Development of Small-Molecule Tools for Cell Therapy

Cell Biology empowered by small molecules

Professor Motonari Uesugi – Institute for Chemical Research *and* iCeMS

Taking advantage of technology available in fields ranging from organic chemistry to clinical medicine, Prof Motonari Uesugi and his research team seek to discover and use synthetic small molecules that modulate fundamental processes in human cells, specifically small-molecule adhesion factors and small-molecule growth factors. Their goals extend beyond the discovery of clinically useful molecules, to include design innovations and chemical synthesis that will lead to new, broad, and cost-effective general applications of synthetic organic molecules.

Prof Uesugi's discoveries have made possible the investigation of complex cellular events and the improvement of cell therapies. The team has already discovered a synthetic small molecule, "adhesamine," which boosts adhesion and growth of cultured human cells. Using this molecule as a seed, Prof Uesugi and colleagues designed a synthetic molecule that behaves just like fibronectin, a naturally-occurring protein commonly used in a range of fields from basic biology to cosmetics. The team has additionally shown that it is possible to replace fibronectin, a large protein, with a synthetic compound appropriate in size for mass chemical production. The development of this "small molecule fibronectin" is a groundbreaking contribution to chemistry, biology, and medicine.

www.icems.kyoto-u.ac.jp/e/pr/2011/05/12-tp.html

Receptor Behaviors Observed in Living Cell Membranes

Expanding drug development horizons

Professor Akihiro Kusumi [left] – iCeMS
Rinshi Kasai PhD [right]

Unprecedented single molecule imaging movies of living cell membranes, taken by a research team based at Kyoto University and the University of New Mexico, have clarified a decades-old enigma surrounding receptor molecule behaviors. The work focuses on G protein-coupled receptors (GPCRs), a class of molecules in cell membranes that comprise the largest superfamily in the human genome. According to iCeMS Prof Akihiro Kusumi, "We obtained a parameter called the dissociation constant, which will allow us to predict numbers of monomers and dimers if the total number of GPCRs in a cell is known. The ability of scientists to obtain such key numbers will be essential for understanding GPCR signaling, as well as defects leading to diseases from the neuronal to the immune systems. The blocking of signal amplifications by monomer-dimer interconversions and its implications for drug design are profoundly important."

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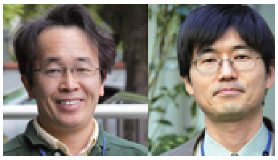


DNA Engine Observed in Real-Time,Traveling Along Base Pair Track

Applicable to the development of advanced drug delivery methods and molecular manufacturing systems

Professor Hiroshi Sugiyama [left] – Graduate School of Science *and* iCeMS
Masayuki Endo [right] – iCeMS

In a complex feat of nanoengineering, a team of scientists at Kyoto University and the University of Oxford have succeeded in creating a programmable molecular transport system, the workings of which can be observed in real time. Resembling a monorail train, the system relies on the self-assembly properties of DNA origami and consists of a 100 nm track together with a motor and fuel. Using atomic force microscopy (AFM), the research team was able to observe in real time as this motor traveled the full length of the track at a constant average speed of around 0.1 nm/s. "DNA origami techniques allow us to build nano- and meso-sized structures with great precision," elaborated iCeMS Prof Hiroshi Sugiyama. "We already envision more complex track geometries of greater length and even including junctions. Autonomous, molecular manufacturing robots are a possible outcome."
www.icems.kyoto-u.ac.jp/e/pr/2011/02/07-nr.html

Shining New Light on Air Pollutants Using Entangled Porous Frameworks

Applicable to the development of a new range of portable, solid-state pollution detectors, and possibly even new types of light sources

Professor Susumu Kitagawa [right] – iCeMS *and* Graduate School of Engineering
Associate Professor Shuhei Furukawa [left] – iCeMS

Associate Prof Shuhei Furukawa and Prof Susumu Kitagawa at iCeMS, and Dr. Yohei Takashima (currently at the University of Glasgow, Scotland, UK) have synthesized a newly-formulated entangled framework of porous crystals (porous coordination polymers, or PCPs) that can not only capture a variety of common air pollutants, but are distinguishable with a corresponding easily-detected color. The research team has created what amounts to interlocking jungle-gyms that move relative to each other and are therefore able to capture molecules of varying sizes. This PCP based on naphthalenediimide, known as NDI, expands and contracts to confine air-born aromatic volatile organic compounds (VOCs) such as benzene, toluene, xylene, anisole, and iodobenzene, which are common pollutants in the lower atmosphere. When exposed to ultraviolet light, the enhanced NDI-VOC interaction luminesces in an unusually wide range of colors, sufficiently intense enough to be observed even with the naked eye. The cooperative structural transition in mesoscopic crystal domains result in a nonlinear response to the guest concentration. Thanks to its high emission intensity in the full range of visible light, this new material may demonstrate new types of light emitters – even including white-light.
www.icems.kyoto-u.ac.jp/e/pr/2011/01/26-nr.html

Flow-microreactor Approach to Protecting-group-free Synthesis Using Organolithium Compounds

Potential applications in the mass production process for drugs and specialty chemicals.

Professor Jun-ichi Yoshida – Graduate School of Engineering

Protecting-group-free synthesis has received significant recent research interest in the context of ideal synthesis and green sustainable chemistry. In general, organolithium species react readily with ketones, and therefore ketone carbonyl groups should be protected before an organolithium reaction, if they are not involved in the desired transformation. If organolithium chemistry could be freed from such a limitation, its power would be greatly enhanced. Prof Yoshida and his research group have shown that a flow microreactor enables such protecting-group-free organolithium reactions by greatly reducing the residence time (0.003 s or less). Aryllithium species bearing ketone carbonyl groups are generated by iodine–lithium exchange reactions of the corresponding aryl iodides with mesityllithium and are reacted with various electrophiles using a flow-microreactor system. The present method has been successfully applied to the formal synthesis of Pauciflorol F.
dx.doi.org/10.1038/ncomms1264

Peptides and Genes that Enhance the Formation of Stoma in Plants

Improvement of growth and biomass productivity

Professor Ikuko Hara-Nishimura – Graduate School of Science

Stomata, in the epidermal tissues of leaves, are valves through which CO_2 passes, influencing the global carbon cycle. The two-dimensional pattern and density of stomata in the leaf epidermis are genetically and environmentally regulated to optimize gas exchange.

Prof Ikuko Hara-Nishimura at the Graduate School of Science and her research team have found that a novel secretory peptide, known as STOMAGEN, is a positive intercellular signaling factor that is conserved among vascular plants. STOMAGEN is a 45-amino-acid peptide and is able to enhance the formation of stoma in plants. If the technology is further developed, it will be possible to modify plants to absorb CO_2 much faster, without genetically modifying the genome of the target plants. Such plants should grow faster and be able to remove CO_2 more effectively from the atmosphere.

The advantages include: (1) STOMAGEN positively regulates stomatal density without modifying the genome (2) It may be possible to enable plants to absorb CO_2 much faster (3) Plants should be able to grow faster.
www.nature.com/nature/journal/v463/n7278/abs/nature08682.html

Highly Efficient and Precise Processing Inside Transparent Materials Using Femtosecond Laser

Potential applications in optical waveguides, 3D optical data storage, space selective light emission, coloration, ion migration inside glasses and transparent and flexible solar cells

Professor Kazuyuki Hirao – Graduate School of Engineering

Graduate School of Engineering Prof Kazuyuki Hirao and his research team have developed a series of techniques to create refractive index distribution inside various transparent materials with a spatial resolution of less than a micrometer, by focusing femtosecond laser pulses.

The techniques include: (1) Highly efficient laser processing with an LCOS-SLM (Liquid Crystal on Silicon - Spatial Light Modulator), e.g. multiple light spots can be generated by modulating the phase distribution of a laser pulse. (2) Ultrafast microscopic photography of laser processing inside various transparent materials, e.g. the material deformation process after irradiation with a focused laser pulse can be observed with a time resolution of 10^{-13} second. With this technique, the research team was able to elucidate the origin of damage after loading external forces on to various solid materials, and (3) Nanostructuring inside a glass – Nanograting – which leads to rewritable 5D optical storage with a capacity of 37GB/cm^3, which corresponds to about 10 times the size of Blue-ray discs.

The above mentioned laser techniques are now being applied to the fabrication of high efficiency transparent and flexible solar cells.

int.icc.kyoto-u.ac.jp/video.htm

Softening Crystals without Heat Using Terahertz Pulses to Manipulate Molecular Networks

Possibilities in manipulating large molecules, thereby increasing understanding of the properties of molecular complexes such as proteins

Professor Koichiro Tanaka [right] – iCeMS
Assistant Professor Masaya Nagai [left] – Graduate School of Science

Prof Koichiro Tanaka at iCeMS and his research team have successfully developed a kind of tractor beam that can be used to manipulate networks of molecules. The research team has succeeded in generating intense terahertz (far-infrared) pulses with the electric field exceeding 1 MV/cm [*1] and demonstrated that it is possible to use the intense terahertz pulses to climb 20 ladder steps on the anharmonic intermolecular potential in the microcrystals [*2]. In this case, intense terahertz pulses were used to successfully increase the amplitude of movement between amino-acid molecules in crystalline form, essentially softening the crystals. Previous softening methods have always correspondingly raised the temperature, resulting in unwanted changes to the crystals' structure and properties. This novel technique using terahertz pulses may have broad applications in the chemical and pharmaceutical industries.

www.icems.kyoto-u.ac.jp/e/pr/2010/11/01-nr.html

[*1] http://apl.aip.org/resource/1/applab/v98/i9/p091106_s1

[*2] http://prl.aps.org/abstract/PRL/v105/i20/e203003

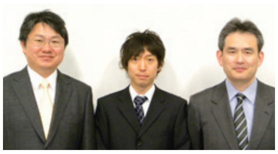
Selective Dye Loading at the Polymer/Fullerene Interface

Improving efficiency of plastic solar cells by using dye surfactants similar to soap

Associate Professor Hideo Ohkita – Graduate School of Engineering

Graduate School of Engineering Associate Prof Hideo Ohkita and his research group have succeeded in improving the efficiency of plastic solar cells based on a blend of poly(3-hexylthiophene) (P3HT) and a fullerene derivative (PCBM) by incorporating a light-harvesting dye, silicon phthalocyanine derivative (SiPc), and revealing the underlying mechanism of selective dye loading. Focusing on a similarity between the dye they used and surfactants in soap, both of which spontaneously segregate to form an interface, they found that SiPc was located at the P3HT/PCBM interface from the absorption and surface energy measurements. Such interfacial segregation of dye molecules can be rationally explained in terms of the surface energy of each component similar to the effects of surfactant compounds in soap. Crystallization of P3HT by annealing also induces additional enhancement of segregation. As a result, the photocurrent density and power conversion efficiency of the ternary blend solar cells were most improved by loading SiPc with a content of 4.8 wt%.

dx.doi.org/10.1002/aenm.201100094



High Power Silicon Carbide Bipolar Junction Transistors

Fabrication of silicon carbide power device for high energy efficiency

Associate Professor Jun Suda [left] – Graduate School of Engineering
Dr. Hiroki Miyake [center] – Graduate School of Engineering
Professor Tsunenobu Kimoto [right] – Graduate School of Engineering

Prof Tsunenobu Kimoto and Associate Prof Jun Suda of the Graduate School of Engineering have reported achieving world-record current gains in silicon carbide (SiC) bipolar junction transistors (BJTs) by using original fabrication technologies. SiC BJTs are promising power semiconductor devices for high-efficiency energy conversion, when employed in a variety of motor control (including EV/HEV) and power supplies (including solar cells). However, SiC BJTs have suffered from low current gains, typically 50-70. The research team was able to significantly reduce carrier recombination in bulk SiC as well as at the SiC surface, based on their recent inventions on defect elimination. This defect elimination includes the annihilation of point defects by thermal oxidation and the reduction of surface states by passivation with deposited oxides annealed in nitric oxide. The research team successfully demonstrated high-voltage SiC BJTs with record current gains ( ) of 257-335, which is a two- or three-fold improvement on the previous best BJT.

ispsd2011.e-papers.org/ESR/paper_details.php?PHPSESSID=66kfvn7o4arvt9o3u344249j64&paper_id=1161
www.ispsd2011.com/index.htm