

Sensing the Future: The Future of Sensing

Workshop 1: Sensing Inside Us

Poster Session Abstracts

Monday, May 7, 2018



Kavli Foundation



Smalley-Curl Institute

Presenter Information

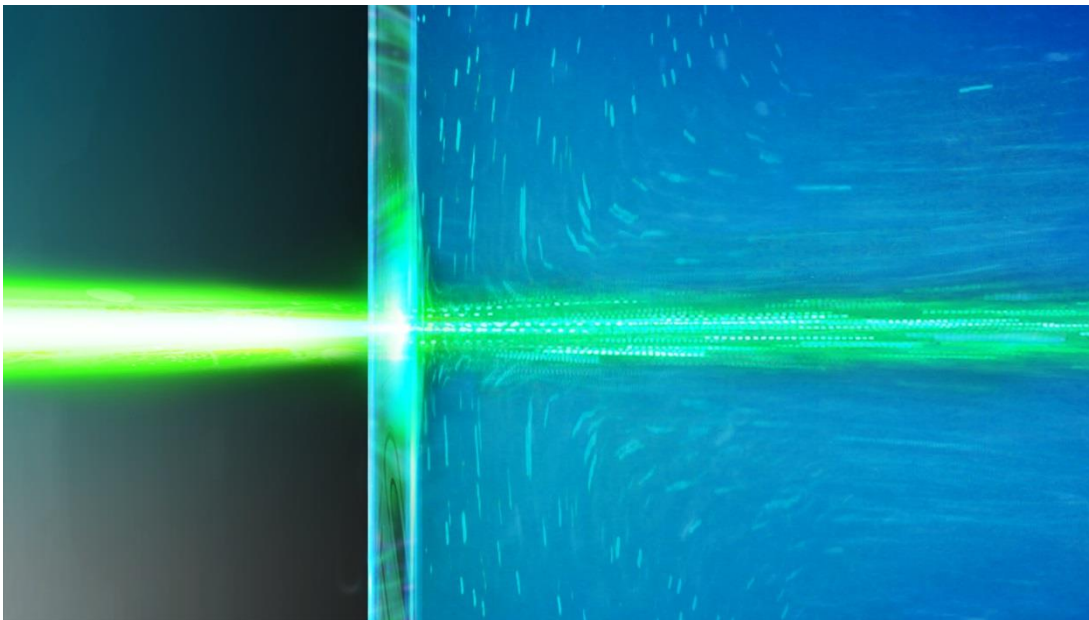
Presenter Name	Affiliation	Poster Title
Jiming Bao; Feng Lin	University of Houston	Laser Streaming: Turning a Laser Beam into a Liquid Jet Flow
Jianbo Chen	Rice University	Hybrid optical-computational CNN with DMD based imaging system
Sean Collins	Rice University	Single nanoparticle spectroelectrochemical sensing
Nicola Di Marzio	Houston Methodist	PLGA Particles Based Delivery System For Intrapericardial Delivery Of Prostaglandin through HeartPAS™ Device
Hamin Jeon	Rice University	Spectrally Encoded Miniature Objective for High Resolution Endomicroscopy
Michal Pawlowski	Rice University	High Performance Image Mapping Spectrometer for remote sensing and biomedical applications
Wenlan Qiu	University of Houston	Spin-Valve Based Magnetoresistive Nanoparticle Detector for Applications in Biosensing
Xiaonan Shan	University of Houston	IMAGING THE MEMBRANE MECHANICAL FLUCTUATIONS OF SINGLE CANCER CELLS WITH PLASMONIC MICROSCOPE
Veronica Vighetto	Houston Methodist	A novel <i>in ovo</i> system to treat lung cancer
Wenxiao Wang	Rice University	A robust and generalized method for phase mask designs
Cynthia Wong	Rice University	Filter-less Fluorescence Imaging Using Ultraviolet Illumination for Acridine Orange Stained Whole Blood
Yibo Xu	Rice University	Compressive Hyperspectral Microscopy
Qingfeng Zheng		Origin of Plasmonic Circular Dichroism from Au Nanorod-Protein Complex: A single-particle spectroscopic study

Laser Streaming: Turning a Laser Beam into a Liquid Jet Flow

Jiming Bao

University of Houston

Transforming a laser beam into a mass jet flow has been a challenge both scientifically and technologically. I will present our recent demonstration of the generation of a liquid jet by simply focusing a pulsed laser into water through a glass window. The jet originates from the laser focusing spot on the glass and moves in the same direction as the refracted beam. Microscopically, this transformation is made possible by an underlying plasmonic nanoparticle-decorated cavity which is self-fabricated on the glass by nanoparticle-assisted laser etching and exhibits size and shape uniquely tailored to the incident beam profile. Hydrophone signals indicate that the jet is driven via acoustic streaming by a long-lasting ultrasound that is resonantly generated by laser and the cavity through the photoacoustic effect. The principle of this light-driven flow via ultrasound, i.e. photoacoustic streaming by coupling photoacoustics to acoustic streaming, is general and can be applied to any liquids, and will create new research in optofluidics and open up enormous light-controlled microfluidics applications.



Reference: *Science Advances* **3**, e1700555 (2017)

Laser Streaming: Turning a Laser Beam into a Liquid Jet

Yanan Wang^{1,2,†}, Qiuhui Zhang^{3,2,†}, Zhuan Zhu², Feng Lin^{2,1}, Jiangdong Deng⁴, Geng Ku⁵, Shuo Song², Md Kamrul Alam⁶, Dong Liu⁷, Zhiming Wang^{1,*} and Jiming Bao^{2,1,6,*}

¹Institute of Fundamental and Frontier Sciences, University of Electronic Science and Technology of China, Chengdu, Sichuan 610054, China

²Department of Electrical and Computer Engineering
University of Houston, Houston, Texas 77204, USA

³College of Optical and Electronic Information, Henan University of Engineering
Xinzheng, Henan 45119, China

⁴Harvard CNS, Harvard University, Cambridge, MA 02138, USA

⁵Department of Mechanical Engineering, University of Kansas
Lawrence, KS 66045, USA

⁶Materials Science and Engineering, University of Houston
Houston, Texas 77204, USA

⁷Department of Mechanical Engineering
University of Houston, Houston, Texas 77204, USA

[†]Equal contributions

*To whom correspondence should be addressed, Zhiming Wang (zhmwang@uestc.edu.cn);
Jiming Bao (jbao@uh.edu)

Transforming a laser beam into a mass jet has been a challenge both scientifically and technologically. Here we demonstrate the generation of a liquid jet by simply focusing a pulsed laser into water through a glass window. The jet is ejected from the laser spot on the glass and moves in the same direction as the refracted beam. Microscopically, this transformation is made possible by an underlying plasmonic particle-decorated cavity which is self-fabricated on the glass by nanoparticle-assisted laser etching and exhibits size and shape uniquely tailored to the incident beam profile. Hydrophone signals indicate that the jet is driven via acoustic streaming by a long-lasting ultrasound that is resonantly generated by laser and the cavity through photoacoustic effect. The self-fabrication of plasmonic ultrasonic cavity by laser and its subsequent generation of ultrasound to drive a laser-like liquid jet show that macroscopic structures and devices can be created from microscopic interaction of light with nanoparticles at the interface between liquid and solid substrate, thus laser streaming creates new research in optofluidics and opens up enormous light-controlled device applications.

Hybrid optical-computational CNN with DMD based imaging system

Jianbo Chen, Yibo Xu, Matthew Herman, and Kevin F. Kelly

Rice University, Department of Electrical and Computer Engineering

We are proposing a hybrid operation convolution system to perform image classification tasks. The field of compressive sensing lays the foundation for this work, as embodied in the Single-Pixel Camera invented at our lab and modified to a multi-pixel version. It is shown that not only can the multi-pixel compressive architecture replace one or more computational layers in a neural network, but that the amount of data required for classification tasks is a fraction of that required for traditional networks.

Single nanoparticle spectroelectrochemical sensing

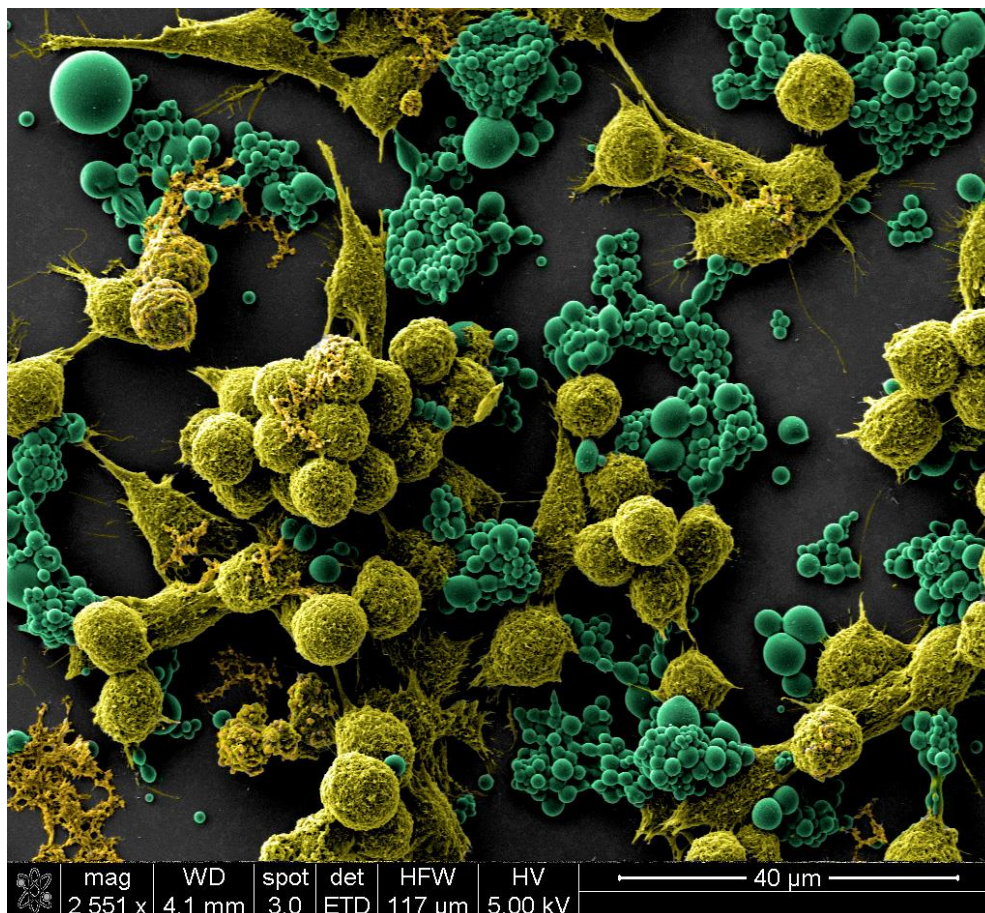
Sean S. E. Collins, Benjamin S. Hoener, Thomas S. Heiderscheidt, Charlotte F. Flatebo,
Alexander Al-Zubeidi, Wei-Shun Chang, Stephan Link, Christy F. Landes

Advanced electrode designs for applications like electrocatalytic biosensing and electrolyzing are increasingly incorporating nanoparticles to enhance Faradaic current for target chemical substrates. It is well known that the inherent morphological heterogeneity of nanoparticles with respect to shape, size and crystallinity result in a significant distribution of their individual contributions to the total measured current. Using nanoscale optical spectroscopy techniques, our lab senses the electrochemical activity of individual metal nanoparticles by monitoring changes in their localized surface plasmon resonance (LSPR). The LSPR is the collective oscillation of conduction band electrons coupled to on-resonance incident light at the surface of a metal nanoparticle. This light-matter interaction generates a strong scattering signal from the nanoparticle which we use to examine the electrochemical properties of multiple individual gold nanoparticles using Hyperspectral Dark-Field Imaging. We have optically monitored the following electrochemical processes on single gold nanoparticles using externally controlled applied potentials: electron density modulation, ion adsorption, oxide formation, metal/metal halide shell active switching, and nanoparticle dissolution. All of the processes listed impact the intensity, dephasing time, and/or energy of the LSPR which we analyze to extract single particle quantities such as electron transfer rates, and ion adsorption, oxide formation, and dissolution onset potentials. In addition, we have used electrochemiluminescence imaging to spatially resolve where light is emitted from when electrochemically excited dye molecules are electro-oxidized on the surface of a nanoparticle electrode. Most recently, we have implemented Snapshot Hyperspectral Imaging to achieve high-throughput spectroelectrochemical sensing by capturing LSPR changes on multiple particles undergoing irreversible and heterogeneous electrochemical reactions simultaneously, with millisecond time resolution.

PLGA Particles Based Delivery System For Intrapericardial Delivery Of Prostaglandin through HeartPAS™ Device

Abstract

Our knowledge on drugs and on their capability to treat diseases is huge. However, there are a lot of problems due to administration methods. For example, adverse side effects are known to be a critical problem as a result of systemic delivery. After a Myocardial Infraction (MI), caused by sudden coronary artery occlusion, soluble factors are released by the myocardium into the coronary circulation and pericardial fluid. In patients after MI, enhanced secretion of cardiac hepatocyte grow factor (HGF) from the infarct region is associated with reduced ventricular remodeling and improved cardiac function. Prostaglandins stimulate the production of endogenous myocardial HGF and offer a therapeutic avenue to pursue. PGE-1 (Alprostadi) is an FDA approved small molecule drug that acts as a potent vasodilator with anti-platelet aggregation properties. Clinically, infusion of PGE-1 increases local HGF production. The HeartPAS™, our novel device, can be used to deliver PLGA-encapsulated Alprostadi into the pericardial fluid. In this study, we investigate PLGA particle production, characterization, biocompatibility, and the interaction between PLGA particles and cells. Furthermore, the drug encapsulation and sustained release are evaluated by changing the PLGA polymer ration, which influences the degradation properties. The interaction of PLGA with cells is observed with Scanning Electron Microscopy imaging. Use of PLGA as a controlled release drug delivery system can be coupled with the HeartPAS™ to offer a powerful way to release a wide variety of therapeutics into the pericardium.



Spectrally Encoded Miniature Objective for High Resolution Endomicroscopy

Hamin Jeon¹, Michal E. Pawlowski¹, Tomasz S. Tkaczyk^{1,2,*}

1. Department of Bioengineering, Rice University, 6500 Main Street, Houston, TX 77030, USA

2. Department of Electrical and Computer Engineering, Rice University, 6500 Main Street, Houston, TX, 77030, USA

**tkaczyk@rice.edu*

Fiber optic endomicroscopy technique serves as an important tool for early diagnosis of cancers. The technique utilizes a compact and flexible fiber bundle, which enables clinicians to minimally invasively access and detect cancerous sites. However, the fiber bundle's sampling capability is limited due to the sparse distribution of fiber cores inside the fiber bundle. Spatial gaps exist between individual cores, which lead to increased core-to-core distance and decreased spatial sampling capacity of the fiber bundle. This may prevent fiber-coupled imaging systems from resolving subcellular details of cancerous lesions, which might lead to lowered sensitivity in detecting cancers. Here, we present a custom-fabricated miniature objective that can be coupled to a fiber bundle to surpass its sampling threshold. The combined objective-fiber bundle system will require no bulky scanning mechanisms. The objective includes a prism in its optical train, which disperses image of the sample over the distal face of a fiber bundle. The fiber bundle, which acts as an imaging conduit, captures spectrally encoded and laterally shifted signals and transmits them onto the Image Mapping Spectrometer (IMS) as a 3D data cube (x, y, λ). The 3D data cube is subsequently split into 2D (x, y) narrowband images, which are combined by custom MATLAB reconstruction algorithm into a single high-resolution image. The objective was designed using ZEMAX software and fabricated using an in-house single point diamond turning machine. Its expected performance was verified through a preliminary evaluation using 1951 USAF resolution target.

High Performance Image Mapping Spectrometer for remote sensing and biomedical applications

Michal E. Pawlowski, Jason G. Dwight, Thuc-Uyen Nguyen, Tomasz Tkaczyk
Department of Bioengineering, Rice University, 6500 Main St, Houston TX 77030, USA
E-mail: tkaczyk@rice.edu

KEYWORDS: snapshot spectrometry, multispectral imaging, fluorescence, remote sensing

The snapshot hyperspectral imaging modality allows acquisition of multidimensional data. Typically 3D (x,y,λ) data cube is recorded during single integration period of a imaging detector [1,2]. Due to the operation principle, hyperspectral snapshot imaging systems are best suited to applications requiring monitoring of transient event, with areas of application ranging from remote sensing by satellites [3] to analysis of dynamics of cellular processes [4]. We report here development of new Image Mapping Spectrometer built around pco.edge 5.5 sCMOS camera. Newly developed spectrometer is capable of acquisition of 16 bit data at 100 Hz frame rate over spectral range 515-842 nm. System is capable of reconstruction of $(210 \times 210 \times 46)$ hyperspectral data cube due to optimal utilization of detector photosensitive area. The newly developed imaging spectrometer is by order of magnitude faster than previous generations of IMS imagers, has lower read noise and higher dynamic range. Schematic drawing of newly developed system is presented in Fig.1a). Photograph of prototype attached to a side port of an Olympus microscope is given in Fig. 1b). Fluorescent images of a BPAE cells slide stained with MitoTracker™ Red, Alexa Fluor™ and DAPI acquired using newly developed and reference, previous generation IMS system are given in Fig. 1c). Please note that images acquired by high performance IMS have higher dynamic range, better contrast and lower noise floor.

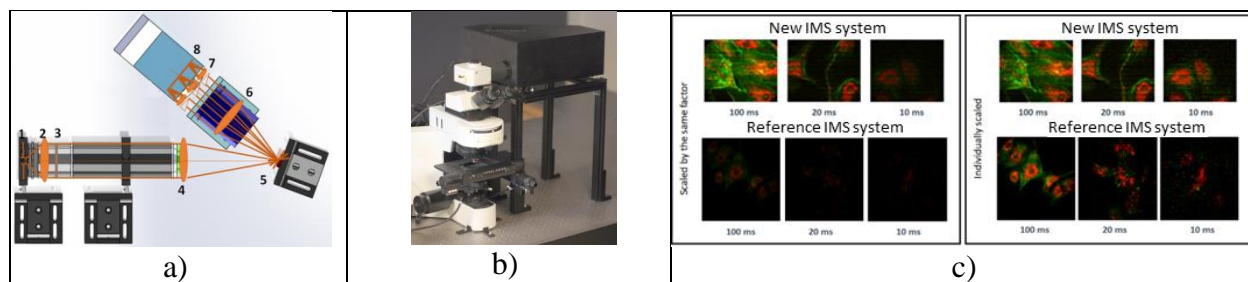


Fig.1. Schematic of newly developed IMS system a). Pictures of high performance imaging spectrometer attached to a side port of an Olympus microscope b). Hyperspectral data cubes of BPAE cells acquired using new and reference previous generation IMS system c).

Literature:

- [1] N. Hagen, M. W. Kudenov, "Review of snapshot spectral imaging technologies," *Opt. Eng.* **52**(9), 090901 (2013).
- [2] N. Bedard, N.A. Hagen, L. Gao, and T. S. Tkaczyk. "Image mapping spectrometry: calibration and characterization," *Optical Engineering* **51**(11), 111711 (2012).
- [3] M. J. Khan, H. S. Khan, A. Yousaf, K. Khurshid and A. Abbas, "Modern Trends in Hyperspectral Image Analysis: A Review," *IEEE Access* **6**, 14118-14129 (2018).
- [4] J. Vermot, S. E. Fraser and M.Liebling. "Fast fluorescence microscopy for imaging the dynamics of embryonic development," *HFSP journal* **2**(3),143-155 (2008).

Spin-Valve Based Magnetoresistive Nanoparticle Detector for Applications in Biosensing

Wenlan Qiu^{1,2}, Long Chang^{2,3}, Yu-Chi Liang⁴, Julia Litvinov⁵, Jing Guo², Yi-Ting Chen⁶, Binh Vu⁴, Katerina Kourentzi⁴, Shoujun Xu⁶, T. Randall Lee⁶, Youli Zu⁷, Richard Willson^{2,4}, and Dmitri Litvinov^{1,2,3,4,6,*}

- 1- Materials Science & Engineering, University of Houston, Houston, USA
- 2- Center for Integrated Bio & Nano System, University of Houston, Houston, USA
- 3- Department of Electrical & Computer Engineering, University of Houston, Houston, USA
- 4- Department of Chemical & Biomolecular Engineering, University of Houston, Houston, USA
- 5- Department of Internal Medicine, University of Texas Medical Branch, Galveston, USA
- 6- Department of Chemistry, University of Houston, Houston, USA
- 7- Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, USA

Key Words: *Bioinstrumentation, magnetic particle detection, magnetoresistive sensors*

A magnetoresistive sensor platform for the detection of individual magnetic reporter particles is presented. The sensing scheme is based on the detection of the shift in the sensor's magnetoresistance-switching field in the presence of magnetic particle. A bottom-pinned spin-valve multilayer (Co/Ru/Co)/Cu/(Co/Ru/Co) device structure (with Ta/Ru seed and Ta capping layers) used for the sensor was deposited using ultra-high vacuum magnetron sputtering and patterned using conventional microfabrication techniques. Inexpensive electronics to measure device magnetoresistance (using DC currents) was used for testing. The detection of individual 500nm Fe₃O₄ nanoparticles was demonstrated and verified using scanning electron microscopy (SEM). The developed sensors are readily integratable into a biosensing platform for the detection of biomolecules at ultra-low concentration using magnetic nanoparticles as reporters.

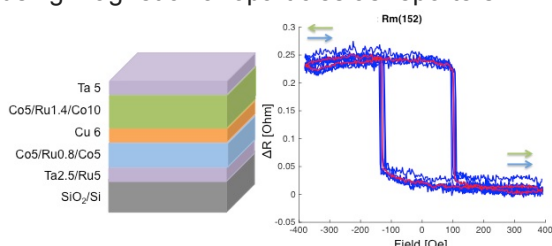


Figure 1

As illustrated in Fig. 1(L), (Co 5nm/Ru 0.8nm/Co 5nm) is chosen to be the pinned layer to retain the direction of magnetization during the measurement, and the free layer (Co 5nm/Ru 1.4nm/Co 10nm) is designed to switch in a relatively

low magnetic field. The sensors are coated with a 100nm thick pinhole-free Al₂O₃ to prevent corrosion and serve as a base for attaching biomolecules. Fig. 1(R) shows a ΔR -H loop describing a typical sensor behavior.

500nm Fe₃O₄ nanoparticles suspended in water are used here as demonstration. The ΔR -H loops for the sensor with and without MNPs are shown in Fig. 2. The switching field positions were approximately +200 Oe and -180 Oe when there was no magnetic nanoparticle (MNP) above the sensor, as shown in the upper right inset of Fig. 2. Then one MNP was artificially moved onto the sensor using the tungsten tip in the Focused Ion Beam system, as shown in the bottom right inset of Fig. 2. The presence of the artificially placed MNP above the sensor changed the switching fields to approximately +250 Oe and -170 Oe. There was significant distinction in the switching fields of a single MNP in proximity to the sensor versus a single MNP in proximity plus a single MNP above the sensor.

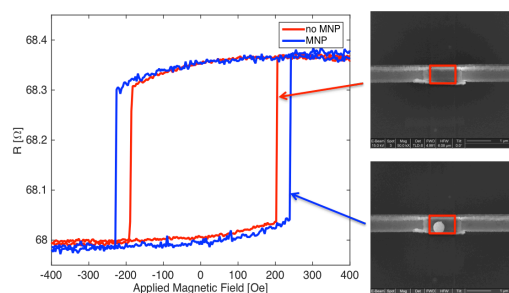


Figure 2

IMAGING THE MEMBRANE MECHANICAL FLUCTUATIONS OF SINGLE CANCER CELLS WITH PLASMONIC MICROSCOPE

Suraj Khochare and Xiaonan Shan
Department of Electrical and Computer Engineering
University of Houston
Houston, TX 77204-4005

Abstract

The plasma membrane of cells is undergoing continuous motion, part of which is driven by the active processes while the other part is purely thermal. This membrane fluctuations are highly relevant for the biological system and many physiological processes, including fusion of liposome vehicles, cell division, and cell's mechanoresponse. In addition, the membrane fluctuations also provide us with the inside information of viscoelastic properties of the cells. Therefore it is very important to image the localized cell membrane vibration. However, it is difficult to quantify the cell membrane fluctuations experimentally due to its small movement. We have used the plasmonic microscope to image the cell membrane fluctuations at single cell level. A 1-2 nm cell membrane vibration has been imaged with 0.5 um spatial resolution in real time. Cancer cells which are alive exhibit active fluctuations like any normal living cells. Quantitative analysis of these mechanical vibrations provides us with mechanical properties of the cell membrane, information about the cell structure and metabolism in the cancer cells. This analysis is essential to analyze activity of biomarkers when cancer cells are exposed to different drug treatments.

A novel *in ovo* system to treat lung cancer

Veronica Vighetto
Houston Methodist

It has been demonstrated that the use of gold nanoparticles (AuNPs) in tumor treatments provides advantages due to radiative enhancement effects. Intratumoral injection of AuNPs combined with X-ray radiation as therapy for Lewis Lung carcinoma is presented for C57BL/6 mice inoculated with cells expressing luciferase (LLC-Luc). In this work, results are also presented for the chick chorioallantoic membrane (CAM) as tumor model. This study showed that the CAM can be used as preliminary *in vivo* model to study the effects of different treatments, using a simpler and faster system in which the influence of the immune system is not present and which does not require the IACUC approvals.

A robust and generalized method for phase mask designs

Wenxiao Wang[†], Fan Ye[†], Hao Shen[‡], Nicholas A. Moringo[‡], Jacob T. Robinson[†], & Christy F. Landes^{†‡§}.*

[†]Department of Electrical and Computer Engineering, Rice University, MS 366, Houston, Texas 77251-1892, United States

[‡]Department of Chemistry, MS 60, Houston, Texas 77251-1892, United States

[§]Smalley-Curl Institute, Rice University, Houston, Texas 77251, United States

Phase modulation and PSF engineering appears as a novel approach in recent years to achieve 3D detection in super-resolution microscopy. Multiple 3D engineered point spread functions have been proposed for specific applications. However the shape of point spread functions is always not under the control. There is not a robust algorithm to design the phase mask of arbitrary shaped point spread functions. In this work a generalized and robust phase mask design method is proposed by solving it in a convex optimization schema. Stochastic gradient descent algorithm and Gauss-Newton algorithm are applied to recover the phase mask. Previously reported phase masks are recovered in this work but with the new approach. A novel stretching-lobe point spread function is designed for the first time to encode 3D spatial information. All the designed phase masks are fabricated using multi-level light lithography method and then validated in single molecule experiments. Finally the algorithm is challenged to generating 4 different letters at different depths as a demonstration that the algorithm is capable of generating arbitrary shaped PSFs.

Filter-less Fluorescence Imaging Using Ultraviolet Illumination for Acridine Orange Stained Whole Blood

Cynthia Wong¹, Michal E. Pawlowski¹, Tomasz S. Tkaczyk^{1,2}

¹Department of Bioengineering, Rice University, 6500 Main Street, Houston, TX 77005, USA

²Department of Electrical and Computer Engineering, Rice University, 6100 Main Street, Houston, TX 77005, USA

Key Words: Fluorescence microscopy, filter-less imaging, ultraviolet illumination, white blood cell imaging

Fluorescence microscopy is a powerful tool that has been used in the biological sciences to image everything from bacteria to cells both *in vitro* and *in vivo*. While most fluorescent dyes have excitation in the visible wavelength range, many of these dyes are also excitable by ultraviolet (UV) wavelengths. Recently, Dr. Richard Levenson and his research group at the University of California Davis successfully implemented slide-free histology and pathology imaging using UV illumination [1]. Since UV wavelengths are not typically visible on camera detectors and are absorbed by most glass components, UV illumination may potentially be used in a filter-free fluorescence microscopy system. This may help decrease the cost of manufacturing diagnostic devices, especially for low-cost diagnostic applications. A prototype system was developed as follows. The system consists of two light emitting diodes (LED) at 280 nm and 455 nm as the illumination source. Both LEDs were aligned in an oblique-angle cis-illumination. No filters were needed for imaging with the 280 nm LED since glass naturally absorbs UV wavelengths and the detector is not sensitive to UV. For the 455 nm LED, a 470 nm excitation filter and a 532 nm longpass emission filter were added to allow for standard fluorescence imaging. The imaging optics and detector consist of off-the-shelf components. Initially, the system was tested by imaging highlighted lens paper. After seeing similar images from both UV and standard fluorescence, whole blood stained with acridine orange was then imaged to test the systems' ability to visualize biological samples.

[1] Fereidouni F, Datta-Mitra A, Demos S, Levenson R. (2015) Microscopy with UV Surface Excitation (MUSE) for slide-free histology and pathology imaging. Proc. SPIE 9318, Optical Biopsy XIII: Toward Real-Time Spectroscopic Imaging and Diagnosis. doi:10.1117/12.2080408.

Compressive Hyperspectral Microscopy

Yibo Xu, Liyang Lu, Jianbo Chen, Kevin F. Kelly

Rice University

Imaging with hyperspectral microscopy using conventional techniques typically involves a trade-off between resolution, acquisition time, and expense due to a combination of low pixel-by-pixel signal intensity and detector sensitivity. In this work, we applied compressive sensing theory to hyperspectral microscopy so that the combination of compressive light modulation with sparsity-based reconstruction algorithms enhances the measurement signal-to-noise ratio and allows for rapid acquisition of the full spectrum at every pixel in the image, even though the total hypercube is sub-sampled. We present the successful demonstration in bright field transmission and reflection mode as well as dark field imaging modality. The utility of this approach is verified by measuring the changes in plasmon resonances as a function of position along gold nanoparticles and nanobelts. We also demonstrate the application of this technique to characterizing the optoelectronic properties of two-dimensional transition metal dichalcogenides thin films and nanoflakes. Beyond these initial results, the tradeoffs between algorithmic restrictions and hardware limitations will also be discussed. An additional compelling feature of this design is its straightforward extension to imaging optical properties outside the spectral responsivity of silicon which has limited various array-based hyperspectral approaches such as pushbroom and snapshot imaging systems where infrared focal plane arrays are prohibitively expensive.

Origin of Plasmonic Circular Dichroism from Au Nanorod-Protein Complex: A single-particle spectroscopic study

Qingfeng Zhang, Taylor Hernandez, Kyle W. Smith, Lauren Warning, Lauren McCarthy, Christy F. Landes, and Stephan Link

Rice University

While plasmonic circular dichroism (PCD) has been widely investigated in the system that combining plasmonic nanostructure with chiral biomolecules (protein, peptide, DNA, etc.), a mechanistic understanding of the origin of PCD from the nanoparticle-biomolecule complex is often missing in current ensemble PCD measurements. When ensemble PCD is observed from the nanoparticle-biomolecule complex in solution, a key question to address is that: does the PCD come from the molecular dipole-plasmon interaction between chiral biomolecules and achiral plasmonic nanoparticles, or the formation of chiral plasmonic nanoparticle aggregates? Here we used single-particle circular differential scattering (CDS) spectroscopy to quantitatively investigate the origin of PCD from Au nanorods-protein complex. We demonstrated that positively charged Au nanorods underwent different interaction pathways upon mixing with bovine serum albumin (BSA) at varying BSA concentration. At relatively high BSA concentration, single Au nanorod was stabilized with the formation of BSA monolayer. However, at low BSA concentration we found nanorods aggregation, and meanwhile, a significant ensemble PCD was observed. The Au NRs-BSA complex that formed at low BSA concentration was chosen as a model system to investigate the origin of PCD at single-particle level. By taking advantage of single-particle CDS spectroscopy with correlated 3D high-resolution scanning electron microscopy, we built the statistical distribution of CDS on different nanorod aggregates (single nanorod, dimer, trimer, etc.). We demonstrated that single Au nanorods-BSA complex is CDS non-active, and Au nanorod dimer, trimer, and larger aggregates show structure-dependent CDS. To gain more quantitative insight into the structure-property relationship of Au nanorods-BSA complex, correlated transmission electron microscopy, electron tomographic reconstruction, and structural simulation is further employed to understand the contribution of chiral configuration and chiral protein to the overall CDS. This work provides significant insights into the understanding of nanoparticle-biomolecule interaction and the origin of PCD in the nanoparticle-protein complex at single-particle level.