S1c1-1  
Femtoliter chamber for single-molecule analysis  
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Micro/nano technology enables to fabricate micro/nanometer-sized devices for fast and highly sensitive detection of biological reaction. We developed micron-sized reaction chambers to enclose reaction mixture with a volume of a few femtoliter. Such an extremely small reaction chamber allows us to detect very small amount of chemical products generated by a single enzyme molecule. The enzymatic reaction activities of beta-galactosidase and horse radish peroxidase were detected at a single molecule level by entrapping fluorogenic reaction mixture. Combination of this highly sensitive detection method with a single-molecule manipulation of a rotary molecular motor, FI-ATPase offers the way to the single-molecule analysis of chemomechanical coupling efficiency of FI-ATPase. Recently, another group reported that stochastic expression of protein molecules in a single bacteria cell was monitored at a single-molecule level using similar reaction chamber. These experiments certify the large potential of the chamber for highly sensitive analysis of biological reactions.

S1c1-2  
Digital Microfluidics  
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Digital microfluidics is an emerging class of microfluidic technologies, where fluids are handled in discrete volumes rather than continuous flows. For processing of liquids, droplets can be moved by various actuation methods, including thermal, surface wave, electrostatic, dielectrophoretic, and electrowetting, currently the last being the most common. A common feature of the droplet-driving schemes is the droplet actuation being highly localized at each droplet. Since droplets are not moved by the pressure around them, digital microfluidic systems can be built without microchannels, pressure sources (e.g., micropumps) or regulatory elements (e.g., microvalves), greatly simplifying the devices and systems. Our current emphasis on digital microfluidics is to establish a lab-on-a-chip platform by the mechanism of electrowetting-on-dielectric (EWOD). Demonstrated to manipulate aqueous droplets in the air or in oil, EWOD-based microfluidics development has accomplished many physical functionalities: creating, dividing, and merging droplets, mixing different droplets, separating and concentrating particles in a droplet, and printing such droplets. As a biochemical application example of the EWOD chip, we demonstrate on-chip sample processing for MALDI Mass Spectrometry. To demonstrate the simplicity EWOD digital microfluidics allows for system development, we showcase a stand-alone handheld prototype system complete with a battery pack. With the ability to create EWOD chips capable of manipulating multiple droplets on a two-dimensional grid array, build an entire system on a printed circuit board, and accurately control droplet volumes on chip through real-time feedback, a complete handheld lab-on-a-chip system seems within the horizon.

S1c1-3  
Soft-state Biological ASICs and Nanofluidic SERS for Quantitative Systems Biology  
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In order to create high-content Integrated Quantitative Molecular Diagnostics (QMD) chip, microfluidic-based Biological Application Specific Integrated Circuits (BioASICS) and quantum nanophotonic probes such as nanostructured surface enhanced Raman scattering (SERS) substrates are developed. Soft-state BioASICS are created by connecting existing and novel microfluidic circuits for high-content experimental biology in new ways. We are creating a library of these "building blocks" to develop multifunctional biological microprocessors. To build a solid foundation of future high-speed micro- and nanofluidic bioprobes for experimental systems biology and biomarker discovery, we have developed design rules and critical modules of BioASICS such as single cell analysis chip, integrated multiple patch-clamp array, dynamic cell culture array, on-chip cell lysing device, sample preparation chip, cell separation device, high-density single cell analysis chip, molecular harvesting device, cell-cell communication array. Recently, we also accomplished artificial livers on a chip for drug screening and drug discovery. For nanoscale spectroscopic molecular imaging and photothermal therapeutic applications, nanosensitive SERS probes are developed. The formation of asymmetric nanophotonic crescent structure is accomplished by the interfacing both bottom-up and top-down methods, which allows to create effective local field enhancement structures, batch nanofabrication, and precise controls of hot spot coupling distance for in-vivo molecular imaging. Gold-based nanocrescents have structures with a sub-10 nm sharp edge, which can enhance local electromagnetic field at the edge area. The advanced nanocrescent SERS probes can be applied for sensitive molecular detection and electron transfers of biomolecules. In addition, integrated nanofluidic SERS device can provide a new solution for label-free genomics and proteomics. The functional BioASICS and quantum nanophotonics have a potential to impact on systems biology, quantitative cell biology, biophysics, and molecular medicine.

S1c1-4  
Microfluidic Systems for Membrane Protein Analysis  
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The University of Tokyo

Membrane proteins play very important roles in cells (e.g., recognition or transportation of molecules). They are also useful in various industrial fields, including next-generation diagnosis techniques, drug discovery, and highly sensitive ion-channel-based biosensors. In this presentation, I will introduce our approach toward membrane protein chips; an array of single-species-specific membrane proteins reconstituted into planar lipid bilayers formed in microfabricated holes and channels. In this approach, a highly reproducible method was developed for planar lipid bilayer reconstitution. Planar lipid bilayers are formed at apertures, 100 micron in diameter, by flowing lipid organic solution and buffer alternately into an integrated microfluidic channel. Using this technique, multiple lipid bilayers are formed simultaneously in a single chip, and channel currents through peptide ion channels was recorded to prove the compatibility of the chip with single molecule electrophysiology. We believe that these devices are useful for an efficient and rapid analysis of single-species-specific membrane proteins.