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Japan Symosium 2015

(Abstract)

SYMPOSIUM Session 980

JAIMA - The State-of-the-Art Technologies from Japan: Analytical Instruments with/for Nano-Bio Technology and Advanced Diagnosis I

arranged by Koichiro Matsuda, JAIMA

Tuesday Morning, Room 260

Koichiro Matsuda and Takeshi Kawamoto, JAIMA, Presiding

8:30 **Introductory Remarks –** SHIGEHIKO HATTORI

8:35 (980-1) **Nano- and Quantum-Biodevices for Cancer Diagnosis, Cancer Therapy, and iPS Cell Based Regenerative Medicine** YOSHINOBU BABA, Nagoya University

9:10 (980-2) **Luminescent Sensors and Switches for Single Cell Analysis** TAKEAKI OZAWA, The University of Tokyo

9:45 (980-3) **Designing Mechanized Nanoparticles for Cancer Therapy and Diagnosis: Toward Developing Nanorobots** FUYUHIKO TAMANOI, University of California, Los Angeles

10:20 **Recess**

10:35 (980-4) **Innovative Electron Microscope for Nano-Biology** BARBARA ARMBRUSTER, Hitachi High Technologies America, Inc.

11:10 (980-5) **How to Explore the Bio-Nano World with Surface Piasmon Resonance lmaging** CHIRAZ FRYDMAN, Horiba Scientific and MARINELLA G.SANDROS, University of North Carolina at Greensboro

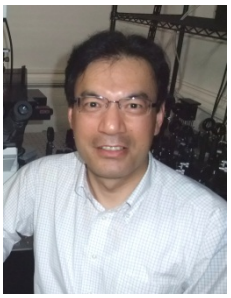
Nano- and Quantum-Biodevices for Cancer Diagnosis, Cancer Therapy, and IPS Cell Based Regenerative Medicine

Yoshinobu Baba, PhD, Professor
Department of Applied Chemistry, School of Engineering, FIRST Research Center for Innovative Nanobiodevices, Nagoya

Abstract

Nano-/quantum-biodevice is a piece of contrivance, equipment, machine, or component, which is created by the overlapping multidisciplinary activities associated with nano-/quantum-technology and biotechnology, intended for biological, medical, and clinical purposes. In this lecture, I will describe the development of nano-/quantum-biodevices for biomedical applications, including single cancer cell diagnosis for cancer metastasis, circulating tumor cell (CTC) detection by microfluidic devices, nanopillar devices for ultrafast analysis of genomic DNA and microRNA, nanopore devices for single DNA and microRNA sequencing, nanowire devices for exosome analysis, single-molecular epigenetic analysis, quantum switching *in vivo* imaging of iPS cells and stem cells, and quantum technology-based cancer theranostics. Immunopillar devices realized the fast and low invasive “from blood to analysis” type biomarker detection of cancer with fM detection sensitivity within 2 min. Additionally, nanopillar devices give us ultrafast separation of DNA and microRNA within 60 μs and nanopillar-nanopore integrated nanobiodevice enables us ultarafast single molecular DNA sequencing. Nanowire devices coupled with super-resolution optical microscopy are extremely useful to analyze exosomes from cancer cells and exosomal microRNA analysis. Quantum dots are applied to develop nanobiodevice for single cancer cell diagnosis, single molecular epigenetic analysis, quantum switching *in vivo* imaging for iPS cell and stem cell therapy and theranostic device for cancer diagnosis/therapy.

Imaging and analysis of biomolecules in living cells



Takeaki Ozawa, PhD, Professor
Department of Chemistry, School of Science,
University of Tokyo

Abstract

Engineered fluorescent and bioluminescent proteins are now widely used for analysis of small molecules and various intracellular events in live cells. The luminescent proteins are entirely genetically encoded and can be engineered to generate functional probes. I herein describe a novel design of engineered fluorescent proteins and luciferases for the analysis of intracellular signaling; the principle is based on complementation and reconstitution of the split-reporter fragments when they are brought sufficiently close together. To demonstrate the usefulness of the split reporters, I will focus on imaging technology of cell survival and death: Using fluorescence imaging, I show methods for imaging dynamics of telomeric RNAs and different apoptotic signals in a single living cells. I also show novel techniques of bioluminescence imaging of caspase activation and intracellular acidification of living mice in a pathological condition. These less-invasive techniques are widely applicable for understanding complex biological systems with high spatiotemporal resolution.

Nanorobots for Cancer Diagnosis and Therapy

Fuyuhiko Tamanoi, PhD, Professor
Dept. of Microbio., Immunol. & Molec. Genet.
Jonsson Comprehensive Cancer Center
California NanoSystems Institute
University of California, Los Angeles

Abstract

One of the challenges in cancer therapy and diagnosis is to develop novel nanomaterials that can carry out targeted, controlled release of anticancer drugs and siRNA as well as to enhance imaging and diagnosis. We have been developing mechanized nanoparticles based on mesoporous silica nanoparticles (MSNs) that contain thousands of pores where chemicals can be stored. MSNs can be surface modified to provide tumor targeting capability. Efficacy of camptothecin-loaded MSNs to inhibit tumor growth was demonstrated in animal model systems. Extensive analysis of safety and biocompatibility of this type of material was carried out.

We equip MSNs with nanovalves that can cap the pore opening with a bulky chemical group. By opening and closing nanovalves, it is possible to achieve controlled release of the content. One type of nanovalves responds to change in pH and opens in acidic pH conditions that are encountered inside the cell or in the tumor environment. Another type of nanovalve contains a disulfide bond so that the nanovalve can respond to reducing conditions inside the cell. We have also developed MSNs that respond to light. This system uses azobenzene, a photosensitive chemical that changes conformation in response to light exposure. We call this drug delivery system nanoimpeller that releases anticancer drugs in response to blue light. More recently, we have developed a second generation nanoimpeller by incorporating a two-photon responsive fluorophore. This enabled the use of red or near infrared red light that is tissue penetrating. Finally, we have developed MSNs that respond to magnetic field. This MSN contains iron oxide core that has super paramagnetic property. Exposure to oscillating magnetic field increases temperature of MSNs opening the nanovalve and releasing contents. Iron oxide core also provides MRI enhancing property. Thus, these MSNs have multiple features that are ideal for imaging and therapeutic purposes.

Innovative Electron Microscope for Nano-Biology

Barbara L. Armbruster

Hitachi High Technologies America
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Abstract

Discoveries at the nanoscale continue to affect all of us at the global and local scales. This is especially true for the next generation of biomaterials as their development demands improved imaging and analytical

performance. Hitachi is responding to this challenge with its HT7700 and the EXALENS, a high resolution objective lens that sets the new performance standard for 40-120kV microscopy. By achieving a smaller spherical aberration coefficient, a lattice resolution of 1.4Å is demonstrated. EXALENS excels at high resolution transmission electron microscopy (TEM) imaging at low accelerating voltages with minimal beam damage, facilitating analyses of soft materials, carbon-based nanomaterials, polymers and catalysts. It is the superior choice for brightfield/darkfield scanning transmission electron microscopy (STEM), where thick biological specimens are imaged with reduced chromatic aberration. These improvements in electron optics, as well as recent developments in TEM instrumentation, have made it possible to study dynamic in-situ reactions of nanoparticles engineered for disease diagnosis and treatment.

How to Explore the Bio-Nano World with Surface Plasmon Resonance Imaging

Chiraz Frydman, PhD, Horiba Scientific
Marinella G. Sandros, PhD, University of North Carolina at Greensboro

Abstract

Analysis of the affinity and the binding between bio-molecules and between molecule and cell tends to be more and more towards label-free approaches. Biosensors and Biochips are developed worldwide to propose new, fast cheap, reliable and multiplexed tools to meet these demands.

SPR Imaging is moving the molecular interaction analyis a step further by offering the multiplex, label-free and real time detection. However, biological samples often contain attomolar or femtomolar concetrations of biomolecules, which is below the detection limit of SPRi. It is not common to combine the SPR to nanotechnology investigation. The high flexibility of the SPRi instrument as well as the biosensor itself open the way to reach ultra low sensitivity measurements.

SYMPOSIUM Session 1320

JAIMA - The State-of-the-Art Technologies from Japan: Analytical Instruments with/for Nano-Bio Technology and Advanced Diagnosis II

arranged by Koichiro Matsuda, JAIMA

Tuesday Afternoon, Room 260

Koichiro Matsuda, JAIMA, Presiding

Yoshinobu Baba, Nagoya University, Presiding

1:30 **Introductory Remarks –** NORIO TERAMAE

1:35 (1320-1) **Enhanced Nano-Drug Delivery After Photoimmunotherapy: Oncologic Applications** HISATAKA KOBAYASHI, NCI/NIH

2:10 (1320-2) **Single Molecule Electrical Sequencing Technology** MASATERU TANIGUCHI, Osaka University

2:45 (1320-3) **SAMPLE PREPARATION; The Achilles Heel of Rapid Mass Spectral Analysis;** FRED REGNIER, Purdue University

3:20 **Recess**

3:35 (1320-4) **Next Generation LCMS Approaches: From Multivariate Panels to Targeted Bioanalysis** CHRISTOPHER GILLES, Shimadzu Scientific Instruments

4:10 (1320-5) **Biological Applications of Fine Structure Analysis and Peripheral Technology Using Cryo-Scanning Electron Microscopy**
N. KIKUCHI, Y. HASEBE, T. KANEKO, Y. TAKASHIMA, K. KAWAUCHI, M. SUGA, T. SUZUKI and T. NOKUO, JEOL Ltd.

Enhanced nano-drug delivery after photoimmunotherapy:Oncologic applications

Hisataka Kobayashi, MD, PhD, Chief scientist
Molecular Imaging Program/NCI/NIH

Abstract

Target-specific drug delivery that treats cancers but leaves normal tissue unharmed, is the ultimate goal of cancer therapy. Nano-sized drugs have virtually limitless synthetic possibilities enabling a variety of payloads to be delivered to the tumor resulting in effective therapy. Tumors have relatively higher concentrations of nano-sized drugs than normal tissue due to the leaky nature of tumor vasculature, a phenomenon known as enhanced permeability and retention (EPR). The EPR effect, while permitting an increase in intratumoral nano-drug concentration, nonetheless has a limited ability to achieve concentrations that take full advantage of the capabilities of nano-sized drugs. Thus, a method for better nano-drug delivery might lead to improved cancer therapy. We have recently developed a new type of highly selective, molecularly-targeted cancer therapy, named photoimmunotherapy (PIT), that is based on conjugating a near infrared silica-phthalocyanine dye, IR700, to a monoclonal antibody (MAb) thereby targeting cancer-specific cell-surface molecules. After the administration of the conjugate and the targeted application of light, the intratumoral vascular barrier is significantly disrupted enabling a dramatic (up to 24 fold) increase in nano-drug concentration in PIT treated cancer tissue compared with non-treated control tumors. In this lecture I will discuss general pharmacokinetic characteristics of nano-sized molecules in the body, especially focusing on drug delivery in cancer tissue and routes of excretion that are important for improving the safety profile. In addition, I will discuss the basis and applications of the PIT-induced super-enhanced permeability and retention (SUPR) effect that could dramatically improve nano-drug delivery thereby enhancing the therapeutic effects of nano-sized anti-cancer agents.

Single-Molecule Electrical SequencingTechnology

Masateru Taniguchi, PhD, Professor
The Institute of Scientific and Industrial Research, Osaka University

Abstract

Cost per genome has decreased much more rapidly than predicted by Moore's law, which famously predicts the growth of the semiconductor industry, whereas the sequencer market has grown at an annual rate of approximately 18%. This rapid reduction in cost, along with the growth of the market, indicates a rapid expansion of new industries using DNA sequencers. The market for DNA sequencers is estimated to increase to $700 billion by 2025. To realize such rapid growth of this market, we must develop innovative technologies that can read an entire human genome within an hour and at a cost of only $100. This is in contrast with the Human Genome Project, which cost $2.7 billion and required 13 years to read a single genome. Targeted technologies are the 4th generation DNA sequencing technologies, and this study will introduce the most influential candidate—single-molecule electrical sequencing technology.

Single-molecule electrical sequencing technologies can identify single molecules by passing them through nanopores and measuring the tunneling currents generated between nanoelectrodes. This method of sequencing DNA, RNA, and peptides is expected to revolutionize molecular biology, medical science, and drug development. Our technique has the potential to sequence chemically modified bases and amino acids, which cannot be performed by any other existing direct sequencing methods.

SAMPLE PREPARATION; The Achilles Heel of Rapid Mass Spectral Analysis.

Fred Regnier;
Distinguished Professor of Chemistry, Purdue University and C.E.O. of Novilytic, West Lafayette, IN, USA

Abstract

Identification and quantification of substances in biological samples is a subject of great interest today, particularly in drug metabolism and pharmacokinetics, biomarker discovery and validation, clinical diagnostics, and translational medicine. The fact that mass spectrometry (MS) can analyze hundreds of metabolites, drugs, and proteins in milliseconds would suggest it could be an enormous asset in environments requiring rapid data acquisition for decision making. But mass analysis is preceded by a lengthy set of sample preparation steps involving sampling, the removal of cells or cellular debris, taking a sample aliquot, chemical modification in some cases, analyte enrichment, and selection of a portion of the sample for MS analysis. Execution of these steps can require hours and involves multiple sample transfers. Clearly sample preparation limits the potential of MS. Efforts to address limitations in sample preparation often involve the use of robotics to replace manual components of sample preparation. Although this reduces the amount of labor involved, robots generally fail to integrate individual steps and reduce the necessity of transferring the sample between multiple preparation vessels. These objectives were achieved in the membrane system described here by integrating multiple sample preparation steps within a single vessel where samples were transported through spatially staged, miniaturized sample preparation components preloaded with reagents. Sampling, reagent addition, mixing, sample splitting, collection of fixed sample aliquots, affinity chromatography, filtration, and chemical modifications were all achieved by a combination of capillary action and simple diffusion. Sampling and sample preparation from a single drop of blood has been achieved with this system.

Next Generation LCMS Approache From Multivariate Panels to Targeted Bioanalysis

Christopher Gilles
Shimadzu Scientific Instruments, Inc.

Abstract

The quantitative analysis of multiple protein biomarkers is an emerging area in biological mass spectrometry research. The translation of discovery-based data into targeted quantitative analysis is critical for the successful advancement of biomarker research projects. Typical workflows require either many methods for optimization or select only a small number of peptides for quantitative analysis. A procedure for rapid method optimization is described, with a goal to achieve multivariate quantitative analysis.

Biological applications of fine structure analysis and peripheral technology using Cryo-Scanning Electron Microscopy

N.Kikuchi, Y.Hasebe, T.Kaneko, Y.Takashima, K.Kawauchi, M.Suga, T.Suzuki and T.Nokuo
SM Business unit, JEOL Ltd.

Abstract

The Cryo-SEM is the tool which can be observed the water containing specimen in a frozen hydrate. This Cryo-SEM is comprised of the Cryo preparation chamber and the cooling stage.

Recently, the SEM equipped the Cryo system is improved the spatial resolution at low accelerating voltage and also it can be taken the variety of images with a low vacuum.

In this presentation, it will present the results of images of biological and food specimens including water with using the Cryo-SEM, FE-SEM (JEOL JSM-7100F/ TTLS/ LV) equipped with Cryo system (Quorum Technologies PP3000T).