include biomolecular diagnostics, micro total analysis system (μTAS), cell-based high-throughput screening, and nanobio device.

Cell-Based Assay Platform



The physical forces to which living cells are most commonly exposed are fluid shear, pressure, and stretch. These mechanical stimulations influence the physiological and pathological condition of the organism, which induces many aspects of human health and disease. We recently develop a new kind of microfluidic biomechanical device for compressive stimulation and lysis of cells. Mechanical stress is applied to the cells with the deflection of the poly(dimethylsiloxane) (PDMS) membrane between two microchannels, formed by multilayer soft lithography. The membrane functions as an on?off valve for closing the fluid channel and a loading membrane for applying compressive stress. As a demonstration of the feasibility of this microfluidic device, the viability of mammary gland epithelial (MCF7) cells in response to compressive stress is assessed by the change of fluorescence intensity with calcein AM [1]. It is also confirmed that the cells are deformed and lysed under compression by the deflected membrane. This device serves as an enabling tool for investigating the cellular response to mechanical stresses. Furthermore, mechanical lysis of cells can be exploited in a microchannel by the compressive force through the membrane deflection. This lysis method could be applied to develop the integrated microfluidic devices for sample preparation and cell-based assays.

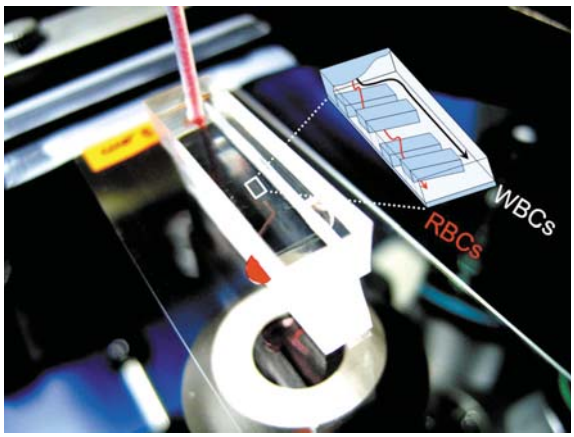
Dielectrophoretic Separation Platform



We report a lens-integrated liquid crystal display (LCD)-based optoelectronic tweezers (OET) system for interactive manipulation of polystyrene microspheres and blood cells by optically induced dielectrophoretic force. When a dynamic image pattern is projected into a specific area of a photoconductive layer in an OET, virtual electrodes are generated by spatially resolved illumination of the photoconductive layer, resulting in

dielectrophoresis of microparticles suspended in the liquid layer under nonuniform electric field. In this study, the simple-structured OET system has been easily constructed with an OET device, an LCD and a condenser lens integrated in a conventional microscope. By using a condenser lens, both stronger dielectrophoretic forces and higher virtual electrode resolution than previously reported lens-less LCD-based OETplatform are obtained. The effects of blurred LCD image and liquid chamber height on the performances of optoelectronic particle manipulation are investigated by measuring the bead velocities according to their sizes. An interactive control program for OET-based microparticle manipulation is also developed by Flash language. The integrated system is successfully applied to the parallel and interactive manipulation of red and white blood cells [2]. Due to its simple structures, cheap manufacturing costs, and high performances, this new LCD-based OET platform may be a widely usable integrated system for optoelectronic manipulation of microparticles including living cells.

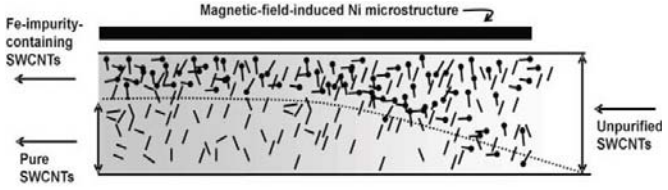
Hydrophoretic Separation Platform



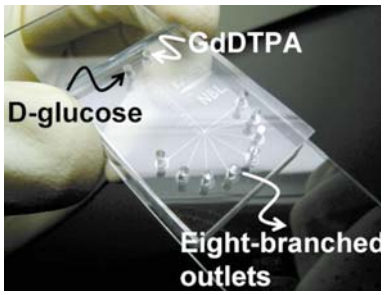
We recently report a microfluidic separation and sizing method of microparticles with hydrophoresis – the movement of suspended particles under the influence of a microstructure-induced pressure field. By exploiting slanted obstacles in a microchannel, we can generate a lateral pressure gradient so that microparticles can be deflected and arranged along the lateral flows induced by the gradient [3]. The slanted obstacle as a microfluidic control element in a microchannel is analogous to the electric, magnetic, optical, or acoustic counterparts in that their function is to generate a field gradient. Since our method is based on intrinsic pressure fields, we could eliminate the need for external potential fields to induce the movement of particles. Therefore, our hydrophoretic method will offer a new opportunity for power-free and biocompatible particle control within integrated microfluidic devices.

Magnetophoretic Separation Platform

A magnetophoretic, continuous purification platform has been developed to rid single-walled carbon nanotubes (SWCNTs) of superparamagnetic iron-catalyst nanoparticles using the enhanced magnetic force of ferromagnetic microstructures in a microfluidic device, as shown in the image. By employing microfluidics and a magnetic field-induced saw-tooth nickel microstructure, a highly enhanced magnetic force in adjoining microchannels is exploited. The iron impurities of SWCNTs are attracted towards areas of higher magnetic-flux density in the microchannels where magnetic field was asymmetrically generated perpendicularly to the streamline. We obtained highly purified SWCNTs at a rate of 0.36 mgh-1 and that are estimated to be about 99% purity [4].



Recently, we also report an improved magnetophoretic method, isomagnetophoresis, employing the magnetic susceptibility gradient across a microfluidic channel applied by magnetic field and we have successfully discriminated the polystyrene (PS; 14.78±0.20 ㎛ in diameter), poly(methyl methacrylate) (PMMA; 15.00±0.77 ㎛) and borosilicate (BS; 14.01±1.00 ㎛) microspheres, where PS and PMMA particles have similar diamagnetic susceptibility that cannot be distinguished by conventional magnetophoresis [5]. This platform can be applied to label-free discrimination of the biological cells and nanotubes.



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4.1.8. NanoBiotech Laboratory

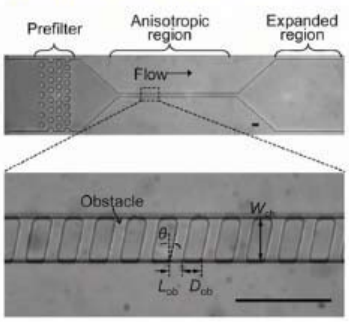
(Prof. Je-Kyun Park, http://nanobio.kaist.ac.kr)

Nanobiotechnology is the application of nanotechnology into the life sciences. This research area consists of two closely related sides. One focuses on developing nanoscaled products with biologically related approaches while the other applies nanoscaled tools to biological systems. Nanobiotechnology creates new opportunities in wide areas of science and engineering based on the interplay between nanotechnology and biotechnology. 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 areas and covers bioMEMS, micro/nano fluidics and bioelectronics. 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 cell-based assay, hydrophoretic separation, magnetophoretic assay, and optoelectrofluidic manipulation. From June 2008, his laboratory has been selected to receive a National Research Laboratory (NRL) Program grant funded by the Korea government (MEST).

Optoelectrofluidic Manipulation Platform

A novel programmable microfluidic platform by which particles are manipulated by electrofluidic forces such as dielectrophoretic or electro-osmotic force generated with a light, has been developed. When a dynamic image pattern is projected into a specific area of a photoconductive layer, virtual electrodes are generated, resulting in electrokinetic motions of micro/nanoparticles under a nonuniform electric field. By using a compact, integrated LCD-based optoelectrofluidic platform, we have characterized the frequency-dependent phenomena of the optoelectrofluidic concentration of microparticles due to the image-driven AC electrokinetics including dielectrophoresis and AC electro-osmosis. This new platform may be a widely usable integrated system for optoelectrofluidic manipulation of micro/nano particles including living cells and biomolecules [1].

Hydrophoretic Separation Platform



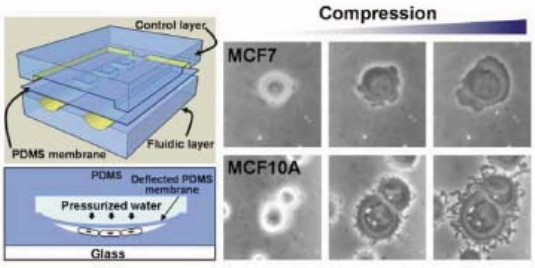
Separation and sorting of micros pheres and blood cells were achieved by using a novel microfluidic mechanism, hydrophoresis, which is hydrodynamic interaction between microfluidic obstacles and particles subject to rotational flows induced by the anisotropic fluidic resistance of the obstacles [2]. The equilibrium positions of the particles by the hydrodynamic interaction depend on their size. Recently, we report a hydrophoretic device that uses rotational flows induced by regularly patterned obstacles only on the top wall for preparing samples of biological particles, including micrometer and submicrometer particles, and DNA

molecules. Continuous separation of these particles was achieved using the obstacles, demonstrating the potential of hydrophoresis for biological sample preparation on the micro- and nanoscales, with the advantages of continuous flow and sheathless passive operation.

Magnetophoretic Assay Platform

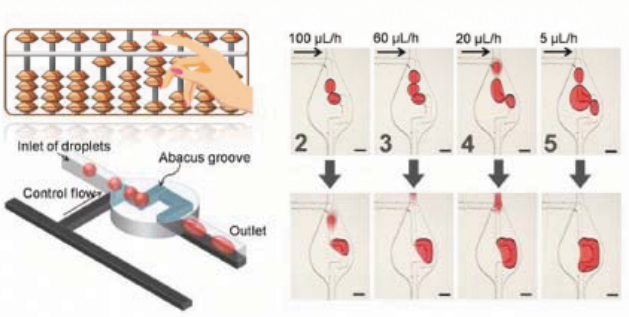
A new immunoassay system based on magnetophoretic mobility of a superparamagnetic nanoparticle conjugated microbead has been developed. By measuring the magnetophoretic deflection of the microbeads varied by the concentration of analytes, the multiple disease markers are simultaneously quantified [3a]. We have also reported a novel magnetophoretic principle, isomagnetophoresis, employing the magnetic susceptibility gradient across a microfluidic channel [3b]. By using this method, the subtle magnetic susceptibility of microparticles was successfully discriminated.

Cell-Based Assay Platform



We have developed a microfluidic device that can be used to spot the difference between cancerous cells and healthy ones by squeezing them until they deform – a discovery that could lead to a cheap tool for cancer detection [4]. Cancer cells are known to have a less extensive internal cytoskeleton than healthy cells, so behave differently when squeezed. We have exploited this property in their two-channel microfluidic device. The first channel holds the sample, and is separated from the second channel by a flexible membrane. Pressurizing the second channel compresses the cells in the sample until they deform. We found that compressed cancerous cells were left with a series of bulges across their surface. But the healthy cells looked very different, being covered with worm-like projections. The device could be used to further study cytoskeleton changes within cells, as well as other diseases, from malaria to Alzheimer's, which are associated with cell cytoskeleton changes.

Microdroplet Technology



Microfluidic abacus channels are demonstrated for the sequential addition of droplets at the desired location [5]. We created a wide microfluidic chamber with a sharply bending groove cut into it. When droplets enter the chamber, they are guided by the groove but get stuck at its rectangular corners. As more droplets enter the groove, they merge at the bend to form a bigger droplet, which is eventually forced out of the chamber as the pressure builds up behind it. Although the droplets enter the chamber at a fixed rate, we introduced a control flow to vary the number of merging droplets – as the flow rate increases, the number of droplets merging decreases because the merged droplet is forced out the chamber more quickly.?The device allows programmable

and autonomous operations of complex two-phase microfluidics as well as new applications for the method of analysis and computations in lab-on-a-chip devices.

References

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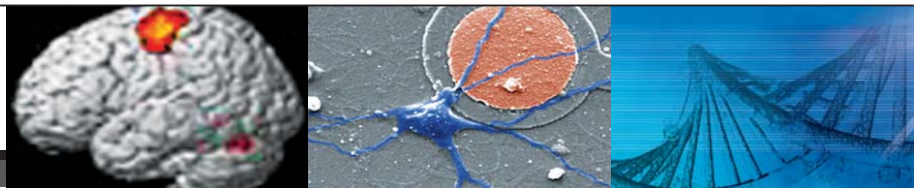
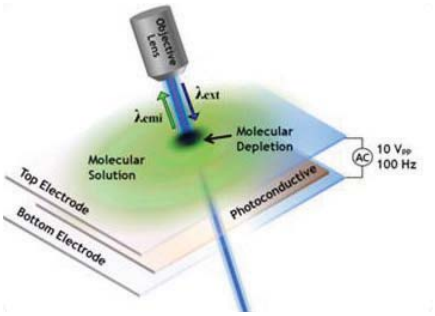


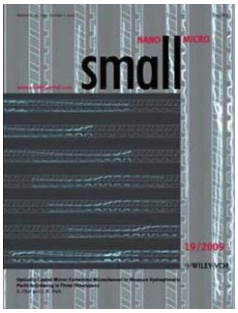
4.1.13. NanoBiotech Laboratory
(Prof. Je-Kyun Park, http://nanobio.kaist.ac.kr)

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.



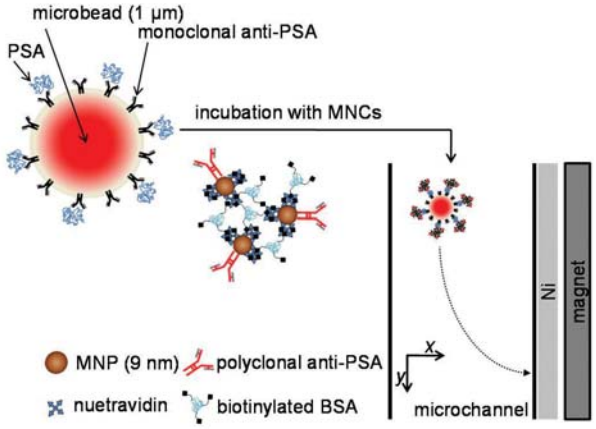


Hydrophoretic Separation Platform

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

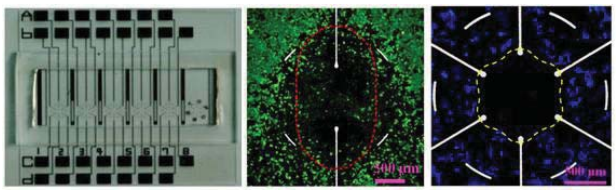
be deflected and arranged along the lateral flows induced by the gradient. The equilibrium positions of the particles by the hydrodynamic interactions depend on their size. The hydrophoretic principles were successfully applied to the particle sizing, sheathless particle focusing, isolation of white 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

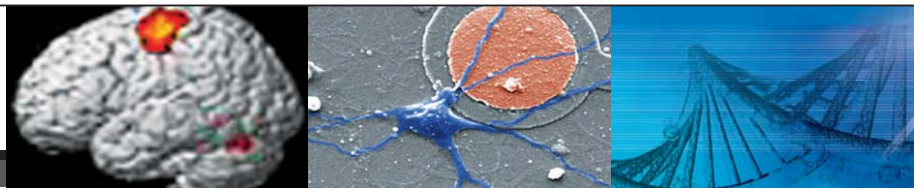


We developed a new immunoassay system based on the magnetophoretic mobility of a microbead, depending on the amount of associated superparamagnetic nanoparticles under magnetic field gradient in a microfluidic channel. By measuring the magnetophoretic deflection velocity of microbeads as the signal for 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].

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04 Research Activities

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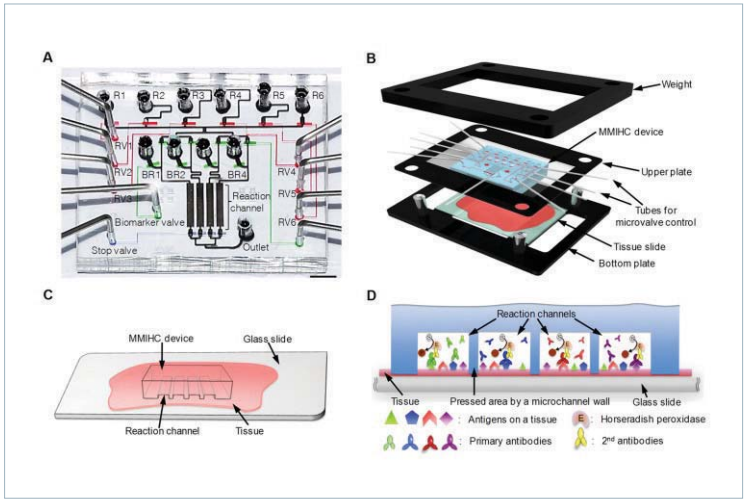
NanoBiotech Laboratory

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

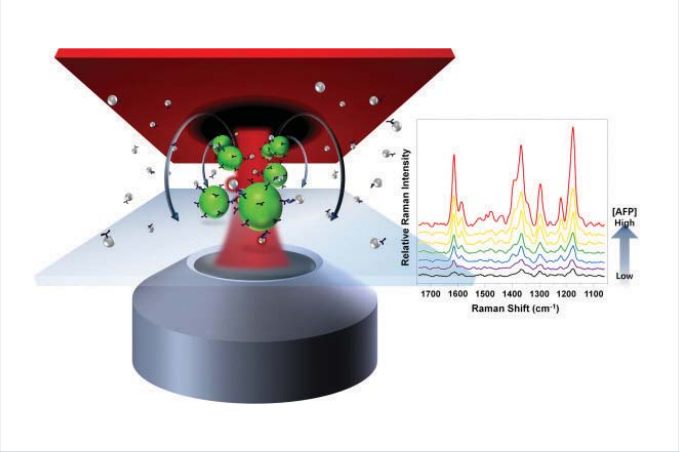
Recent progress of lab-on-a-chip technology is challenging for the development of nanobiotechnology and integrative bioengineering. Particularly, micro/nano fluidics has been a key technology for the realization of micro total analysis systems (μTAS) or lab-on-a-chip as well as the next generation bio-tools 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



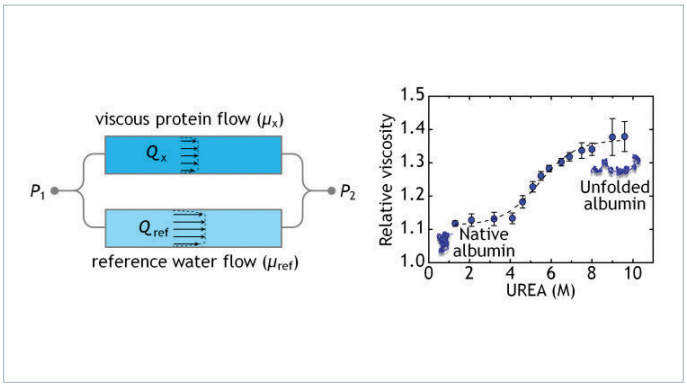
Breast cancer is a heterogeneous disease with many subtypes, and it is difficult to accurately monitor the treatment response of the disease, and to predict the clinical outcome of individual neoplasms. We recently succeeded in developing a microfluidic interface that enables multiplexed immunohistochemistry (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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