Table of Contents

1 Message from the Chair
2 About BME
4 Department of Biomedical Engineering Faculty
14 Faculty Research Areas
15 Active Faculty Research Grants
16 Research Highlight: Using Light to Control the Heart: Leading Research in Cardiac Optogenetics at BME-GW: Drs. Entcheva and Kay
17 Meet Our New Faculty: Dr. Anne-Laure Papa
18 BME Alumni Q&A: Kara Garrott
19 Ph.D. Dissertations
22 Contact Us
On behalf of the faculty and staff of the GW Department of Biomedical Engineering (BME), I would like to welcome you to our fall newsletter. These are exciting times for biomedical engineering at GW. The formation of our new Department of Biomedical Engineering in fall 2014 followed by the launch of our new Science and Engineering Hall in 2015, which is across the street from the School of Medicine and Health Sciences and GW Hospital, make it a unique time to study biomedical engineering in the heart of the nation’s capital. We are also just a few blocks away from the White House, Washington Monument, Lincoln Memorial, Smithsonian National Museums, and many other national capital landmarks and Federal government institutions.

Undergraduates in the department can obtain a Bachelor of Science degree in biomedical engineering, which is accredited by the Engineering Accreditation Commission of the Accreditation Board for Engineering and Technology (ABET). The wide range of expertise of our faculty allows us to prepare undergraduates for immediate entrance into the practice of biomedical engineering, or graduate, medical, policy, or law schools, and also to provide the breadth of fundamental knowledge that will prepare them for the lifelong learning that is necessary to remain productive as professionals in the future. We encourage and provide opportunities for study abroad, internships, and undergraduate research experiences.

At the graduate level, students can enroll for the Master of Science, Master of Engineering, and Doctor of Philosophy (Ph.D.) degrees in Biomedical Engineering. The BME department maintains a diverse program of research, directed at areas such as medical imaging, medical image and signal analysis, optogenetics, microfluidics and lab-on-a-chip development, and neural and cardiovascular engineering. Opportunities for graduate student support are available in many of these areas, and we invite prospective graduate students to contact the department office or individual faculty members for detailed information about teaching and research assistantships. Every year we attend annual sessions of Biomedical Engineering Society, where we present research conducted in our department and our programs to prospective graduate students. We are also proud to present these training opportunities to qualified prospective graduate students during our annual BME Day, which is now traditionally held the first week of November, one month after the BMES conference.

Whether you are a prospective undergraduate or graduate student, we welcome the chance to talk with you and discuss all the options that are available to you in the BME department. Please contact me at biomed@gwu.edu or at 202-994-3740 with any questions you have, including your interest in visiting GW’s BME department in Washington, DC.

Sincerely,

Igor Efimov, Ph.D., F.A.I.M.B.E., F.A.H.A., F.H.R.S.
The Alisann & Terry Collins Professor and Chairman
Department of Biomedical Engineering
The Department of Biomedical Engineering, newly formed in 2014, offers unique opportunities for our students, who can take advantage of our location in the heart of the nation’s capital and near numerous federal agencies and research labs involved in biomedical and health-related enterprises.

What is Biomedical Engineering?

Biomedical engineering is the application of engineering practices to human health issues. Biomedical engineers have developed and improved the technologies used to diagnose and treat a wide range of diseases. Examples of new and exciting technologies under development by biomedical engineers are:

- Improved imaging methodologies for cancer detection
- Novel methods to analyze medical images and present additional information to physicians
- New technologies to understand electrical conduction abnormalities in the heart to better respond to heart attacks and arrhythmias
- New technologies to provide selective delivery of drugs, such as chemotherapy agents, to areas of interest in the body without damaging healthy tissues

EXPENDITURES

Research expenditures: $2.4 million/year

STUDENT POPULATION

Full-time faculty/ Affiliated faculty: 10/8

Undergraduate students: 230

Graduate students: 63
Biomedical Engineering at GW

GW’s BME program takes advantage of the unique combination of resources and opportunities that the School of Engineering and Applied Science can provide to our BME students through its connection with the School of Medicine and Health Sciences and GW Hospital, as well as the biotech industries and world-class laboratories in the Washington, D.C. metropolitan area. Potential focus areas include bioinformatics, telemedicine, instrumentation, pre-medicine, biomechanics, imaging, and other areas as directed by the student’s academic advisor.

Our undergraduate and graduate students conduct internships and research experiences at places like the NIH, NASA, and the FDA, as well as private industry including Medtronic, Boston Scientific, and St. Jude Medical. This provides cutting-edge real world experience that often leads to job offers at the places where students intern.

LABORATORIES, CENTERS, & INSTITUTES

- Cardiac Ischemia Research Laboratory
- Cardiovascular Engineering Lab
- Optical and Acoustic Imaging Laboratory
- Medical Imaging and Image Analysis Laboratory
- Therapeutic Ultrasound Lab
- Cardiac Optogenetics and Optical Imaging Lab
- Assistive Robotics and Tele-Medicine (ART-Med) Lab
- Nanomedicine, Cellular Therapeutics, and Diagnostic Platforms Lab
- Cardiovascular Research Lab
- Nanophotonics and Microfluidics Laboratory

RESEARCH AREAS

- Biomedical signal processing and signal analysis
- Cardiac optogenetics
- Cardiovascular engineering
- Robotics and human robot interactions
- Biosensors
- Cancer detection and therapy
- Disease and pathogen detection
- Drug delivery
- Electrophysiology (cardiac and neural)
- Heart disease and heart failure
- Medical Imaging and Image analysis
- Microfluidics and nanotechnology
- Physiological flows
- Simulation and modeling
- Therapeutic ultrasounds
- Nanomedicine, cellular therapeutics and diagnostic platforms

DEGREES AND PROGRAMS

- Undergraduate: Biomedical Engineering (B.S., 5-year B.S./M.S.)
- Graduate: Biomedical Engineering (M.S., Ph.D.)
- Master of Engineering in Regulatory Biomedical Engineering (rBME)

AFFILIATED LABORATORIES & INSTITUTES

- Bioengineering Laboratory for Nanomedicine and Tissue Engineering
- Biofluid Dynamics Lab
- GW Institute for Biomedical Engineering
- Laboratory for Computational Physics and Fluid Mechanics
- Micro propulsion and Nanotechnology Lab

BME RESEARCH EXPENDITURES

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>Expenditure Dollars</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY-15</td>
<td>$502,262</td>
</tr>
<tr>
<td>FY-16</td>
<td>$1,183,812</td>
</tr>
<tr>
<td>FY-17</td>
<td>$2,414,234</td>
</tr>
</tbody>
</table>

RESEARCH EXPENDITURE DOLLARS
Igor Efimov
ALISANN AND TERRY COLLINS PROFESSOR AND CHAIR
DIRECTOR, CARDIOVASCULAR ENGINEERING LAB

B.S./M.Sc., Physics, Moscow Institute of Physics and Technology, 1986
Ph.D., Biophysics/BME, Moscow Institute of Physics and Technology, 1992
Postdoctoral, University of Pittsburgh, 1994

TEACHING
BME 6994: Biomedical Engineering Regulatory Practicum
BME 3820: Principles and Practice of Biomedical Engineering
BME 1010: Introduction to Biomedical Engineering
BME 3915, BME 4920, and BME 4925: Engineering Capstone Project Lab I, II, and III
BME 301B: Quantitative Physiology II

SELECTED PUBLICATIONS


RESEARCH
Our NIH-funded research laboratory studies the biophysical mechanisms of cardiac conduction and arrhythmia, and has developed novel anti-arrhythmia therapies, including low-energy defibrillation therapy. The lab works on future treatments for heart rhythm disorders and on engineering the pacemaker and conduction system of the heart, using electrical engineering, molecular biology, and multimodal imaging techniques.

Office: Science and Engineering Hall, Room 5000C
Phone: (202) 994-2152
Email: efimov@gwu.edu
Website: http://efimovlab.org

Above: Igor Efimov with Bill Clinton at Heart Rhythm Society Meeting
Emilia Entcheva
PROFESSOR
DIRECTOR, CARDIAC OPTOGENETICS AND OPTICAL IMAGING LAB

B.S./M.S. Electrical Engineering, Technical University - Sofia, Bulgaria
Ph.D. Biomedical Engineering, The University of Memphis, 1998
Postdoctoral, Biomedical Engineering, Johns Hopkins University, 2000

TEACHING
BME 3907: Bioelectricity
BME 6045: Cell and Molecular Imaging
BME 6999: Thesis Research
BME8999: Dissertation Research

SELECTED PUBLICATIONS


RESEARCH
Our group leads efforts in the concept and development of new fully automated high-throughput all-optical electrophysiology platforms to improve drug testing, human stem cell research, and gene therapies for the treatment of cardiac arrhythmias. We collaborate with companies or other researchers to characterize the electromechanical function of disease-specific patient-derived iPS-CMs in a massively parallel fashion.

Office: Science and Engineering Hall, Room 5660
Phone: (202) 994-7807
Email: entcheva@gwu.edu

Above: Light-sensitized cells (green) can be used to optically stimulate cardiomyocytes (red) for improving drug discovery.
Matthew Kay

PROFESSOR
ASSOCIATE CHAIR FOR RESEARCH
& GRADUATE AFFAIRS
DIRECTOR, CARDIAC ISCHEMIA RESEARCH LABORATORY

B.Sc. in Mechanical Engineering, North Carolina State University, May 1993
M.Sc. in Biological Engineering, North Carolina State University, August 1996
D.Sc. in Biomedical Engineering, Washington University in St. Louis, May 2000
Postdoctoral in Biomedical Engineering, University of Alabama in Birmingham, June 2001

TEACHING

BME 3820: Principles and Practice of Biomedical Engineering
BME 6484: Biomedical Signal Analysis
BME 3915, 4920, and 4925: Biomedical Engineering Capstone Project Labs I, II, and III
BME 1010: Introduction to Biomedical Engineering

SELECTED PUBLICATIONS


RESEARCH

Research in Dr. Kay’s laboratory is focused within the areas of heart failure and neurocardiology. Dr. Kay and his research team have specific expertise in high-speed optical assessments of cardiac physiology, including optical mapping and absorbance spectroscopy, and have developed powerful algorithms to analyze time-varying optical signals. Projects include aspects of cardiac metabolism, hypoxia, electromechanical function, and targeted activation of cardiac autonomic nerves using optogenetics and DREADDs.

Office: Science and Engineering Hall, Room 5670
Phone: (202) 994-2898
Email: phymwk@gwu.edu
David Lee
ASSOCIATE PROFESSOR OF PRACTICE
B.A., Maryville College, 1982
M.S, San Jose State University, 1995
Ph.D., Ohio State University, 2002

TEACHING
BME 1010: Introduction to Biomedical Engineering
BME 1020: Introduction to Biomedical Engineering
BME 3915W: Biomedical Engineering Project Lab I
BME 4925W: Biomedical Engineering Capstone Project Lab II
BME 6045: Biomedical Engineering Methods

SELECTED PUBLICATIONS

RESEARCH
Dr. Lee’s interests are in developing project- and laboratory-based curriculum for educating undergraduate biomedical engineers, and in developing assistive and adaptive devices for underserved markets. He currently directs the biomedical engineering capstone courses and is developing lab-and project-based activities throughout the four-year undergraduate program.

Office: Tompkins Hall, Room 104B
Phone: (202) 994-2183
Email: dtlee@gwu.edu

Top: Mouse ECG Vest Team
The mouse vest is a device used to collect ECG data from a mouse and wirelessly transmit that data to a computer.
BME: Kathleen Lockhart, Allison Przybylowicz, Sabrina Wallace
ECE: Annette Brown, Christian Escotto

Below: Respiration Monitor
Team: Aisling Casey, Topher Copeland, Srineil Nizambah, Camille Roberts, Abigail Thorpe
Screenshot: The respiration monitor collects data from a ventilator, and calculates a measure of the patient’s synchronicity with the ventilator. The screenshot shows the monitor at startup.
Zhenyu Li
ASSOCIATE PROFESSOR
DIRECTOR, NANOPHOTONICS AND MICROFLUIDICS LABORATORY

B.S., Tsinghua University, 1999
M.S., University of California, 2000
Ph.D., California Institute of Technology, 2007
Postdoctoral Scholar, Howard Hughes Medical Institute (HHMI) Janelia Farm, 2008-2010

TEACHING
BME 6482: Medical Measurement
BME 6483: Medical Instrumentation Design
BME 4920 & 4925: Biomedical Engineering Capstone Project Lab

SELECTED PUBLICATIONS
A. Guan, A. Shenoy, R. Smith and Z.Y. Li, “Streamline based design guideline for deterministic microfluidic hydrodynamic single cell traps”, Biomicrofluidics 9, 024103, Mar. 2015.

RESEARCH
Professor Zhenyu Li’s research focuses on the development of wearable biosensors and miniaturized medical devices using micro and nanotechnology, namely microfluidics, MEMS, nanophotonics, and flexible electronics. Our current projects include a handheld automated blood analyzer using microliter blood samples, a wearable ECG sensor on a finger ring, and soft robotics with embedded medical sensors and actuators for automated health care delivery.

Office: Science and Engineering Hall, Room 5590
Phone: (202) 994-4272
Email: zhenyu@gwu.edu
Website: https://sites.google.com/site/gwulilab
Murray Loew

PROFESSOR
DIRECTOR, MEDICAL IMAGING AND IMAGE ANALYSIS LABORATORY

B.S.E.E., Drexel Institute of Technology, 1965
M.S.E.E., Purdue University, 1967
Ph.D., Electrical Engineering, Purdue University, 1972

TEACHING

BME 3915, BME 4920, and BME 4925: Biomedical Engineering Capstone
Project Lab I, II, and III
BME 6485: Medical Imaging I
BME 6840: Digital Image Processing
BME 6850: Pattern Recognition
BME 6885: Computer Vision
BME 8484: Medical Imaging II

SELECTED PUBLICATIONS


RESEARCH

Medical imaging and image analysis: image registration, compression, and quality evaluation; Computer-aided diagnosis; Image processing and computer vision: segmentation, multispectral analysis, statistical methods, image fusion, and human perception; Pattern Recognition: feature extraction, classifier design, and validation.

Current work: quantitative thermal imaging for breast cancer detection; hyperspectral image analysis for assessment of success of cardiac ablation; salience measures for diagnosis and anomaly detection; development of simple imaging tools for characterization of glass.

Office: Science and Engineering Hall, Room 6660
Phone: (202) 994-5910
Email: loew@gwu.edu
Website: http://loewlab.seas.gwu.edu
Anne-Laure Papa

ASSISTANT PROFESSOR
DIRECTOR, NANOMEDICINE, CELLULAR THERAPEUTICS AND DIAGNOSTIC PLATFORMS LAB

M.Sc. Chemistry of Interfaces and Materials, University of Bourgogne, France
Ph.D. in Physical Chemistry in partnership with NVH Medicinal Biotechnology, University of Bourgogne, France

SELECTED PUBLICATIONS


RESEARCH

Development of novel translationally directed therapeutic systems including programmable nanoparticles and ex vivo modified cells (e.g., platelets), utilizing surface modifications and biomimicry to ensure optimal circulation times and multifunctional therapeutic effects on various disease models. Our current research interests are inspired by platelet physiology and their implications in cancer metastasis and vascular diseases.

Office: Science and Engineering Hall, Room 5665
Email: alpapa@gwu.edu
Chung Hyuk Park
ASSISTANT PROFESSOR
DIRECTOR, ASSISTIVE ROBOTICS AND TELE-MEDICINE (ART-MED) LAB

B.S., Electrical Engineering, Seoul National University, 2000
M.S., Electrical Engineering & Computer Science, Seoul National University, 2002
Ph.D., Electrical & Computer Engineering, Georgia Institute of Technology, 2006-2012
Postdoctoral, Electrical & Computer Engineering, Georgia Institute of Technology, 2012-2013

TEACHING
BME 6045: Socially Assistive Robotics and Interactive Learning
BME 3907: Introduction to Assistive Robotics
BME 1010: Introduction to Biomedical Engineering
BME 4920 & 4925: Biomedical Engineering Capstone Project Lab

SELECTED PUBLICATIONS

RESEARCH
In our Assistive Robotics and Tele-Medicine (ART-Med) Lab, we study the collaborative innovation between human intelligence and robotic technology, integrating human-robot interaction, machine learning, and computer vision, haptics, and telepresence robotics. We investigate the impacts of multi-modal feedback on the aspects of human-robot interaction and its application in assistive scenarios, such as telepresence for individuals with visual impairments or emotionally and socially interactive robotic systems for children with autism spectrum disorder (ASD). We also study the computational methodologies of machine learning for robotic learning of human behaviors and intelligence for biomedical scenarios, from simple care-giving tasks to intelligent surgical assistance and training systems.

Office: Science and Engineering Hall, Room 6655
Phone: (202) 994-5147
Email: chpark@gwu.edu
Website: www.chunghyukpark.com

Jason Zara
ASSOCIATE PROFESSOR
ASSOCIATE CHAIR FOR ACADEMIC AFFAIRS
DIRECTOR, OPTICAL AND ACOUSTIC IMAGING LABORATORY

B.S., University of Illinois at Urbana-Champaign, 1996
Ph.D., Duke University, 2001

TEACHING
BME 2810: Biomedical Engineering Seminar
BME 3910: Capstone Design Preparation
BME 4830: Introduction to Medical Imaging Methods
BME 4920: Biomedical Engineering Capstone Laboratory II
BME 4925: Biomedical Engineering Capstone Laboratory III

SELECTED PUBLICATIONS
PLOS ONE, 9(11) e113339, 2014.

RESEARCH
Optical Coherence Tomography, Ultrasound, Medical Image Analysis, Epithelial Cancer Detection, and Treatment Monitoring.

Office: Science and Engineering Hall, Room 5610
Phone: (202) 994-2402
Email: jzara@gwu.edu

From top to bottom: In one OCT imaging application, murine hearts were perfused with Tyrode’s solution and arrested using a bolus of potassium chloride prior to imaging. OCT imaging was performed under two conditions: under control Tyrode’s perfusion (first image) and then after infusion with Tyrode’s and mannitol to induce edema (second image). The degree of the edema was measured by assessing void areas in the images before and after mannitol perfusion.
Vesna Zderic
ASSOCIATE PROFESSOR
DIRECTOR, THERAPEUTIC ULTRASOUND LAB

B.S., University of Belgrade, Serbia, 1998
Ph.D., University of Washington, Seattle, WA, 2004
Postdoctoral fellowship, National Space Biomedical Research Institute, 2006

TEACHING

BME 2815: Biomedical Engineering Seminar II
BME 4820: Anatomy and Physiology for Engineers
BME 4920 and BME 4925: Biomedical Engineering Capstone Project Lab II and III
BME 6486: Clinical Medicine for Engineers

SELECTED PUBLICATIONS


Suarez Castellanos I, Balteanu B, Singh T, Zderic V. Therapeutic Modulation of Calcium Dynamics using Ultrasound and Other Energy-based Techniques. IEEE Reviews in Biomedical Engineering, Apr 2016;99 DOI: 10.1109/ RBME.2016.2555760.


RESEARCH

Our laboratory conducts modeling and experimental work in the area of ultrasound therapy. Current projects include the application of ultrasound to enhance drug delivery through different biological barriers, studies of safety of therapeutic ultrasound application, and ultrasound application for functional modification of cells and tissues.

Office: Science and Engineering Hall, Room 6670
Phone: (202) 994-7593
Email: zderic@gwu.edu
Website: zdericlab.seas.gwu.edu
The Cardiovascular Research Lab.
Dr. Igor Efimov’s primary research in the Cardiovascular Research Lab investigates the arrhythmicogenic and metabolic mechanisms of physiological remodeling during heart failure using human donor hearts, which are rejected for transplantation and human end-stage failing hearts procured at the time of transplantation. Our work has resulted in the development of low energy defibrillation therapy, which is currently being translated by startup company Cardialen, Inc. (cardialen.com). We continue our research in the field of medical devices focusing on novel concept organ mounted conformal electronics, based on flexible and stretchable electronics platform, developed by our collaborator John A. Rogers from UIUC, who recently moved to Northwestern University.

Cardiac Ischemia Research Lab
Research in Professor Matthew Kay’s laboratory is focused on studying cardiac electrical activity and mitochondrial function during normal and disease conditions. Work is primarily focused on understanding how hypoxia, ischemia, and heart failure alter myocardial energy supply and demand and identifying how that may motivate deadly arrhythmias. Professor Kay and his research team have specific expertise in high-speed optical assessments of cardiac physiology, including optical mapping and absorbance spectroscopy, and have developed powerful algorithms to analyze time varying optical signals.

Cardiac Optogenetics and Optical Imaging Lab
Dr. Emilia Entcheva’s lab, the Cardiac Optogenetics and Optical Imaging Lab, uses state-of-the-art engineering approaches and methods to gain insights about the electrical and mechanical function of cardiac cells and heart tissue. New tools for optical actuation and sensing/imaging/control are used to elucidate the mechanisms of normal and abnormal excitation in the heart, including the origin of life-threatening arrhythmias. This work can yield new experimental models for physiomics type of studies, drug and gene therapy testing 3D cellular platforms, an experimental setting for validation of computer models of excitable tissue.

Nanophotonics and Microfluidics Laboratory
Professor Zhenyu Li’s laboratory focuses on the integration of nanophotonics and microfluidics, or optofluidics, for life sciences and medicine. His research also concentrates on the innovation of novel biosensors and medical devices using micro and nanotechnology, namely microfluidics, MEMS, nanophotonics and flexible electronics. Multiple projects analyze single cells for stem cell and cancer research. The lab also develops portable integrated biosensors for point-of-care diagnostics, environmental monitoring, and food safety inspection.

Medical Imaging and Image Analysis Laboratory
Professor Murray Loew’s laboratory for Medical Imaging and Image Analysis develops new methods for acquiring and extracting useful information from medical images. The disciplines involved include pattern recognition, biomedical image and signal processing, and computer vision, with occasional bits of psychophysics and statistics.

Tele-Medicine Lab (ART-Med)
Professor Chung Hyuk Park’s primary research interest centers on the coexistence and collaborative innovation between human intelligence and robotic technology, and spans machine learning, computer vision, haptics, and telepresence robotics. Professor Park and his research team’s current research focuses on the investigation of two main areas: 1) multi-modality in human-robot interaction and assistive robotics, where they study the impact of multi-modal feedback on the aspects of human-robot interaction and its application in assistive scenarios; and 2) robot learning and humanized intelligence, where they focus on computational methodologies of machine learning in the aspect of robotic learning of human behaviors and intelligence.

Assistive Robotics & Therapeutics
Dr. Anne-Laure Papa’s current research interests are inspired by platelet physiology and their implications in cancer metastasis and vascular diseases. Her research consists of development of novel translational therapeutic systems including programmable nanoparticles and ex vivo modified cells (e.g. platelets), utilizing surface modification and biomimicry to ensure optimal circulation times and multifunctional therapeutic effects on various disease models.
### NATIONAL INSTITUTES OF HEALTH

- **Title of Project:** Anrhythmogenic Remodeling in Human Heart Failure  
  PI: Igor Efimov  
  Funding Agency: National Heart, Lung, and Blood Institute
- **Title of Project:** Low Energy Defibrillation  
  PI: Igor Efimov  
  Funding Agency: National Heart, Lung, and Blood Institute
- **Title of Project:** Unpinning Termination Therapy for Ventricular Tacharyrhythmias  
  PI: Igor Efimov  
  Funding Agency: National Institute of Biomedical Imaging and Bioengineering
- **Title of Project:** Exploration of Arrhythogenic Triggers and Substrates in Heart Failure  
  PI: Igor Efimov  
  Funding Agency: National Heart, Lung, and Blood Institute
- **Title of Project:** Cardiac Optogenetics: A Cell Delivery Approach  
  PI: Emilia Entcheva  
  Funding Agency: National Heart, Lung, and Blood Institute
- **Title of Project:** Oxygen-Rich Perfusion that is Compatible with Optical Assessments of Myocardial Physiology  
  PI: Matthew Kay  
  Funding Agency: National Heart, Lung, and Blood Institute
- **Title of Project:** Restoration of Cardiac Parasympathetic Activity in Heart Failure  
  PI: David Mendelowitz  
  Co-Investigator and Key Personnel: Matthew Kay  
  Funding Agency: National Heart, Lung, and Blood Institute
- **Title of Project:** Ambulatory Sensor Arrays for Real-Life Monitoring of Pediatric Patients with Asthma  
  PI: Zhenyu Li  
  Funding Agency: National Institute of Biomedical Imaging and Bioengineering
- **Title of Project:** New Generation of Catheters for Treatment of Atrial Fibrillation  
  PI: Namine Sarvazyan  
  Co-Investigator and Key Personnel: Murray Loew  
  Funding Agency: National Heart, Lung, and Blood Institute
- **Title of Project:** Novel Ultrasound Device for Treatment of Type 2 Diabetes  
  PI: Vesna Zderic, Kevin Cleary

### NATIONAL SCIENCE FOUNDATION

- **Title of Project:** All-Optical Interrogation System for Cardiac Dynamics  
  PI: Emilia Entcheva  
  Funding Agency: National Science Foundation, Biophotonics Division
- **Title of Project:** Light-Enabled Gene Control  
  PI: Emilia Entcheva  
  Funding Agency: National Science Foundation, Biophotonics Division
- **Title of Project:** FDA Scholar-in-Residence - On-Chip Optical Biosensing Methods for Quantitative Measurement of Antibiotic Resistance  
  PI: Zhenyu Li  
  Funding Agency: National Science Foundation
- **Title of Project:** The Role of p38 Isoforms in Cardiac Toxicity of Anti-Cancer Doxorubicin Therapy in Mice  
  PI: Igor Efimov, Tatiana Efimova  
  Funding Agency: GW BME and Cancer Center Fund

### INDUSTRY

- **Title of Project:** Microfluidics for Quantifying Deposition on Contact Lens  
  PI: Zhenyu Li  
  Funding Agency: Johnson & Johnson Vision
- **Title of Project:** Multi-modal Sensor Technology Development for the Evaluation of Virtual-Reality Based Content Training  
  PI: Chung Hyuk Park  
  Funding Agency: Korea Technological National University, MWN Tech

### PRIVATE FUNDING

- **Title of Project:** RHYTHM: Repolarization Heterogeneity Imaging for Personalized Therapy of Heart Arrhythmia  
  PI: Igor Efimov, Michel Haissaguerre  
  Funding Agency: Leducq Foundation
- **Title of Project:** Cultivating an Entrepreneurial Mindset in Capstone Design Preparation  
  PI: Jason Zara  
  Funding Agency: Kern Family Foundation, Kern Entrepreneurial Engineering Network (KEEN)
- **Title of Project:** Construction of Bio-Inspired Bee-Stinger Glass Microelectrodes  
  PI: Matthew Kay  
  Funding Agency: Amgen Corporation

### TOTAL DEPARTMENT ACTIVE RESEARCH GRANTS:

$12.4$ MILLION
Using Light to Control the Heart: Leading Research in Cardiac Optogenetics at BME-GW

Drs. Emilia Entcheva and Matthew Kay

Cardiac optogenetics is an emerging field, where light-sensitive proteins are genetically expressed in cardiac cells and tissues and permit sophisticated optical control of function. Drs. Entcheva and Kay have been at the forefront of this new field.

Dr. Entcheva’s research in this area started in 2011 and has been supported by grants from the National Institutes of Health and the National Science Foundation. Her research group, which joined GW in 2016, leads the efforts in the biophysical characterization of new optogenetic tools for cardiac application and the development of massively-parallel all-optical cardiac electrophysiology. This new approach leverages the scalability of optical methods and combines optogenetic actuation, optical sensing, automation, and feedback control. Dr. Aleks Klimas, a former Ph.D. student and now research fellow in the lab, led the efforts to develop the OptoDyCE system; she won the university innovation competition for this technology. This is the first implementation of high-throughput cardiac electrophysiology, applicable to phenotyping stem-cell derived cardiomyocytes, disease modeling, testing of gene control strategies, and a wide range of drug-testing applications. OptoDyCE was found superior to any existing cardiotoxicity approach in blind testing of 12 compounds of different pro-arrhythmic risk as part of FDA-overseen initiative to update regulations for cardiotoxicity testing. The same concept is applied to genetically modified intact rat hearts to derive conceptually new very-low energy strategies for “wave steering” and arrhythmia control in the heart by the use of patterned light. Dr. Entcheva’s research has been published in Nature Communications, Nature Photonics, and other top-tier journals.

Dr. Kay’s group has pioneered the use of optogenetic control to dissect neural-cardiac interactions. His team has provided the first evidence of the power of optical interrogation of the sympathetic and the parasympathetic system using transgenic mouse models and a

Above: The high-throughput all-optical cardiac electrophysiology system, OptoDyCE, developed by Drs. Klimas and Entcheva, increases the predictive power of stem-cell derived cardiac models for drug testing.
**MEET OUR NEW FACULTY**

**Dr. Anne-Laure Papa**

Anne-Laure Papa will be joining the Department of Biomedical Engineering from the Wyss Institute for Bio-inspired Engineering at Harvard University in the fall, as assistant professor. Her research interests include blood cell-based cellular therapeutics for applications in thrombosis and cancer, as well as novel methods of drug/DNA delivery. She is interested in exploring the intersection of biology, chemistry, engineering, and medicine to develop new methods of targeted therapeutics using blood cells and particles as vehicles, as well as novel diagnostic methods, particularly in cancer and vascular diseases.

In the case of cancer, there is a dramatic increase in mortality when cancer transforms from locally advanced to being metastatic in distant organs. One of Dr. Papa’s current projects deals with the ability to hinder metastatic cancer cells in the circulation from establishing new niches and reducing overall metastatic efficiency. These circulating tumor cells (CTCs) have been seen in multiple cancers and seem to be seen even when there is no clinical evidence of metastatic spread. These CTCs form the scouts who will eventually find their way to other organs through the circulation and disrupting this process before metastases is established is an attractive target for future therapeutics. Preventing or delaying this form of metastatic spread can make meaningful changes to patients’ morbidity and mortality in the long run.

Preventing thrombosis is also a key aspect of Dr. Papa’s work as aberrant platelet activity, conjugated with locally exacerbated coagulation, manifest in a plethora of clinical scenarios from deep vein thrombosis, stroke, pulmonary embolism and cancer-associated thrombosis. Her work to engineer therapeutic platforms could potentially be fine-tuned to adapt to various clinical needs, ranging from acute scenarios to established pathologies.

Dr. Papa received her Ph.D. in the fields of Physical Chemistry and Nanomedicine from the University of Bourgogne, France. Her initial postdoctoral training was at Brigham and Women’s Hospital and Harvard-MIT Program of Health Sciences and Technology in the field of nanoparticle-based cancer drug delivery. She subsequently pursued a postdoctoral fellowship at the Wyss Institute for Biologically Inspired Engineering at Harvard University where she focused on drug delivery and cellular therapeutics. Anne-Laure is a recipient of the Department of Defense Breast Cancer Breakthrough Award to develop ex-vivo modified platelets to delay cancer metastasis.

**Above:** Selective expression of optogenetic channels and chemigenetic receptors are used by Dr. Kay’s trainees to investigate novel aspects of cardiac physiology and disease.
Can you please tell us a little about yourself?

KG: I am originally from Florida and completed my B.S. degree in BME from the University of South Carolina (Go Gamecocks!). After spending a summer in Tanzania repairing medical equipment after graduation, I moved my way up the East Coast to DC to start my Ph.D. at GW. I’ve loved my time here, and in my free time I enjoyed running, biking, reading, and taking advantage of everything going on in DC!

After graduation, did you continue your career in the Biomedical Engineering field?

KG: Immediately following graduation I spent a few months backpacking around the Western states followed by a trip to the UK. I plan on continuing work in the Biomedical Engineering field, specifically in the realm of cardiac device development. I will be working as a R&D Scientist at Boston Scientific! My research on cardiac electrophysiology in Dr. Matthew Kay’s lab has prepared me with a dynamic and adaptable skill set to succeed in the field of cardiac devices.

What degrees did you obtain at GW?

KG: I obtained my Ph.D. in Biomedical Engineering at GW.

What influence has your education at GW had on your career?

KG: My education at GW gave me the tools and skill set to excel at a career in cardiac device development or device regulation. I believe the most valuable skill I learned through my research at GW was troubleshooting, which will serve me well in any future role.

What might you tell someone who’s interested in becoming a Biomedical Engineer?

KG: Biomedical Engineering is a broad field, but that allows for exploration into many different subject areas. I would advise a student interested in Biomedical Engineering to explore all the different facets of the field and eventually expand on the one or two areas he or she is most interested in. The beauty of BME is having the broad knowledge of the entire field while delving deeper into a specific subject area.

What are some of your favorite memories during your time at GW?

KG: One of my favorite memories was presenting my dissertation defense. It was so rewarding to share my work of the past four years with both colleagues from GW and my family and friends.

What advice would you give to current BME students on how they can optimize their time, learn, and gain experience here at GW?

KG: My advice would be to absorb all the information you can and use that to figure out what you are truly passionate about. GW BME is full of incredible faculty with many different backgrounds—so take advantage of their expertise!
Kara Garrott
DEPARTMENT OF BIOMEDICAL ENGINEERING

Title: Adapting Novel Techniques to Elevate Physiological Relevance to Study Heart Failure and Oxygenation in the Isolated Heart

Advisor: Professor Matthew Kay

Cardiovascular disease is the leading cause of death in the United States with severe repercussions on society and individual lives. Despite recent research advancements, additional work is needed to more effectively diagnose and treat the wide range of cardiac afflictions. The isolated heart, developed by Oskar Langendorff in 1895, is a valuable tool to study cardiac function and disease. This preparation allows researchers to investigate whole organ function without confounding variables associated with in vivo methods, such as hormonal changes and spectral interference of blood.

The isolated heart led to a greater understanding of cardiac electrophysiology and metabolism, which spurred the development of methods to diagnose and treat cardiovascular disease. Moving forward, ex vivo heart experiments must move closer to in vivo physiology in order to effectively recapitulate human conditions and reach translational potential.

The purpose of the studies presented in this dissertation is to implement and validate new techniques to study cardiac function and disease with more physiologically relevant conditions in the isolated heart model. The widespread effects of heart failure motivate the development of potential treatments. The research of this dissertation aims to reinstate the parasympathetic withdrawal that is characteristic of heart failure (HF) in a rat model by activation of parasympathetic oxytocin neurons. Application of Designer Receptors Exclusively Activated by Designer Drugs (DREADDS) to increase cardiac parasympathetic tone in a rat model of HF reveals significant improvements in cardiac function and reductions in cardiac injury. Additionally, this dissertation more closely replicates in vivo physiology in fully contracting, working rabbit hearts to study electromechanical function and oxygen requirements. An innovative optical mapping technique to remove motion artifact in contracting hearts allows for sensitive measurements of electrical, mechanical, and metabolic function. Studying these parameters in tandem, rather than in isolation, allows for a more comprehensive understanding of cardiac function under conditions of hypoxia and increased work. These experiments also elucidate that KATP channels, ion channels that link the heart’s metabolic state to electrical function, are more readily activated in isolated heart preparations with greater work demands. The results of these studies and the previously established oxygen limitation due to crystalloid perfusate used in isolated heart experiments motivate the adaptation of a perfusate with 35% greater oxygen carrying capacity. Perfluorocarbon (PFC) solution binds oxygen with a greater affinity than crystalloid perfusate to bring studies of cardiac electrophysiology closer to physiological oxygenation conditions. The use of PFC solution in contracting heart optical mapping studies builds upon the developments previously established by this dissertation and moves closer towards in vivo physiology. PFC perfusate eliminated the oxygen limitation inherent to isolated heart preparations and provided enhanced protection against arrhythmogenesis. The clinical need for improved diagnosis and treatment of cardiovascular disease necessitates experimental research that mimics physiology with greater fidelity. This dissertation moves isolated heart experiments closer to in vivo physiology by using a new approach to reinstate parasympathetic tone in HF, revealing the role of KATP channels in contracting, working hearts, and vastly improving oxygenation in perfused heart studies.
Aleksandra Klimas  
DEPARTMENT OF BIOMEDICAL ENGINEERING  
Title: All-Optical Cardiac Electrophysiology: Design, Validation and Applications in Vitro and in Vivo  
Advisor: Professor Emilia Entcheva

Biological systems are inherently dynamic, requiring active interrogation and recording to provide a full understanding of their underlying mechanics. In order to fully characterize such a system, both readily quantifiable signals as well as a means of dynamic control are necessary. In the heart, the propagation of electrical waves driving contraction is mediated by the flow of ions through various ion channels working in concert to drive de- and re-polarization of the cell membrane. Typically, the culprit of electrical dysfunction in the heart is due to some disruption of normal function of one or more of these ion channels. In order to study these complex electrical disturbances, known as arrhythmias, high spatiotemporal resolution imaging and interrogation are necessary.

Traditional methods of interrogation have relied on the use of electrodes and patch clamp methods, which are inherently low throughput and have limited spatial resolution. Additionally, these approaches do not lend well for in vivo use. While studies of cardiac tissue have also employed optical mapping techniques where voltage- or calcium-sensitive fluorescent reporters provide detailed information about cell activation, repolarization, and wave propagation maps, stimulation has remained primarily limited to electrical means. However, recently developed optogenetic tools provide a means of high-spatiotemporal resolution (and potentially tissue-type specific) means of interrogation. By combining both of these methods, high-spatiotemporal dynamic characterization of cardiac electrophysiology can be achieved.

Here we present how all-optical approaches can be achieved via employing optogenetics in order to explore cardiac electrophysiology at the in vitro as well as in vivo scale. The main optical design is first implemented for in vitro use, where we demonstrate how OptoDyCE, our all-optical dynamic cardiac electrophysiology platform, can be used to screen drug effects in both isolated primary myocytes and human induced pluripotent stem-cell derived cardiomyocytes (hiPSC-CMs) grown in monolayers and 3D tissue constructs. We then characterize an upgraded version of OptoDyCE, capable of simultaneous imaging of membrane voltage and intracellular calcium signals. The system is used for screening of 12 blinded compounds to demonstrate how the platform can be used for pro-arrhythmia prediction at the high-throughput (HT) scale. All compounds were properly identified as ‘safe’ or ‘unsafe’ using the multi-parameter endpoints, made possible with high-spatiotemporal resolution recordings under spontaneous and paced conditions. To further demonstrate how all-optical approaches improve proarrhythmia prediction, we tested vanoxerine, a compound that failed Phase III clinical trials, and demonstrate OptoDyCE’s ability to easily identify the compound as pro-arrhythmic, unlike techniques employing patch clamp and in silico modeling that deemed the compound safe for use in humans. As hiPSC-CMs provide a novel testbed for drug testing and disease modeling, we then use OptoDyCE to characterize these cells, both in terms of their potential immaturity (a common criticism) and their ability to recapitulate genetic diseases for use in disease modeling. Finally, the requirements for translating OptoDyCE for in vivo use are considered and successful demonstration in vivo expression of ChR2 in the rat heart by employing systemic viral delivery, providing a model for development and testing of an optical system in intact tissue and for long-term use in behaving animals. Ultimately, we demonstrate the OptoDyCE platform has capacity to revolutionize pre-clinical drug testing, reduce cost, reduce animal use, and make clinically implemented personalized medicine an obtainable goal.
Angel Moreno Entrenas
DEPARTMENT OF BIOMEDICAL ENGINEERING
Title: Engineering Cellular Level Tools to Measure and Control Cardiac Physiology During Normal and Pathologic Conditions
Advisor: Professor Matthew Kay

Despite decades of extensive research, heart-related diseases remain a major global burden, taking countless lives every year and decreasing the quality of life of many more. Animal models have been essential in cardiovascular research but significant differences among species and inherent limitations related to study preparations have hampered the effective translation from basic science to clinical practice needed for the development of improved therapies that restore proper cardiac function. This dissertation seeks to develop and improve current techniques to adequately measure key components of cardiac physiology and pathophysiology that will ultimately lead the way to reduce the gap between animal models and humans. We present, a new kind of detachable microelectrodes for action potential recordings from cells within fully contracting hearts without the need of any constraints, an improved non-destructive and reproducible optical technique to measure the metabolic activity within the myocardium of perfused hearts and an optogenetic approach for selectively activating and modulating intrinsic parasympathetic and sympathetic pathways recapitulating true autonomic tone response.

Ivan Suarez Castellanos
DEPARTMENT OF BIOMEDICAL ENGINEERING
Title: Ultrasound Stimulation of Insulin Release from Pancreatic Beta Cells
Advisor: Professor Vesna Zderic

Type 2 Diabetes (T2D) mellitus is a complex metabolic disease that has reached epidemic proportions in the United States and around the world. Controlling T2D is often difficult as pharmacological management routinely requires complex therapy with multiple medications, and loses its effectiveness over time. The objective of this dissertation was to explore a novel, non-pharmacological approach that utilizes the application of ultrasound energy to stimulate insulin release. Our experiments have focused on determination of effectiveness and safety of ultrasound application in stimulation of insulin release from the pancreatic beta cells. Our results showed that ultrasound treatment, applied at frequencies of 800 kHz and 1 MHz and intensities of 0.5 W/cm² and 1 W/cm², did not produce any significant effects on cell viability compared to sham group as assessed with trypan blue dye exclusion test and MTT cytotoxicity assay. ELISA quantification of insulin release from beta cells resulting from ultrasound treatment showed clinically-significant amounts of released insulin as compared to sham-treated beta cells. Carbon fiber amperometry detection of secretory events from dopamine-loaded beta cells treated with ultrasound showed that release of secretory content could be temporally controlled by careful selection of ultrasound parameters. Both ELISA and amperometry experiments demonstrated that ultrasound-stimulated insulin release is a calcium-dependent process, potentially mediated by the mechanical effects of ultrasound. This study demonstrated that therapeutic ultrasound is a technique capable of stimulating the release of insulin from pancreatic beta cells in a safe, effective and controlled manner.