Data and Health

PLUS
MIT IS COMING TO A CITY NEAR YOU P. 31
Civil and environmental engineering professor Lydia Bourouiba, pictured with graduate student Yongji Wang, collects and analyzes data on the spread of infectious disease (see page 13).

PHOTO: LILLIE PAQUETTE

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In this space last spring, I described a simple, unifying vision for MIT’s campaign: to make a better world. I believe we should see the MIT Campaign for a Better World as a mechanism for magnifying MIT’s distinctive strengths in education, research, and innovation, to help us make progress against grand, global problems.

This issue of Spectrum explores one of the grandest: human health.

From radically inexpensive diagnostics for detecting early stage disease to life-saving treatments for cancer, our faculty, students, and alumni are increasingly renowned for inventing novel solutions that improve patient care. And we are equally focused on applying MIT’s expertise in analyzing massive data sets and optimizing complex systems to unravel the big, complicated underlying problems that plague the health care system itself.

Whether at MIT’s health-related academic units—including the Institute for Medical Engineering and Science (IMES) and the Departments of Biological Engineering, Biology, and Brain and Cognitive Sciences—or at MIT’s many cutting-edge research centers and programs focused on a single disease, the work under way on our campus to advance solutions in human health and health care is already breathtaking.

Today, I believe we have the opportunity to sharply increase our impact precisely because our work on human health and health care isn’t limited to any single school. More than 50% of MIT’s science and engineering faculty and students are engaged in biological research, often specifically focused on human health. These diverse research efforts branch and intertwine all across MIT, engaging colleagues in fields from transportation, management, economics, and public policy to health care delivery. And many also make the most of our exceptional location, in easy reach of a fleet of world-class hospitals, research centers, and biotechnology firms. No wonder MIT now anchors what is arguably the biotech capital of the world.

And of course, throughout our work on health and health care, we lead with data. With new efforts like the Institute for Data, Systems, and Society, and MIT Big Data, we bring to bear exciting new analytical tools and MIT’s signature strength in systems thinking to address crucial societal problems. Using knowledge for the betterment of humankind. That is MIT at its core.

To invent a health and health care system that works well for everyone—to make a better, healthier world—demands bold ambitions and innovative thinking. I am delighted to share with you such a wide range of evidence that MIT is up to this most important challenge.
“Even though it’s made of humble materials, the geometry and pattern of the brick makes it possible to achieve beauty.”

John Ochsendorf

8×10m
Each bay measures 8×10 meters, and can be replicated in an undulating pattern.

3×6
The prototype bay in Venice was built in only three weeks by six people.

Stabilized by double vault curvature, the structure is held in place by friction and compression forces.

Reusable steel tubes form a temporary framework over which the vault is built.
In the not-so-distant future, Droneports may dot the African continent. These instant architectural landmarks are designed to become community hubs—not unlike the cathedrals their vaulted curves bring to mind.

The Droneport project, initiated by Red Line, within Switzerland’s Afrotech-EPFL, seeks to create a route for drones to carry medical supplies to off-grid African communities, circumventing the need for traditional transportation infrastructure. These miniature bays for unmanned aerial vehicles would enable a technological shift that Class of 1942 Professor of Architecture and Professor of Civil and Environmental Engineering John Ochsendorf likens to the advent of mobile telecommunication, when cell phones connected communities where telephone lines had never been installed.

The project’s lead architect, Lord Norman Foster, of Foster + Partners, turned to Ochsendorf’s structural engineering consulting firm ODB Engineering, cofounded with MIT graduates Matthew DeJong SM ’05, PhD ’09 and Philippe Block SM ’05, PhD ’09, to develop the technical aspects of these buildings, which must rely as little as possible on imported materials and labor. The resulting structure is a self-supporting tile vault made of interlocking bricks, using techniques of the 19th-century architect Rafael Guastavino, whom Ochsendorf has been studying for more than a decade. (He directs MIT’s Guastavino Project, which documents and preserves tile vaults designed by the Guastavino Company in nearly a thousand US buildings, including New York’s Grand Central Terminal, the Boston Public Library, and Fariborz Maseeh Hall at MIT.)

“This is an example of research going into practice—and of universities collaborating with industry to create new possibilities,” says Ochsendorf. The team, also including Sixto Cordero MA ’16 and Luisel Zayas MA ’16, traveled to Venice in May to debut a prototype at the 2016 Architecture Biennale.

“The three-layer brick construction uses clay tiles from Spain for the base layer. “Durabric,” a naturally cured block of compressed earth and cement designed for local manufacture in the developing world, makes up the two outer layers. France’s LafargeHolcim Research Center developed Durabric and provided 18,000 units for the Droneport construction.
Dynamic System
A core chemistry course that activates engagement, even beyond the MIT campus

TITLE
5.111 Principles of Chemical Science

INSTRUCTOR
Cathy Drennan, professor of chemistry and biology

PHOTO: JAMES KEGLEY

PLATFORM
OpenCourseWare

COURSE FEATURES
- Video lectures with subtitles, transcripts, and notes
- Reading assignments
- Problem sets and exams, with solutions
- “Behind the Scenes at MIT” videos
- “Clicker questions” and graphs of student responses

DESCRIPTION
Introduction to the chemistry of biological, inorganic, and organic molecules. The emphasis is on basic principles of atomic and molecular electronic structure, thermodynamics, acid-base and redox equilibria, chemical kinetics, and catalysis.

BACKSTORY
When Cathy Drennan decided to pursue biology as an undergraduate at Vassar, she was skeptical about the relevance of chemistry to her education. Thanks to some dynamic teachers, however, she came to appreciate the connection between the two fields. Now a professor in both biology and chemistry at MIT, she is also the only person ever to have been named both an investigator and a professor with the prestigious Howard Hughes Medical Institute (HHMI).

As one of MIT’s most frequent teachers of 5.111—which is taken each year by more than 500 first-year students—for the past 16 years, Drennan has employed educational innovation to inspire others the way she was once inspired. For students coming to MIT to study the dynamic fields of computer engineering or biotechnology, learning about molecules and reactions can seem like a chore. Drennan, a MacVicar Faculty Fellow, has worked to dispel that perception by showing how basic chemical reactions underlie almost everything that happens in science.

DIGITAL ASSETS
In 2011, Drennan used a grant from HHMI to establish an Education Lab, and produced a series of two-to-three-minute videos called “Behind the Scenes at MIT.” Most of the segments feature graduate students or undergrads describing their research in MIT faculty labs. Using illustrations and animations, the students explain how a basic chemistry concept helped them pursue solutions to real-world challenges as diverse as cancer, terrorism, and climate change. In companion videos, the up-and-coming chemists relate a personal story about how they became interested in science. Since the videos were produced, many of these subjects have moved on to pursue a chemistry-related career.

In a study conducted with MIT’s Teaching and Learning Laboratory, students who had watched the videos rated their motivation to learn chemistry a full 1 out of 7 points higher, on average, than during the half semester in which they had not seen the videos. (The spike in ratings was even sharper among female students; notably, two-thirds of the video subjects are female.) Drennan posted these videos to chemvideos.mit.edu, so they are available to anyone around the world with an interest in chemistry. They continue to be used by other instructors in the MIT classroom, as well. Assistant chemistry professor Matthew Shoulders, who co-teaches 5.111 with colleague Troy Van Voorhis, says he constructs portions of his lectures around the videos, and notices “the level of engagement spark up” in response.

These videos are far from the only resources Drennan has made available to online chemistry learners. Since 2009, extensive materials from 5.111 as taught by Drennan and co-instructor Elizabeth Vogel Taylor PhD ’07 have been freely available on OpenCourseWare (OCW), MIT’s pioneering web-based publication of virtually all the Institute’s course content. Drennan is launching an extensively updated version of 5.111 on OCW this fall, featuring new edits of lectures that are divided into subject modules. Visitors to OCW can download 5.111 lecture notes, homework problems, and handouts, and tally their success in answering onscreen “clicker questions” identical to those Drennan has used on campus to keep her students engaged and motivated by friendly competition.
Benjamin Ofori-Okai SM ’13, PhD ’16

Concepts: atomic energy levels, degeneracy

MIT research (Christian Degen Lab):
Energy-level differences detected with nanoscale MRI can lead to the generation of three-dimensional images of biological molecules. “The thing I would love to see this technology be able to do is: we’ve got this virus, let’s watch it in real time, let’s see if we can see how it attaches to cells and invades them.”

Stefanie Sydlik PhD ’13

Concepts: VSEPR (valence shell electron pair repulsion) theory, geometry of molecules

MIT research (Timothy Swager Lab):
Amplifying small-scale changes in bond angles following interaction with a target molecule could improve detection of explosives. “If we can come up with a handheld device...that will be attached to a robot and sent to sniff out the area before the soldiers got there, it can really save a lot of the soldiers’ lives.”

“Do people actually use the stuff they learn in intro chemistry?”

Benjamin Ofori-Okai SM ’13, PhD ’16

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Data + Health
By its Latin root, if not always in conversation, “data” is a plural noun. Arguably, nowhere is that plural nature so evident than in the realm of human health. We are sequenced, imaged, surveyed, examined—and documented. From 2008 to 2015, the percentage of non-federal acute care hospitals using electronic health record systems rose from 9.4% to 84%. Outside hospital walls, in everything from insurance records to credit card statements, digital details about our bodies and habits are proliferating.

New technologies and ballooning data sets allow us to model problems and test solutions in ways inconceivable just a decade ago, but we must learn how to organize, share, and interpret these resources effectively. Researchers representing MIT’s broad range of strengths are meeting that challenge—collecting the data we need, making sense of the data we have. From this plurality of information, they are extracting insights that could improve countless lives.
Leading with Data

In their own words: MIT faculty on advancing health in a data-rich era

When we say “Big Data”—what do we mean by big? MIT faculty member Sandy Pentland, who is numbered by Forbes among the world’s seven most powerful data scientists, says we’re not talking about sheer size. Researchers amassed enormous data sets, he points out, long before Big Data coalesced as a capital-letter concept. But, says Pentland, the scope of data at our fingertips “is far more pervasive than ever, far more continuous.” Spectrum asked Pentland and six other MIT researchers working in the sphere of human health to discuss the challenges and opportunities they face in this new landscape.

MARIANA ARCAYA explores relationships between geographic contexts and health. An assistant professor in the Department of Urban Studies and Planning, she is one of the leaders of a new Health Initiative in the School of Architecture and Planning.

EMERY BROWN, an anesthesiologist at Massachusetts General Hospital, leads the Neuroscience Statistics Research Laboratory in the Department of Brain and Cognitive Sciences. He is MIT’s Edward Hood Taplin Professor of Medical Engineering and of Computational Neuroscience, director of the Harvard-MIT Health Sciences and Technology Program, associate director of the Institute for Medical Engineering and Science (IMES), and an investigator at MIT’s Picower Center for Learning and Memory.

MUNTHER DAHLEH is the director of MIT’s Institute for Data, Systems, and Society (IDSS), which has just celebrated its first anniversary, and the William A. Coolidge Professor in the Department of Electrical Engineering and Computer Science.

JOSEPH DOYLE is the Erwin H. Schell Associate Professor of Management in applied economics. He is a co-director of the MIT Sloan Initiative for Health Systems Innovation and a co-chair of the Health Sector of the Abdul Latif Jameel Poverty Action Lab (J-PAL), a research center at MIT dedicated to reducing poverty by ensuring that policy is informed by scientific evidence.

AMY FINKELSTEIN PhD ’01 is the John and Jennie S. MacDonald Professor of Economics at MIT, the co-scientific director of J-PAL North America, and chair of J-PAL’s US Health Care Delivery Initiative, which supports randomized evaluations of innovative strategies to improve the efficiency and effectiveness of health care in the United States.

JOHN GUTTAG is the Dugald C. Jackson Professor in the MIT Department of Electrical Engineering and Computer Science. He leads the Data-Driven Inference Group at the Computer Science and Artificial Intelligence Laboratory (CSAIL).

ALEX “SANDY” PENTLAND, Toshiba Professor at MIT, is a computer scientist and entrepreneur who co-created the MIT Media Lab, where he now directs the Human Dynamics research group. He also leads the Connection Science initiative, based in IDSS.

EVALUATING CARE MANAGEMENT

Five percent of the US population accounts for more than half of our health care expenditures. The Camden Coalition of Healthcare Providers developed a care management program, pictured, that uses a data-driven “hotspotting” process to identify these high-needs patients and to provide them with medical management and assistance in accessing social programs. With support from J-PAL, professors Joseph Doyle and Amy Finkelstein (see above) and their colleagues have partnered with the New Jersey organization on a randomized evaluation of its program. The study will generate evidence on whether the Camden approach is effective—as measured by hospital readmissions, health care utilization, participation in social programs, earnings, employment, and mortality. PHOTO: COURTESY OF J-PAL

Blending perspectives

DAHLEH: “By hiring new faculty and bringing together the larger community of researchers at MIT who focus on data, IDSS aims to promote the development of data science theoretically, algorithmically, and in the various ways it is applied to real challenges. IDSS faculty collaborate on health care research with major departments and institutes at MIT, including the Broad Institute, the Koch Institute for Integrated Cancer Research, and the Institute for Medical Engineering and Science (IMES). This kind of research follows the general theme of ‘data to models to decisions/insights.’ Our faculty, in collaboration with experts in their fields, brings in new powerful methods in statistics and machine learning, graphical models and causal inference, dynamic system theory, optimization, and decision theory to address difficult challenges in health care. Our research addresses ‘big data’ questions (this includes general electronic hospital data sets or genomic data), ‘small data’
MATH AND PHYSIOLOGY

IMES faculty Thomas Heldt PhD ’04 develops modeling techniques to understand physiological signals, such as arterial blood pressure or cerebral blood flow velocity waveforms. For example, his group is refining an algorithm that estimates intracranial pressure, which is important to measure in a variety of neurological conditions, including traumatic brain injury, hydrocephalus, or hemorrhagic stroke. “We try to incorporate our understanding of the underlying physiology into the analysis tools,” Heldt, the W. M. Keck Career Development Professor of Biomedical Engineering, recently told MIT News. “We can represent the physiology mathematically through differential equations or algebraic equations, and then interpret the data within the context of those mathematical relationships.”

PHOTO: LILIE PAQUETTE

questions (such as those related to clinical trials), learning model structures of underlying phenomenon (e.g., learning gene regulatory networks), dynamic effects (e.g., contagion), and control and decision effects (e.g., targeting immunization, pandemics), as well as policy questions like the effects of funding on cancer research.”

GUTTAG: “We can sit in our lab at MIT and do fancy mathematics, but if we actually want to have an impact on health, it’s crucial that we work with people in the clinical environment. A lot of what we do in computer science is based upon statistical models, but clinicians have a probably healthy skepticism about statistical models that have no obvious relation to what they observe in practice. I don’t let a week go by where I’m not in conversation with people who are actually on the front line.”

FINKELESTEIN: “J-PAL’s US Health Care Delivery Initiative (HCIDI) hosted a ‘matchmaking’ conference in October 2014 that brought together more than 75 health care practitioners, policy makers, and scholars to spur more data-based evaluations of programs and policies in health care delivery. We’re looking to hold another conference this November, with a portion open to the public. We also convene smaller gatherings around specific, high-priority topics. In May, we brought together policy makers from four states and from the White House’s Office of National Drug Control Policy (ONDCP) with medical experts and researchers from J-PAL’s network to discuss opportunities to evaluate innovative approaches to drug abuse and addiction. The roundtable has already spurred a project with the ONDCP, a potential academic research collaboration in two states, and has

4 BATCHES

Philippe Rigollet, associate professor of mathematics, core member, Center for Statistics; affiliate member, Broad Institute

The design of ethical clinical trials must compromise between caution (testing one subject at a time) and efficiency (all of them simultaneously). The former optimizes outcomes for the most patients but is impractical; the latter maximizes the speed of research, but sacrifices potential benefits to a large segment of study enrollees. A solution is to group subjects into smaller batches: the FDA currently recommends four batches, but their size is not precisely regulated. Rigollet and collaborators developed a mathematical technique for sizing each batch. They have demonstrated that by applying their rule, four batches can yield patient outcomes comparable to the most cautious procedure of testing subjects one at a time, while presenting almost no loss of efficiency in relation to current standards.
“We can sit in our lab at MIT and do fancy mathematics, but if we actually want to have an impact on health, it’s crucial that we work with people in the clinical environment,” says Guttag.

New York City’s Department of Health, and several community-based organizations, aimed at reducing hospitalizations for asthma. As a team, we’re saying: let’s look at the data on which buildings are sending residents to the hospital for asthma in high numbers. Then, let’s go into those buildings and talk to the residents, owners, and landlords. Can we retrofit the buildings for energy conservation and lower utility bills, while improving indoor air quality? And can we do it in a way that’s providing work for local low-income people? We think about a place-based, higher-level intervention that will help reduce not just health care utilization for asthma but at the same time provide some kind of economic, social, and environmental benefit.”

Navigating challenges

Brown: “Recent technological and experimental advances in the capabilities to record signals from neural systems have led to an unprecedented increase in the types and volume of data collected in neuroscience experiments and hence, in the need for appropriate techniques to analyze them. My laboratory develops algorithms to characterize how the brain represents and transmits information. A primary focus of our research is the development of algorithms to characterize, monitor, and control the brain states of patients receiving general anesthesia and sedation.”

Finkelstein: “Administrative data are an invaluable resource for rigorously evaluating health programs, but come with a unique set of challenges. J-PAL has developed a 45-page practical guide on how to obtain and use nonpublic administrative data. As a companion, a growing catalog of administrative data sets outlines specific requirements and processes for obtaining data from several key agencies. For example, we’ve compiled cost estimates — some data, such as Medicare claims data, can cost thousands of dollars to acquire — and an estimated timeline, since some can take several months to more than a year to obtain. Since their creation in January, our guide and catalog have each been downloaded about 1,000 times.”

Pentland: “Data access, data preservation, and data privacy are big issues. If researchers can’t get at the data, they can’t find the patterns. And we want to enable people to keep track of their health. When encouraged one state to make evidence-based adjustments to its opioid prescription policies.”

Arcaya: “My expectation in advancing the School of Architecture and Planning’s Health Initiative [with urban studies associate professor J. Phillip Thompson] was that a lot of the work going on at SA+P — housing, economic development, environmental work — would be very important for health, even if it’s not labeled that way. For example, Phil and I have a project in the Bronx with Montefiore Hospital, designing the buildings for energy conservation and lower utility bills, while also improving indoor air quality. And can we do it in a way that’s providing work for the local low-income people? We think about a place-based, higher-level intervention that will help reduce not just health care utilization for asthma but at the same time provide some kind of economic, social, and environmental benefit.”

Informing decisions

Doyle: “There’s a lot of talk about care redesign, but to figure out if the redesign is effective I advocate for smart piloting. You could say a program was implemented and costs went down 20%, but you might have gotten that 20% regardless of what you did. Or they might have gone down 15% regardless, and you achieved a 5% relative improvement. That’s why we develop tools such as real-time, low-cost, randomized controlled trials to show a causal effect on outcomes. Providers need data to figure out how to streamline and improve health care at the same time.”

Laurie Boyer, associate professor of biology and biological engineering / Manolis Kellis ’99, MEng ’99, PhD ’03, professor of computer science; faculty at CSAIL and Broad Institute

Heart disease is the leading cause of death in adults, accounting for one in four deaths in the US. Genetic variants from genome-wide association studies can reveal new therapeutic targets, but their discovery requires impractically large patient groups. To speed up this search, researchers from the Boyer and Kellis labs analyzed known genetic markers that increase heart disease risk, and found that they show common epigenetic signatures. Those signatures enabled them to identify several additional genetic contributors to heart disease with much smaller cohorts than would otherwise be necessary. The researchers plan to apply this strategy to help reveal new therapeutic targets in diverse inherited diseases, including Alzheimer’s, schizophrenia, and type 2 diabetes.
FINKELEIN: J-PAL’s US Health Care Delivery Initiative (HCDI) provides a coordinated platform to support randomized evaluations of strategies that aim to improve the quality and value of health care delivery. At the outset of the initiative, [research scientist] Sarah Taubman and I published a review paper in Science, documenting the scarcity of randomized evaluations of health care delivery strategies. We also outlined priority research questions in health care delivery, and provided specific guidance on potential research designs to answer those questions. The paper was covered by the New York Times and the Freakonomics podcast, and has guided the development and funding of specific studies and influenced policy conversations. HCDI has funded or otherwise supported the development of 15 randomized evaluations to date.”

COMMUNITY-BASED DATA
The nonprofit creators of the Healthy Neighborhoods Equity Fund have partnered with an MIT team—led by urban studies and planning faculty Mariana Arcaya—on a longitudinal study of how its investments in transit-oriented development projects affect residents’ health. Focusing on three Boston-area communities experiencing interventions and six control communities, the MIT researchers (including grad students Rob Call and Leigh Carroll, pictured center and at right in Roxbury) partnered this summer with community members (including Shannon Simpson, left) to field surveys on topics from health to violence and displacement. This fall, the residents will help the researchers analyze the survey results, which will be integrated with findings from a statewide All-Payer Claims Database. Says Arcaya, “We want to combine the power of big data with rich, qualitative data that is coproduced and co-owned with community-based organizations.”

PHOTO: PETER GUMASKAS

spectrum.mit.edu
A year ago I cofounded a company called HEALTH[at]SCALE Technologies. Hospital stays are getting shorter and shorter, and a lot of people now go from the hospital to skilled nursing facilities. How do you match the patient to the right facility? Right now, it’s an ad hoc procedure. With our sophisticated machine learning technology, we help providers be more efficient in matching patients with both therapies and institutions. They enter information about the patient and our tool tells them what facility we think will result in the lowest probability of readmission and shortest predicted length of stay. Our clients are the hospitals, but indirectly they’re also the patients. Increasingly these are decisions that are made together by the providers and the patients—and the payers as well—and it should be an informed decision.

Extracting insights

My group is working with Massachusetts General Hospital (MGH) on infection control. There are certain kinds of infections that exist more strongly in clinical environments than in the population at large. One of the most common is an intestinal infection called Clostridium difficile. In the US, about 1% of inpatients...
contract this. It has serious complications, and it’s very hard to treat. The spores can live a long time outside the human body and are not killed by typical room cleaning procedures, so it’s very tricky. We’re working with MGH, using many years of medical records, to build models predicting who is most likely to get infected so that preemptive actions can be taken. Going forward, we’re also trying to understand the source of the infection. I think we’re going to be able to have a real impact on MGH, and also, I hope, show how you can do this more generally.”

DAHLEH: “The complexity of many current systems stems from the interaction between people, institutions, and engineered systems. Such interactions have become much more interesting as mobile devices have allowed people to assess the state of the system and react to it. Think of Google Maps and how it impacts the patterns of congestion; high velocity trading and how it impacts the fragility of the financial system; or the continuous monitoring of people’s vital signs from smart watches and devices—an unprecedented opportunity for both risk analysis and intervention. In order to correctly predict future behavior and mitigate risks, it is essential that models incorporate both the physical protocols and people’s patterns of behavior on the system.”

PENTLAND: “A sea change would be to move from a disease system—when you get sick, you engage with the system—to a health system. Recognizing early signs, understanding how to take care of yourself: Doctors don’t know what you do 99% of the time. Now, using things like cell phones and credit cards, you could make a map of your life: when did you get up, how many people did you talk to, how far did you walk, what did you eat, how much sunlight did you get? Over time, these are excellent predictors of quality of life, which is perhaps the best measure we have of how healthy you are. These are not complicated things. But we never had the data before. This insight led to my cofounding both Ginger.io [see page 14] and CogitoHealth.com.”

“Students in my course on econometrics for managers tell me they want to be able to speak to data scientists,” Doyle says.

Educating for impact

DAHLEH: “Decision theory has a new challenge, namely co-designing the feedback control system for the physical system (e.g., management of health care protocols) and simultaneously designing incentive mechanisms, like subsidized fitness programs, for people to maximize social benefits. More so, higher-level decisions become extremely important in setting various policy questions, such as 30-day hospital readmission policies. This particular view is now reflected in our newly designed PhD program on Social and Engineering Systems. The objective is to educate the new generation of students to be deeply knowledge-able with engineering, social, and economic principles as they approach societal challenges.”

DOYLE: “At Sloan, we’re starting a master’s program in data analytics. There’s been an explosion of interest among students regarding how to evaluate credible arguments. Students in my course on econometrics for managers tell me they want to be able to speak to data scientists. It’s exciting that we have a lot more data-literate people — and that includes doctors, patients, and payers, who have to recognize value when they see it. This is the time to be a health economist, especially a data-driven one.”

GUTTAG: “If you look at resumes of thought leaders around the country, an awful lot of them have MIT pedigrees. First and foremost, MIT is an educational institution. Our research certainly has an impact, but our graduates have a bigger impact. I think computer science is going to revolutionize medicine — so there’s a group of us trying to train the next generation, not just of data scientists but health care data scientists. Health care data are not like the data that you see at Amazon, or Google, or Facebook. These data are very different, and learning how to derive actionable information from them is not easy. We’re working hard to figure out better ways to do it, and better ways to educate our students, because they’ll really be the ones who will transform medicine.”
Data into Action

Medical tech entrepreneur and investor
Zen Chu on the digital reinvention of health care

“Health care today is similar to the Internet in 1995 with respect to its digital and business model transformation,” says Zen Chu, senior lecturer in health care innovation at MIT Sloan School of Management and Harvard-MIT Health Sciences and Technology program. “Health care research and redesigned products are being transformed by new sources of data, new tools for analyzing that data, and new services for putting that data into action in real time.”

Chu has served as founding CEO of three health care companies and has helped to build many more in his role as venture investor for AccelMed Ventures. Chu is also the cofounder and lead faculty advisor of MIT’s Hacking Medicine Initiative, which has taught more than 10,000 health professionals, engineers, and entrepreneurs a process for tech-centric health care innovation, culminating each year in a “Grand Hack” on the top floor of the MIT Media Lab. In 2016, one of the Grand Hack’s three tracks was the data-focused “Connected Health” (sponsored by InterSystems, a pioneering company in the data/health space founded by Phillip T. Ragon ’72).

We asked Chu to explain how harnessing data can reinvent health care, and how MIT researchers and entrepreneurs are leading the way. –Kara Baskin

Digital health has been a hot category of global entrepreneurship, with more than $8 billion in venture funding invested in each of the past two years. What’s your view of digital health?

ZC: The digital transformation of health is one of the most significant shifts in the history of medicine. When people ask me to explain digital health, I say it’s not just the Silicon Valley model of “faster, better, cheaper.” It’s not enough to digitize everything. It’s about society’s broader goals of increasing access, convenience, better patient experiences, and trust. Redesigning fundamental health experiences can improve trust, behaviors, and patient satisfaction.

Many clinicians and public health professionals want to be a part of the solution in health care, but that doesn’t mean more care. Optimal health systems must focus limited resources on increasing access, increasing quality, and decreasing cost. The digital transformation of health care and tech-enabled services can simultaneously impact all three aims.

We hear a lot about big data being used in health care. Where is it applied?

ZC: Take Arsenal Health, also known as Smart Scheduling, which came out of Hacking Medicine and was acquired by Athenahealth. One of the attendees said, “My wife is a doctor, and her days are governed by her schedule: Either everyone shows up, and she runs two hours late, or nobody does. Why can’t we have the Ozzy Osborne patient scheduled with the reliable grandmother so it averages out?”

A team of MIT engineers said, “Hey, this is a supply chain optimization issue, and we know how to do that.” They mined a deidentified patient data set from Athenahealth to pinpoint no-shows or habitual cancellers and optimized schedules based around these patterns; for instance, by double-booking with a reliable patient to cause minimal disruption.

Can you give another example of a company maximizing new sources of real-world data?

ZC: Ginger.io is a great example, started by two MIT grad students [Anmol Madan SM ‘05, PhD ’10 and Karan Singh MBA ’11] with no health care experience but with fresh insights from Sandy Pentland’s group at the Media Lab. They viewed the smartphone as a set of sensors and developed algorithms to predict episodes of depression, based on behavioral data like how many calls you made, whether you left your
More than $100 million in venture funding has gone into startups that emerged at MIT from HST.978 Healthcare Ventures and Hacking Medicine.

You co-teach a class called HST.978 Healthcare Ventures. What does it cover?

zo: Our class serves as an action-learning lab to teach entrepreneurial techniques amid the complexities of health care innovation. It grew out of the Hacking Medicine process and allows us to take teams deeper during a full semester. We teach them how to be intentional about business models, choosing and using only the data that are predictive of a real effect in the real world. It’s not enough to invent something; it has to impact the real world. More than $100 million in venture funding has gone into startups that emerged from this course and Hacking Medicine.

How are MIT students and faculty equipped to creatively improve health care?

zo: MIT has an amazing culture of engineering and applied sciences. If there’s any industry that needs more engineers, it’s health care. As Edward Roberts, our famous entrepreneurship professor, says: “Impact equals invention times commercialization.”

At Hacking Medicine, we’ve emphasized that health professionals cannot shy away from addressing business models in the redesign of health care.

MIT and Boston are at the center of this transformation. MIT doesn’t have a medical school, but our focus on health and technology has an outsized impact on health care. There is no other place on Earth with this concentration of basic research, world-class clinical institutions, and company R&D centers from high tech, biotech, pharma, and med tech.

We believe that students outside of medical and life sciences can contribute to the noble mission of health care innovation. Many inventions and ventures will be founded by engineers with fresh eyes on the massive problems in health care. This is the best time in the history of medicine to be an innovator focused on human health.

Data-driven Spinouts with Big Impact

The combination of expert MIT faculty and entrepreneurial MIT students and alumni is a powerful one. Young companies with MIT origins are leveraging data to improve human health in bold, creative ways—spanning such areas as insurance plans, neurological research, and drug development, as these three examples illustrate.

Benefits Science Technologies

Spun out of MIT in 2012, Benefits Science Technologies (BST) takes a three-pronged approach—descriptive, predictive, and prescriptive analytics—to helping companies optimize their health plans in a way that benefits both employer and employee. BST analyzes complex data on companies’ current health care spending and provides insights on the efficacy of the health care plan. Then, it predicts employees’ future health care costs, and based on these predictions optimizes the design of the health plan. The company’s science team is led by longtime MIT faculty member Dimitris Bertsimas SM ’87, PhD ’88, the Boeing Leaders for Global Operations Professor of Management at MIT Sloan, who co-directs MIT’s Operations Research Center.

LeafLabs

Among the ambitious computing challenges being tackled at LeafLabs, founded by MIT alumni in 2009, is how to wrangle one of the biggest data producers in the world: the brain. In collaboration with the MIT Media Lab’s Synthetic Neurobiology group—which is led by professor of biological engineering and brain and cognitive sciences Ed Boyden ’99, MNG ’99—LeafLabs has created Willow, a system for collecting and storing massive amounts of neural data. The system can process and store thousands of channels of electrophysiological data. This enables researchers to observe the activity of entire populations of neurons as they study crucial topics such as development and cognition, as well as brain diseases such as Alzheimer’s, epilepsy, and depression.

Tamr

The path from clinical trial to FDA approval of new drugs and devices is lengthy and complicated. Spun out of the work of MIT CSAIL’s Turing Award–winning faculty member Michael Stonebraker in 2013, Tamr is shortening the path of clinical data conversion to standardized (CDISC) format through a combination of machine learning and human guidance. Tamr’s solution aggregates, cleans, validates, and converts study data into the submission standards mandated by the FDA, reducing data prep time by 85% to 90%. When CDISC standards are changed, Tamr updates older submissions to match new requirements. Tamr recently made headlines by offering to lend its technology and expertise to the White House Cancer Moonshot Task Force, free of charge.
Descending to water level to collect and filter individual sewage samples, this slim robot is designed for quick assembly from off-the-shelf parts. Its pumping mechanism has been validated to produce the same microbiome data as manual collection and filtration in the lab.

Groups of MIT researchers banded together in 2015 to develop a “smart sewage platform” for collecting and analyzing information about the bacteria, viruses, and chemical compounds that live in the human gut and converge in our communal wastewater. Tapping into this real-time data can help monitor urban health patterns, shape more inclusive public health strategies, and push the boundaries of urban epidemiology. This fall, the team is sampling sewage as a proof of concept in 10 locations across Cambridge and Boston, Massachusetts, as well as Kuwait City.

The Underworlds team imagines a future where data mined from sewage informs public health action. The likely first application is contagious disease monitoring and prediction. Other applications could include tracking biomarkers for diseases such as obesity and diabetes, or creating a biobank of antibiotic-resistant bacteria.

Analysis begins at the Underworlds Lab.
city of Cambridge, a team of MIT biologists and urban planners, their intrepid robot Luigi, are tapping into a vast reservoir health and behavior. Illustration by Mark S. Fisher

Ibuprofen, normalized to urine content of samples

Observation: Presence of ibuprofen peaks at 3 a.m.
Context: Clearance time of drug from body is 2-3 hours.
Implication: Ibuprofen use peaks around midnight.
Hypothesis: Do people consume ibuprofen to aid sleep?

- ibuprofen-glucuronide
- flow rate (millions of gallons per day), averaged over 15 weekdays
- +/-1 standard deviation

Wastewater data can be noisy and hard to interpret. The Underworlds team takes hourly samples at a single manhole to better understand the daily dynamics of the system.

Viral genomes sequenced to identify strains and new mutations

Public health authorities disseminate recommendations

Medical providers adjust treatment

Underworlds was pioneered at MIT by the Senseable City Lab in the Department of Urban Studies and Planning, and the AI Lab in the Department of Biological Engineering, led by faculty members Carlo Ratti and Eric Alem, respectively. The project manager is Neha Shaib. Collaborating MIT groups include the Computer Science and Artificial Intelligence Laboratory, Ramseyer Lab, Poli Lab, and the China Research Group. The project is sponsored by the Kavli Foundation for the Advancement of Sciences through the Kavli-MIT Center for Biomedical Innovation and the Environment. Learn more: underworlds.mit.edu
Intensive Analysis

A clinical database of unprecedented scope opens new avenues for improving critical care

It’s one thing for data to be captured, and quite another for them to surrender their secrets. Hospital intensive care units (ICUs) are a case in point. They generate an abundance of information about their closely monitored patients: vital signs, medications, lab results, providers’ notes, fluid balance, diagnostic codes, imaging reports, and more. Of course, this information is tracked primarily because it can make a life-or-death difference in steering an individual patient’s care. But through the application of data science and machine learning technology, it has the potential to improve the quality of intensive care as a whole.

Led by Roger Mark ’60, PhD ’66—Distinguished Professor of Health Sciences and Technology and of Electrical Engineering and Computer Science—MIT’s Laboratory of Computational Physiology (LCP) has unlocked the aggregate power of such data, by building and maintaining the Medical Information Mart for Intensive Care, or MIMIC. The most accessible database of its kind, MIMIC archives clinical data going back to 2001 from nearly 60,000 patient stays in intensive care units at Boston’s Beth Israel Deaconess Medical Center (BIDMC), where Mark is senior physician. The updated version released last year, MIMIC-III, is the culmination of a decade-long collaboration among that hospital, MIT, and Philips Healthcare, with support from the National Institute of Biomedical Imaging and Bioengineering.

Among the challenges the project faced early on was the hospital’s switch to a new information system. Data elements such as blood pressure or laboratory results have had to be mapped across incompatible systems. Leo Anthony Celi SM ’09, a LCP research scientist and BIDMC physician, ruefully labels such clean-up work “the bane of medical informatics.” In fact, the goals of LCP, which is part of MIT’s Institute for Medical Engineering and Science, begin rather than end with the onerous task of curating MIMIC’s data. The group’s interest in the ICU is tied to the acute need for
reproducible studies that support best practices in that space. Decisions about treatments or interventions for critically ill patients can vary widely, often based on an individual clinician’s training, knowledge, and habits.

Several of LCP’s researchers have medical backgrounds like Mark and Celi; others have expertise in computer science, electrical engineering, physics, mathematics, or some combination thereof. Pooling their expertise, teams of clinicians, engineers, and scientists design studies using MIMIC that evaluate variations in clinical practice, weigh the effectiveness of diagnostics and therapies, and create predictive models for patient outcomes.

“Our group has engendered a cross-disciplinary research ecosystem around MIMIC with activities such as ‘datathons,’ and an upcoming fall course on secondary analysis of health records that will be streamed live online.”

Working with MIMIC: Two Student Perspectives

SuperUROP, launched in 2012, is an expanded version of MIT’s Undergraduate Research Opportunities Program (UROP). Hosted by the Department of Electrical Engineering and Computer Science and now open to students throughout the School of Engineering, the yearlong program provides students the opportunity to partner with faculty on publication-worthy research. In 2015, Erin Hong and Aaron Zalewski worked with the MIMIC database under faculty advisor Roger Mark. Now seniors, they revisit the goals they stated going into last year’s SuperUROP experience, and reflect on what they learned.

Erin Hong ’17
Actifio Undergraduate Research and Innovation Scholar

**Before:** “I plan to expand the database….While merging data sets, I will have to account for gaps in the database due to flawed data and different hospital information formatting, all while finding the best way to capture and communicate implicit information to researchers….I hope to learn how to study and manipulate data through the eyes of a clinical technician and with the mind of an engineer.”

**After:** “Before working toward building a federated data model for heterogeneous electronic health records (EHR), I naïvely dedicated a few weeks of my work to read over system documentation and understand the organization of several EHR schemas. Soon enough, I was daunted by the low quality in electronic health system documentation, erroneous data, and vast amounts of unmapped implicit knowledge. These observations not only pointed to the lack of standardized health record systems but also indicated how difficult consolidating various data sets was. Building a federated data model and fully understanding the distinctions of individual data sets therefore necessitated a more stepwise approach….Since the end of my SuperUROP program, I have joined a team of oncologists, roboticists, computational biologists, and engineers as an intern at Driver, a cancer genomics company whose mission is to provide patients access to clinical trials.”

Aaron Zalewski ’17
Angle Undergraduate Research and Innovation Scholar

**Before:** “We will analyze data from physiological time series by using machine learning algorithms to predict patient mortality and the likelihood of the patient developing sepsis. We will model physiological time series using machine learning techniques to discover ‘clusters’ of time series segments with similar trajectories and transient dynamics. Our goal is to identify prototypical temporal patterns from vital sign time series that we can use to generate early warning signs to alert doctors of patients with worsening conditions.”

**After:** “While the MIMIC database has done a great deal to simplify working with ICU data, dealing with inconsistent frequencies in the measurement of patient data was a particular challenge. It’s difficult to determine the best way to standardize and then analyze patient data when the raw data aren’t uniform. I ended up solving this problem by using interpolation and some custom-made feature vectors to generate the input for my clustering algorithms….The biggest thing I learned is that how you process the data beforehand is just as important, if not more important, than the algorithms that you use to analyze those data.”
“This type of research is one of the building blocks of precision medicine.”

— Nicole Estvanik Taylor

globally free of charge,” says Celi, adding that the group will publish an open-access textbook to coincide with the course.

LCP’s computer scientists have stripped MIMIC’s data of patient-identifying characteristics in accordance with Health Insurance Portability and Accountability Act (HIPAA) standards—the key to providing colleagues around the world with entrée to its treasures.

More than 2,500 credentialed researchers from some 32 countries have signed a basic data-use agreement to gain full access to MIMIC since it first became widely available in 2007. A subset of the data—consisting of multichannel waveform recordings of physiologic signals and vital signs sampled hundreds of times each second—is available to the public without restrictions, and heavily used for education as well as research, including in Health Sciences and Technology coursework at MIT itself.

Despite its unprecedented scope, the fact that MIMIC taps into the data of a single hospital does put a caveat on the findings that can be gleaned from it. “The use of a single-center database is always problematic in that the findings may only apply to patients at BIDMC and may not be generalizable to other intensive care unit populations,” Celi notes. Last year, Philips and LCP launched a new, separate database compiling close to 3 million ICU admissions from across the US. Researchers may apply to Philips for use of that full database, but the team plans to publicly release a subset representing 200,000 admissions.

Meanwhile, plans to expand MIMIC are international in scope. According to Celi, the researchers are in discussion with colleagues building similar ICU databases in the UK, France, Belgium, Brazil, and Greece.

Even in its current form, MIMIC has produced an average of one publication per month over the past three years. “There have been a number of findings that have changed the way I and my colleagues practice in the intensive care unit,” says Celi. “For example, we learned that in the 10-year period covered by the database, not a single patient with advanced liver disease who required dialysis during his or her hospitalization has survived to discharge. We previously viewed kidney failure as a complication that we can treat with dialysis while the patient recovers from an acute illness. It turns out that among those with advanced liver disease, it is a marker of unsurvivable critical illness. This information is powerful when we discuss goals of care with these patients and their families.

“We have evaluated numerous interventions in the intensive care unit that have been widely implemented with little evidence that they improve outcomes—arterial catheterization for invasive blood pressure monitoring, echocardiography to assess heart function, routine blood testing—and found that their effect varies across patient subsets: some benefit and some are harmed,” he continues. “This type of research is one of the building blocks of precision medicine. We are now in the process of creating decision-support tools based on our findings.”
Collectors’ Items
A closer look at two next-generation devices for capturing medical data

Arterial blood pressure waveform monitor

Team
Joohyun Seo SM ’14 and Sabino Pietrangelo SM ’13, graduate students, Department of Electrical Engineering and Computer Science
Hae-Seung Lee, Advanced Television and Signal Processing Professor of Electrical Engineering; director, Center for Integrated Circuits and Systems
Charles Sodini, Clarence J. LeBel Professor of Electrical Engineering; co-director, Medical Electronic Device Realization Center

Size
Portable ultrasound monitor: 14.7 cm × 13.2 cm; transducer: 2.5 cm × 5 cm × 5 cm

Purpose
Use ultrasound to take a comprehensive measurement of blood pressure at the carotid artery.

How it works
When arterial blood pressure (ABP) is measured at an ambulatory clinic, it’s usually recorded as two numbers. The higher of the two represents the pressure in the arteries when the heart muscle contracts; the lower marks the pressure when the muscle rests between heartbeats. In reality, of course, there are many data points in between these “systolic” peaks and “diastolic” lows. This monitor is designed to capture the pressure waveform (i.e., the blood pressure as a function of time). The device collects the data noninvasively, without squeezing or blocking the artery, by using ultrasound to continuously measure the artery’s cross-sectional area and elasticity.

Status
In 2015 the device was tested on nine healthy subjects, and the results of the clinical study—validating the potential of the approach—were published. The next step is to make the measurements insensitive to mispositioning of the transducer, which would lower the level of skill required to operate it. Its creators are also considering miniaturization of the components for implementation as a wearable device.

The big picture
The use of a portable ABP waveform monitoring device—less expensive and less risky than the current practice of measuring ABP at central circulatory sites through arterial catheterization—could improve routine monitoring of hypertensive patients. The massive new data sets it could provide to researchers would also open the door to greater understanding of cardiovascular disease and other health conditions.

Miniaturized, biopsy-implantable chemical sensor

Team
Michael Cima, David H. Koch Professor in Engineering in the Department of Materials Science; investigator at the Koch Institute for Integrative Cancer Research
Vincent Liu SM ’09, PD ’14, PhD ’14, MIT postdoc (former)
Christophoros Vassiliou ’04, MNG ’06, PhD ’13, MIT postdoc (former)

Size
2.2 mm in diameter; 6 mm in length

Purpose
Provide ongoing information about cancerous tissue’s chemical response to treatment.

How it works
The sensor is designed for long-term implantation in a tumor by means of a biopsy needle, in order to collect longitudinal data related to two biomarkers: pH and dissolved oxygen. The data are actionable. For example, decreased acidity of cancerous tissue is an indication that chemotherapy is working; and low-oxygen levels can signal the need to increase radiation therapy. The sensor is filled with responsive nuclear magnetic resonance contrast agents for chemical sensitivity, similar to those used in magnetic resonance imaging (MRI). The device contains onboard circuitry and sends its data wirelessly to an external reader device, on which it relies as a power source through a magnetic process called mutual inductance.

Status
In July 2015 the team published a paper in the journal Lab on a Chip summarizing its work on the sensor; currently, it is engaged in building a clinically acceptable reader device.

The big picture
As an alternative to MRI, the sensor could enable less expensive and more frequent measurements. Real-time data help doctors make nimble adjustments to therapies and drug dosages, rather than waiting months for an indication of whether treatments are working. The data also help them see past misleading symptoms such as inflammation, which can make tumors falsely appear to grow. The bottom line for cancer patients is a shot at better outcomes with fewer unnecessary side effects.
Wearable sensors may soon know us better than we know ourselves—and that is both tremendously exciting and a cause for caution, according to MIT experts who study the technology and its implications.

“While we still can’t measure your thoughts, and I think that’s a good thing, we can measure manifestations of them,” says Rosalind W. Picard ScD ’91, founder and director of the Affective Computing Research Group at the MIT Media Lab, and cofounder of Empatica, a company that sells wearable devices to medical researchers and to consumers for monitoring their personal health. “If you’re not getting good sleep or physical activity. If you’re not getting out of your dorm or apartment. Those can be early warnings that you’re physically sick or that your mental health is not where you want it to be.”

Wearable sensors are moving health care closer to personalized treatment regimens, real-time patient monitoring, and earlier detection of serious conditions. However, collecting data from new, unregulated sources that can reveal activity levels, mood, and more also raises questions about how all these data will be used.

“Why should you have to deal with a recommendation that is for some average group of people, when almost nobody is that average person?” Picard says.

asks Kenneth Oye, director of MIT’s Program on Emerging Technologies, who has spent decades studying and influencing technology policy.

Today, most consumer wearables are fairly limited, mainly tracking movement. The wearable sensors developed in Picard’s lab and by Empatica, however, use software that can track a much wider range of signals. In addition to gathering accelerometer data, these more sophisticated sensors can track gyroscope data, temperature, and skin conductance—from which researchers can derive heart rate, heart rate variability, respiration, and even posture. By collecting such data from a broad spectrum of people and combining them with user input (shared with permission) and advanced computer analytics, researchers are gaining a nuanced understanding of how the technology records different moods and behaviors.

“We are building tools that will allow people to see if behaviors in their life related to their physical activity, their stress, their sleep, are impacting their mood or not,” Picard says, noting that the devices often detect signs of stress before users do. “I liken it to your personalized weather forecast.”

Such information can prompt individuals to make behavioral changes, but there are wider benefits. Gathering and analyzing such data could help health care professionals to better personalize their advice, and manufacturers to custom-tailor drugs. “Why should you have to deal with
While US law protects against discrimination by health insurers, such rules don’t currently apply to life insurance or disability coverage, he notes. “Now the simple technology that we have in our phones and in other locations is being used by doctors and nurses to improve the quality of the practice of medicine by prompting follow-ups.”

At a more basic level, the electronics we carry with us already provide a tool for medical professionals to enhance patient care. “Doctors all say the hardest part of practicing medicine is behavioral. Physicians will tell us to do stuff, but we don’t,” Oye says. “Now the simple technology that we have in our phones and in other locations is being used by doctors and nurses to improve the quality of the practice of medicine by prompting follow-ups.”

However, Oye points out that such societal benefits need to be weighed against individual concerns about how all the data that can be collected will be used. “There are very strong concerns that the information that you’re providing could be used against your interests,” says Oye, who is also an associate professor of political science. While US law protects against discrimination by health insurers, such rules don’t currently apply to life insurance or disability coverage, he notes.

As a first step to address such concerns, both Oye and Picard recommend that technologists educate both the public and the policy-making community about the capabilities of wearable devices. “This is an area where relatively open access to the technologies developed, how they’re being used, is critical,” says Oye. “There’s a public interest in having information to be able to evaluate, and adapt, and adjust.” — Kathryn M. O’Neill

DataHub for Smarter Sharing

Last year, the MIT Computer Science and Artificial Intelligence Laboratory (CSAIL) teamed up with MIT Medical to develop an iPhone app called getfit@mit. The app was used by about 600 of the 2,000 participants in the 2015 getfit@mit challenge, an annual on-campus program sponsored by MIT Medical, to log details of their fitness activities—including type, duration, and location—and analyze their progress via charts and graphs. On its surface, the product resembled any number of existing commercial apps for tracking exercise and other personal metrics. But its backend holds great potential for how health and wellness data may be handled in the future.

The getfit@mit app was built on a new platform called DataHub, which was developed at CSAIL by PhD candidate Anant Bhardwaj and his advisors, professors David Karger and Sam Madden ’99, MNG ’99. This hosted database system and interface allows users to freely own, edit, share, and delete their data. In the words of its creators: “Think of it as a mashup of [version control software] GitHub and [relational database] PostgreSQL, accessible through your web browser.” The MIT Big Data Living Lab at CSAIL conducted the getfit@mit project as one of its on-campus pilot programs exploring the platform’s technical and social implications for data collection.

This past June, DataHub was released as open source under the MIT License to enable continued innovation by others. Stephen Buckley, director of the Living Lab, sees significant opportunities for those who manage electronic medical records. “DataHub could help health care providers to allow their patients to more easily and privately share their information across different networks,” he says. For example, a patient referred to an orthopedist by his primary care physician could allow that specialist to view related x-rays and other diagnostic information, without granting access to the entire health record. This ability would enhance patient privacy, while reducing risk for physicians when it comes to maintaining regulatory compliance in protecting patient information.

Possibilities like this lie at the heart of the Living Lab, says Buckley: “We want to help accelerate the pipeline of innovation coming out of MIT so that people can use it to solve problems out in the real world.” — Genevieve Rajewski
Astrophysicist Anna Frebel studies the oldest stars for clues about how the universe was formed.
The Las Campanas Observatory is perched atop a barren mountain ridge 8,200 feet above the Atacama Desert in southern Chile. Equipped with two 6.5-meter, single-mirror Magellanic telescopes, the remote facility offers astronomers splendid and unobstructed views of the star-rich southern sky. Which is what draws Anna Frebel and her team of graduate students and postdocs to travel there several times a year from MIT; the Institute is a partner in the observatory.
“In the evening, after dinner, our whole group meets on the catwalk at the telescope to watch the sunset,” says Frebel, the Silverman Family Career Development Assistant Professor in MIT’s Department of Physics, and a member of the Kavli Institute for Astrophysics and Space Research. “It’s a beautiful ritual. Then, once the sun goes down, we get to work observing the stars until morning.”

Anna Frebel is a leading light—one is tempted to say a rising star—in a new generation of astronomers who call themselves “stellar archeologists.” Frebel studies metal-poor stars—stars whose percentage of heavy elements, known in astronomy as “metals,” is significantly lower than that of our sun. Metal-poor stars are some of the oldest stars in existence, and contain precious information about the early universe and the origins of the matter that composes the universe. Like scientists sifting through ruins of past civilizations to understand our human past, stellar archeologists analyze these ancient stars to sketch the history of the universe.

“Every star in the universe contains a record of the elements in the gas cloud out of which it was formed,” says Frebel, who joined the MIT faculty in 2012. “When we analyze the contents of these metal-poor stars, which were formed in the first billion years after the Big Bang, we’re unearthing a record of a significant period in the early universe. And from this record, we can begin to reconstruct how our universe took shape, how galaxies formed, and how nature, in this amazing way, creates the elements that compose the stars, the planets, and even our bodies.”

As Frebel explains in her recently published book, Searching for the Oldest Stars: Ancient Relics from the Early Universe, the first stars emerged out of giant clouds of gas approximately 13.5 billion years ago, a few hundred million years after the Big Bang. Composed only of hydrogen and helium—with trace quantities of lithium—these first stars were massive and not particularly dense. They burned for a scant few million years, generating energy by fusing hydrogen and helium into heavier elements such as carbon and oxygen in their cores. Then they exploded as supernovae, spewing these heavier elements into the interstellar medium. With their superior cooling qualities, these newer elements enabled the formation of smaller, denser stars—of the kind Frebel and colleagues are studying—with lifespans measuring into billions of years. The ongoing nuclear reactions in the cores of these stars produced increasing amounts of elements heavier than hydrogen and helium.

With the exception of hydrogen and helium, which were formed by the Big Bang, all of the elements in our universe were synthesized by stars—including iron, one of the principal components of our planet, and carbon, the basis of all life on earth. (The formation of elements heavier than iron requires either an extraordinary stellar event, such as a supernova explosion or neutron star merger, or a particular late stage in the life of lower-mass stars.) The production of elements continues. When our sun was born some 4.6 billion years ago, heavy elements constituted about 1.5% of the matter in the universe. Today they account for close to 2%.

The goal of stellar archeologists is to answer fundamental questions about the origins and evolution of the universe. What elements were present 300 million years after the Big Bang? At what point were there sufficient quantities of heavy elements to form galaxies and planets? Where does the carbon that forms the basis of life on Earth originate? “By analyzing the different chemical and physical processes involved in this evolution,” writes Frebel in her book, “astronomers can inch their way closer to understanding the nature of the whole universe.”

Frebel’s precise, painstaking quest for knowledge begins with a thorough examination of large sky surveys—photographic and photometric surveys of large swaths of the night sky, like the Sloan Digital Sky Survey or the Hamburg/ESO Survey—to identify potential objects of interest. Once identified, these objects are reexamined with medium-resolution spectroscopy, and, if still of interest, through high-resolution spectroscopy. Spectroscopy analyzes the light that emanates from a star’s core and passes through its outer shell, where most of the star’s metals reside. Each heavy element on the outer shell absorbs a specific wavelength of light. The light that emerges produces a spectrum much like a chemical fingerprint that identifies each element present in the star. The spectra appear on screens during observation times at Las Campanas.

Each new metal-poor star constitutes a piece of the puzzle scientists like Frebel are trying to put together. “It’s amazing that we can even begin to gather evidence to try and answer these fundamental questions about the universe,” says Ani Chiti, a second-year graduate student who came to MIT specifically to work with Frebel. “And it’s mind-boggling that we try to answer them by staring at tiny points of light in the sky.”

Educated both in Germany—where she was born in 1980—and in Australia, Frebel first drew international attention with her PhD thesis, which she completed in 2006 at the Mount Stromlo Observatory at the Australian National University (ANU). Sifting through data from close to 2,000 stars, Frebel identified two immensely significant objects: HE1523-0901, which is one of the earliest stars ever observed and contains significant quantities of thorium and uranium; and HE1327-2326, the most chemically

Previous spread: Frebel studies stars residing on the halo of the Milky Way, visible here above Chile’s Las Campanas Observatory. PHOTO: YURI BEITSKY

“As humans, we have a strong urge to bridge heaven and earth, to connect the dots around us.”
primitive object observed to date, with an iron content more than 100,000 times lower than the sun’s. The thesis was awarded the Charlene Heisler Prize by the Astronomical Society of Australia.

“It’s true that Anna was perhaps more lucky than we might have dared to hope,” says John Norris, her PhD supervisor at ANU, and now a close colleague. “But what was truly impressive was the manner in which she took the opportunity these objects presented to obtain high-resolution spectra and unlock their secrets.”

“She has a clear idea of what questions are important, and an uncanny ability to synthesize the answers,” says Alex Ji, a fourth-year graduate student in Frebel’s group, who cites his mentor’s contagious enthusiasm as well as her “superhuman” focus. “I don’t think I would have been interested in stars were it not for her.”

In addition to her research in metal-poor stars, Frebel and her group are investigating ultrafaint dwarf galaxies, which can yield information about how the Milky Way galaxy and its extended halo were formed. “Stars tend to be formed in these ultrafaint dwarf galaxies,” Frebel explains. “They then ride these small galaxies like a gondola into larger galaxies, where they are disbursted and absorbed.” Frebel and her group have also created a large supercomputing project, Caterpillar, in collaboration with MIT physics professor Mark Vogelsberger, to simulate this galactic assembly process.

Frebel says she always knew astronomy was what she was born to do. “As humans, we have a strong urge to bridge heaven and earth, to connect the dots around us. I have a two-year-old son, and I’m waiting for the day very soon when he starts to ask ‘why’ about the things he sees around him. My work is just the grown-up version of his ‘why’.” — Ken Shulman

“What is true for bones is also true for human language”

When I returned to MIT last year as director of the MIT Press, I was delighted to discover that we had a new book from computer scientist Bob Berwick and the eminent linguist Noam Chomsky on our Spring 2016 list. I had studied with both MIT faculty members in the 1980s, as a Course 9 doctoral student. Their first co-authored book, Why Only Us, is Berwick’s fifth with the MIT Press and Chomsky’s eighth, and builds on years of research on the biological basis of language. This excerpt from Chapter 2 emphasizes that the study of how human language evolved requires a closer examination of what language is for. — Amy Brand PhD ’89

The inference of a biological trait’s “purpose” or “function” from its surface form is always rife with difficulties. [Richard] Lewontin’s remarks in The Triple Helix (2001) illustrate how difficult it can be to assign a unique function to an organ or to a trait even in the case of what at first seems like a far simpler situation: bones do not have a single, unambiguous “function.” While it is true that bones support the body, allowing us to stand up and walk, they are also a storehouse for calcium and bone marrow for producing new red blood cells, so they are in a sense part of the circulatory system.

What is true for bones is also true for human language. Moreover, there has always been an alternative tradition, expressed by [Robbins] Burling (1993) among others, that humans may well possess a secondary communication system like those of other primates, namely a nonverbal system of gestures or even calls, but that is not language, since, as Burling notes, “our surviving primate communication system remains sharply distinct from language.”

Language can of course be used for communication, as can any aspect of what we do: style of dress, gesture, and so on. And it can be and commonly is used for much else. Statistically speaking, for whatever that is worth, the overwhelming use of language is internal—for thought. It takes an enormous act of will to keep from talking to oneself in every waking moment—and asleep as well, often a considerable annoyance. The distinguished neurologist Harry Jerison (1973) among others expressed a stronger view, holding that “language did not evolve as a communication system.... The initial evolution of language is more likely to have been...for the construction of a real world,” as a “tool for thought.” Not only in the functional dimension, but also in all other respects—semantic, syntactic, morphological, and phonological—the core properties of human language appear to differ sharply from animal communication systems, and to be largely unique in the organic world.

Excerpted from Why Only Us: Language and Evolution by Robert C. Berwick and Noam Chomsky, published by the MIT Press in 2016. Copyright Robert C. Berwick and Noam Chomsky. All rights reserved.
More than 150 years ago, Henry David Thoreau pondered the biology of Massachusetts peat bogs, calling them “little oases of wilderness in the desert of our civilization.” He would likely be troubled to learn that today in a wetland named for him, MIT biogeochemist Harold Hemond PhD ’77 is extracting the airborne metals released by industrialized society, including rare earth elements (REEs), increasingly indispensable in consumer electronics, computers, and clean energy technologies.

For Hemond, William E. Leonhard Professor in the Department of Civil and Environmental Engineering, the presence of these substances in Thoreau’s Bog—a body of water he has studied for four decades—is an opportunity to anticipate and perhaps prevent problems as society changes its chemical footprint: “We need to be proactive in understanding what kind of impacts we are making,” he says.

Hemond’s research is part of a novel investigation, supported by MIT’s new Environmental Solutions Initiative (ESI), into the potential effects of REEs on the environment and humans.

“Use of these materials has gone up tenfold in a decade, but there’s been very little testing of their toxicity,” says John Essigmann SM ’72, PhD ’76, the William R. and Betsy P. Leitch Professor in Residence, whose lab straddles the departments of chemistry and biological engineering. “Many materials released in large amounts in the past, like asbestos, DDT, and lead in gasoline, seemed very constructive at the time but ultimately proved destructive to biological systems.” Along with Bevin Engelward, professor of biological engineering, Essigmann became Hemond’s partner on the ESI grant through the activities of the MIT Center for Environmental Health Sciences.

Essigmann and Engelward are studying how these new environmental chemicals might affect human health. This means closely examining Hemond’s bog sediments, which date further back in time as they increase in depth. The sediments are vital records of atmospheric emissions, since this bog is fed exclusively by rainwater.

Measurements by the Hemond Lab reveal a host of REEs, likely released in large part by metal smelting processes. According to a preliminary chronology, these elements barely registered in 1900, but grew through the century and spiked to hundreds of parts per billion by mid-century. Then they began to decline, Hemond says: “Our working hypothesis is that increasing industrial activity put more of these chemicals in the air, and then the 1970 Clean Air Act helped reduce their presence.”

While this appears reassuring, Essigmann finds reason for concern. The bog reflects historic, regional atmospheric concentrations of REEs, so concentrations in regions lacking air regulations, or regions with aggressive mining and manufacturing practices, might currently be much higher. With expanding global use and discard of products incorporating REE-based technologies, concentrations could rise again as REEs find their way into the environment at unprecedented levels.

One element from Hemond’s bog samples drew Essigmann’s particular attention: cerium, now turning up as a fuel additive to make diesel engines burn more efficiently and at lower temperatures. This epitomizes why Essigmann calls REEs “a double-edged sword.” He explains, “On the one hand cerium oxide particles are good for the environment and sustainability, but on the other it’s been discovered that they escape from tailpipes, and we have to worry about the health consequences if we breathe them.” Using technology developed in the Engelward laboratory for measuring DNA damage, Essigmann’s preliminary research indicates that while these particles alone are not very toxic, hydrogen peroxide produced by the body’s inflammatory response to small particles can combine dangerously with cerium oxide. Together, says Essigmann, “they produce a very harsh chemical byproduct that breaks DNA.”

Before drawing conclusions about health impacts, Essigmann and Engelward await ongoing testing by Hemond, which will try to correlate concentrations of REEs taken from air samples with those from rain-fed bogs. “We will be able to tell you based on what you see in a bog anywhere in the world how much people breathe of REEs at any given time,” says Essigmann. Using concentrations typical in countries manufacturing REEs, Essigmann hopes to pursue further tests with these compounds using mouse models. If these experiments demonstrate lung damage, he believes the work might influence regulatory policy.

“Think of our work as due diligence,” says Hemond. “We want to be ahead of the curve this time.”

—Leda Zimmerman
Rosa Lafer-Sousa exhibited her first piece of artwork at age four. She’s been painting ever since — for enjoyment and for the challenge — but it wasn’t until college that put her passion for art together with an abiding interest in science. “Color was the most difficult topic covered in my undergraduate neuroscience classes,” says Lafer-Sousa, a fourth-year MIT brain and cognitive sciences doctoral student. “It is also a challenging aspect of painting.”

Aspiring painters often start by learning to draw in black and white. Color adds complexity. There are variations in hue — the quality most people are referring to when they use the word “color”— but also in saturation and brightness. And the perception of a color changes depending on the surroundings. “The moment you take a color from palette to canvas, it changes based on the colors already there,” says Lafer-Sousa.

The brain’s visual system has specialized neurons to process these phenomena. Signals from the retina separate into parallel tracks representing lines, motion, and color. Deeper in the visual system, the compartmentalization becomes more sophisticated, with regions dedicated to recognizing faces, such as the fusiform face area (FFA) discovered by MIT neuroscientist Nancy Kanwisher ’80, PhD ’86, as well as regions for bodies, shapes, and places.

As an undergraduate at Wellesley College, Lafer-Sousa and her advisor Bevil Conway, a visual neuroscientist and artist, decided to look at how color is processed in these deeper regions of the visual pathway. Using functional magnetic resonance imaging (fMRI) in macaque monkeys, she found that the ventral visual pathway, deep in the visual cortex, is systematically organized into non-overlapping sets of regions that are specialized not only for faces and places, but also for color.

The finding of independent regions so deep in the cortex biased to process color signals was surprising, says Lafer-Sousa, because researchers historically have considered color as a low-level feature of visual input, similar to lines. “The assumption was that by the time you’re in this high-level cortex that deals with objects, color is already bound to form,” she says. “So why do we see a segregation? What are these color signals doing?”

To answer these questions, Lafer-Sousa came to the MIT McGovern Institute for Brain Research to work with Kanwisher, who is the Walter A. Rosenblith Professor of Cognitive Neuroscience. Kanwisher’s longstanding expertise in functional imaging was one draw, but her lab also is exploring novel imaging methods that will allow Lafer-Sousa to study how the brain processes complex visual images, such as faces with different skin tones that convey information about mood or health status.

First, Lafer-Sousa had to determine whether the organization she found in the macaque brain was the same in the human brain. With Kanwisher and Conway, she repeated her fMRI experiment on humans and found the same patterns. “Color regions were neatly sandwiched between face and scene regions, without overlap, mirroring what we saw in the macaque,” says Lafer-Sousa, who published the findings in February in the Journal of Neuroscience.

Her next step involves using diffusion tensor imaging (DTI) to reveal the connections between these specialized regions. The work is on the cutting edge of imaging because the regions are small and close together, but Lafer-Sousa has help. Zeynep Saygin PhD ’12, a postdoc in the Kanwisher Lab, recently had success in using this approach to look at the connectivity of the FFA and the visual word form area, which are as close spatially as Lafer-Sousa’s sandwiched regions.

“I was apprehensive, not sure we’d be able to separate face and color streams, but Zeynep showed you can separate such fine streams and see what’s connected,” says Lafer-Sousa, who will also be working with experts in DTI at Massachusetts General Hospital to do this work. “If it’s possible with these technologies, I’m in a position to do it.”—Elizabeth Dougherty
In May, to mark the launch of the MIT Campaign for a Better World, groups of MIT leaders, faculty, alumni, and students gathered to discuss in detail what the Campaign’s priorities mean in the context of MIT’s ongoing education, research, and innovation. How are we making a difference now? And what will this bold fundraising effort enable us to achieve? Videos of these discussions, including candid audience Q&As, can now be viewed online.

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The MIT Campaign for a Better World hits the road

Alumni and friends are invited to join President L. Rafael Reif for a celebration of MIT, our vibrant global community, and our mission to build a better world.

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The MIT Road

Reza “Rae” Pourian has a document framed on the wall of his Northern California home: his daughter’s acceptance letter to MIT. In the years since that piece of paper arrived in the family’s mailbox, Jessica Pourian ’13 earned a degree from MIT’s Department of Brain and Cognitive Sciences. She gained valuable experience along the way through Undergraduate Research Opportunities Program (UROP) placements at the McGovern Institute for Brain Research, spending time in the labs of Ann Graybiel PhD ’71, who studies the basis of neurodegenerative and developmental brain disorders, and Nancy Kanwisher ’80, PhD ’86, whose group specializes in a brain imaging method called fMRI (see page 29) to build fundamental understanding of how the brain works.

These days, Jessica is attending medical school, pursuing an interest in pediatrics and autism that was sparked by her undergraduate research experience. Meanwhile, work in the Graybiel and Kanwisher labs is moving forward, bolstered by a gift from the Pourian family.

The Pourians have also provided generous unrestricted support to the Koch Institute for Integrative Cancer Research (KI) in support of its mission to confront cancer through the convergence of life sciences and engineering. “It looks like they are truly on the road—I call it the MIT road—to resolve the issue of many, many diseases, not only cancer, through the approach to research they have developed at the Koch Institute,” says Rae Pourian. KI has identified five areas of critical interdisciplinary research: nanotechnology-based cancer therapeutics; novel devices for cancer detection and monitoring; exploring the molecular and cellular basis of metastasis; advancing personalized medicine through analysis of cancer pathways and drug resistance; and engineering the immune system to fight cancer.

According to Pourian, the family’s gift to both the Koch Institute and the McGovern is aimed at supporting scientific discoveries that benefit the health of future generations—“we are the beneficiaries of a lot of pure research done by generations before us,” he says—and also to enhance the education of the current generation of MIT students. This is a factor he witnessed firsthand as an MIT parent: “What MIT offers is a culture of cooperation, opening their hearts and labs to undergraduate students so they can learn cutting-edge research.”

Born in Iran, Pourian came to the United States more than 50 years ago and built a long and varied career in manufacturing, with a focus on the automotive industry. His wife, Julia Madidi Pourian, works in banking, and older daughter Kristin is a practicing physician. He sees a common thread in all of their fields—something he believes his daughter Jessica is well prepared for no matter where her career takes her, thanks to her time in Cambridge. “More than anything else, MIT teaches their students problem solving and teamwork, and in any industry, in any aspect of life, the person who solves problems is the successful one,” he says. “MIT truly trains everybody equally and gives them the confidence to step out there and succeed.”

We are the beneficiaries of a lot of pure research done by generations before us,” says Rae Pourian.

Above: Jessica Pourian ’13, center, with mentor Nune Lemaire Martiros ’08, PD ’16, PhD ’16, left, and Professor Ann Graybiel PhD ’71.
PHOTO: COURTESY OF MCGOVERN INSTITUTE

Below: Reza Pourian, on a recent visit to the MIT campus.
PHOTO: JOHN GILLOOLY
Providing the Opportunity

When Stephen Hoffman ’66 decided to endow a scholarship at MIT, he knew at once whom it should honor. “In your lifetime, you meet very few people like Jim,” he says of the namesake of the James E. Brown III Memorial Scholarship. Not coincidentally, Brown came to MIT on full scholarship. “Aside from being an outstanding student, as well as fulfilling his non-academic workload, Jim always found time to help anybody who asked him for academic assistance,” Hoffman recalls of his friend, who went on to apply his degree in electrical engineering to a career in academia and the oil industry.

This past June, Hoffman returned to MIT for his 50th Reunion. Though Brown, who died in 1992, could not be there, his memory was celebrated in the back room of a Kendall Square restaurant that weekend as it filled with people exchanging lively greetings: Hoffman and his wife, Mindy; Brown’s daughter Emily ’96, in town for her own 20th Reunion; Richard ’66 and Emily Levine, also contributors to the scholarship fund and close friends of Brown; and student Geronimo Mirano and his family. Mirano had been supported throughout his entire four years at MIT as the first Brown Scholar, and was now graduating with a degree in computer science and mathematics.

Hoffman converses in the practical tones of a businessman (he recently retired from the helm of a food and beverage company), but he says he saw the hand of fate in that June encounter: marking his half-century as an MIT alumnus the same weekend Mirano became one, all while MIT celebrated 100 years in Cambridge. And it wasn’t just the timing. If you pictured the ideal candidate for a scholarship in Brown’s name, “Geronimo is that person,” Hoffman says. “He reflects a lot of Jim’s attributes: inquisitive, hardworking, personable. He didn’t just ‘get through’ MIT—he took it very seriously and I think has gotten a lot out of it.”

Mirano, now beginning his master’s of engineering at MIT, says he relished a period of academic exploration before settling on his undergraduate major. He also credits opportunities for research through the Undergraduate Research Opportunities Program (UROP), as well as travel with the MIT International Science and Technology Initiatives (MISTI) program in Japan, for honing his focus.

“I want to develop engineering solutions to real problems,” Mirano says. One of his interests is automating aspects of manual labor to decrease strain on workers “and elevate the engagement people have with their jobs.” To that end, he is working with his master’s advisor, computer scientist Russell Tedrake PhD ’04, on robotic grasp control.

Looking back at Commencement weekend, Mirano says, “It was a highlight for my parents and grandparents to meet the Hoffmans for the first time.” He recalls his own first meeting with them and Brown’s widow, Cathy, and elder daughter Kate: “I remember being floored by their stories about James Brown. To know I was being sponsored in his memory was humbling.”

That’s the kind of reaction Hoffman hopes will continue to inspire the fund’s future recipients for decades to come. “Naming a scholarship is about turning the financial aid transaction between MIT and the recipient into a more personal relationship,” he believes—and not just through donor/student interactions, but in a big-picture sense, by demonstrating someone cared enough to provide the student with an opportunity. Hoffman hopes this might even prompt some recipients to establish a scholarship fund themselves, down the road: “It multiplies, and makes it that much easier for MIT to thrive and help more students.”—Nicole Estvanik Taylor

The Need: Endowed Scholarship Funds

MIT has a long-standing commitment to ensuring access to an undergraduate education. We consider each applicant on merit alone, regardless of his or her family’s financial circumstances. At the same time, we meet 100% of every student’s demonstrated financial need through a mix of loans, work opportunities—and, most crucially, scholarships. MIT embraces this approach because it enables us to admit, retain, and graduate the very best students who will, in turn, create, invent, and sustain a better world.

Endowed scholarship funds play an essential role in the lives of the students they support—and of the Institute as a whole. By reducing MIT’s dependence on the operating budget to fund student aid, scholarship gifts benefit the entire student body by freeing up MIT operating resources for other priorities and strengthening the environment in which all MIT students have come to learn.

DATA FROM 2015–2016

70% of MIT undergraduates receive a scholarship from some source.

24% of MIT’s annual expenditure on undergraduate financial aid ($25M of $103.4M) comes from the general operating budget.
WE LOOK AT THINGS DIFFERENTLY.

An anamorphic sculpture appears distorted from most angles but, viewed from a certain vantage point, it snaps into focus. Look up from the lobby of MIT’s McGovern Institute, and you’ll see a tangle of neurons. Look again from the third-floor atrium, and it comes together: the gleaming outlines of the human brain.