

## Institute for Medical Engineering and Science

Founded in 2012, the [Institute for Medical Engineering and Science](#) (IMES) pioneers novel research and graduate education paradigms by bringing together engineering, science, and clinical medicine to advance human health. IMES is an integrative force, catalyzing academic and strategic partnerships within MIT and with hospitals and industry to confront major challenges, particularly in the areas of infectious and autoimmune disease, neurological disorders, cardiovascular disease, and diagnostics.

IMES is home to the Harvard-MIT Division of Health Sciences and Technology (HST). HST also maintains an office at the Harvard Medical School (HMS) quadrangle campus in Boston as one of the five medical societies at HMS. HST director Emery Brown reports to the IMES director, and the director at Harvard Medical School reports to the HMS dean of medicine and dean for graduate education.

This year IMES also became the home of the Medical Electronic Device Realization Center, directed by professor Charles Sodini, and the MIT Clinical Research Center, led by professor Elazer Edelman.

### New Faculty

This year we welcomed Thomas Heldt to the IMES core faculty as a new assistant professor; he holds the Hermann von Helmholtz Career Development Professorship. He was also appointed as an assistant professor of electrical and biomedical engineering in the Department of Electrical Engineering and Computer Science (EECS). Thomas studied physics at Johannes Gutenberg University (Germany), Yale University, and MIT. In 2004, he received a PhD in medical physics from HST and commenced postdoctoral training at MIT's Laboratory for Electromagnetic and Electronics Systems. Prior to joining the faculty, Heldt was a principal research scientist with the Research Laboratory of Electronics (RLE), where he cofounded and codirected (with professor George Verghese) the Computational Physiology and Clinical Inference Group. Heldt's research interests focus on signal processing, mathematical modeling, and model identification to support real-time clinical decision making, monitoring of disease progression, and titration of therapy, primarily in neurocritical and neonatal critical care. In particular, Thomas is interested in developing a mechanistic understanding of physiological systems and in formulating appropriately chosen computational physiological models for improved patient care. His research is conducted in close collaboration with colleagues at MIT and clinicians from Boston-area hospitals.

We anticipate the arrival of Kwanghun Chung as an assistant professor in the fall as he completes his relocation from Stanford. Kwanghun completed his undergraduate studies at Seoul National University in 2005, majoring in chemical and biological engineering. He then completed his thesis work in 2009 at the Georgia Institute of Technology. After completing collaborations stemming from his PhD work, he joined the Karl Deisseroth lab at Stanford University for postdoctoral training in 2010. In his time there, he invented a novel technology, CLARITY, that enables systemwide structural and molecular analysis of large-scale intact biological samples, including rodent brains

and human clinical samples. Kwanghun will hold the Hermann von Helmholtz Career Development Professorship as an assistant professor in IMES and the Department of Chemical Engineering.

## Academic Program

### Graduate Degree Programs

HST is among the largest biomedical engineering and physician scientist training programs in the United States, with 325 students enrolled in its graduate degree programs during AY2013:

- 187 MD and MD/PhD students
- 119 Medical Engineering and Medical Physics Program (MEMP) PhD students, including 11 MEMP/MD students
- 29 Speech and Hearing Bioscience and Technology (SHBT) program PhD students
- 1 Biomedical Enterprise Program SM student

HST graduate students work with faculty and affiliated faculty members from MIT, Harvard, and affiliated teaching hospitals. Whether pursuing careers in medicine, research, industry, or government, HST graduates have made outstanding contributions to advances in human health care.

The MEMP PhD program trains students as engineers or physical scientists who also possess extensive knowledge of medical sciences. The program provides preclinical and clinical training to students. On average, students complete the PhD program in six years, and in some cases they also pursue an MD.

The HST MD program is aimed at students interested in a research-based medical career. While eligible to complete the program in four years, many students take an optional fifth year to engage in more extensive research. Approximately 80% of HST MD alumni follow a career path in academia.

### Summer Institute

Patterned after MIT's Summer Research Program, HST offers two specialized Summer Institute programs, one in biomedical optics (offered in collaboration with the Wellman Center for Photomedicine at Massachusetts General Hospital) and the other in bioinformatics (offered in collaboration with the i2b2 National Center for Biomedical Computing at Brigham and Women's Hospital). Thirty-eight students participated in these two programs in summer 2012, and 33 are enrolled for summer 2013.

These programs offer a unique opportunity for outstanding undergraduate college students considering a career in biomedical engineering and/or medical science. Through hands-on research and in-depth lectures, participants learn about either biomedical optics or bioinformatics and engage in the application of these fields to solve problems in human health. Through individual tutorials and workshops, students learn to communicate their research findings effectively in written and oral formats. Shared living arrangements and a variety of technical and social activities enable Summer Institute participants to develop a network of peers and build strong, enduring connections with faculty working in the field.

### **Faculty Honors and Promotions**

Dr. Emery Brown was appointed associate director of the Institute for Medical Engineering and Science and codirector of the HST program. In addition, he was awarded the NIH (National Institutes of Health) Director's Transformative Research Award.

Dr. Elazer Edelman was appointed faculty director of the Clinical Research Center.

Dr. Matthew Frosch was appointed associate director of HST at the Harvard Medical School.

Dr. Jeffrey M. Karp was inducted into the American Institute for Medical and Biological Engineering College of Fellows.

Dr. Robert Langer was awarded the National Medal of Technology and Innovation, making him one of only three Americans to have won both that medal and the National Medal of Science.

Dr. Peter Szolovits was the recipient of the 2013 Morris F. Collen Award of Excellence from the American College of Medical Informatics.

Dr. Larry Young received the National Space Biomedical Research Institute 2013 Pioneer Award.

### **Faculty Mentoring and Teaching Awards**

Dr. Chinfei Chen was honored with HST's Seidman Prize for MD Research Mentorship.

Dr. Wolfram Goessling and Dr. Daniel Solomon were honored with HST's Irving M. London Teaching Award.

Dr. Richard Mitchell received the Robbins Distinguished Educator Award from the American Society for Investigative Pathology.

Dr. Shiv Pillai was honored with HST's Thomas A. McMahon Mentoring Award.

## Student Honors and Awards

MD/PhD candidates Omar Abudayyeh and Dayan (Jack) Li were awarded Paul and Daisy Soros Fellowships for New Americans.

MEMP program PhD candidates Pamela Basto and Ashley Wessendorf and SHBT program PhD candidate Annalisa Pawlosky were recipients of MIT Graduate Women of Excellence Awards from the Office of the Dean for Graduate Education.

Kevin Chen, PhD candidate in the MEMP program, received a National Defense Science and Engineering Graduate Fellowship.

Isha Jain, a PhD candidate in the MEMP program, received a Department of Energy Computational Science Graduate Fellowship. She was also offered and declined a National Defense Science and Engineering Graduate Fellowship.

Gabrielle Merchant, PhD candidate in the SHBT program, received the Helen Carr Peake Research Award from RLE.

Nuria Oliva-Jorge, PhD candidate in the MEMP program, received the William Asbjornsen Albert Memorial Fellowship from the Office of the Dean for Graduate Education.

Bryan Ranger, PhD candidate in the MEMP program, received a National Science Foundation Graduate Research Program Fellowship.

Andrew Schwartz, PhD candidate in the SHBT program, was a member of the Sana AudioPulse team that won the Groupe Speciale Mobile Association Mobile Health Challenge competition.

Luke Shaheen, PhD candidate in the SHBT program, was awarded the 2013–2014 Amelia Peabody Scholarship from the Massachusetts Eye and Ear Infirmary.

Jordan Spatz, PhD candidate in the MEMP program, received a Hugh Hampton Young Memorial Fund Fellowship from the Office of the Dean for Graduate Education.

## Research Program

### Core Faculty

Professor Elfar Adalsteinsson's research group conducts medical imaging work with magnetic resonance imaging (MRI), primarily at the Martinos Center for Biomedical Imaging. Their current research activities aggregate around estimation of brain oxygenation parameters via MRI, development of parallel transmission technology and applications in MRI, and image reconstruction methods for accelerated acquisitions and compressed sensing. The group recently launched efforts in fetal imaging with Boston Children's Hospital. A presentation by group member Audrey Fan described what she has termed quantitative oxygenation venography. She is able to visualize venous-side

vasculature with quantitative estimates of oxygen saturation. Professor Adalsteinsson is excited to further develop and validate this methodology since the potential applications range from evaluation of stroke and tumors to fetal and neonatal brain development. Professor Adalsteinsson's lab is also tightly involved with the [Madrid-MIT M+Visión Consortium](#), within which several diverse and interdisciplinary imaging research projects are under way.

Professor Daniel G. Anderson is continuing his research on new biomaterials for cellular therapy and drug delivery. In particular, his research has led to significant advances in the development of nanotherapeutics and RNA-based therapy. He has been actively involved in the MIT/Skolkovo Institute of Science and Technology project, and he will be the director of the new Skoltech Center for RNA Therapeutics and Biology. This center will feature research on drug delivery, chemistry, biology, and medicine by experts in the United States and Russia, including the efforts of three Nobel Laureates. This multidisciplinary effort seeks to advance science, generate new therapeutics, and build collaborations between Russian and American scientists.

Professor Anderson's work has led to a number of high-impact publications in journals such as *Nature Biotechnology*, *Nature Nanotechnology*, and *Science*. In addition to IMES, he is a member of the Department of Chemical Engineering, HST, and the David H. Koch Institute for Integrative Cancer Research and an associate member of the Broad Institute.

Professor Sangeeta Bhatia's laboratory made substantial progress this year toward engineering replacement livers. Two of the key challenges in this field are the sourcing of human hepatocytes (the functional cells of the liver) and connection of the transplanted tissue to the blood supply. This year, they identified small molecules via high throughput that could take advantage of the human hepatocyte's unusual ability to undergo mitosis in liver regeneration. Though recognized as a property of the human liver for centuries, this has never been achieved previously through conventional biological approaches. The alternative to using adult hepatocytes is to use stem cells; however, personalized stem cells (so-called induced pluripotent stem cells) do not mature beyond the fetal stage. As a result of the high-throughput screen, chemicals that mature iPS cells into hepatocytes were also identified. In addition to their potential for providing cells for tissue engineering, these molecules are being developed as possible medicines for liver failure using zebrafish models of liver injury. Also described was a method for accelerating the vascularization of the transplanted tissue by constructing tissues with prefabricated endothelial vessels that "hook up" to the host, allowing an understanding of the 3D architecture of the transplanted tissue and resulting in improved transplant performance. These techniques are being scaled up to build implantable organs with multiscale precision architecture using 3D organ printing.

Beyond efforts to engineer replacement livers, Bhatia's group also has miniaturized human livers to build models of disease. This year her group demonstrated the ability to model the liver stages of the two most virulent human malarias: *Plasmodium falciparum* and *Plasmodium vivax*. These miniature models were used for vaccine and drug testing and allowed the growth of a hibernating form of malaria that had never been seen

before in culture, and that serve as a key barrier to malaria eradication. These models contribute to a growing program in which she is modeling liver pathogens such as hepatitis B and C and dengue virus. The models are now being used for antimalarial drug screening in collaboration with the Gates Foundation.

Dr. Bhatia was profiled in the *Scientist* and the Howard Hughes Medical Institute *Bulletin* and *Forbes India* as one of 18 “Indian Scientists Changing the World.” She gave more than 40 invited talks, including a lecture at the National Biomedical Engineering Society meeting and a keynote lecture at the Gates Grand Challenges Meeting.

Dr. Bhatia has been asked to serve on Harold Varmus’ Board of Scientific Advisors to the National Cancer Institute, Francis Collins’ National Institute of Health Working Group on Diversity, and Eric Lander’s Broad Institute Strategic Advisory Committee.

Dr. Bhatia is currently overseeing the training of 40 postgraduates, graduates, and undergraduates, most of whom have been presented one or more training awards, including a Hertz Graduate Fellowship in 2012. She has authored over 150 publications that have been cited more than 11,000 times.

Professor Emery Brown’s laboratory made substantial progress in defining the neuroscience of general anesthesia. The group established in humans how anesthetic induction of electroencephalogram oscillations in the 8 to 10 Hz (alpha oscillations) and less than 1 Hz (slow-wave oscillations) ranges can lead to unconsciousness. They also reported new insights into burst suppression, a brain state of profound inactivation. They found that, contrary to current beliefs, burst suppression is not necessarily a global brain state. Parts of the brain can be in burst suppression while others are not. The group established in simulation and animal studies that closed-loop control of burst suppression is a highly feasible way to automate maintenance of medical coma as a therapy for patients with head injuries or intractable epilepsy. They demonstrated that administration of a D1 dopamine agonist can be used to induce rapid emergence of rodents from general anesthesia.

Professor Brown received a 2012 NIH Director’s Transformative Research Award for his project “Redesigning General Anesthesia.” In addition, he has been asked to serve on the working group for the NIH BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative announced by President Obama in April 2013.

Professor Arup K. Chakraborty continued his research at the convergence of physical science, engineering, and medicine. Perhaps the most important finding emerging from his laboratory this year was the development of a general method that allows the translation of virus sequences into a quantitative fitness landscape. The availability of viral fitness landscapes makes possible the rational design of immunogens for vaccines against scourges such as HIV. The laboratory has designed such an immunogen based on the Gag polyprotein of HIV, which is being moved to animal trials in laboratories at MIT and Massachusetts General Hospital. In addition to directing the successful launch of IMES, Chakraborty led an effort that raised philanthropic support for a \$10 million renovation of space that will help attract outstanding new faculty to MIT who

work at the intersection of engineering, science, and medicine. Chakraborty continues to serve the National Academy of Engineering, the American Academy of Arts and Sciences, and the Dreyfus Foundation in numerous ways. The US secretary of defense recently appointed him a member of the Defense Science Board, an influential group in determining the country's defense research priorities.

Sudden cardiac death accounts for approximately 300,000 deaths per year in the United States. In appropriate patients, implantable defibrillators can reduce the risk of sudden cardiac death but are associated with their own significant risks. Professor Richard Cohen's laboratory has developed a noninvasive technology—microvolt T-wave alternans (MTWA) testing—that analyzes microvolt-level fluctuations in the surface electrocardiogram in order to identify patients at high and low risk of sudden cardiac death. Professor Giulio Molon of the Cardiology Department, Sacro Cuore Hospital in Negrar, Verona, Italy has used MTWA testing in his clinical practice for many years to make decisions regarding defibrillator implantation. Professors Cohen and Molon published this past year in the *International Journal of Cardiology* the long-term follow-up results in 178 consecutive patients all of whom met standard clinical criteria for defibrillator implantation. Over 64 months of follow-up, patients who tested MTWA negative and did not receive a defibrillator had substantially better survival rates than MTWA-abnormal patients who did receive a defibrillator. This analysis indicates that many patients who test MTWA negative can safely avoid defibrillator therapy even if they meet other criteria for defibrillator implantation.

During AY2013, professor Elazer Edelman's lab published 24 peer-reviewed papers, received a competing renewal of its NIH R01 grant, and was awarded three new large grants. Professor Edelman was named to the Association of University Cardiologists, served as chair of the Food and Drug Administration (FDA) Science Board, testified before the US Congress on the state of innovation in the United States, and presented a number of plenary and honorary lectures, including keynote addresses at the Society for Biomaterials meeting, the 11th International Congress on Medical Librarianship, the 7th International Conference of Animal Health Information Specialists, and the 6th International Clinical Librarian Conference.

Professor Lee Gehrke's lab continued progress on two NIH-funded projects aimed at learning how cells sense invading viruses and mount an immune response and designing and building a point-of-care diagnostic device to detect hemorrhagic fever viruses. The group is also working with the FDA to design a device that will detect food pathogens in the field. Professor Gehrke taught HST-010 Functional Human Anatomy, required for HST MD candidates and an elective for other graduate students. He also serves as a member of the HST advisory, MD advisory, and graduate committees.

The primary focus of professor Martha Gray's research during the last two years has been on developing, implementing, and documenting training approaches that promote and accelerate translational biomedical research with the potential for high impact. Professor Gray conducts this work through the M+Visión fellowship program. Program fellows function more or less as principal investigators and work on teams that include other fellows as well as collaborators they recruit from Madrid and Boston.

A portfolio of projects emerged that are ambitious and creative, address a major unmet medical need, and have a high potential for impact. Outcomes so far include patents, publications, and a strong intellectual basis for continuity. Despite the newness of the projects, the accomplishments are impressive and have motivated the faculty, together with experts in innovation and educational assessment, to document the approach.

Professor Roger G. Mark's lab is working on critical care informatics, and they are making progress toward their goal of expanding their critical care database to other hospitals in the United States, Europe, and, possibly, Singapore. The group had a very fruitful workshop in Paris involving 25 enthusiastic participants, including major leaders from Europe in the area of critical care medicine. They continue to engage in a number of collaborative research projects involving clinicians and engineers who are deriving new knowledge from their massive data archives.

Professor Leonid Mirny's lab made significant progress in two directions: characterizing the folding of the human genome in 3D, and understanding cancer progression through accumulation of driver and passenger mutations. A computational pipeline for analysis of experimental data has revealed new principles of 3D genome organization. The group also demonstrated that cancer accumulates passenger mutations that are damaging to cells but that there is the potential for new therapeutic strategies. The group has also been actively involved in high-school outreach via MIT PRIMES program.

### **Associate Faculty**

In 2012 and 2013, professor Robert Langer received honorary degrees from Boston University, Tel Aviv University, and Ben Gurion University. He was elected as a fellow of the American Institute of Chemical Engineers and as a charter fellow of the National Academy of Inventors. Langer received the Wolf Prize in Chemistry, the US National Medal of Technology and Innovation, the American College of Clinical Pharmacology's Distinguished Investigator Award and Honorary Fellow Award, and the Industrial Research Institute Medal, among other awards. Along with a number of other lectures, he presented the DuPont Inaugural Thomas H. Chilton Lecture, the Warren L. McCabe Lecture (North Carolina State University), the Reed Izatt and James Christensen Lecture (Brigham and Young University), and the Eliahu Caspi Memorial Lecture (University of Massachusetts Medical School).

Institute Professor Phillip A. Sharp (Koch Institute and Department of Biology) was involved in many activities relating to the MIT community during the past year. Professor Sharp's lab recently published some very exciting results on how cells make sense of transcriptional direction. They hope further investigation will reveal how cells carry out normal functions and change with respect to malignancy. In addition to teaching 7.60 Cell Biology, he serves as an advisor and as a member of the Department of Biology's graduate committee. He also serves on two MIT commissions, the Production in the Innovation Economy initiative and the Committee for Innovation and Entrepreneurship.

Professor Charles Sodini's research group had several significant research results during the past year including the demonstration of a wearable wireless device that attaches to the ear to monitor vital signs. The device has the form of a hearing aid and is wirelessly connected to a PC for data recording and analysis. It monitors electrocardiograms in a single lead configuration, ballistocardiograms with a triaxial accelerometer, and photoplethysmograms with LED sources and a static photocurrent subtraction analog front end. The group also developed a four-channel analog front-end transceiver chip for medical ultrasound imaging. This high-voltage transmitter uses a three-level pulse-shaping technique to deliver over 50% more acoustic power than traditional methods for the same power dissipation. The design requires minimum off-chip components and is scalable for more channels.

During Professor Sodini's stay at the Hong Kong University of Science and Technology (HKUST) in January 2012, as well as trips in March and June, he developed the HKUST-MIT Research Alliance Consortium, which will fund research in the areas of Internet infrastructure, cloud computing, smart green buildings, and biomedical systems.

Professor Peter Szolovits (EECS/Computer Science and Artificial Intelligence Laboratory) received the 2013 Morris F. Collen Award of Excellence from the American College of Medical Informatics. This award is presented to "an individual whose personal commitment and dedication to biomedical informatics has made a lasting impression on healthcare and biomedicine."

## Events

### HST Faculty Poster Session

Approximately 50 faculty members and 100 students attended the eighth annual HST Faculty Poster Session, held on October 16 at the Tosteson Medical Education Center at Harvard Medical School. Forty-six faculty posters were on exhibit, representing all HST programs. Some posters represented broad research programs, while others presented specific research projects; some included student coauthors. This annual event familiarizes faculty members with their colleagues' research and allows them to recruit students to their laboratories. It also assists students beginning the process of selecting laboratories and mentors for their research.

### HST Forum

The 26th HST Forum was held on April 11 at the Tosteson Medical Education Center at Harvard Medical School. At this annual event showcasing student research, the exciting depth and breadth of HST science and accomplishment are highlighted for MD and PhD candidates, current students, faculty, staff, and other members of the HST, HMS, and MIT communities.

This year approximately 125 people attended the forum, including 38 students who presented posters on their current research. The poster session was followed by a keynote address given jointly by HMS professor of systems biology Vamsi Mootha (HST MD '98) and his advisee, HST MD student Molly Plovanich, who treated the audience to a unique view of a dynamic mentor/mentee relationship. The joint address was well received by current and prospective members of the HST community.

In the context of an impressive array of articulately presented student research, the following students received the Martha Gray Prize for Excellence in Research in the categories named:

- Milena Andzelm (MD/PhD program), Cell and Molecular Biology
- Pam Basto (MEMP), Regenerative and Rehabilitative Biomedical Engineering
- Ronn Friedlander (MEMP), Biomedical Devices
- Mark Lee (MD/PhD program), Bioinformatics and Integrative Genomics
- Xenos Mason (MD program), Physiology and Systems Biology
- Daniel Oh (MD program), Imaging, Acoustics and Optics

### **IMES Distinguished Lecture Series**

This year IMES held three well-received invited lectures that included the following speakers and subjects:

- J. J. Collins, "Network Biology Approaches to Microbial Threats" (February 7)
- Steve Quake, "Is the Genome Useful in Medicine?" (April 10)
- Konstantina Stankovic, "Auditory Neuroscience: Nexus of Surgery and Biotechnology" (May 9)

### **Priorities**

IMES has three important immediate goals: to serve as an integrative force across MIT and create an intellectual hub of research and education at the convergence of engineering, science, and translational and clinical medicine; to create strategic partnerships with collaborating hospitals and industry that can transform health care and medicine; and to provide a robust home for the HST program. Achievement of these goals is expected to benefit all units at MIT and collaborating institutions in the Boston area. In support of these ambitions, IMES draws on HST's 40-plus years of providing world-class training to leaders in medicine and health care. HST's MD and PhD educational programs and its partnership with the Harvard Medical School represent a significant historical, structural, and administrative underpinning that is important for IMES' potential and growth.

IMES anticipates significant growth in educational and research programs as partnerships with hospitals are put in place and new faculty members are recruited in partnership with MIT departments. In the past year, IMES has made significant progress toward these goals. It is expected that, with full support from the senior administrations of MIT and Massachusetts General Hospital, a strategic partnership between the two institutions will be established. This partnership is anticipated to focus on confronting major challenges to human health: making diagnosis accurate and efficient, guiding clinical decisions based on historic and real-time data, and studying neurological and infectious diseases.

In partnership with HMS, IMES has strengthened the HST educational program, thereby enhancing the ability to educate physician-scientists and physician-engineers who can integrate approaches from the physical sciences and engineering with the practice and science of medicine. IMES aims to build on these early successes to enhance MIT's ability to advance health and educate engineers and scientists who will be at the leading edge of the convergence of medicine, engineering, and science.

**Arup K. Chakraborty**

**Director**

**Robert T. Haslam Professor of Chemical Engineering, Chemistry, Physics,  
and Biological Engineering**