



















French Family Science Center Duke University December 19, 2011



# Duke University

Center for Molecular and Biomolecular Imaging

Warren S. Warren, Director

James B. Duke Professor of Chemistry, Radiology and Biomedical Engineering French Family Science Center, Box 90346 Durham, NC 27708-0346 Phone (919) 660-1604 (919) 681-2691 Fax (919) 287-2454 warren.warren@duke.edu

December 19, 2011

Welcome to the "Imaging the Essence: From Medical Diagnosis to Art Resoration" meeting, which is the annual meeting of the Center for Molecular and Biomolecular Imaging at Duke. The meeting takes place in the French Family Science Center (dedicated November 2007), which I think you will agree provides an outstanding venue for research and education.

The 2011 annual meeting will focus on the application frontiers of modern imaging. Dramatic advances in imaging methods, hardware, and image processing concepts have lead to a wide range of novel clinical applications. But many of these approaches have additional uses far removed from the clinical area. The same optical technologies that image a retina with high precision or diagnose skin lesions can penetrate darkened varnish or yellowed paint binders to reveal the intended beauty of centuries-old paintings or distinguish restoration from original. The same MR physics that images soft tissue can vereal rock porosity to extract more oil from a well, or detect water behind wall frescoes. The goal of this meeting is to bring together disparate communities with distinct expertise and identify opportunities to transcend disciplinary bounds.

CMBI is a Provost-level or ganization which unites several different schools at Duke (interconnecting Trinity College of Arts and Sciences, the Pratt School of Engineering, the Medical School, and the Nicholas School of the Environment) to support the transform ative and inherently interdisciplinary nature of modern imaging science. This has a natural connection with one of Duke's greatest strengths, which can best be appreciated on *Google Maps*. If you locate the French Family Science center at 124 Science Drive, and go to the 200 foot scale, you will find all of physics, biology, chemistry, engineering, and computer science, and virtually all of the basic science buildings of the medical school. This extremely unusual proximity can, and does, foster strong connections between departments. To support this very broad field, our meetings have widely varying themes and foci. The preceding meeting (Dec. 2010), for example, focused on the frontiers of image analysis and the relationship of signal and contrast.

These meetings do not happen spontaneously. I am very grateful for the continuing efforts of Mike Conti (CMBI Manager), for helping to organize the meeting, and to the CMBI steering committee for their thoughts and guidance.

Warren S. Warren Director, Center for Molecular and Biomolecular Imaging Duke University

Marran A Marian



# **Schedule of Events**

8:30	Warren Warren & Keith Whitfield	Welcome and Introduction
8:40	Maria Perla Colombini -University of Pisa	Macromolecules in Art
9:10	Gregory Smith -Indianapolis Museum of Art	Science Serving Art Conservation: Fast Compositional and Structural Analysis of an 18th C. Italian Oil Sketch
9:40	Martin Fischer -Duke University	Optical Pump-probe Spectroscopic Imaging of Art Pigments
10:00	Morning Session Break and Poster Viewing	
10:20	Jens Stenger -Harvard Art Museums	Mark Rothko's Harvard Murals: From Chemical Imaging to Digital Projection
10:50	William Brown -North Carolina Museum of Art	Artists' Intent Revealed Through Materials Analysis and Er:YAG Laser: Examination and Restoration of Old Master Paintings at the North Carolina Museum of Art
11:15	Ingrid Daubechies -Duke University	
11:35	Michael Toth -RB Toth Associates	Integrating Advanced Imaging Technology to Address Challenges in Cultural Heritage Studies
12:00	Lunch and Poster Viewing	
1:00	Yi-Qiao Song -Schlumberger-Doll	Magnetic Resonance of Porous Media
1:30	Mara Camaiti -Consiglio Nazionale delle Ricercehe	Magnetic Resonance Imaging in Stone Artworks Conservation
1:50	Tuan Vo-Dinh -Duke University	Plasmonic SERS Nanoprobes: From Medical Diagnostics to the Analysis of Works of Art
2:15	Cynthia Toth -Duke University	Imaging the Growth of Human Photoreceptors (our "art-receptors") in Infancy
2:40	David Brady -Duke University	High Pixel Count Wide Field Microscopy
3:00	Afternoon Session Break and Poster Viewing	
3:15	Elizabeth Hillman -Columbia University	Hyperspectral and Dynamic In-Vivo Molecular Imaging and Microscopy
3:50	Anuj Kapadia -Duke University	Neutron and Gamma Stimulated Spectroscopy for Molecular Diagnostic Imaging
4:10	Cristian Badea -Duke University	Expanding Micro-CT Imaging Along Temporal and Spectral Dimensions
4:30	Zackary Cleveland -Duke University	Functional MR Imaging of Gas Uptake and Elimination in the Lungs

#### Macromolecules in Art



Maria Perla Colombini, PhD Professor of Analytical Chemistry University of Pisa

Professor Colombini teaches courses in Analytical Chemistry and Chemistry of Cultural Heritage. She is the Director of the "Materials and Diagnostic Techniques in the Cultural Heritage Field" program at the University of Pisa.

Her research activity is related to the development of analytical procedures based on spectroscopic and chromatographic techniques for the characterization of micropollutants in the environment and, above all, of organic materials and their degradation products in works of art and archaeological objects.

She is leader of several national and international research projects for the safeguard of Cultural Heritage. She coordinates the research group of the Laboratory of Chemical Sciences for the Safeguard of Cultural Heritage and is specialized in the characterization of binders, organic dyes and resins by chromatographic and mass-spectrometric techniques. Professor Colombini is the President of the Italian Association of Archaeometry (AIAr).

Abstract:

Since ancient times, natural organic materials have been employed as paint binders, adhesives, waterproofing materials, ointments, balms, pharmaceutical preparations and so on, as reported in classical literature by Plinius the Elder and Vitruvius.

The chemical characterisation of macromolecules and polymers in works of art allows us to obtain information useful to set up conservation and restoration procedures. Anyway, the identification of aged natural organic materials is particularly arduous because organic materials are complex mixtures of many chemical species, quite often very similar each other and their chemical composition, and have been altered by the action of man and by the environmental conditions. Moreover, organic material composition deeply changes in the course of ageing.

Since long time, Fourier Transform Infrared (FTIR) is very effective in the identification of materials and compounds in the field of Cultural Heritage, particularly after the development of accessories like ATR crystals, diffuse reflectance cells, diamond anvil cells and IR microscopy. The application of IR mapping microspectroscopy to cross sections of paint samples allows the characterization of the organic substances together with their spatial distribution within the different paint layers. Indeed, spectroscopy imaging methods have shown to be extremely effective for a precise mapping of complex and heterogeneous samples such as paint samples.

Mass spectrometry, alone or interfaced to chromatographic techniques, has demonstrated a powerful tool in cultural heritage researches, for its ability to resolve and characterise complex mixtures even at very low concentration, as those represented by organic residues in works of art and to reveal complex pattern of degradation. Since they require a small amount of sample (<<1 mg) they may be considered microdestructive methods.

This lecture shows how MS techniques, integrated in a unique analytical protocol, helps in the characterisation of organic materials in paintings.

Case studies on Etruscan, Medieval, Renaissance and Contemporary wall paintings will be presented.

#### Science Serving Art Conservation: Fast Compositional and Structural Analysis of an 18th C. Italian Oil Sketch



Gregory Smith, PhD Otto N. Frenzel III Senior Conservation Scientist Indianapolis Museum of Art

Gregory Smith obtained an undergraduate education at Centre College of Kentucky in chemistry and anthropology. He continued his studies in science and archaeology at Duke University before earning his doctorate in analytical chemistry. During this time, he served as a field supervisor at two archaeological excavations in Israel's Galilee region. Following his doctoral studies, Dr. Smith was a Marshall Sherfield Scholar at University College London, a postdoctoral researcher at the National Synchrotron Light Source, and the Samuel Golden Research Fellow at the National Gallery of Art in Washington, DC.

In 2005 he became the first Andrew W. Mellon Professor of Conservation Science at the graduate training program for art conservators at Buffalo State College. In 2010, Smith joined the Indianapolis Museum of Art as Senior Conservation Scientist to design, outfit, and operate a 3000 ft<sup>2</sup> facility for applied research into the museum's encyclopedic collections and to perform basic science into the degradation of artists' materials. His research interests span the field of conservation and include degradation reactions of inorganic pigments, treatment strategies for modern artists' materials, and the use of analytical techniques in authentication studies.

Abstract:

Cross-section sample analysis is essential for obtaining layered structural and compositional information on many kinds of artworks, especially paintings. While many non-invasive analytical techniques are effective in characterizing artists' materials, they usually provide either surface information or mixed atomic information from all layers. Conversely, collecting micro samples and preparing cross-sections is the most convenient and easiest way to identify and characterize the layered structure of a painting.

This presentation will describe the cross-section sample analysis of an oil sketch on canvas in preparation for its conservation. The painting, *The Madonna Appearing to St. Philip Neri*, was created by Italian artist Sabastiano Conca (1680–1764) in 1740 and had previously been heavily restored. The interplay of macroscopic imaging (X-ray, UV, near-IR), optical microscopy, and electron microscopy will be highlighted. Additionally, the use of a new correlative light and electron microscopy package called "Shuttle & Find" will be discussed. Correlative microscopy is convenient for the routine analysis of cross-section samples since it combines the optical properties of light microscopy (LM) with detailed structural and chemical analysis from the scanning electron microscope (SEM) with energy dispersive X–ray spectroscopy (EDS). LM shows the optical appearance of layered structures in the samples, while SEM-EDS provides information on pigment particle shape, size, and chemical composition within different layers. The new technology also enables precise, automated relocation of ROIs between the LM and SEM.

### **Optical Pump-probe Spectroscopic Imaging of Art Pigments**



Martin Fischer, PhD Assistant Research Professor of Chemistry Duke University

Professor Fischer received his PhD in Physics from the University of Texas at Austin. He worked as an optical engineer for Lucent Bell Labs/Agere Systems and has lead microscopy research projects at the University of Texas at Austin, the University of Pennsylvania, and Duke University.

His research explores novel nonlinear contrast mechanisms such as two-photon absorption and self-phase modulation for structural and functional imaging in tissue.

#### Abstract:

Identification of pigments used in historical artwork has long been of great value for authentication, restoration and conservation of art. Important additional information can be obtained by characterizing the composition of successive paint layers, recognizing the structural form of the involved pigment or even identifying the pigment origin. However, in most cases destructive bulk chemical analysis methods are not an option. Current non-destructive techniques include elemental analysis (such as x-ray fluorescence or particle-induced x-ray emission) and molecular analysis (such as linear optical microscopy), each with their own shortcomings in resolution, sensitivity or specificity.

Nonlinear optical microscopy could alleviate these problems by providing detailed chemical and structural information about the pigments in intact paintings. While existing nonlinear techniques, such as harmonic generation and multi-photon fluorescence, offer advantages in multilayer structures, they still lack chemical specificity. Here we demonstrate a nonlinear optical technique that can combine good three-dimensional resolution with high specificity for paint layer analysis. The basis is a recently developed nonlinear optical pump-probe microscopy technique that uses modulation transfer to sensitively extract excited-state dynamics with high spatial resolution, for use in biological tissue. This technique has the ability to uniquely identify a variety of biological pigments, for example it has been demonstrate the use of the pump-probe microscopy technique to characterize several inorganic and organic pigments used in historical art.

#### Mark Rothko's Harvard Murals: From Chemical Imaging to Digital Projection



Jens Stenger, PhD Associate Conservation Scientist Harvard Art Museums

Jens Stenger received his doctorate in Chemical Physics from Humboldt-Universität zu Berlin. He joined the Harvard Art Museums in 2004 as an Andrew W. Mellon Postdoctoral Fellow. Four years later he was awarded a position as Associate Conservation Scientist at Harvard Art Museums' Straus Center for Conservation and Technical Studies. His research into Mark Rothko's Harvard murals led *Popular Mechanics* to dub Jens an "Art Detective".

#### Abstract:

The American abstract expressionist Mark Rothko donated five large canvas paintings to Harvard University in 1962, now known as his Harvard Murals. The paintings were displayed in a dining room in Holyoke Center and were subject to large amounts of natural light. Due to the excessive light exposure and the presence of the fugitive pigment Lithol Red, the color of the Murals changed dramatically. In 1979 the painting were removed and sent to dark storage. The paintings have since been exhibited three times for short periods of time, but otherwise have remained in storage. A technical investigation has been conducted to understand the paintings and their deterioration from a chemical point of view and to assess possibilities of their restoration.

Analysis of cross sections reveal the paint stratification and give key information on how the paintings were executed. Chemical imaging of these sections using Raman and Infrared spectroscopy show which pigments are located in which paint layer. In addition, the presence of several different binding media were detected. The inhomogeneity of the materials clearly indicate that the paints were not industrially produced but rather mixed by hand from dry pigments and a binding medium. Proteinaceous media were further analyzed with state of the art proteomics techniques. Trypsin digestion into small peptides with subsequent application of liquid chromatography and mass spectrometry accesses amino acid sequence information and makes protein identification possible.

Because of the color change all over the paintings and the thin application of the paint it is impossible to restore the works in a conventional way by adding restoration material to the surface. Instead we developed an approach to restore the original appearance using light from a digital projector. By comparison of the current state of the art work with a color photograph from 1964 we calculate a compensation image that is projected onto a painting. This procedure takes into account the reflectance of the painting surface in two million pixel locations. As a result the viewer of the mural cycle can experience the original color as well as the physicality of the paintings.



Mark Rothko's Harvard Murals, Panels One, Two, and Three, Holyoke Center, 1963. Photo: James K. Ufford and Michael Nedzweski. © President and Fellows of Harvard College (Harvard Art Museums)

December 19, 2011

#### Artists' Intent Revealed Through Materials Analysis and the Er:YAG Laser: Examination and Restoration of Old Master Paintings at the North Carolina Museum of Art



William Brown Chief Conservator North Carolina Museum of Art

William Brown received his M.A. and Certificate of Advanced Studies in Conservation from the State University College at Buffalo, NY in 1989. Since 2001 he has held the title of Chief Conservator for the Art Conservation Center of the North Carolina Museum of Art. After graduation he joined the NCMA first as assistant conservator then as associate conservator. His responsibilities at the NCMA include the management of the conservation department and the care and restoration of the collections. He has been awarded many grants and gifts to support the Art Conservation Center from sources including IMLS, Henry Luce Foundation, Hanes Family Grant, ABB Corporation, and the McCrindle Foundation.

Abstract:

The treatment of a work of art by a conservator must be informed by a respect for and understanding of the artist's intention. What were the materials and techniques used by the Old Masters Painters to creatively express their unique vision? The restoration of a four or five hundred year old painting is never straightforward; rarely is it in pristine condition, rather what we have inherited has surely been modified by the passing of time and the actions of past restorers. Conservators rely on the art historian and conservation scientist to provide the context within responsible treatment choices can be made. In this presentation, Mr. Brown discusses the examination and treatment of several Old Master Paintings in the Museum's collection with an emphasis on materials analysis technology.



Ingrid Daubechies, PhD James B Duke Professor of Mathematics Duke University

Professor Daubechies was born and educated in Belgium. She moved to the United States in 1987 where she first worked for Bell Laboratories and then at Princeton University where she was full Professor of Mathematics from 1993 until 2011, when she joined Duke University.

Professor Daubechies is best known for her work with wavelets in image compression, and she is a leader in the field of signal processing, a branch of applied mathematics that is concerned with transmitting, analyzing, manipulating, reconstructing and storing signals. She was awarded the Guggenheim Fellowship in 2010.

### Integrating Advanced Imaging Technology to Address Challenges in Cultural Heritage Studies



Michael Toth President, RB Toth Associates Technology Consultant, The Walters Art Museum

Michael Toth has been imaging art and historical documents for the past 12 years. Since graduating from Wake Forest University, he has lead several hyperspectral imaging studies, including St. Catherine's Monastery, Sinai, the National Library of Scotland, and the Library of Congress. Among his current projects are the Archimedes Palimpsest, a 13<sup>th</sup> century Byzantine prayer book that was written onto parchment which previously held treatises by Archimedes in their original Greek formulation.

#### Abstract:

The development of digital imaging capabilities from earth resource and medical systems into more commonly available systems suitable for use in cultural heritage studies, poses challenges for scholars, scientists and institutions in digitizing and integrating data for permanent storage, access and study. Advances in digital *imaging technology* must capitalize on parallel developments in *information technology* to ensure the continued utility of critical cultural heritage data for storage, sharing and study by a broad base of researchers, especially for the integration of overlapping technologies.

Digital imaging poses significant challenges with large and potentially complex data files that serve as facsimiles of the physical object. Key to integrating new imaging technology developed for other applications – including earth resource and astronomical studies – for cultural heritage studies is not just the adaptation of the technology with new imaging methods, set-ups, and processing techniques, but the technical integration of data systems and metadata collection to broadly accepted, international standards. This allows the data to be effectively and efficiently shared and studied globally with commonly available software and information technology and storage systems. Effective digitization and digital restoration of objects requires not just leading edge or exceptional digital technology, but the integration of the data and metadata collection, processing, storage and retrieval systems and processes into a useful end-to-end technical system that can efficiently handle the large digital image files.

This presentation will discuss the potential offered by the integration of a spectral camera and lighting system with data acquisition and dissemination technologies, standards and processes for cultural heritage studies. It will discuss the technical applications and challenges of integrating an effective spectral imaging system with case studies of the Archimedes Palimpsest and most recently palimpsests at St. Catherine's Monastery. It will also discuss the challenges in integrating a standardized capability and processes to collect high-resolution spectral images of historic manuscripts, including the Waldseemuller 1507 World Map, drafts of the Declaration of Independence and Gettysburg Address, and watermarks on a Beethoven Piano Sonata at the Library of Congress. It will address the use of spectral imaging, data management and global access technologies to provide standardized data as effective tools for scholars, preservation experts and curators.

### **Magnetic Resonance of Porous Media**



Yi-Qiao Song, PhD Program Manager Schlumberger-Doll Research

Yi-Qiao Song spent his undergraduate career at Peking University and earned his PhD in Physics at Northwestern University. He joined Schlumberger-Doll in 1997, and has since been applying the principles of magnetic resonance to the problems of geological survey and oil exploration.

Abstract:

MR has become an important technique for characterization of porous materials in recent years. In particular, its importance in petroleum exploration has been increased by the recent progress in MR well-logging techniques for the characterization of both rocks and the natural fluids. Such advanced techniques are increasingly used as a valuable characterization especially in the technically challenging areas, such as deep-sea exploration for the continuous rise of global energy demand. The techniques developed for oilfield rocks have also found interesting applications for other porous media. This talk will outline the MR technical development and their applications in the study of pore structure, rock heterogeneity, composition and molecular dynamics of crude oils, and biological materials and medical application.

#### Magnetic Resonance Imaging in Stone Artworks Conservation



Mara Camaiti, PhD Consiglio Nazionale delle Ricerche

Mara Camaiti is a researcher at the Institute for Conservation and Enhancement of Cultural Heritage, part of the Consiglio Nazionale delle Ricerche. She specializes in the chemistry of synthetic polymers, a subject which she has taught since 2004 at the Ravenna campus of the University of Bologna for their program in the conservation of cultural heritage.

Abstract:

Monumental buildings, sculptures and any other kind of stone objects exposed to outdoor conditions are subject to degradation phenomena mainly due to the interaction of the rock minerals with pollutants and other substances dissolved in rain and/or in liquid water coming from vapor condensation or soil uptake.

Protection of cultural assets and repair of degraded stone objects are complex operations which require suitable products (chemical compounds) and methodologies of treatment for obtaining effective and durable interventions.

In order to study the performances of traditional and innovative compounds, as well as the effectiveness of different treatment methods, Magnetic Resonance Imaging (MRI) may be considered a powerful tool for evaluating the distribution and penetration depth of hydrophobic treatments, and to follow the kinetics of water absorption. MRI, an accurate not destructive and spatially resolved technology, in fact allows us to visualize and quantify the liquid water confined in opaque porous mediums (i.e. rocks).

MR images of stone samples, treated with different compounds and applied with different methodologies, will be presented in order to show the validity of MRI in the selection of the best suitable hydrophobic materials and their application methods when restoration and conservation interventions (protection and consolidation operations) of cultural assets must be planning. An example of the information obtained with this technique is reported in Fig. 1. The MR images show the different penetration and distribution of two hydrophobic compounds, widely used as protective agents in stone artworks conservation.



MR images of biocalcarenite (Lecce stone) samples after different times of water capillary absorption through the untreated face: a) treatment with alkyl alcoxy silane (440mg/10g stone) b) treatment with poly(ethyl methacrylate-*co*-methyl acrylate) (395g/100g stone)

December 19, 2011

#### Plasmonic SERS Nanoprobes: From Medical Diagnostics to the Analysis of Works of Art



Tuan Vo-Dinh, PhD Director, Fitzpatrick Institute of Photonics Professor of Biomedical Engineering and Chemistry Duke University

Professor Vo-Dinh earned a Ph.D. in biophysical chemistry from the ETH (Swiss Federal Institute of Technology) in Zurich, Switzerland. He joined Oak Ridge National Laboratory in 1977 as a staff research scientist and ultimately became a corporate fellow in 1994. He became director of the Center for Advanced Biomedical Photonics at Oak Ridge in 2003 before joining Duke University in 2006, when he was named director of the Fitzpatrick Institute of Photonics.

Abstract:

Plasmonics refers to the research area of enhanced electromagnetic properties of metallic nanostructures that produce ultrasensitive and selective detection technologies. This presentation provides an overview of the development and applications of the plasmonics and surface-enhanced Raman scattering (SERS) nanoprobes for various applications ranging from biomedical diagnostics to analysis of works of art. Nanoparticle-based SERS technology has enabled sensitive detection of DNA damage and gene defects. The SERS technology can also be used for direct analysis of dyes used in works of art. This SERS procedure has potential applications in analyzing solid samples of color layer from paintings, which will be demonstrated and discussed in detail.

### Imaging the Growth of Human Photoreceptors (our "art-receptors") in Infancy



Cynthia Toth, MD Department of Ophthalmology Duke University

Dr. Toth is the Duke Retina Fellowship Director. She specializes in the evaluation and surgical treatment of vitreoretinal diseases in adults and children and has pioneered the development of macular translocation surgery for agerelated macular degeneration (AMD).

Dr. Toth is also a professor in the Department of Biomedical

Engineering in the Pratt School of Engineering. Her primary research interests are in translational research and early-application clinical trials with a focus on novel retinal imaging with spectral domain optical coherence tomography (SDOCT).

Abstract:

Optical coherence tomography (OCT) is an optical imaging tool used very early in ophthalmology and subsequently in other fields of medicine and for examination of artwork. Dr. Toth worked in the field of ophthalmic OCT imaging since its infancy in the early 1990's using this tool to image the changes in living human eye structures.

Anatomic specialization of the central retina within the eye into a fovea endows this neurosensory tissue with better acuity than non-foveal retina. Foveal maturation begins in utero, extends through early childhood and parallels normal human central visual development. Until now, maturation of the fovea has not been studied in the living infant eye. Dr. Toth has obtained the first view into development of living cellular layers of the retina and of subcellular specialization at the fovea in premature infant eyes using a novel portable spectral domain optical coherence tomography system. Mapping three-dimensional regional changes in human retinal thickness by age, she has documented the complex and lengthy progress of retinal ontogeny at the fovea in vivo after premature birth. With the translation of adult diagnostic technology into pediatric application, she has established a framework of the timeline of foveal development in the living human. Three-dimensional mapping of foveal structures from infancy to adulthood may be integral in future studies of vision and visual cortex development and may allow us to better understand what and how we see.

### High Pixel Count Wide Field Microscopy



David Brady, PhD Michael J. Fitzpatrick Professor of Electrical & Computer Engineering Duke University

Professor Brady leads the Duke Imaging and Spectroscopy Program (DISP), which builds computational imaging systems. Current DISP projects focus on snapshot gigapixel photography using multiscale optics, gigapixel holography, x-ray scatter tomography and compressive spectral imaging.

Abstract:

Advances in lens fabrication and design, micro-electronic focal planes and information processing enable imaging systems of unprecedented scale. For example, the Duke Imaging and Spectroscopy Program is developing snapshot gigapixel imagers using multiscale lens system.

This talk describes the design philosophy of wide field high resolution cameras and discusses current imaging capabilities. We consider implications of this technology for stand-off microscopic resolution imaging of art and other artifacts.

### Hyperspectral and Dynamic In-vivo Molecular Imaging and Microscopy



Elizabeth Hillman, PhD Assistant Professor of Biomedical Engineering & Radiology Columbia University

Professor Hillman received her PhD in Medical Physics and Bioengineering from the University of London. Before joining Columbia, she worked in imaging at Massachusetts General Hospital and has been an instructor in Radiology at Harvard Medical School.

Her research interests include 3D brain imaging and in-vivo skin cancer imaging. She is the recent recipient of Adolph Lomb Medal, presented by the Optical Society of America for contributions to optics before the age of 35.

#### Abstract:

Optical imaging harnesses the diverse interactions of light with matter. Living tissues contain many sources of optical contrast including intrinsic absorbers such as oxy- and deoxy-hemglobin, intrinsic fluorophores such as NADH and FAD and scatterers whose properties can reveal nanoscale morphology. Additionally, a wide range of optical contrast agents are available that can specifically target key cell types, actively report changes such as intracellular calcium, or be genetically expressed. Optical imaging platforms vary widely depending on the kind of tissue being imaged and the scale of detail sought. Optical microscopy can reveal sub-micron detail, but with tissue penetration generally limited by scattering to less than a millimeter. Wide-field imaging systems can be used to image an entire small animal, but have more limited resolution and sensitivity to deeper tissues. This range of size and scale means that there are many opportunities to develop hybrid approaches that exploit the unique benefits of optical imaging while overcoming the challenges imposed by light scattering.

Here we will describe optical imaging methods that exploit either hyperspectral or dynamic data to extract quantitative information about living tissues beyond conventional contrast. Small animal dynamic contrast enhanced imaging (DyCE) acquires optical images of a fluorescent dye bolus, capturing organ-specific dynamics of the dye as it circulates in the body. We demonstrate that while static images of fluorescence in small animals can lead to confusion over quantitation and identification of the anatomical location of a region of interest, dynamic contrast provides unique temporal signatures that can allow quantitative analysis of organ function, as well as accurate and simple anatomical organ mapping. Hyperspectral two-photon microscopy acquires images of tissue at the cellular level by acquiring data at a range of excitation and emission wavelengths. This generates a rich data set in which each 3-dimensional voxel has a unique spectral signature, allowing quantification and identification of its composition of fluorophores. We have demonstrated that this technique can not only delineate a large number of dyes or other forms of exogenous contrast, but that it can also provide exquisite imaging of native endogenous contrast in fresh of living tissues such as the colon or skin.

#### Neutron and Gamma Stimulated Spectroscopy for Molecular Diagnostic Imaging



Anuj Kapadia, PhD Assistant Professor of Radiology Duke University

Professor Kapadia received his PhD in Biomedical Engineering from Duke University. He is now an Assistant Professor of Radiology, a faculty member of the Carl E. Ravin Advanced Imaging Laboratories, and on the faculty of the Duke Medical Physics Graduate Program. His research focuses on developing innovative neutron and gammabased imaging modalities for tomographic imaging of elements in the human body.

#### Abstract:

In this talk, we describe the development of neutron- and gamma-stimulated emission imaging techniques for determining the elemental compositions of objects at a molecular level. We have developed a spectroscopic imager that uses high-energy neutron or gamma beams to image naturally occurring elements in a sample through gamma-ray spectroscopy. The imager provides quantitative information about the elemental composition of the sample, the location of the elements within the object, and the intensity of elements within the localized regions. We will describe the development of these techniques and discuss their applications in element-based molecular diagnostic imaging in the human body.

### **Expanding Micro-CT Imaging Along Temporal and Spectral Dimensions**



Cristian Badea, PhD Associate Professor of Radiology Duke University

Professor Badea received his PhD in Biomedical Engineering from the University of Patras in Greece. He is an academic researcher with the Center for In Vivo Microscopy. His research interests include image formation and image reconstruction algorithms for tomosynthesis, CT, microCT, and fluorescence tomography

Abstract:

The availability of genetically modified murine models for many human diseases provides biomedical scientists the controlled environment required to link genotype and phenotype. Micro-CT is widely used for anatomical preclinical imaging. But in many applications, such as in cardiac or pulmonary studies, both structural and functional information are required. Our work has been focused on extending micro-CT imaging along temporal dimension.

At Duke's Center for In Vivo Microscopy, we have built an unique dual source micro-CT instrument and developed novel strategies in gating/sampling/reconstruction/analysis of 4D data. We have shown that 4D cardiac micro-CT is an important tool for morphological and functional phenotyping in rodents. Furthermore, we have exploited the dual source micro-CT system in dual energy studies to discriminate between Iodine and gold based nanoparticles in cancer studies. Currently, we are developing novel reconstruction algorithms that combine 3D anatomy with time and energy in a 5D image. We believe that the final result from the combined temporal and spectral reconstruction will be especially useful for cardiac and perfusion applications, in which we are interested in the spatial distribution of a contrast agent that is changing over time.

#### Functional MR Imaging of Gas Uptake and Elimination in the Lungs



Zackary Cleveland, PhD Postdoctoral Associate, Department of Radiology Duke University

Zack works at the Center for In Vivo Microscopy, and his research interests have centered on developing novel <sup>129</sup>Xe MR techniques for imaging lung function in rodents and humans. A particular focus has been on visualizing diffusive gas uptake in the lungs by imaging HP <sup>129</sup>Xe as it dissolves in the alveolar walls and adjacent capillary blood. He is also studying diffusive gas elimination in rats by first delivering HP <sup>129</sup>Xe to the blood using hydrophobic gas exchange membranes and then imaging the gas as it diffuses from the capillary bed into the alveolar spaces.

Abstract:

The primary function of the lungs is to facilitate the uptake of oxygen and the elimination of carbon dioxide. Therefore, elucidating the physical processes that enable the exchange of these metabolically active gases is a central goal of pulmonary physiology. However, conventional methods of assessing gas exchange detect and quantify these gases (or surrogate tracer gases) after they are exhaled. As a result, most measures of lung physiology provide only global information, and cannot assess the regional heterogeneity in lung function that occurs even in healthy individuals. Moreover, the character of this functional heterogeneity is altered by disease and injury, making spatially resolved measures of lung function essential for understanding pathological changes in gas exchange. Unfortunately, currently available modalities cannot image the distribution of  $O_2$  and  $CO_2$  within the lungs or the flux of these gases between the alveolar spaces and gas-exchange tissues. To address this need, we have developed functional imaging methods to assess pulmonary gas exchange using hyperpolarized (HP) <sup>129</sup>Xe as a tracer.

HP <sup>129</sup>Xe is a novel MRI contrast agent that provides high MR signal intensities, soluble in tissues, and possesses a large (>200 ppm) chemical shift range that is sensitive to the local chemical environment. Moreover, HP <sup>129</sup>Xe displays unique NMR peaks when in the alveolar spaces, when dissolved in the red blood cells, and when dissolved in the blood plasma and parenchymal tissues. Thus, inhaled <sup>129</sup>Xe can serve as a surrogate for O<sub>2</sub> and provide spatially resolved information about gas uptake. Furthermore, HP <sup>129</sup>Xe can be dissolved by a biologically comparable carrier solution or even blood. When these <sup>129</sup>Xe-saturated solutions are delivered to the vasculature, HP <sup>129</sup>Xe flows into the pulmonary capillaries and then, via perfusion and diffusive exchange, passes into the alveolar airspaces, where it can be selectively detected and imaged. That is, <sup>129</sup>Xe travels the same physical path as CO<sub>2</sub>, making it a unique, spatially resolved probe of gas elimination. Here we will present recent advances in using HP <sup>129</sup>Xe MRI to assess regional gas exchange in rodents, healthy human subjects, and patients with chronic obstructive pulmonary disease.