The Smalley-Curl Institute and the Kavli Foundation present “Sensing the Future: The Future of Sensing” Workshop Series, a trio of visionary, cross-disciplinary meetings at Rice University that will focus on the future of sensing technology. These meetings bring together scientists and engineers from academia, government and industry to identify the grand challenges that could potentially be met by next-generation sensing technologies, and the fundamental scientific capabilities that will be needed to address those challenges. The second workshop in the series, “Biosensing II”, continues and expands upon the discussion from the first workshop on topics such as biomedical diagnostics and imaging, and implantable and wearable sensors.
Program Overview

The workshop will take place at the **Bioscience Research Collaborative building** (all talks will be in the Main Auditorium; lunch will be held in the Event Space)

<table>
<thead>
<tr>
<th>DATE / TIME</th>
<th>SPEAKER</th>
<th>TALK TITLE</th>
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<tr>
<td>Day 1 (Thursday Dec 6)</td>
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<tr>
<td>8:30 AM</td>
<td>Breakfast and Coffee (outside Main Auditorium)</td>
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<tr>
<td>9:00 AM</td>
<td>Welcome and Introduction to Workshop 2</td>
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<td>Session A Chair: Dr. Christy Landes</td>
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<tr>
<td>9:15 AM</td>
<td>Francois St-Pierre (Baylor College of Medicine)</td>
<td>“Hacking fluorescent proteins to image bioelectricity”</td>
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<td>10:00 AM</td>
<td>Markita del Carpio Landry (University of California - Berkeley)</td>
<td>&quot;Imaging Striatal Dopamine Release Using a Non-Genetically Encoded Near-Infrared Fluorescent Catecholamine Nanosensor&quot;</td>
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<td>10:45 AM</td>
<td>Break</td>
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<tr>
<td>11:00 AM</td>
<td>Hanyu Zhu (Rice University)</td>
<td>“Piezoelectric two-dimensional materials for mechanical biosensing”</td>
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<td>11:45 AM</td>
<td>Roundtable Panel Discussion</td>
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<td>12:30 PM</td>
<td>Lunch</td>
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<tr>
<td>1:15 PM</td>
<td>Romain Quidant (ICFO - The Institute of Photonic Sciences)</td>
<td>“Combining Photonics and Nanotechnology for Sensing: From On-a-Chip Molecular Detection to Tissue Interrogation”</td>
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<td>Session B Chair: Dr. Kaitlyn Crawford</td>
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<tr>
<td>3:00 PM</td>
<td>Jonathan Rivnay (Northwestern University)</td>
<td>“Polymer Mixed Conductors for Bi-Directional Neural Interfacing”</td>
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<td>3:45 PM</td>
<td>Break</td>
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<tr>
<td>4:30 PM</td>
<td>Jacob Robinson (Rice University)</td>
<td>&quot;Distributed Neural Sensing and Actuation to Regulate Physiological States&quot;</td>
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<tr>
<td>5:15 PM</td>
<td>Roundtable Panel Discussion</td>
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</table>
5:30 PM  Reception and Poster Session

Day 2 (Friday Dec 7)

8:30 AM  Breakfast and Coffee

9:00 AM  Opening Remarks for Day 2

Session C Chair: Dr. Naomi Halas

9:15 AM  Tzahi Cohen-Karni (Carnegie Mellon University)  "Organ-on-e-Chip: Biosensors for Electrical Interrogations of Engineered 3D Micro-Tissues"

10:00 AM  Lisa Biswal (Rice University)  “Biochemo-mechanics: The development of supported lipid-membranes on microcantilevers to evaluate therapeutics”

10:45 AM  Break

11:00 AM  Hui-wang Ai (University of Virginia)  “Directed Evolution of Luciferase-Luciferin Pairs for Biocompatibility and In Vivo Sensitivity”

11:45 AM  Roundtable

12:30 PM  Lunch and Conclusion
**Presenter information (in alphabetical order by presenter last name):**

**Huiwang Ai**, Associate Professor of Molecular Physiology & Biophysics, Chemistry, and Biomedical Engineering, University of Virginia School of Medicine

“**Directed Evolution of Luciferase-Luciferin Pairs for Biocompatibility and In Vivo Sensitivity**”

Bioluminescence, a phenomenon of production and emission of light as the result of a biochemical reaction, has broad applications in biology, biotechnology, and biomedical sciences. The current bioluminescence imaging systems have several limitations, such as very low photon flux and a limited choice of compatible colors. In particular, red-shifted bioluminescence reporters are desirable for in vivo imaging. We developed red-shifted luciferins based on synthetic coelenterazine (CTZ) analogs and corresponding mutants of NanoLuc that enable bright bioluminescence. Also, the substrates, including CTZ and the recently developed furimazine (FRZ) and diphenylterazine (DTZ), have poor solubility in aqueous solutions, and thus require organic cosolvents for in vivo injection, thereby limiting their applications. We further developed a family of pyridyl CTZ and DTZ analogs that exhibit improved water solubility and spectrally shifted emission. We selected pyDTZ, a substrate with the most red-shifted emission, and further engineered a pyLuc luciferase to pair with this new substrate. We compared the resultant pyLuc-pyDTZ pair to several benchmark reporters in a tumor xenograft mouse model. Our new pair, which does not need organic cosolvents for in vivo injection, surpasses other reporters by detecting early tumors.

Dr. Ai received his B.S. degree from Tsinghua University in 2003 and Ph.D. degree from the University of Alberta in 2008 (advisor: Robert E. Campbell). He received his postdoctoral training from 2008 to 2011 in the lab of Peter G. Schultz at The Scripps Research Institute. He then became an assistant professor at the University of California, Riverside. In 2017, he moved to the University of Virginia (UVA) Department of Molecular Physiology and Biological Physics as a tenured associate professor. He is a resident faculty member of the Center for Membrane and Cell Physiology. He is also affiliated with the Departments of Chemistry and Biomedical Engineering, and the UVA Cancer Center. His research interest is the development of genetically encoded probes for biological imaging, including the engineering and use of fluorescent and bioluminescent biosensors to understand the spatiotemporal organization of redox and brain signaling.

**Lisa Biswal**, Associate Professor, Chemical and Biomolecular Engineering, Materials Science and NanoEngineering, Rice University

“**Biochemo-mechanics: The development of supported lipid-membranes on microcantilevers to evaluate therapeutics**”

Abstract:

I will discuss how biochemical interactions can translated into a nanomechanical measurements: biochemo-mechanics. Specifically, supported lipid–membranes on microcantilevers are used to probe the interactions between phospholipid membranes and membrane-active macromolecules.
for assessing the efficacy of therapeutics. This biosensing method integrates two well-developed techniques: the solid-supported lipid bilayers (SLBs) and the microcantilever sensors. As lipids and macromolecules adsorb onto the surface of the microcantilever, it induces a nanomechanical deflection of the microcantilever due to induced compressive or tensile surface stresses. By monitoring this nanomechanical deflection, the real–time surface stress changes in supported lipid membranes can be detected. Macromolecules, such as PEP1, a synthetic amphipathic peptide resembling a segment of the nonstructural protein (NS5A) of hepatitis C virus, and Pluronics with lipid membranes cause a measurable deflection change. In both systems, we are able to observe macromolecules adsorb onto and crowd the lipid membranes. For concentration greater than the critical concentration, the macromolecules start to aggregate leading to membrane pore formation. At even higher concentrations, the macromolecules further destabilize and induce the solubilization of membrane. The membrane coated microcantilever sensor is capable of characterizing the kinetics and dynamics of membrane-peptide interactions with great sensitivity.

Dr. Sibani Lisa Biswal is an Associate Professor at the Department of Chemical and Biomolecular Engineering at Rice University in Houston, TX and leads the Soft Matter Engineering Laboratory. She has a B.S in chemical engineering from Caltech (1999) and a Ph.D. in chemical engineering from Stanford University (2004). She is the recipient of an ONR Young Investigator Award (2008), a National Science Foundation CAREER award (2009), Rice U. Professional Excellence Award from the Rice CHBE Alumni Advisory Committee (2017), the Southwest Texas Section AICHE Best Applied Paper Award (2018), and the George R. Brown Award for Superior Teaching (2015).

Tzahi (Itzhaq) Cohen-Karni, Assistant Professor, Biomedical Engineering and Materials Science & Engineering, Carnegie Mellon University

“Organ-on-e-chip: Biosensors for electrical interrogations of engineered 3D micro-tissues”

We focus on developing a new class of nanoscale materials and novel strategies for the investigation of biological entities at multiple length scales, from the molecular level to complex cellular networks. Our highly flexible bottom-up nanomaterials synthesis capabilities allow us to form unique hybrid-nanomaterials, such as 3D out-of-plane single- to few-layer fuzzy graphene (3DFG) grown on a Si nanowire (SiNW) mesh template. By varying graphene growth conditions, we control the size, density, and electrical properties of the NW templated 3DFG (NT-3DFG). I will discuss the formation and use of complex hybrid-nanomaterials with tailored optical and electrical properties in biosensing, and bioelectronics. Our current efforts target the limits of cell-nanodevices interfaces using biosensor array assembled in 3D with subcellular spatial resolution (<5μm) and μsec temporal resolution. Our approach enables simultaneous multiplexed electrical measurements to directly monitor the development of electrical activities of microscale tissues (μtissues, ca. 100-400μm) which are engineered from embryonic stem cell (ES) derived cardiomyocytes. Last, we have developed a unique transparent graphene-based electrical platform that enables concurrent electrical and optical investigation of ES-derived cardiomyocytes’ intracellular processes and intercellular communication. In summary, the exceptional synthetic control and flexible assembly of nanomaterials provide powerful tools for fundamental studies and applications in life science and open up the potential to seamlessly merge
either nanomaterials-based platforms or unique nanosensor geometries and topologies with cells, fusing nonliving and living systems together.

Tzahi Cohen-Karni is an Assistant Professor at the Departments of Biomedical Engineering and Materials Science and Engineering in Carnegie Mellon University, Pittsburgh, PA, USA. He received both his B.Sc. degree in Materials Engineering and the B.A. degree in Chemistry from the Technion Israel Institute of Technology, Haifa, Israel, in 2004. He obtained his M.Sc. degree in Chemistry from Weizmann Institute of Science, Rehovot, Israel, in 2006 and his Ph.D. in Applied Physics from the School of Engineering and Applied Sciences, Harvard University, Cambridge MA, USA, in 2011. He was a Juvenile Diabetes Research Foundation (JDRF) Postdoctoral Fellow at the Massachusetts Institute of Technology and Boston Children’s Hospital at the labs of Robert Langer and Daniel S. Kohane from 2011 to 2013. Dr. Cohen-Karni received the Gold Graduate Student Award from the Materials Research Society in 2009, and received the 2012 International Union of Pure and Applied Chemistry Young Chemist Award. Dr. Cohen-Karni was awarded the Charles E. Kaufman Foundation Young Investigator Research Award (2014), the NSF CAREER Award (2016) and the Cellular and Molecular Bioengineering Rising Star Award (2017) and the Office of Naval Research Young Investigator Award (2017).

Markita Landry, Assistant Professor, Chan-Zuckerberg Biohub Investigator, Department of Chemical and Biomolecular Engineering, University of California, Berkeley

“Imaging Striatal Dopamine Release Using a Non-Genetically Encoded Near-Infrared Fluorescent Catecholamine Nanosensor”

For over 60 years, drugs that alter, mimic, or block modulatory neurotransmitters have formed the core arsenal for the treatment of neurological disorders such as depression, addiction, schizophrenia, anxiety, and Parkinson’s disease. However, methods to diagnose and validate drug efficacy have remained largely the same: questionnaires and behavioral observations. The archaic nature of neurological disorder diagnosis results from the lack of tools to detect the molecular ‘key players’ of neuronal communication – the three primary modulatory neurotransmitters dopamine, serotonin, and norepinephrine. Therefore, new optical tools are needed that can image neuromodulation with high spatial and temporal resolution, which will add an important new dimension of information to neuroscience research. Here, we demonstrate the use of a catecholamine nanosensor (nIRCat) with fluorescence modulation ∆F/F of up to 2400% in the 1000-1300 nm near-infrared window (Beyene*, Alizadehmojarad*, et al. bioRxiv 2018) to measure dopamine transmission in ex vivo brain slices. We show that nIRCats can be used to detect catecholamine efflux in brain tissue driven by both electrical or optogenetic stimulation (Beyene et al. bioRxiv 2018). Spatial analysis of electrically evoked signals revealed dynamic regions of interest approximately 2 microns in size in which transients scaled with simulation intensity. Optogenetic stimulation of dopaminergic terminals produced similar transients, while optogenetic stimulation of glutamatergic terminals showed no effect on nIRCat signal. Furthermore, bath application of nomifensine, a dopamine reuptake inhibitor, prolonged nIRCat fluorescence signal as expected. Bath application of dopamine receptor agonist quinpirole decreased nIRCat signal, whereas bath application of dopamine receptor antagonists sulpiride or haloperidol increased nIRCat signal. We discuss insights gained from computational work to rationalize experimental findings (Beyene et al. ACS Chem Neurosci 2017). These nanosensors may be advantageous for future use because they i) do not require virus delivery, gene delivery, or protein expression, ii) their near-infrared fluorescence facilitates imaging in optically scattering brain tissue and is compatible for use in conjunction with other optical neuroscience tool sets, and iii) the broad availability of unique near-infrared colors have the potential for simultaneous detection of multiple neurochemical signals.
Markita Landry is an assistant professor in the department of Chemical and Biomolecular Engineering at the University of California, Berkeley. She received a B.S. in Chemistry, and a B.A. in Physics from the University of North Carolina at Chapel Hill, a Ph.D. in Chemical Physics from the University of Illinois at Urbana-Champaign, and completed a postdoctoral fellowship in Chemical Engineering at the Massachusetts Institute of Technology. Additionally, she has held interim research positions at the Biophysics Institute at the Technical University of Munich, and at the center for nanobiosciences at Osaka University.

Her current research centers on the development of synthetic nanoparticle-polymer conjugates for imaging neuromodulation in the brain, and for the delivery of functional biomolecules and nutrients into living systems. The Landry lab exploits the highly tunable chemical and physical properties of nanomaterials for the creation of bio-mimetic structures, molecular imaging, and gene editing. She is a recent recipient of early career awards from the Brain and Behavior Research Foundation, the Burroughs Wellcome Fund, The Parkinson’s Disease Foundation, the DARPA Young Investigator program, the Beckman Young Investigator program, the Howard Hughes Medical Institute, is a Sloan Research Fellow, an FFAR New Innovator, and is a Chan-Zuckerberg Biohub Investigator.

**Romain Quidant**, Professor, ICFO - The Institute of Photonic Sciences

**“Combining Photonics and Nanotechnology for sensing: from on-a-chip molecular detection to tissue interrogation”**

*Abstract pending*

After a PhD in Physics from the University of Dijon, France, Quidant joined ICFO- The Institute of Photonic Sciences as a postdoctoral researcher. In 2006, he was appointed junior Professor (tenure-track) and group leader of the *Plasmon NanoOptics* group at ICFO. In 2009, he became tenure Professor both at ICFO and ICREA. His research focuses on nano-optics, at the interface between Photonics (the science of light) and Nanotechnology. His teams uses the unique optical properties of nanostructures as an enabling toolbox to design solutions to scientific and technological challenges, in a wide set of disciplines, from fundamental physics to biotechnology and medicine. This makes his activities highly multidisciplinary, and spanning all the way from basic to applied research. The most fundamental part of his work is mainly directed towards enhanced light/matter interaction and quantum physics. From a more applied viewpoint, the Quidant's team investigates news strategies to control light and heat at the nanometer scale for biomedical applications, including lab-on-a-chip technology and targeted hyperthermia. Quidant is also extensively involved in tech-transfer, with three technologies being incubated in the ICFO KTT Launch pad.

**Jonathan Rivnay**, Assistant Professor of Biomedical Engineering, Northwestern University

**“Polymer mixed conductors for bi-directional neural interfacing”**

Direct measurement and stimulation of electrophysiological activity is a staple of neural and cardiac health monitoring, diagnosis and therapy. Such bi-directional interfacing can be enhanced by the attractive properties of organic electronic materials which can favorably bridge the biotic/abiotic interface. These materials are mixed ionic/electronic conductors: they allow for intimate interaction of the electron transporting polymer with the biological environment, including swelling and bulk interaction with ions and biomolecules. This feature improves both electrochemical properties and mechanical matching with surrounding tissue, critical for recording and stimulation in biomedical devices, and can be used to advance the state of the art. Organic electrochemical
transistors, for example, have shown considerable promise as amplifying transducers for electrophysiology and biomolecular sensing due to their stability in aqueous conditions and high transconductance. The volumetric gating of these devices and steep subthreshold switching characteristics are used to demonstrate human electroencephalography measurements with significant signal enhancement at low frequency and low power operation. The same class of materials, conducting polymers and polyelectrolytes, are then demonstrated as active elements in organic electronic ion pumps -- devices which allow for localized electrophoretic delivery, without the adverse effects of fluidic delivery. In this work, release of an endogenous inhibitory neurotransmitter from such a device is shown to stop seizure-like activity locally in brain tissue. Finally, ionic and electronic transport properties of organic mixed conductors can be controlled through synthetic and processing variations, modulating device performance, and establishing design guidelines for next-generation polymeric bioelectronic materials. Jonathan Rivnay earned his B.Sc. in 2006 from Cornell University (Ithaca, NY). He then moved to Stanford University (Stanford, CA) where he earned a M.Sc. and Ph.D. in Materials Science and Engineering studying the structure and electronic transport properties of organic electronic materials. In 2012, he joined the Department of Bioelectronics at the Ecole des Mines de Saint-Etienne in France as a Marie Curie post-doctoral fellow, working on conducting polymer based devices for bioelectronics. Jonathan spent 2015-2016 as a member of the research staff in the Printed Electronics group at the Palo Alto Research Center (Palo Alto, CA) before joining the Department of Biomedical Engineering at Northwestern University in 2017. He is a recipient of the Faculty Early Career Development (CAREER) award from the National Science Foundation (2018).

Jacob Robinson, Assistant Professor, Electrical and Computer Engineering; Bioengineering, Rice University

“Distributed neural sensing and actuation to regulate physiological states”

Technological advances in nanoscale materials and devices are allowing us to manipulate and measure brain activity with unprecedented precision leading to deeper understanding of the brain and improved methods to treat brain disorders. In this talk I will discuss how emerging nanotechnologies enable tiny distributed devices that can be implanted in the body to sense and actuate neural activity. With these electronic, photonic, and magnetic technologies we expect to develop feedback control systems to help regulate physiological states to more effectively treat a number of disorders.

Jacob Robinson is an Assistant Professor in Electrical & Computer Engineering and Bioengineering at Rice University and an Adjunct Assistant Professor in Neuroscience at Baylor College of Medicine. Dr. Robinson earned a B.S. in Physics from UCLA and a Ph. D. in Applied Physics from Cornell. Following his Ph. D., he worked as a postdoctoral fellow in the Chemistry Department at Harvard University. Dr. Robinson joined Rice University in 2012 where he currently works on nanoelectronic, nanophotonic, and nanomagnetic technologies to manipulate and measure brain activity. Dr. Robinson is currently a co-chair of the IEEE Brain Initiative, and the recipient of a Hammill Innovation Award, NSF NeuroNex Innovation Award, DARPA Young Faculty Award, and Materials Today Rising Star Award.

Francois St-Pierre, Assistant Professor and McNair Scholar, Neuroscience, Baylor College of Medicine

“Hacking fluorescent proteins to image bioelectricity”
A longstanding goal in neuroscience is to understand how spatiotemporal patterns of neuronal electrical activity underlie brain function, from sensory representations to decision making. An emerging technology for monitoring electrical dynamics is voltage imaging using Genetically Encoded Voltage Indicators (GEVIs) — light-emitting protein indicators whose brightness reports voltage. In this talk, I will discuss our efforts at developing novel voltage indicators with millisecond-timescale kinetics and their application in brain slices and in Drosophila.

Francois St-Pierre received his doctorate in Computational and Systems Biology from the Massachusetts Institute of Technology in 2009. He then went on to be a postdoctoral fellow in Bioengineering & Pediatrics at Stanford University before joining Baylor College of Medicine, Department of Neuroscience, in 2015. His research focuses on the design, developments and deployment of genetically encoded sensors of neural activity.

Luisa Torsi, Professor, Chemistry, University of Bari Aldo Moro

"Single Molecule Detection of Markers with a Label-Free Bio-Electronic Sensor"

Label-free single-molecule detection has been achieved so far by funnelling a large number of ligands into a sequence of single-binding events with few recognition elements host on nanometric transducers. Such approaches are inherently unable to sense a cue in a bulk milieu. Conceptualizing cells’ ability to sense at the physical limit by means of highly-packed recognition elements, a millimetric sized field-effect-transistor is used to detect a single molecule. To this end, the gate is bio-functionalized with a self-assembled-monolayer of trillions of capturing anti-Immunoglobulin-G and is endowed with a hydrogen-bonding network enabling cooperative-interactions. The selective and label-free single-molecule IgG detection is strikingly demonstrated in diluted saliva while 15 IgGs are assayed in whole serum. The suggested sensing mechanism triggered by the affinity binding event, involves a work-function change that is assumed to propagate in the gating-field through the electrostatic hydrogen-bonding network. The proposed immunoassay platform is general and can revolutionize the current approach to protein detection.

Luisa Torsi is full professor of Chemistry since 2005 and is the immediate past-president of the European Material Research Society, the largest in its field in Europe. She is the first women to hold this role. Torsi received her laurea degree in Physics from the University of Bari in 1989 and the PhD in Chemical Sciences from the same institution in 1993. She was post-doctoral fellow at Bell Labs from 1994 to 1996. In 2005 and 2006 she was invited professor at the University of Anger and Paris 7, respectively. Presently she is adjunct professor at the Abo Academy University in Finland. In 2010 she has been awarded with the Heinrich Emanuel Merck prize for analytical sciences, this marking the first time the prestigious award is given to a woman and to an Italian scientist. She is also the recipient of the main overall platinum 2015 prize of the Global-Women Inventors and Innovators Network. Torsi had been serving extensively as expert reviewer for the European Commission being for three years the Chair of the Chemistry Panel for the evaluation of the Marie Curie Research Fellowships. She was also member the Physical and Engineering Science 05 panel of the European Research Council for the evaluation of the consolidator grants. In 2014 she has been appointed as member of the H2020 Program Committee by the Italian Minister for Education and Research and is still serving in this role. Torsi has authored almost 190 ISI
papers, including papers published in Science, Nature Materials, Nature Communications, PNAS, Advanced Materials, Scientific Reports and is co-inventor of several international awarded patents. Her works gathered almost 11,000 Google scholar citations resulting in an h-index of 50. She has given more than 170 invited lectures, including almost 25 plenary and key notes contributions to international conferences. Awarded research funding comprises several European contracts as well as national and regional projects. She is coordinating the “Single molecule bio-electronic smart system array for clinical testing – SiMBiT” a H2020-ICT-2018-2020 research and innovation action finance with over 3 M€. She has also coordinated a “European Industrial Doctorate” Marie Curie project in collaboration with Merck and was principal investigator in a Marie Curie ITN. She has also coordinated a Marie Curie ITN European network, several national PRIN projects and was principal investigator in an ICT STREP proposal. The total budget awarded to Torsi and to the consortia she has coordinated is over 8 M€. She has also been the scientific coordinator of a Structural Reinforcement PON Project awarded to UNIBA for 2012-2014 with 13 M€. Prof. Torsi is committed to the role of model for younger women scientists. She has been giving a number of talks on this topic such as a TEDx talk and she was also member of the National Board of the STAGES European project that aims at implementing strategies to trigger structural changes addressing the issues connected with gender inequality in science.

**Hanyu Zhu**, Assistant Professor, Materials Science & Nanoengineering, Rice University

“Piezoelectric two-dimensional materials for mechanical biosensing”

*Abstract pending*

Dr. Zhu is an assistant professor of Materials Science and NanoEngineering. He earned his B.S. in Mathematics and Physics in Tsinghua University in China studying carbon-based nanomaterials. He obtained his Ph.D. in Applied Science and Technology in the University of California at Berkeley for the discovery of piezoelectricity in atomically thin crystals, and then performed postdoctoral research at Berkeley to develop novel optical spectroscopy for quantized and topological lattice vibration. In July 2018 he started the Emerging Quantum and Ultrafast Activity Laboratory at Rice University.