Institute for Medical Engineering and Science

Founded in 2012, the Institute for Medical Engineering and Science (IMES) pioneers novel research and education paradigms by bringing together engineering, science, and 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 diseases, neurological disorders, cardiovascular disease, and diagnostics.

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

IMES is also the home to the Medical Electronic Device Realization Center (MEDRC), directed by Professor Charles Sodini; the Clinical Research Center, led by Professor Elazer Edelman; and the Center for Microbiome Informatics and Therapeutics. IMES also led the creation of the strategic partnership between MIT and the Massachusetts General Hospital (MGH), and a separate partnership with Brigham and Women's Hospital (BWH). The latter effort led to MIT and BWH winning the $75 million "One Brave Idea" competition, which aims to transform the diagnosis and care of cardiovascular diseases.

New Faculty Arrivals

In the past year, IMES recruited two new core faculty members and one associate faculty member to expand upon the research areas that are integral to advancing human health. Additionally, IMES appointed two professors of the practice to bring in further clinical and industrial expertise.

Core Members

David Sontag: Associate Professor David Sontag's research aims to advance the fields of machine learning and artificial intelligence, and to apply these to transform healthcare. His lab develops algorithms that use data to better understand diseases such as Type 2 diabetes and multiple myeloma. He also plans to develop the foundation for next-generation intelligent electronic health records. His appointment as Hermann L. F. von Helmholtz Career Development Professor was made in partnership with the Department of Electrical Engineering and Computer Science.

Tami Lieberman: Assistant Professor Tami Lieberman's research group focuses on uncovering the principles governing colonization, niche range, and personalization in the human microbiome. Her group conducts studies that help predict which therapeutic strains and co-administered treatments (prebiotics) provide the most potential for colonization and to identify which microbial-based therapies have the potential to treat a

wide range of diseases. Her appointment as assistant professor was made in partnership with the Department of Civil and Environmental Engineering.

Charles Sodini: Professor Sodini moved from associate status to become a core member of the IMES faculty this year. His research fields of interest are electronics and integrated circuit design and technology. His group explores novel integrated technology, device physics, and circuit design—and its application to specific microsystems, including medical electronic systems for monitoring and imaging.

Associate Member

Brett Bouma: Professor Bouma's research focuses on novel technologies for disease diagnosis and treatment, many of which have been translated into clinical applications, including for esophageal cancer and coronary artery pathology. He is internationally recognized for his contribution to the development of optical coherence tomography, a medical imaging technique. Bouma teaches in the Harvard-MIT Health Sciences and Technology Program.

Professor of the Practice Members

Joseph Frassica: The chief technology officer and vice president of Philips Healthcare, Joseph Frassica focuses on leading a broad-based, medical, science, and technology team to bring clinically meaningful innovation to the bedside. Frassica also is a senior consultant in pediatric critical care at Massachusetts General Hospital, a research affiliate at MIT, and serves as pediatric editor for the *Journal of Intensive Care Medicine*.

Bruce Walker: Professor Walker is director of the Ragon Institute of MGH, MIT, and Harvard. , Dr. Walker's lab performs research on cellular immune responses in chronic human viral infections, with a focus on HIV immunology and vaccine development. He is an adjunct professor at the Nelson Mandela School of Medicine in South Africa and a principal investigator at the Doris Duke Medical Research Institute at the University of KwaZulu-Natal in the HIV Pathogenesis Program, an initiative that seeks to understand the evolution of HIV and the immune responses effective in controlling the virus.

These appointments have been made in partnership with eight different MIT units.

Academic Program

HST is among the largest biomedical engineering and physician scientist training programs in the United States, with 297 students enrolled in its graduate degree programs during AY2017:

- 110 Medical Engineering and Medical Physics (MEMP) PhD students, including five MEMP/MD students
- Three Speech and Hearing Bioscience and Technology PhD students
- 189 MD and MD/PhD students, including five MEMP/MD students

HST graduate students work with 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.

HST's MEMP PhD program, housed in IMES at MIT, 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 also pursue an MD. MEMP students are extremely successful in obtaining outside funding support for their graduate studies, with 32% of MEMP students holding external fellowships in AY2017.

Two specialized programs within MEMP are the Neuroimaging Training Program and the Mentored Research Program in Bioastronautics.

The Neuroimaging Training Program is supported by a training grant from the National Institute of Biomedical Imaging and Bioengineering. Professors Bruce Rosen and Randy Gollub—both members of the HST faculty based at the Martinos Center for Biomedical Imaging at MGH—co-direct the program. Trainees are identified from among those already enrolled in MEMP with specific interests in neuroimaging. They take additional classes in a curriculum tailored for the program and participate in networking and enrichment activities with faculty and students with related research interests.

The PhD Program in Bioastronautics is directed by Professor Laurence Young, the Apollo Program Professor Emeritus of Astronautics, a member of the HST faculty, and an associate member of the IMES faculty. This program combines the biomedical training of HST's MEMP PhD curriculum with hands-on research exposure at NASA's Johnson Space Center. One or two new students enroll in MEMP/Bioastro each year, joining a small, focused cohort of approximately seven students. This program was founded in 2006 with the support of an education grant from the National Space Biomedical Research Institute. This financial support ended in 2017, and alternative funding sources have not yet been secured. IMES/HST will continue to offer the academic program as part of MEMP without dedicated funding.

The HST MD program, housed in the London Society at Harvard Medical School, is aimed at students interested in a research-based medical career. Although students may 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 career paths in academia.

Graduate Education in Medical Sciences Certificate Program

Graduate Education in Medical Sciences (GEMS) is a certificate program open to doctoral students in MIT's Schools of Engineering and Science who are interested in working at the intersection where engineering and science meet medicine and real-world healthcare. GEMS runs concurrently with the normal course of an MIT PhD program and can be completed in two years without prolonging a typical PhD career. In addition to coursework in pathology and pathophysiology, participants attend seminars with HST

students and engage in an individually tailored clinical experience. GEMS students learn how advances in basic science and engineering become medically relevant therapies and tools for the improvement of human health, while developing a professional network that includes medical researchers, clinicians, and physician-scientists.

GEMS was initially founded with support from a Howard Hughes Medical Institute (HHMI) program that encouraged graduate schools to integrate medical knowledge and an understanding of clinical practice into PhD curricula. Thirty-two MIT PhD students enrolled in GEMS between 2007 and 2011. The program, which became dormant after the HHMI funding ended, was revitalized after the founding of IMES. Two new students enrolled in AY2017.

Summer Institute

Patterned after MIT's Summer Research Program, HST offers a specialized Summer Institute program in biomedical optics, offered in collaboration with the Wellman Center for Photomedicine at Massachusetts General Hospital. Eighteen students are enrolled in summer 2017.

This program offers 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 solving 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.

Honors and Awards

Faculty Honors and Promotions

Sangeeta Bhatia was elected to the National Academy of Sciences in May 2017.

Lydia Bourouiba was awarded a *professeur invité* position—a competitive, international award—by the Foundation of Aix-Marseille University, France.

Emery Brown was named a fellow of the Institute of Mathematical Statistics.

Kwanghun Chung won a National Institutes of Health (NIH) New Innovator Award for his work developing new techniques to produce comprehensive, high-resolution maps of complex organs such as the brain.

James Collins was named one of the Bostonians of the Year in 2016 by *The Boston Globe* for his work on the development of a cutting-edge system that could diagnose Zika quickly, cheaply, and accurately—helping to reduce the impact of the outbreak until a vaccine is ready to be rolled out.

Thomas Heldt was appointed the W.M. Keck Career Development Chair in Biomedical Engineering at MIT. He was also promoted to the rank of associate professor without tenure in the Department of Electrical Engineering and Computer Science.

Robert Langer received honorary degrees from the Gerstner Sloan Kettering Graduate School of Biomedical Sciences, Carnegie Mellon University, the Karolinska Institute, and the Hong Kong University of Science and Technology. He received the Memorial Sloan Kettering Medal for Outstanding Contributions to Biomedical Research, the Raymond and Beverly Sackler Award for Sustained National Leadership, the Benjamin Franklin Medal in Life Science, the Irving Weinstein Foundation Distinguished Lecture Award, and the European Inventor Award (in the category of Non-European Countries).

Alex Shalek was appointed to the Pfizer-Laubach Career Development Professorship.

Faculty Mentoring and Teaching Awards

Dr. Eliezer Van Allen was honored with HST's Seidman Prize for MD Research Mentorship.

Dr. Richard Mitchell and Dr. Robert Padera were honored with HST's Irving M. London Teaching Award.

Dr. Loren Walensky was honored with HST's Thomas A. McMahon Mentoring Award.

In addition, HST Director's Awards recognized Dr. Rebecca Betensky, Dr. Mary-Jo Good, and Dr. Byron Good for their outstanding teaching contributions in HST.

Student Honors and Awards

Melis Anahtar, MD-PhD, received the HMS Leon Reznick Memorial Prize.

MEMP PhD students Melodi Anahtar, Max Cotler, Shoshana Das, and Christina Tringides received National Science Foundation Graduate Research Fellowships.

HST MD students Annabelle Anandappa, Brandon Law, Selena Li, and Connie Zhao received Howard Hughes Medical Institute Medical Research Fellows Awards.

MEMP PhD students Jenny Chen and Emily Lindemer were named MIT Graduate Women of Excellence.

Jenny Chen, MEMP PhD student, and Quinlan Sievers, HST MD-PhD student, received HST Director's Awards for outstanding teaching contributions.

Daniel Chonde, MD-PhD student, received the HMS Multiculturalism and Diversity Award for the London Society.

Tyler Clites, MEMP PhD student, received a Hugh Hampton Young Memorial Fellowship from MIT.

Avilash Cramer, MEMP PhD student, received the 2017 Broshy Fellowship, awarded by IMES.

Aaron Deutsch, HST MD student, received the HMS Seidman Prize for Outstanding HST Senior Medical Student Thesis.

Luke Funk, MEMP PhD student, received a National Defense Science and Engineering Graduate Fellowship.

Wilfredo Garcia-Beltran, HST MD student, received the HMS Jeffrey Modell Prize.

David Gootenberg, HST MD-PhD student, and Justin Rice, HST MD student, both received HIV Medicine Association Medical Student Program Awards.

Nil Gural, HST MEMP PhD student, received a Howard Hughes Medical Institute International Student Research Fellowship.

HST MD-PhD students Morgan Hennessy and Divya Jayaraman received the HMS Henry Asbury Christian Awards.

Robert Hinshaw, MEMP PhD student, was awarded a NASA Space Technology Research Fellowship.

Markus Horvath, MEMP PhD student, received an ERP (European Recover Program) Study Scholarship from the Studienstiftung des deutschen Volkes (German National Academic Foundation).

Lucy Hu, MEMP PhD student, received the SITA Foundation Fellowship, awarded by IMES.

Isha Jain, MEMP PhD student, received a Harold M. Weintraub Graduate Student Award.

Jibril Kedir, HST MD-PhD student, received the HMS Linnane Scholarship.

Christopher Lee and Emily Lindemer, both MEMP PhD students, were named as MedTech Boston “40 Under 40 Healthcare Innovators.”

Jared Mayers, HST MD-PhD, received the HMS James Tolbert Shipley Prize.

Mohamad Ali Najia and Shriya Srinivasan, both MEMP PhD students, received MIT IDEA2 Global –IMES Awards (as members of team SmartClot).

Y. Ray Shao, HST MD student, was named a Scholars’ Abstract Award Finalist for the International Anesthesia Research Society 2016 Annual Meeting and International Science Symposium.

Priya Srikanth, HST MD-PhD, received both the American Academy of Neurology Medical Student Prize and the HMS Sirgay Sanger Award.

Shriya Srinivasa, MEMP PhD student, received the William Asbjornsen Albert Memorial Fellowship, awarded by MIT.

Claudia Varela, MEMP PhD student, received a Ford Foundation Fellowship.

Staff Awards

Academic Programs Administrator Traci Anderson was recognized for exceptional service to the HST community at the sixth annual Harvard Heroes Award Ceremony. This highly selective honor is given to only 60 employees—0.5% of staff—university-wide. Anderson was nominated in the areas of Service Excellence, Teamwork, and Innovation/Continuous Improvement.

Melinda Lyman-Wright, IMES personnel administrator, and Michelle Morrison, IMES administrative assistant II to the Collins and Shalek laboratories, were both awarded a School of Engineering Infinite Mile Award for Excellence. These awards are given to individuals whose work is of the highest quality, along with a high level of commitment and enthusiasm.

Research Program

Core Faculty

Elfar Adalsteinsson: The mainstay of research in the MRI group at MIT continues to be medical imaging with magnetic resonance. Two multi-institutional grants from the National Institutes of Health now support work on fetal imaging and MRI of the placenta, respectively, on teams with colleagues at MIT, MGH, and Boston Children's Hospital. Imaging in pregnancy is an underserved area relative to decades of productive developments for adult MRI, and the domain poses multiple open questions across disciplines of engineering, science, and clinical practice. Active topics in this group include parallel transmission technology, quantitative MRI, and image reconstruction and machine learning applications.

Daniel G. Anderson: The research done in Anderson's laboratory is focused on developing new materials for medicine. His work has led to advances and products in a range of areas, including medical devices, cell therapy, drug delivery, gene therapy, and materials science. In the past year, particular progress has been made in the development of nanoparticles capable of in vivo genome editing (Yin et al, *Nature Biotechnology*), as well as the generation of a pancreas from human stem cells for the treatment of diabetes (Vegas et al., *Nature Medicine*). These technologies are now being advanced clinically at companies based on MIT patents.

Sangeeta Bhatia: There is an enormous clinical need for liver transplant tissue. Bioengineered livers might ultimately be used to serve as a bridge or alternative to whole organ transplantation. In work published in *Science Translational Medicine*, Bhatia and colleagues fabricated human artificial liver "seeds" in biomaterials that can grow and expand inside the body, when the animals harbor a liver injury. After growth, the human artificial liver seeds were able to carry out normal liver functions, such as production of human transferrin and albumin. This work introduces a new paradigm of engineering tissues to expand in response to the body's own repair signals.

Emery Brown: Brown delivered the 2017 Severinghaus Award Lecture at the American Society of Anesthesiologists meeting and a 2017 Medallion Lecture at the Joint Statistical Meeting.

The manuscript "Optogenetic activation of dopamine neurons in the ventral tegmental area induces reanimation from general anesthesia" shows that it is possible to bring rats out of general anesthesia by optogenetic stimulation of the dopamine neurons in the ventral tegmental area in the midbrain. The results give a precise mechanism to explain reviously reported results showing that intravenous administration of methylphenidate (Ritalin) induces reanimation from general anesthesia in rodents most probably through a dopaminergic mechanism. This work has laid the groundwork for a phase II clinical trial in humans testing administration of Ritalin to induce emergence from general anesthesia. If the trial is successful, this may make regular use of Ritalin a way to wake patients up from general anesthesia and to mitigate the post-operative dysfunction that is commonly seen in elderly patients after surgery.

Emery's work "Gamma frequency entrainment attenuates amyloid load and modifies microglia" suggests that auditory or visual stimuli at 40 Hz decrease amyloid load in a rodent model of Alzheimer's disease. In addition, this 40 Hz stimulation is associated with behavioral improvement. The results suggest that either auditory or visual stimulation at 40 Hz may be a therapy for Alzheimer's disease in humans.

Arup K. Chakraborty: Chakraborty continued efforts to understand the mechanistic bases of how a specific and systemic immune response to pathogens occurs and how its aberrant regulation leads to disease. Research aimed toward understanding how this knowledge can be harnessed for the rational design of vaccines and therapies is also an important facet. In the last year, Chakraborty, in collaboration with Phillip Sharp and Laurence Young, also launched a new project on understanding how genes critical for maintaining healthy cell states are regulated. Chakraborty served as the director of IMES and co-chair of MIT's committee on Digital Health. Along with Tyler Jacks, he coordinated the crafting of the campaign white paper on health. He continues to serve as a member of the US Defense Science Board and as a senior editor of *eLife* (one of the premier journals in biology).

Kwanghun Chung: Kwanghun Chung started his position in October 2013 in the Department of Chemical Engineering and IMES as the Samuel A. Goldblith Career Development Assistant Professor. He is also a principal investigator at the Picower Institute for Learning and Memory. His laboratory is an interdisciplinary research team that is devoted to developing and applying novel technologies for holistic understanding of large-scale, complex biological systems. In the past year, his group has continued to develop their recent technologies (SWITCH, MAP, Stochastic Electrotransport) to accelerate the pace of scientific discovery and development of therapeutic strategies in a broad range of biomedical research. Recent research advances by the lab include advancing their SWITCH 3D imaging to reveal network-specific amyloid progression and subcortical susceptibility related to Alzheimer's disease (bioRxiv 2017). Chung was named a 2016 National Institutes of Health New Innovator awardee. He has traveled extensively, including to Seoul National University and Yale University, as well as to

the VIB and Gordon research conferences, to speak about his group's technologies and their applications. Chung taught 10.302 Transport Processes and HST.562 Imaging and Sample Processing in Biology and Medicine. He also served on the IMES Committee for Academic Programs, as well as the IMES graduate admission and faculty search committees. Chung has recently founded a start-up, LifeCanvas Technologies, that aims to advance the adoption and usage of Chung lab technologies developed at MIT.

Richard Cohen: Cohen continued to support MIT's entrepreneurship efforts and the Sloan Healthcare Certificate program by directing one of the core required courses (15.132/HST.972 Medicine for Managers and Entrepreneurs Proseminar) and one of the elective courses (HST.973/15.124 Evaluating a Biomedical Business Concept) for this program. In addition, he served as one of two faculty members on the certificate program's board. Also, as co-founder and consultant, he worked with Sirona Medical Technologies, Inc. to develop a novel catheter technology for the treatment of cardiac arrhythmias. This technology combines local electrical mapping with focused radiofrequency ablation and promises to improve both the efficacy and safety of this important and rapidly growing means of therapy.

James Collins: Collins is the Termeer Professor of Medical Engineering and Science, and is affiliated with both IMES and the Department of Biomedical Engineering. He continues to develop innovative, synthetic biology platforms that can be used to address critical issues in medicine, biotechnology, and the life sciences. Live cells are increasingly becoming the mainstay for the bioproduction of therapeutic proteins and other commodities. However, these living molecular foundries require specialized equipment for operation, and biosafety concerns further restrict their utility, gating them within laboratory walls. Collins and his team proposed and developed a novel solution to these challenges in the form of a portable, on-demand, biomolecular manufacturing platform rooted in freeze-dried, cell-free reaction pellets. The team showed that this approach can be used to produce antimicrobial peptides, vaccines, antibody conjugates, and small molecules, rapidly and inexpensively in the field. This innovative work, which was published in *Cell*, establishes a framework for the portable biomanufacturing of diagnostic and therapeutic tools for use in research and clinical settings, as well as for global health—particularly in developing region—and as a rapid response to pandemics.

Elazer Edelman: Edelman's research combines his scientific and medical training, integrating multiple disciplines. This year he and his group have published some 20 critical papers and been acknowledged on the international stage. He and investigators at Brigham and Women's Hospital received $75 million as part of the One Brave Idea initiative, which aims to better understand the earliest stages of coronary heart disease. He was honored by the Irish Royal Society, Simon Dack Memorial Lectureship, Sharma Visiting Professorship, and the Mount Sinai School of Medicine—as well as with plenary lectures at the Woodrow Wilson Innovation Mexico Summit, MIT Portugal Program, Massachusetts Biotechnology Council, and the annual meeting of the American Institute for Medical and Biological Engineering. His work with the US Food and Drug Administration was honored with an award from the Office of Regulatory Affairs.

John Gabrieli: Gabrieli's team made advances in understanding two difficulties that affect many children, dyslexia (difficulty in learning to read) and depression (feelings of severe despondency and dejection). For dyslexia, both adults and children with dyslexia exhibited reduced brain plasticity. This offers a novel understanding of why about 15% of children struggle to read. For depression, children at familial risk for developing depression have brain difference relative to children not at risk. Such brain measures of risk for depression in children could be used to promote early intervention to reduce the likelihood of developing depression.

Lee Gehrke: Gehrke is a molecular virologist who directs the HST Human Functional Anatomy course at Harvard Medical School and the HST Medical Maker course at MIT. He studies RNA viruses, including Zika, West Nile, dengue, and others. The Gehrke laboratory has been active in designing and building rapid diagnostic tests to detect viruses in blood serum and urine. In collaboration with the laboratories of Rudolf Jaenisch and David Sabatini (Whitehead Institute), the Gehrke lab is developing 2D and 3D tissue models for investigating neurotropic virus infections.

Martha Gray: Gray leads the Biomedical Technology Innovation Group. Her research program focuses on formalizing approaches that drive innovation to create impact, particularly in the context of pre- and post-doctoral research training.

One particular highlight relates to the neuroQWERTY project. This work demonstrated that people with very early stage Parkinson's can be distinguished from healthy controls by analyzing subtle differences in timing while typing. This work leverages advanced machine learning and the pervasive availability of the Internet, and opens the door to the possibility of monitoring new therapies—as well as possibly screening for Parkinson's. ("Computer keyboard interaction as an indicator of early Parkinson's disease," *Scientific Reports*, April 20, 2016). This project has attracted commercial interest and a new start-up, nq-medical, recently licensed this technology from MIT.

Thomas Heldt: Heldt directs the Integrative Neuromonitoring and Critical Care Informatics Group at IMES. Using physiologically based dynamic models, his group leverages multivariate bedside monitoring data—on the second to hour timescale—to understand the physiology of the injured brain, to improve diagnoses, and to accelerate treatment decisions in the critically ill. A key research accomplishment over the past year has been further improvements in the group's model-based noninvasive and patient-specific approach to intracranial pressure estimation, specifically in pediatric patients. Additionally, the group's work has led to the filing of three patent applications over the past year.

Heldt's group continues active collaborations with clinicians at Boston Children's Hospital, Boston Medical Center, Massachusetts General Hospital, and Beth Israel Deaconess Medical Center in neurocritical and neonatal critical care, as well as in other areas of patient monitoring. The group's collaborative work with MGH on developing an early warning system for sepsis has led to a reduction in the (median) time to appropriate antibiotic administration in septic patients in the MGH Emergency Department by almost an entire hour. This is highly relevant, as each hour of delay in the administration of appropriate antibiotics in septic shock patients has been shown to increase mortality by over 7%. This work was highlighted on the MGH website.

Group member Rebecca Mieloszyk completed her PhD this year on assessing levels of sedation in patients under anesthesia, and her thesis was awarded the 2016 Jin Au Kong Prize for an outstanding doctoral thesis in electrical engineering. Rohan Jaishankar submitted his SM thesis, and Jonathan Birjiniuk submitted his MEng thesis. Additionally, Birjiniuk was awarded the Thomas (1959) and Sarah Kailath Fellowship. Incoming graduate student Syed Imaduddin was awarded a Grass Instruments Graduate Fellowship. Both are from the Department of Electrical Engineering and Computer Science (EECS).

This past year, Heldt was appointed the W.M. Keck Career Development Chair in Biomedical Engineering at MIT. He was also promoted to the rank of associate professor without tenure in EECS.

Roger G. Mark: In the past year, Mark taught two courses: 6.022J/HST.542J Quantitative Systems Physiology, for undergraduates and early graduate students from multiple engineering departments, and HST.201 and 202 Introduction to Clinical Medicine and Medical Engineering I and II, for advanced MEMP students. His laboratory's objective is to improve healthcare through the generation of new clinical knowledge and new monitoring technology, and decision support through the application of data science and machine learning technology to large collections of critical care data. His lab has developed the widely-used Medical Information Mart for Intensive Care (MIMIC) database that is freely available to more than 4,000 credentialed investigators worldwide. The lab also developed and supports PhysioNet, an extensive open archive of physiological signals. Mark's administrative and service responsibilities include: MEMP board of advisors (chair), HST-IMES Committee on Academic Programs, MEMP QuEHST (Qualifying Examination) committee, MEMP faculty advisor, and EECS graduate student counselor.

Leonid Mirny: Mirny leads a research program aimed at understanding the organization of the human genome in 3D. He is a co-director of the Center for 3D Structure and Physics of the Genome, funded by the NIH 4D Nucleome Program. In the last year, the Mirny laboratory has published several high-profile papers on 3D genome organization, proposing and supporting a novel mechanism of genome organization by active loop extrusion. In April 2017, *Nature* published an article, "A loop of faith," featuring the work of Mirny on loop extrusion. Mirny teaches a freshman seminar on quantitative biology in which students learn concepts of genomics through interactive games and table-top experiments.

Alex Shalek: This year, the Shalek laboratory has broadly applied Seq-Well, their ultra-high-throughput, low-cost, microwell-based, single-cell RNA-Seq platform to systematically examine how cellular composition and communication drive healthy and diseased tissue behaviors. Through local, national, and international collaborations (in England, Spain, Switzerland, Malawi, South Africa, and Thailand), they have profiled a wide array of human, non-human primate, and murine tissue isolates to define their cellular structures, as well as deviations induced by different cancers (e.g., pancreatic, colon, and lung cancers, and brain metastases), infections (e.g., *M. tuberculosis* in lung tissue and cerebrospinal fluid, HIV-1/SHIV in blood, lymph nodes,

gut, lung, cerebrospinal fluid, and more, across different cohorts and time scales), and inflammatory diseases (e.g., respiratory inflammation (polyps) in nasal epithelia and ulcerative colitis in gut mucosa). While each project alone is affording unprecedented insights into the relevant disease etiology, taken together, they are beginning to reveal common cellular motifs that inform healthy tissue equilibria and immune behaviors, and novel therapeutic and prophylactic paradigms. In parallel, the Shalek lab is actively developing new technologies to facilitate deeper, more mechanistic inquiry into the factors that influence the social structure and fitness of cellular ensembles.

Charles Sodini: The vision of the MIT Medical Electronic Device Realization Center (MEDRC) is to revolutionize medical diagnostics and treatments by bringing healthcare directly to the individual and to create enabling technology for the future information-driven healthcare system.

MIT MEDRC, launched in May 2011, currently has four member companies (ADI, General Electric, Nihon Kohden, Philips Research) supporting approximately 15 projects, with 25 students/postdocs, and seven principle investigators with funding of approximately $2 million annually.The MEDRC serves as a focal point for engagement with researchers across MIT, the medical device and microelectronics industry, venture-funded startups, and the Boston medical community. Recently, there has been tremendous interest in digital biomarkers from local pharmaceutical companies to monitor and track neurodegenerative diseases.

Collin Stultz: Stultz, affiliated with both EECS and IMES, is a principal investigator in the Research Laboratory of Electronics (RLE). He is an HST alumnus and a board-certified internist and cardiologist. He is a member of the American Society for Biochemistry and Molecular Biology and the Federation of American Societies for Experimental Biology. Among his honors are being a recipient of the Burroughs Wellcome Fund Career Award in Biomedical Sciences and the James Tolbert Shipley Prize.

Associate Faculty

Lydia Bourouiba: This past year, the Bourouiba laboratory published key papers at the interface of fluid dynamics and respiratory and agricultural diseases and established fundamental collaborations with the US Department of Agriculture and the FDA in relation to the application of the fundamental fluid dynamics governing foodborne and waterborne diseases. The techniques used by Bourouiba and her team have led to the revisiting of canonical fluid dynamics problems of droplet formation. This is paving the way for new detection, tracking, and capture tools of droplets formed from impacts on contaminated leaves and produce (in the agricultural application domain) and surfaces indoors (in the human health application domain).

Bourouiba continued to develop and teach two classes: 1.631/HST.537/2.250 Fluids and Diseases and 1.068-1.686/18.358/2.033 Nonlinear Dynamics and Turbulence. The material she developed in the past on differential equations is now being converted to the edX platform. She continued to be on the advisory board of the National Institute for Mathematical and Biological Synthesis and was an invited speaker for a range of institutes, universities, and events this year, including Stanford University, University of California at Berkeley, University of Illinois at Urbana-Champaign, University of

Houston, the Joint Division of Applied Mathematics at Brown University, the Applied Mathematics Laboratory at the Courant Institute of New York University, the Global Health Innovation Partnership, the Gates Foundation, the Ragon Institute, the Provincial Infection Control Network of British Columbia's annual conference, and the BioMEMS Resource Center at MGH

Bourouiba's work continues to draw significant attention and she and her laboratory were featured by *Science Friday* and the Howard Hughes Medical Institute (HHMI) in "Breakthrough: Connecting the Drops."

Polina Golland: In collaboration with Adalsteinsson's group and clinical colleagues at Children's Hospital, Golland's group aims to develop MRI-based biomarkers of placental function. The researchers are using MRI to characterize how well oxygen and other nutrients are transferred from the maternal blood stream to the fetus. The collaborative team demonstrated that MRI-based signals can be used to visualize normal function of the placenta and its dysfunctions. The results of this research have been recently published in *Scientific Reports - Nature*.

Robert Langer: During 2016 and 2017, Langer received numerous honorary degrees and awards. He presented several named lectures, include the Inaugural Distinguished Lecture in Bioengineering (University of California, Berkeley), the Inaugural Frank and Grace Yin Distinguished Lecture (Washington University), the Deloitte Endowed Lecture (Dana-Farber Cancer Institute), the Stetson Lecture (Larner College of Medicine at the University of Vermont), the Alfred Stracher Memorial Lecture (State University of New York Downstate Medical Center), the Henry Louis Smith Lecture (Davidson College), the Anderson Distinguished Lecture (University of Virginia School of Medicine), the AACR-Irving Weinstein Foundation Award Distinguished Lecture (American Association for Cancer Research), and the Hunt Lecture (Wound Healing Society Foundation).

Phillip A. Sharp: Recent recognition that liquid-liquid phase transitions in cells can concentrate factors into membraneless bodies in cells, and that RNA is frequently a component of these assemblies, stimulated the speculation that super-enhancers (SEs) might be a manifestation of these phenomena. Richard Young introduced the concept of SEs as large regions of DNA bound by transcription factors that dramatically stimulate transcription from proximal promoters. Further, he showed that SE-associated genes are frequently critical for normal development and that new SEs appear near many disease genes. The research team examined the role of SEs in expression of miRNAs and found that they marked cell type specific microRNA (miRNA) genes, particularly those expressed at high levels. More importantly, when miRNAs that have oncogene activity gain an association with SEs, the prognosis of the cancer patient worsens (Suzuki et al., 2017). Given that phase transitions can concentrate factors in a highly cooperative fashion to enhance the rate of reactions, the team conjectured that SEs function as a large, membraneless assembly of factors that enhanced the rate of transcription from adjacent promoters. In collaboration with the Chakraborty and Young labs, the Sharp lab developed a model of phase transitions that illustrated its high dependence on valences and low dependence on affinity (Hinsz et al., 2017), and outlined how its properties are consistent with many of the known phenotypes of SEs. This research is ongoing and has great potential to open new avenues to investigate dynamic biological phenomena and develop new therapies.

Leia Stirling: While wearable technology is expanding at an incredible rate, current technology is limited as a decision-making aid due to difficulties in interpreting the underlying data in the context of the natural environment. Stirling's research is to extend the ability of subject matter experts to make decisions that rely on understanding human performance when direct visual observation is not possible through the use of wearable technology and biomechanical modeling. Her work bridges the domains of biomechanics, signal processing, and human factors and aims to enable those with limited knowledge (non-experts) in sensor technology and physiological systems to use these data for decision-making. These methods have the potential to inform full-body monitoring for aiding clinicians, as well as individuals in the community. Stirling also applies these methods to evaluate exoskeleton architectures.

Peter Szolovits: Szolovits continued to do research on natural language processing of clinical notes and building predictive models that estimate the risks of various morbid events and the likelihood of success of different therapeutic interventions. He served as overall PI of the medical collaboration between Philips Healthcare and MIT and continues to collaborate with colleagues at MGH, UMass/Lowell, and Harvard Medical School on a variety of projects. Three of his students completed PhDs, one of them will be on the faculty at University of Toronto, and the others are now at Google and Adobe. The group also graduated two master's students and several Undergraduate Research Opportunities (UROP) students. Most of their projects have led to conference and journal publications.

Laurence Young: Young is the Apollo Program Professor Emeritus of Aeronautics and Astronautics, and Professor of Health Sciences and Technology at the Massachusetts Institute of Technology. He was the founding director of the National Space Biomedical Research Institute. He directs the HST PhD program in bioastronautics.

Professors of the Practice

Brett Bouma: Bouma is director of the Center for Biomedical OCT Research and Translation. The center began the first year of its second five-year P41 funding cycle under a grant from the National Institute of Biomedical Imaging and Bioengineering. Bouma served as a guest editor for a feature issue of *Biomedical Optics Express* celebrating the 25th anniversary of optical coherence tomography.

Research advances have included:

- Developing a new method for measuring lymph flow velocity and volumetric flow rates without requiring an exogenous contrast agent (*Scientific Reports* 6, p29035, 2016)
- Demonstrating label-free volumetric optical microscopy of entire, intact murine brains (*Scientific Reports* 7, p46306, 2017)

In addition, Bouma's work on polarimetry for characterizing tissue birefringence, depolarization, and optical axis orientation has advanced on several fronts, including:

- Demonstrating polarimetric imaging through narrow gauge aspiration needles for in situ tumor imaging (*Scientific Reports* 6, p28771, 2016)

- Successfully testing a new system for monitoring airway smooth muscle structure and function in vivo (*Science Translational Medicine* 8, p359ra131, 2016)
- Developing a method for mapping gold nanorod distribution within biological tissues (*Nature Photonics* doe:10.1038/nphoton.2017.128, 2017)

Joseph Frassica: Frassica leads the Philips Research Americas laboratories. His research interests cover a broad range of topics, from the use of high-resolution physiologic data and clinical information to create predictors of patient trajectory in critical care, to developing new measurements for ultra-mobile ultrasound, to the application of whole-genome sequencing to track the spread of multi-resistant bacteria within geographies and health-care environments.

Recently, his acute care data analytics and machine learning team defined a method to predict the deterioration in hemodynamic control in children hours before the event. This predictive algorithm is now in clinical validation. This year, his lab participated in multiple national and international challenges and won first place in this year's ImageCLEF and second place in the National Data Science Bowl.

Philips Research North America Lab also continues collaborations with multiple labs across the Institute including, with the following faculty members and their respective research areas:

- Thomas Heldt, to advance non-invasive intracranial pressure estimation
- Roger Mark lab, to extend MIMIC II to the emergency department
- Una-May O'Reilly, to develop large-scale knowledge mining of physiologic waveforms
- Brian Anthony, to study force-controlled sonography for advanced elastographic diagnosis in the liver, prostate, and thyroid
- Polina Golland, to study imaging analysis of chest x-rays for heart failure
- Roger Mark, developing an MIT-Philips Research Award for clinicians from Harvard hospitals.
- Peter Szolovits and Amar Gupta, for the research project, "Telemedicine Interactions and Face-to-Face Interactions in Critical Care Medicine and Other Clinical Specialties: Enhancing Effectiveness of Virtual Teams thru Systems Engineering"
- Peter Szolovits, MIT-Philips Grand challenge to define the future of healthcare informatics

Bruce Walker: Walker is director of the Ragon Institute of MGH, MIT, and Harvard, and a Howard Hughes Medical Institute investigator. He was appointed a professor of the practice in IMES in 2016. His notable accomplishments in the past year include the establishment of a new MIT undergraduate course, HST.S46 IAP Evolution of an Epidemic, addressing how the medical, scientific, and public health communities

identify the emergence of a new epidemic; looking at how policy and advocacy influence events; and providing a comprehensive view of the many dimensions of and responses to the ongoing HIV epidemic. With support from IMES, MISTI, and the Dean for Undergraduate Education, 19 MIT undergraduates attended the inaugural course, which was taught in South Africa during the January Independent Activities Period and consisted of both lectures and field trips to interact with affected communities and visit traditional healers, hospitals, and clinical research sites. Two of these students returned to conduct research projects this summer, funded through an MIT partnership with the Ragon Institute. On the research front, Walker and investigators from the Ragon Institute, MIT, and Harvard used the new gene-editing technology CRISPR-Cas9 to identify host dependency factors which are required for HIV replication, but dispensable for host cell viability—thereby identifying possible new therapeutic targets for treatment of HIV infection. Their report, published in Nature Genetics was the subject of the feature, "Clinical Implications of Basic Research," in the New England Journal of Medicine. Walker was also involved in collaborative studies with Douglas Kwon at the Ragon Institute, demonstrating high female genital tract (FGT) microbiome diversity in African women, and linked specific FGT bacterial species to increased inflammation, increased numbers of infectable CD4+ T cells, and increased acquisition of HIV infection. This report, published in Immunity, provides a potential pathway for therapeutic intervention through alteration of FGT flora. Walker published 24 peer-reviewed journal papers in the past year. In addition, Walker received the 2017 Heroes in Action Award from the AIDS Action Committee of Massachusetts for his significant and lasting contributions to the fight against HIV/AIDS in Massachusetts.

Events

Health Sciences and Technology Faculty Poster Session

Approximately 125 people attended the 2016 HST Faculty Poster Session, held on October 6 at the Courtyard Café at Harvard Medical School. Forty-eight faculty posters, representing 42 labs, were on exhibit. Some posters represented broad research programs, while others presented specific research projects; some included student co-authors. 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.

Health Sciences and Technology Forum

The 30th HST Forum was held on April 20, 2017, at the Tosteson Medical Education Center at Harvard Medical School. This event highlights the depth and breadth of HST student research for applicants admitted to HST's MD and PhD programs, as well as current students, faculty, staff, and other members of the Harvard and MIT communities.

This year approximately 125 people attended the Forum, including 30 students who presented posters on their current research. The poster session was followed by a keynote address given jointly by Harvard Medical School Professor Douglas Kwon and his advisee, HST MD-PhD student Melis Anahtar, through which they provided the audience with a view of a dynamic mentor/mentee relationship.

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:

- Travis Hughes (MD-PhD) Bioinformatics and Integrative Genomics
- Allison Hamilos (MD-PhD) Physiology and Systems Biology
- Lina Colucci (MEMP) Biomedical Devices
- Rohit Thummalapalli (MD) Cell and Molecular Biology
- Sangyeon Cho (MEMP) Imaging, Acoustics, and Optics
- Hyun-Ho "Greco" Song (MEMP) Regenerative and Rehabilitative Biomedical Engineering

Institute for Medical Engineering and Science Distinguished Lecture Series

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

- Michael Elowitz, "Design principles for signaling, memory, and cell state control pathways in mammalian cells," November 10, 2016
- David Louis, "Crossing the second translational research valley of death: A lesson from tumor classification in the molecular era," February 23, 2017
- Christina Smolke, "Synthetic biology platforms for natural product biosynthesis and discovery," March 21, 2017
- Todd Coleman, "Neuro-gastroenterologic engineering," May 4, 2017

Arup K. Chakraborty
Founding Director
Robert T. Haslam Professor of Chemical Engineering
Professor of Physics, Chemistry, and Biological Engineering