TECHNICAL PRESENTATIONS: SESSION I

Background Suppression in Broadband Coherent Anti-Stokes Raman Scattering (CARS) Microscopy

Marcus Cicerone, Biomaterials Group Leader, Polymers Division, Biomaterials Group, NIST

Coherent anti-Stokes Raman scattering (CARS) microscopy is gaining popularity as a technique for performing three-dimensional chemical imaging of biological and polymeric systems without the need to add fluorescent molecules to the systems of interest. Narrowband CARS microscopes, those that record a narrow spectrum of light wavelengths (colors) scattered from the samples, have already been commercialized, but lack true chemical sensitivity. Broadband CARS, which would record a much wider spectrum of wavelengths from the sample, promises unprecedented noninvasive chemical sensitivity, but the images have been hampered by relatively high levels of noise. We have developed a unique pulse-shaping approach that dramatically enhances the chemical contrast and improves the signal-to-noise ratio of broadband CARS microscopy, in order to remove unwanted background signals while keeping resonant signals of interest.

Optimizing Multi-photon Fluorescence Microscopy Light Collection by Total Emission Detection (TED)

Christian A. Combs, Cell Biology & Physiology Center, NHLBI

Parabolic mirrors and condensers can be combined to collect the totality of solid angle around the spot for tissue blocks, leading to ~8-fold signal gain. We now show a new version of this Total Emission Detection instrument modified to make non-contact images inside tissue *in vivo*. The device is mounted on a periscope to facilitate imaging live animals. Thus, scanning with the same SNR could occur at more than twice the normal rate or at reduced laser power to reduce photodamage. We have also designed a smaller version to directly replace an objective.

Optical Microscopy and Image Analysis at the National Cancer Institute - Frederick with Emphasis on Validation

Stephen J. Lockett, Optical Microscopy and Analysis Laboratory, SAIC/NCI-Frederick

Additional Poster: NCI Optical Microscopy and Analysis Laboratory

Understanding cancer mechanisms requires analysis at the individual cellular level while cells remain in their tissue context. We have developed efficient, interactive tools for whole cell segmentation as well as automatic tools for nuclear segmentation. These software tools offer improvements over existing methods. Anticipated markets are in cancer diagnostics and as software tools for biology researchers.

The Advanced Technology Partnerships Initiative: Access to World-Class Bio Imaging Resources through Collaboration

Bruce Crise, Business Development, Advanced Technology Partnerships Initiative, SAIC/NCI-Frederick

The Advanced Technology Program (ATP) has technology and expertise that accelerates research activities at the National Cancer Institute. Located at the NCI in Frederick and operated by SAIC-Frederick, the ATP provides a wide range of cutting-edge biotechnologies services to support basic and translational research. These technologies include world-class facilities for imaging and nanotechnology characterization. In addition to service activities, the ATP laboratories assist NCI researchers in collaborative projects for technology development resulting in advanced methods and approaches for addressing complex biological problems. Access to these technologies is available to other government agencies, academic institutions, and industry through collaboration

and research development agreements.

Bioimaging Applications of Modern Nanoparticle Constructions
Joseph J. Barchi, Jr., Laboratory of Medicinal Chemistry, NCI-Frederick

Semiconductor nanocrystals, also called quantum dots (QDs), are particles that exhibit unique size- and composition-dependent optical properties and one of their most interesting applications is as luminescent labels for cellular imaging. The Laboratory of Medicinal Chemistry, NCI has prepared QDs coated with the tumor-associated carbohydrate antigen (TACA) disaccharide Galâ1-3GalNAcá (Thomsen Friedenreich antigen), conjugated to various linkers, that are highly stable, luminescent and functional. These conjugates permit efficient imaging of tumor cells and in addition, the novel method of synthesis overcomes other reported problems with short-lived and unstable nanoparticles. These new tools hold great promise for labeling cells that express specific carbohydrate-binding proteins on their surfaces.

Nanoparticles in Lymphatic Imaging
Peter L. Choyke, M.D., Molecular Imaging Program, NCI

The lymphatic system is difficult to image, however, injected nanoparticles of precise size are taken up rapidly by the lymphatics and can be used to image the lymphatic channels and sentinel lymph nodes, which are critical to cancer staging. In the optical realm suitable nanoparticles include quantum dots and upconverting nanocrystals both of which provide excellent target to background ratios. In the realm of MR imaging dendrimers tagged with Gadolinium or iron core particles have shown promise for visualizing the lymph nodes and lymphatic vessels.

Quantitative Molecular Sensors and Imaging Techniques for Diagnostic Detection of Infectious Diseases
Jeeseong Hwang, Biophysics Group, Optical Technology Division, NIST

Quantitative detection of pathogens and infectious agents plays a vital role in biological threat surveillance, agricultural safety, and medical diagnosis. While there is increasing interest in highly sensitive detection assays involving either fluorescent molecules or light-emitting chemical reactions, they often pose challenges to quantitative optical analysis. We embark on efforts to quantitatively characterize and model the unique optical properties of novel fluorescent nanocrystal probes to investigate biological processes involving infectious diseases and bacterial pathogens. We are developing and using new measurement platforms and standards to characterize and model the unique optical properties of these nanoscale materials for their applications as quantitative biosensors and detectors.

Method of Preparing Macromolecular Contrast Agents and Uses Thereof
Martin W. Brechbiel, Radiation Oncology Branch, NCI

We describe a new method of pre-forming a metal-ligand chelate in alcohol prior to conjugation to a dendrimer. The result is a dendrimer-based MRI contrast agent with greatly improved homogeneity and stability, and possessing an unexpectedly greater molar relaxivity that allows the use of much less of the agent than previously required to obtain comparable images. Advantages include the efficient preparation of stable dendrimer-based contrast agents suitable for medical imaging; higher molar relaxivity, hence a lower dosage needed for imaging; an ability to control dendrimer size conducive for development of compartment-specific imaging agents.