



## RESEARCH SURVEY

### Digital Health Care

Big data, clinical decision-making, health information systems, machine learning, prediction, mobile diagnostic tools, implantable, ingestible, wireless devices, sensors...



## Digital Health Care: Clinical Decision-Making, Machine Learning, Mobile Diagnostic Tools, Ingestible, Wearable Devices, etc.

This survey by MIT's Industrial Liaison Program identifies selected research and expertise in digital health care related to clinical decision-making, data, machine learning, mobile diagnostic tools, and implantable/ingestible and wearable devices, etc.

For more information, please contact MIT's Industrial Liaison Program at +1-617-253-2691.

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## BIG DATA, CLINICAL DECISION-MAKING, HEALTH INFORMATION SYSTEMS, MACHINE LEARNING, PREDICTION

### REGINA BARZILAY

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Regina Barzilay is a Delta Electronics professor in the Department of Electrical Engineering and Computer Science and a member of the Computer Science and Artificial Intelligence Laboratory at the Massachusetts Institute of Technology. Her research interests are in natural language processing, applications of deep learning to chemistry and oncology. She is a recipient of various awards including the NSF Career Award, the MIT Technology Review TR-35 Award, Microsoft Faculty Fellowship and several Best Paper Awards at NAACL and ACL. In 2017, she received a MacArthur fellowship, an ACL fellowship and an AAAI fellowship. She received her Ph.D. in Computer Science from Columbia University, and spent a year as a postdoc at Cornell University.

### Learning to Cure

<http://learningtocure.csail.mit.edu/>

...The majority of cancer research today takes place in biology and medicine. Computer science plays a minor supporting role in this process if at all. We firmly believe that recent advances in machine learning, natural language processing and computer vision can revolutionize cancer care. Data collected about millions of cancer patients -- their pathology slides, imaging, and other tests - - contain answers to many open questions in oncology. We are developing algorithms that can learn from this data to improve models of disease progression, prevent over-treatment, and narrow down to the cure.

We are a group of computer scientists from MIT and physicians from MGH who are passionate about making a real clinical impact in oncology. We started our collaboration over a year ago, learning from each other and exploring the vast space of possibilities in cancer research. This journey was rewarding and productive. Tools we have developed are already deployed at MGH, and we are currently expanding them to process data in other hospitals. These early successes only scratch the surface of opportunities, and we excited to explore where this research will lead.

### High-risk breast lesions: A machine learning model to predict pathologic upgrade and reduce unnecessary surgical excision

Bahl, M., Barzilay, R., Yedidia, A.B., Locascio, N.J., Yu, L., Lehman, C.D., Radiology, Volume 286, Issue 3, March 2018, Pages 810-818, <https://doi.org/10.1148/radiol.2017170549>

Purpose: To develop a machine learning model that allows high-risk breast lesions (HRLs) diagnosed with image-guided needle biopsy that require surgical excision to be distinguished from HRLs that are at low risk for upgrade to cancer at surgery and thus could be surveilled. Materials and Consecutive patients with biopsy-proven HRLs who un-Methods: underwent surgery or at least 2 years of imaging follow-up from June 2006 to April 2015 were identified. A random forest machine learning model was developed to identify HRLs at low risk for upgrade to cancer. Traditional features such as age and HRL histologic results were used in the model, as were text

features from the biopsy pathologic report. Results: One thousand six HRLs were identified, with a cancer upgrade rate of 11.4% (115 of 1006). A machine learning random forest model was developed with 671 HRLs and tested with an independent set of 335 HRLs. Among the most important traditional features were age and HRL histologic results (eg, atypical ductal hyperplasia). An important text feature from the pathologic reports was “severely atypical.” Instead of surgical excision of all HRLs, if those categorized with the model to be at low risk for upgrade were surveilled and the remainder were excised, then 97.4% (37 of 38) of malignancies would have been diagnosed at surgery, and 30.6% (91 of 297) of surgeries of benign lesions could have been avoided. Conclusion: This study provides proof of concept that a machine learning model can be applied to predict the risk of upgrade of HRLs to cancer. Use of this model could decrease unnecessary surgery by nearly one-third and could help guide clinical decision making with regard to surveillance versus surgical excision of HRLs.

### *Using artificial intelligence to improve early breast cancer detection*

**Model developed at MIT’s Computer Science and Artificial Intelligence Laboratory could reduce false positives and unnecessary surgeries.**

Adam Conner-Simons, CSAIL, October 16, 2017, <http://news.mit.edu/2017/artificial-intelligence-early-breast-cancer-detection-1017>

Every year 40,000 women die from breast cancer in the U.S. alone. When cancers are found early, they can often be cured. Mammograms are the best test available, but they’re still imperfect and often result in false positive results that can lead to unnecessary biopsies and surgeries.

One common cause of false positives are so-called “high-risk” lesions that appear suspicious on mammograms and have abnormal cells when tested by needle biopsy. In this case, the patient typically undergoes surgery to have the lesion removed; however, the lesions turn out to be benign at surgery 90 percent of the time. This means that every year thousands of women go through painful, expensive, scar-inducing surgeries that weren’t even necessary.

How, then, can unnecessary surgeries be eliminated while still maintaining the important role of mammography in cancer detection? Researchers at MIT’s Computer Science and Artificial Intelligence Laboratory (CSAIL), Massachusetts General Hospital, and Harvard Medical School believe that the answer is to turn to artificial intelligence (AI).

As a first project to apply AI to improving detection and diagnosis, the teams collaborated to develop an AI system that uses machine learning to predict if a high-risk lesion identified on needle biopsy after a mammogram will upgrade to cancer at surgery.

When tested on 335 high-risk lesions, the model correctly diagnosed 97 percent of the breast cancers as malignant and reduced the number of benign surgeries by more than 30 percent compared to existing approaches.

“Because diagnostic tools are so inexact, there is an understandable tendency for doctors to over-screen for breast cancer,” says Regina Barzilay, MIT’s Delta Electronics Professor of Electrical Engineering and Computer Science and a breast cancer survivor herself. “When there’s this much uncertainty in data, machine learning is exactly the tool that we need to improve detection and prevent over-treatment...”

### Machine learning to parse breast pathology reports in Chinese

Tang, R., Ouyang, L., Li, C., He, Y., Griffin, M., Taghian, A., Smith, B., Yala, A., Barzilay, R., Hughes, K., *Breast Cancer Research and Treatment*, 29 January 2018, Pages 1-8, <https://doi.org/10.1007/s10549-018-4668-3>

**Introduction:** Large structured databases of pathology findings are valuable in deriving new clinical insights. However, they are labor intensive to create and generally require manual annotation. There has been some work in the bioinformatics community to support automating this work via machine learning in English. Our contribution is to provide an automated approach to construct such structured databases in Chinese, and to set the stage for extraction from other languages. **Methods:** We collected 2104 de-identified Chinese benign and malignant breast pathology reports from Hunan Cancer Hospital. Physicians with native Chinese proficiency reviewed the reports and annotated a variety of binary and numerical pathologic entities. After excluding 78 cases with a bilateral lesion in the same report, 1216 cases were used as a training set for the algorithm, which was then refined by 405 development cases. The Natural language processing algorithm was tested by using the remaining 405 cases to evaluate the machine learning outcome. The model was used to extract 13 binary entities and 8 numerical entities. **Results:** When compared to physicians with native Chinese proficiency, the model showed a per-entity accuracy from 91 to 100% for all common diagnoses on the test set. The overall accuracy of binary entities was 98% and of numerical entities was 95%. In a per-report evaluation for binary entities with more than 100 training cases, 85% of all the testing reports were completely correct and 11% had an error in 1 out of 22 entities. **Conclusion:** We have demonstrated that Chinese breast pathology reports can be automatically parsed into structured data using standard machine learning approaches. The results of our study demonstrate that techniques effective in parsing English reports can be scaled to other languages.

### Using machine learning to parse breast pathology reports

Yala, A., Barzilay, R., Salama, L., Griffin, M., Sollender, G., Bardia, A., Lehman, C., Buckley, J.M., Coopey, S.B., Polubriaginof, F., Garber, J.E., Smith, B.L., Gadd, M.A., Specht, M.C., Gudewicz, T.M., Guidi, A.J., Taghian, A., Hughes, K.S., *Breast Cancer Research and Treatment*, Volume 161, Issue 2, 1 January 2017, Pages 203-211, <https://doi.org/10.1007/s10549-016-4035-1>

**Purpose:** Extracting information from electronic medical record is a time-consuming and expensive process when done manually. Rule-based and machine learning techniques are two approaches to solving this problem. In this study, we trained a machine learning model on pathology reports to extract pertinent tumor characteristics, which enabled us to create a large database of attribute searchable pathology reports. This database can be used to identify cohorts of patients with characteristics of interest. **Methods:** We collected a total of 91,505 breast pathology reports from three Partners hospitals: Massachusetts General Hospital, Brigham and Women's Hospital, and Newton-Wellesley Hospital, covering the period from 1978 to 2016. We trained our system with annotations from two datasets, consisting of 6295 and 10,841 manually annotated reports. The system extracts 20 separate categories of information, including atypia types and various tumor characteristics such as receptors. We also report a learning curve analysis to show how much annotation our model needs to perform reasonably. **Results:** The model accuracy was tested on 500 reports that did not overlap with the training set. The model achieved accuracy of 90% for correctly parsing all carcinoma and atypia categories for a given patient. The average accuracy for individual categories was 97%. Using this classifier, we created a database of 91,505 parsed pathology reports. **Conclusions:** Our learning curve analysis shows that the model can achieve reasonable results even when trained on a few annotations. We developed a user-friendly interface to the database that



allows physicians to easily identify patients with target characteristics and export the matching cohort. This model has the potential to reduce the effort required for analyzing large amounts of data from medical records, and to minimize the cost and time required to glean scientific insight from these data.

### **DIMITRIS J BERTSIMAS**

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Dimitris Bertsimas is the Boeing Leaders for Global Operations Professor of Management, a Professor of Operations Research, the CoDirector of the Operations Research Center and the Director of the Master of Business Analytics at MIT.

A faculty member since 1988, his research interests include optimization, stochastic systems, machine learning, and their application. In recent years, he has worked in robust optimization, statistics, healthcare, transportation and finance. Bertsimas was a cofounder of Dynamic Ideas, LLC, which developed portfolio management tools for asset management. In 2002, the assets of Dynamic Ideas were sold to American Express. He is also the founder of Dynamic Ideas Press, a publisher of scientific books, the cofounder of Benefits Science, a company that designs health care plans for companies, of Dynamic Ideas Financial, a company that provides financial advice to customers, of Alpha Dynamics, an asset management company, P2 Analytics, an analytics consulting company and of MyA health, a personalized health care advice company.

### **Algorithmic Approaches to Personalized Health Care**

Principal Investigator: Dimitris Bertsimas

Project Dates: October 1, 2012 – September 30, 2017

[https://www.nsf.gov/awardsearch/showAward?AWD\\_ID=1237136](https://www.nsf.gov/awardsearch/showAward?AWD_ID=1237136)

...This proposal puts forth a comprehensive and systematic approach to intelligently process such data aiming at preventing hospitalization, empowering patients to actively participate in managing their health, assessing quality of care, and facilitating cost-effective epidemiology in the emerging data-rich environment. In the proposed framework, early risk assessment starts with algorithms for mining EHR [Electronic Health Records] and PHR [Personal Health Record] data to classify patients in terms of the risk they have for developing an acute condition that would require hospitalization and/or incur large costs. Risk stratification produced by our approach triggers a set of actions, including tests, additional and more intensive monitoring, and physician involvement. As part of this dynamic health management process, patients can have access to tools that enable their active participation in the daily management of chronic conditions, such as diabetes. Our plans include the development of algorithms that leverage experts' opinions to assess quality of care and the development of a distributed epidemiology approach suitable for the emerging landscape where lots of data about each patient are distributed among many different locations.

The proposed work has the potential to achieve revolutionary improvements in the quality of health care. Risk assessment combined with intelligent management of chronic conditions can prevent acute health episodes and dramatically improve health outcomes. Having rigorous and scalable ways of assessing the quality of care has the potential to reduce medical errors and improve

coordination among health care providers. On the educational front, plans include new courses, training a diverse set of graduate students, involving undergraduate students, actively collaborating with medical doctors, and reaching out to high school students through existing programs embraced by the PIs. Dissemination plans include capitalizing on the BU Sensor Network Consortium and organizing a major medical informatics workshop.

### **Optimal healthcare decision making under multiple mathematical models: application in prostate cancer screening**

Bertsimas, D., Silberholz, J., Trikalinos, T., *Health Care Management Science*, Volume 21, Issue 1, 1 March 2018, Pages 105-118, <https://doi.org/10.1007/s10729-016-9381-3>

Important decisions related to human health, such as screening strategies for cancer, need to be made without a satisfactory understanding of the underlying biological and other processes. Rather, they are often informed by mathematical models that approximate reality. Often multiple models have been made to study the same phenomenon, which may lead to conflicting decisions. It is natural to seek a decision making process that identifies decisions that all models find to be effective, and we propose such a framework in this work. We apply the framework in prostate cancer screening to identify prostate-specific antigen (PSA)-based strategies that perform well under all considered models. We use heuristic search to identify strategies that trade off between optimizing the average across all models' assessments and being "conservative" by optimizing the most pessimistic model assessment. We identified three recently published mathematical models that can estimate quality-adjusted life expectancy (QALE) of PSA-based screening strategies and identified 64 strategies that trade-off between maximizing the average and the most pessimistic model assessments. All prescribe PSA thresholds that increase with age, and 57 involve biennial screening. Strategies with higher assessments with the pessimistic model start screening later, stop screening earlier, and use higher PSA thresholds at earlier ages. The 64 strategies outperform 22 previously published expert-generated strategies. The 41 most "conservative" ones remained better than no screening with all models in extensive sensitivity analyses. We augment current comparative modeling approaches by identifying strategies that perform well under all models, for various degrees of decision makers' conservativeness.

### **Accept or Decline? An Analytics-Based Decision Tool for Kidney Offer Evaluation**

Bertsimas, D., Kung, J., Trichakis, N., Wojciechowski, D., Vagefi, P.A., *Transplantation*, Volume 101, Issue 12, 1 Dec. 2017, Pages 2898-2904, <https://doi.org/10.1097/TP.0000000000001824>

**Background** When a deceased-donor kidney is offered to a waitlisted candidate, the decision to accept or decline the organ relies primarily upon a practitioner's experience and intuition. Such decisions must achieve a delicate balance between estimating the immediate benefit of transplantation and the potential for future higher-quality offers. However, the current experience-based paradigm lacks scientific rigor and is subject to the inaccuracies that plague anecdotal decision-making. **Methods** A data-driven analytics-based model was developed to predict whether a patient will receive an offer for a deceased-donor kidney at Kidney Donor Profile Index thresholds of 0.2, 0.4, and 0.6, and at timeframes of 3, 6, and 12 months. The model accounted for Organ Procurement Organization, blood group, wait time, DR antigens, and prior offer history to provide accurate and personalized predictions. Performance was evaluated on data sets spanning various lengths of time to understand the adaptability of the method. **Results** Using United Network for Organ Sharing match-run data from March 2007 to June 2013, out-of-sample area under the receiver operating characteristic curve was approximately 0.87 for all Kidney Donor Profile Index thresholds and timeframes considered for the 10 most populous Organ Procurement

Organizations. As more data becomes available, area under the receiver operating characteristic curve values increase and subsequently level off. Conclusions The development of a data-driven analytics-based model may assist transplant practitioners and candidates during the complex decision of whether to accept or forgo a current kidney offer in anticipation of a future high-quality offer. The latter holds promise to facilitate timely transplantation and optimize the efficiency of allocation.

### Personalized diabetes management using electronic medical records

Bertsimas, D., Kallus, N., Weinstein, A.M., Zhuo, Y.D., *Diabetes Care*, Volume 40, Issue 2, 1 February 2017, Pages 210-217, <https://doi.org/10.2337/dc16-0826>

**OBJECTIVE:** Current clinical guidelines for managing type 2 diabetes do not differentiate based on patient-specific factors. We present a data-driven algorithm for personalized diabetes management that improves health outcomes relative to the standard of care.

**RESEARCH DESIGN AND METHODS:** We modeled outcomes under 13 pharmacological therapies based on electronic medical records from 1999 to 2014 for 10,806 patients with type 2 diabetes from Boston Medical Center. For each patient visit, we analyzed the range of outcomes under alternative care using a k-nearest neighbor approach. The neighbors were chosen to maximize similarity on individual patient characteristics and medical history that were most predictive of health outcomes. The recommendation algorithm prescribes the regimen with best predicted outcome if the expected improvement from switching regimens exceeds a threshold. We evaluated the effect of recommendations on matched patient outcomes from unseen data.

**RESULTS:** Among the 48,140 patient visits in the test set, the algorithm's recommendation mirrored the observed standard of care in 68.2% of visits. For patient visits in which the algorithmic recommendation differed from the standard of care, the mean posttreatment glycated hemoglobin A1c (HbA1c) under the algorithm was lower than standard of care by  $0.44 \pm 0.03\%$  ( $4.8 \pm 0.3$  mmol/mol) ( $P < 0.001$ ), from 8.37% under the standard of care to 7.93% under our algorithm (68.0 to 63.2 mmol/mol). **CONCLUSIONS:** A personalized approach to diabetes management yielded substantial improvements in HbA1c outcomes relative to the standard of care. Our prototyped dashboard visualizing the recommendation algorithm can be used by providers to inform diabetes care and improve outcomes.

### Transforming decision making with analytics

Steve Calechman, ILP Institute Insider, August 7, 2017, <http://ilp.mit.edu/newsstory.jsp?id=23363>

Data holds the potential to predict the future. But without a framework, even the best information is merely quantity. Dimitris Bertsimas is a professor of operations research and an applied mathematician. His work is in analytics, taking old methods of quantification, like statistics, and combining them with computational power to make predictive and prescriptive algorithms. With a particular focus on healthcare, his modeling offers more personalized treatment and cost-saving measures. But the desire to make better decisions and maximize resources isn't the stranglehold of medicine. It applies across industries like finance, transportation, aviation, energy, anything which involves human activity. "That's the beauty of analytics," he says....

### POLINA GOLLAND

Professor of Electrical Engineering and Computer Science, <http://www.csail.mit.edu/user/791>  
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Lab: <https://www.csail.mit.edu/research/medical-vision-group>

Publications: <http://people.csail.mit.edu/polina/pubs.html>

Polina Golland is a professor in the Electrical Engineering and Computer Science Department at MIT and an associate director of the Computer Science and Artificial Intelligence Laboratory (CSAIL). Her primary research interest is in developing novel techniques for biomedical image analysis and understanding. She particularly enjoys working on algorithms that either explore the geometry of the world and the imaging process in a new way or improve image-based inference through statistical modeling of the image data.

Professor Golland is also interested in shape modeling and representation, predictive modeling and visualization of statistical models. Her current research focuses on developing statistical analysis methods for characterization of biological processes based on image information. In this domain, she is interested in modeling biological shape and function, how they relate to each other and vary across individuals.

### **Cardiac MRI analysis**

<https://www.csail.mit.edu/research/cardiac-mri-analysis>

We develop computer vision and machine learning methods for segmentation and interpretation of cardiac MRI in patients with congenital heart disease (CHD), to support simulation and surgical planning. The resulting heart surface models can, for example, be 3D-printed to visualize each patient's individual cardiac anatomy, or be used for dynamic functional analysis of the cardiac cycle (i.e., ejection fraction). Our research focuses on overcoming challenges of dramatic anatomical variability on the heart in CHD patients.

### **Clinical Neuroimaging**

<https://www.csail.mit.edu/research/clinical-neuroimaging>

We build statistical models of brain anatomical and functional structures from large collections of neuroimages. Our approach is to integrate image-derived phenotypes with genetic and clinical indicators. The resulting algorithms provide descriptors of normal anatomy and physiology, disease effects on the brain, and predictions of disease trajectory and recovery.

### **Monitoring Fetal Health**

<https://www.csail.mit.edu/research/monitoring-fetal-health>

We develop algorithms to enable tracking and segmentation of the fetus and placenta in dynamic MRI series. Signal inhomogeneity correction and subsequent analysis of the MRI signal provides measures of placental function and fetal development, which promise to yield novel biomarkers of fetal health for monitoring during pregnancy.

### **Fast geodesic regression for population-based image analysis**

Hong, Y., Golland, P., Zhang, M., Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), Volume 10433 LNCS, 2017, Pages 317-325, [https://doi.org/10.1007/978-3-319-66182-7\\_37](https://doi.org/10.1007/978-3-319-66182-7_37)

Geodesic regression on images enables studies of brain development and degeneration, disease progression, and tumor growth. The high-dimensional nature of image data presents significant computational challenges for the current regression approaches and prohibits large scale studies. In this paper, we present a fast geodesic regression method that dramatically decreases the



computational cost of the inference procedure while maintaining prediction accuracy. We employ an efficient low dimensional representation of diffeomorphic transformations derived from the image data and characterize the regressed trajectory in the space of diffeomorphisms by its initial conditions, i.e., an initial image template and an initial velocity field computed as a weighted average of pairwise diffeomorphic image registration results. This construction is achieved by using a first-order approximation of pairwise distances between images. We demonstrate the efficiency of our model on a set of 3D brain MRI scans from the OASIS dataset and show that it is dramatically faster than the state-of-the-art regression methods while producing equally good regression results on the large subject cohort.

### Population based image imputation

Dalca, A.V., Bouman, K.L., Freeman, W.T., Rost, N.S., Sabuncu, M.R., Golland, P., Lecture Notes in Computer Science (including subseries Lecture Notes in AI and Lecture Notes in Bioinformatics), Volume 10265 LNCS, 2017, Pages 659-671, [https://doi.org/10.1007/978-3-319-59050-9\\_52](https://doi.org/10.1007/978-3-319-59050-9_52)

We present an algorithm for creating high resolution anatomically plausible images consistent with acquired clinical brain MRI scans with large inter-slice spacing. Although large databases of clinical images contain a wealth of information, medical acquisition constraints result in sparse scans that miss much of the anatomy. These characteristics often render computational analysis impractical as standard processing algorithms tend to fail when applied to such images. Highly specialized or application-specific algorithms that explicitly handle sparse slice spacing do not generalize well across problem domains. In contrast, our goal is to enable application of existing algorithms that were originally developed for high resolution research scans to significantly undersampled scans. We introduce a model that captures fine-scale anatomical similarity across subjects in clinical image collections and use it to fill in the missing data in scans with large slice spacing. Our experimental results demonstrate that the proposed method outperforms current upsampling methods and promises to facilitate subsequent analysis not previously possible with scans of this quality.

### *New technique makes brain scans better*

#### **Boosting quality of patient MRIs could enable large-scale studies of stroke outcome.**

Anne Trafton, MIT News Office, June 20, 2017, <http://news.mit.edu/2017/new-technique-makes-brain-scans-better-0621>

People who suffer a stroke often undergo a brain scan at the hospital, allowing doctors to determine the location and extent of the damage. Researchers who study the effects of strokes would love to be able to analyze these images, but the resolution is often too low for many analyses.

To help scientists take advantage of this untapped wealth of data from hospital scans, a team of MIT researchers, working with doctors at Massachusetts General Hospital and many other institutions, has devised a way to boost the quality of these scans so they can be used for large-scale studies of how strokes affect different people and how they respond to treatment.

“These images are quite unique because they are acquired in routine clinical practice when a patient comes in with a stroke,” says Polina Golland, an MIT professor of electrical engineering and computer science. “You couldn’t stage a study like that.”

Using these scans, researchers could study how genetic factors influence stroke survival or how people respond to different treatments. They could also use this approach to study other disorders such as Alzheimer's disease.

Golland is the senior author of the paper, which will be presented at the Information Processing in Medical Imaging conference during the week of June 25. The paper's lead author is Adrian Dalca, a postdoc in MIT's Computer Science and Artificial Intelligence Laboratory. Other authors are Katie Bouman, an MIT graduate student; William Freeman, the Thomas and Gerd Perkins Professor of Electrical Engineering at MIT; Natalia Rost, director of the acute stroke service at MGH; and Mert Sabuncu, an assistant professor of electrical and computer engineering at Cornell University....

### **Video: Making Invisible Obvious: Computational Analysis of Medical Images**

ILP Video, September 19, 2017, <http://ilp.mit.edu/videodetail.jsp?confid=null&ilp-videos=Y&id=2173#>

Polina Golland will discuss her group's research in computational analysis of MRI scans that aims to provide accurate measurements of healthy anatomy and physiology, and biomarkers of pathology. Applications range from fetal development to aging brain.

### **Temporal Registration in In-Utero Volumetric MRI Time Series**

Liao R, Turk EA, Zhang M, Luo J, Grant PE, Adalsteinsson E, Golland P, *Med Image Comput Comput Assist Interv.* 2016 Oct; 9902:54-62. doi: 10.1007/978-3-319-46726-9\_7. Epub 2016 Oct 2., [https://doi.org/10.1007/978-3-319-46726-9\\_7](https://doi.org/10.1007/978-3-319-46726-9_7)

We present a robust method to correct for motion and deformations in in-utero volumetric MRI time series. Spatio-temporal analysis of dynamic MRI requires robust alignment across time in the presence of substantial and unpredictable motion. We make a Markov assumption on the nature of deformations to take advantage of the temporal structure in the image data. Forward message passing in the corresponding hidden Markov model (HMM) yields an estimation algorithm that only has to account for relatively small motion between consecutive frames. We demonstrate the utility of the temporal model by showing that its use improves the accuracy of the segmentation propagation through temporal registration. Our results suggest that the proposed model captures accurately the temporal dynamics of deformations in in-utero MRI time series.

### ***MRIs for fetal health***

#### **Algorithm could help analyze fetal scans to determine whether interventions are warranted.**

Larry Hardesty, MIT News Office, October 2016, <http://news.mit.edu/2016/algorithm-mri-scans-fetal-health-1021>

Researchers from MIT, Boston Children's Hospital, and Massachusetts General Hospital have joined forces in an ambitious new project to use magnetic resonance imaging (MRI) to evaluate the health of fetuses.

Typically, fetal development is monitored with ultrasound imaging, which is cheap and portable and can gauge blood flow through the placenta, the organ in the uterus that delivers nutrients to the fetus. But MRI could potentially measure the concentration of different chemicals in the placenta and in fetal organs, which may have more diagnostic value.

Earlier this year, in a project led by Ellen Grant's group in the Fetal-Neonatal Neuroimaging and Developmental Science Center at Boston Children's Hospital (BCH), members of the research team presented a paper showing that MRI measurements of oxygen absorption rates in the placenta can indicate placental disorders that might endanger the fetus. Grant is a professor of pediatrics and radiology at the Harvard Medical School (HMS).

And at the International Conference on Medical Image Computing and Computer Assisted Intervention this week, a team led by Polina Golland's group at MIT's Computer Science and Artificial Intelligence Laboratory presented a paper demonstrating a new algorithm for tracking organs through sequences of MRI scans, which will make MRI monitoring much more useful.

Much of Golland's prior work has dealt with algorithmic analysis of MRI scans of the brain. "The question is, why can't you just use everything that we've done in the last 25 years in the brain to apply in this case?" says Golland, a professor of electrical engineering and computer science. "And the answer is that for the brain, when the person is performing a particular task in the scanner, they're lying still. And then after the fact, you can use algorithmic approaches to correct for very small motions. Inside the uterus, well, you can't tell the mother not to breathe. And you can't tell the baby not to kick..."

### **JOHN V. GUTTAG**

Dugald C Jackson Professor of Computer Science and Engineering,  
<http://people.csail.mit.edu/guttag/> ; <https://www.csail.mit.edu/person/john-guttag>  
Lab: <https://www.csail.mit.edu/research/data-driven-inference-group>  
Publications: <http://people.csail.mit.edu/guttag/pubs.html>

From January of 1999 through August of 2004, Professor Guttag served as Head of MIT's Electrical Engineering and Computer Science Department. He served as Associate Department Head from Computer Science from 1993 to 1998. EECS, with approximately 1800 students and 125 faculty members, is the largest department at MIT.

Professor Guttag currently co-heads the Computer Science and Artificial Intelligence Laboratory's Networks and Mobile Systems Group. This group studies issues related to computer networks, applications of networked and mobile systems, and advanced software-based medical instrumentation and decision systems.

Professor Guttag has also done research, published, and lectured in the areas of software engineering, mechanical theorem proving, hardware verification, compilation, and software radios...

### **Data-Driven Inference Group**

<https://www.csail.mit.edu/research/data-driven-inference-group>  
Projects: <https://www.csail.mit.edu/research/data-driven-inference-group#projects>

Our group focuses on the application of advanced computational techniques to medicine. Current projects include prediction of adverse medical events, prediction of response to therapies, non-invasive monitoring and diagnostic tools, and tele-medicine.

### ***Hidden Influencers, Risk and Causes of Infection***

<https://www.csail.mit.edu/research/hidden-influencers-risk-and-causes-infection>

When modeling the spread of an infection among members or nodes of a community, each node's probability of getting infected depends on its innate susceptibility and its exposure to the contagion through its neighbors. In many cases, a neighbor's influence is hidden. Such is the case with asymptomatic carriers of the disease. We develop generative models to identify the hidden influencers in both static and dynamic networks. We use the neighbors' hidden influence state to compute an accurate estimate of exposure to the contagion. We propose efficient variational inference algorithms to learn our models' parameters. We also study the causal mechanisms that lead to an elevated risk of infection.

### ***Predicting Adverse Events Across Changing Electronic Health Record Systems***

<https://www.csail.mit.edu/research/predicting-adverse-events-across-changing-electronic-health-record-systems>

Clinical risk models based on Electronic Health Record (EHR) data can facilitate stratifying care, thereby improving outcomes while lowering costs. However, EHRs frequently employ different representations of patient data to tailor functionality to the needs of individual institutions and even different units within an institution. These differences hinder the development and use of clinical risk models that generalize across EHR systems over time and across institutions.

To address this problem, we use auxiliary knowledge from the Unified Medical Language System (UMLS), a collection of medical ontologies, to build clinical risk models that span multiple EHRs. We evaluate our method over an EHR system transition on two clinically relevant tasks, in-hospital mortality and prolonged length of stay. For both outcomes, a feature representation derived from EHR-specific events and the UMLS yields better results than using EHR-specific events alone.

### **Video: Transforming Healthcare Using Machine Learning**

ILP Video, January 26, 2018, <http://ilp.mit.edu/videodetail.jsp?confid=null&ilp-videos=Y&id=2328#>

Many poor healthcare outcomes and the majority of wasted healthcare spending can be attributed to bad decision making. It is widely accepted that decision support systems are needed to address this issue, and that machine learning has a key role to play in constructing such systems. However, learning to predict the impact of care decisions is made challenging by the need to scale out to complex populations being managed for complex diseases across complex care networks. We will present some recent work that addresses these challenges.

### **Predicting clinical outcomes across changing electronic health record systems**

Gong, J.J., Naumann, T., Szolovits, P., Gutttag, J.V., Proceedings of the ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, Volume Part F129685, 13 August 2017, Pages 1497-1506, <https://doi.org/10.1145/3097983.3098064>

Existing machine learning methods typically assume consistency in how semantically equivalent information is encoded. However, the way information is recorded in databases differs across institutions and over time, often rendering potentially useful data obsolescent. To address this problem, we map database-specific representations of information to a shared set of semantic concepts, thus allowing models to be built from or transition across different databases. We demonstrate our method on machine learning models developed in a healthcare setting. In particular, we evaluate our method using two different intensive care unit (ICU) databases and on two clinically relevant tasks, in-hospital mortality and prolonged length of stay. For both outcomes,



a feature representation mapping EHR-specific events to a shared set of clinical concepts yields better results than using EHR-specific events alone.

### *Using machine learning to improve patient care*

**New CSAIL research employs many types of medical data, including electronic health records, to predict outcomes in hospitals.**

Rachel Gordon, CSAIL, August 21, 2017, <http://news.mit.edu/2017/using-machine-learning-improve-patient-care-0821>

...In a new pair of papers, researchers from MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL) explore ways for computers to help doctors make better medical decisions.

One team created a machine-learning approach called "ICU Intervene" that takes large amounts of intensive-care-unit (ICU) data, from vitals and labs to notes and demographics, to determine what kinds of treatments are needed for different symptoms. The system uses "deep learning" to make real-time predictions, learning from past ICU cases to make suggestions for critical care, while also explaining the reasoning behind these decisions.

"The system could potentially be an aid for doctors in the ICU, which is a high-stress, high-demand environment," says PhD student Harini Suresh, lead author on the paper about ICU Intervene. "The goal is to leverage data from medical records to improve health care and predict actionable interventions."

Another team developed an approach called "EHR Model Transfer" that can facilitate the application of predictive models on an electronic health record (EHR) system, despite being trained on data from a different EHR system. Specifically, using this approach the team showed that predictive models for mortality and prolonged length of stay can be trained on one EHR system and used to make predictions in another.

ICU Intervene was co-developed by Suresh, undergraduate student Nathan Hunt, postdoc Alistair Johnson, researcher Leo Anthony Celi, MIT Professor Peter Szolovits, and PhD student Marzyeh Ghassemi. It was presented this month at the Machine Learning for Healthcare Conference in Boston.

EHR Model Transfer was co-developed by lead authors Jen Gong and Tristan Naumann, both PhD students at CSAIL, as well as Szolovits and John Guttag, who is the Dugald C. Jackson Professor in Electrical Engineering. It was presented at the ACM's Special Interest Group on Knowledge Discovery and Data Mining in Halifax, Canada.

Both models were trained using data from the critical care database MIMIC, which includes de-identified data from roughly 40,000 critical care patients and was developed by the MIT Lab for Computational Physiology....

### **THOMAS HELDT**

W M Keck Career Development Assistant Professor in Biomedical Engineering, Assistant Professor of Electrical and Biomedical Engineering, IMES,  
<http://www.rle.mit.edu/people/directory/thomas-heldt/> ; <http://imes.mit.edu/faculty/heldt-thomas/>  
Lab: <http://www.rle.mit.edu/incci/>

Publications: <http://www.rle.mit.edu/incci/publications/>

Professor Heldt's research interests focus on signal processing, mathematical modeling, and model identification to support real-time clinical decision making, monitoring of disease progression, and titration of therapy, primarily in neurocritical and neonatal critical care. In particular, Thomas is interested in developing a mechanistic understanding of physiologic systems, and in formulating appropriately chosen computational physiologic models for improved patient care. His research is conducted in close collaboration with colleagues at MIT and clinicians from Boston-area hospitals.

### **Computational Physiology and Clinical Inference Group (CPCI)**

<http://www.rle.mit.edu/cpci/>

Research: <http://www.rle.mit.edu/cpci/research/>

The overarching objectives of the research in the CPCI Group are to enhance patient monitoring, improve clinical decision-making, and better understand physiological and pathophysiological processes. The group develops and uses mathematical models derived from physiology, along with signal processing and estimation methods, to extract relevant information from clinical data. The models provide the constraints that allow readily observable data streams (such as waveforms of ECG, arterial blood pressure, cerebral blood flow velocity, near-infrared transmission through cerebral tissue, and/or EEG) to be related to physiological variables and parameters that are unmeasured but more directly reflective of changes in pathological state (quantities such as cardiac output, cardiac contractility and ejection fraction, peripheral resistance, intracranial pressure, cerebral metabolism and/or seizure activity). The models thereby form the basis for estimation of unmeasured quantities from measured ones, thus enabling a fuller assessment and tracking of patient state, and a more comprehensive description of the underlying physiology. The group's main research efforts are currently aligned along the following projects:

#### ***Integrating Data, Models, and Reasoning in Critical Care***

<http://www.rle.mit.edu/cpci/research/>

Modern intensive care units (ICUs) employ an impressive array of technologically sophisticated instrumentation to provide detailed measurements of various important variables and parameters for each patient. Providing care in the ICU is becoming an increasingly difficult task, however, because of the growing volume of relevant data that must be screened, integrated, and interpreted in order to extract clinically relevant and actionable information. This project combines the resources of an interdisciplinary team of investigators from academia (research groups from HST, CSAIL and RLE at MIT), industry (Philips Healthcare), and clinical medicine (Beth Israel Deaconess Medical Center in Boston) to develop and evaluate advanced ICU patient monitoring systems that will support improved efficiency, efficacy, and timeliness of clinical decision making in critical care. A substantial part of the effort on this project goes towards assembling a rich and extensive database of de-identified ICU data – the MIMIC II database – comprising high-resolution waveforms from bedside monitors, along with clinical notes and laboratory results, for several thousand patients. This database also constitutes the platform for much of the research on the project, and is being made available to researchers worldwide. The project is funded as a Bioengineering Research Partnership (BRP) by the National Institute for Biomedical Imaging and Bioengineering (NIBIB).

### Model-Based Estimation of Respiratory Parameters from Capnography, with Application to Diagnosing Obstructive Lung Disease

Abid A, Mieloszyk RJ, Verghese GC, Krauss BS, Heldt T., IEEE Trans Biomed Eng. 2017 May 2. doi: 10.1109/TBME.2017.2699972, <https://doi.org/10.1109/TBME.2017.2699972>

**OBJECTIVE:** We use a single-alveolar-compartment model to describe the partial pressure of carbon dioxide in exhaled breath, as recorded in time-based capnography. Respiratory parameters are estimated using this model and then related to the clinical status of patients with obstructive lung disease.

**METHODS:** Given appropriate assumptions, we derive an analytical solution of the model, describing the exhalation segment of the capnogram. This solution is parametrized by alveolar CO<sub>2</sub> concentration, dead-space fraction, and the time constant associated with exhalation. These quantities are estimated from individual capnogram data on a breath-by-breath basis. The model is applied to analyzing datasets from normal (n=22) and chronic obstructive pulmonary disease (COPD) (n=24) subjects, as well as from patients undergoing methacholine challenge testing for asthma (n=22).

**RESULTS:** A classifier based on linear discriminant analysis in logarithmic coordinates, using estimated dead-space fraction and exhalation time-constant as features, and trained on data from 5 normal and 5 COPD subjects, yielded an area under the receiver operating characteristic curve (AUC) of 0.99 in classifying the remaining 36 subjects as normal or COPD. Bootstrapping with 50 replicas yielded a 95% confidence interval of AUCs from 0.96 to 1.00. For patients undergoing methacholine challenge testing, qualitatively meaningful trends were observed in the parameter variations over the course of the test.

**SIGNIFICANCE:** A simple mechanistic model allows estimation of underlying respiratory parameters from the capnogram, and may be applied to diagnosis and monitoring of chronic and reversible obstructive lung disease.

### Prediction of postoperative outcomes using intraoperative hemodynamic monitoring data

Prasad, V., Guerrisi, M., Dauri, M., Coniglione, F., Tisone, G., De Carolis, E., Cillis, A., Canichella, A., Toschi, N., Heldt, T., Scientific Reports, Volume 7, Issue 1, 1 December 2017, Article number 16376, <https://doi.org/10.1038/s41598-017-16233-4>

Major surgeries can result in high rates of adverse postoperative events. Reliable prediction of which patient might be at risk for such events may help guide peri-and postoperative care. We show how archiving and mining of intraoperative hemodynamic data in orthotopic liver transplantation (OLT) can aid in the prediction of postoperative 180-day mortality and acute renal failure (ARF), improving upon predictions that rely on preoperative information only. From 101 patient records, we extracted 15 preoperative features from clinical records and 41 features from intraoperative hemodynamic signals. We used logistic regression with leave-one-out cross-validation to predict outcomes, and incorporated methods to limit potential model instabilities from feature multicollinearity. Using only preoperative features, mortality prediction achieved an area under the receiver operating characteristic curve (AUC) of 0.53 (95% CI: 0.44-0.78). By using intraoperative features, performance improved significantly to 0.82 (95% CI: 0.56-0.91, P = 0.001). Similarly, including intraoperative features (AUC = 0.82; 95% CI: 0.66-0.94) in ARF prediction improved performance over preoperative features (AUC = 0.72; 95% CI: 0.50-0.85), though not significantly (P = 0.32). We conclude that inclusion of intraoperative hemodynamic features significantly improves prediction of postoperative events in OLT. Features strongly associated with occurrence

of both outcomes included greater intraoperative central venous pressure and greater transfusion volumes.

### **MIT Professional Education Course: Quantitative Cardiorespiratory Physiology and Clinical Applications For Engineers (June 2018)**

Lead Instructor: Profs Thomas Heldt and Roger Mark

Dates: Jun 11, 2018 - Jun 15, 2018, \$4750

<http://professional.mit.edu/programs/short-programs/quantitative-cardiovascular-physiology>

Cardiovascular disease and stroke remain the number one and two killers worldwide, according to the American Heart Association. In fact, one in three deaths in the U.S. are caused by heart disease, stroke and other cardiovascular diseases. That's one of the reasons why medical device companies have always considered cardiology to be one of the most important sectors. New digital technologies, such as wearable devices and connected devices (IoT), have made it easier and less intrusive to record physiological and behavioral data. But recording, tracking, and displaying metrics such as heart rate or the number of daily steps taken only takes us so far. The next wave of medical innovation must involve technologies to make sense of the constellation of personal and physiological data being collected, and to accurately relate such constellations to particular disease states.

That's a significant challenge, however, in part because the engineers tasked with designing and developing next-generation devices may not be trained in the medical field. Often, then, a significant gap can emerge between the technologies that engineers develop and the kind of technologies and information clinicians require to track particular disease states.

This course presents the functional anatomy, physiology, and pathophysiology of the cardiovascular and respiratory systems from an engineering perspective. The goal of the course is to enable engineers and managers from industry to understand the normal cardiorespiratory physiology at the systems level, to predict system behavior under normal operation and pathological stresses, and to understand what commonly monitored clinical signals reveal about the state of the system. Strong emphasis will be placed on describing the cardiovascular system quantitatively, drawing on physical principles and deriving models of cardiovascular and respiratory function that illuminate the organ systems' operation. The course is structured into these major blocks:

- Functional anatomy of the cardiovascular systems
- Function of the heart and peripheral circulation
- Function of the intact cardiovascular system
- Control of the cardiovascular system
- Physical basis of electrocardiography
- Clinical electrocardiography
- Functional anatomy of the respiratory system
- Respiratory mechanics
- Respiratory gas exchange...

### **UNA-MAY O'REILLY**

Principal Research Scientist, <https://www.csail.mit.edu/person/una-may-oreilly>

Founder, Co-Leader, The Alfa Group: Any Scale Learning for All, <http://alfagroup.csail.mit.edu/>



Publications: <http://alfagroup.csail.mit.edu/12.x/tiki-index.php?page=Publications>

Dr. Una-May O'Reilly is the leader of the AnyScale Learning For All (ALFA) group at CSAIL. ALFA focuses on scalable machine learning, evolutionary algorithms, and frameworks for large scale knowledge mining, prediction and analytics. The group has projects in cybersecurity, healthcare, and online education.

...Una-May served as chair of the largest international Evolutionary Computation Conference, GECCO, in 2005. She has served on the GECCO business committee, co-led the 2006 and 2009 Genetic Programming: Theory to Practice Workshops and co-chaired EuroGP, the largest conference devoted to Genetic Programming. Una-May serves as the area editor for Data Analytics and Knowledge Discovery for Genetic Programming and Evolvable Machines (Kluwer), as editor for Evolutionary Computation (MIT Press), and as action editor for the Journal of Machine Learning Research...

### **AnyScale Learning for All (ALFA) Group**

<http://alfagroup.csail.mit.edu>, <https://www.csail.mit.edu/research/anyscale-learning-all-alfa>

Publications: <http://alfagroup.csail.mit.edu/12.x/tiki-index.php?page=Publications>

Our vision is data-driven machine learning systems that advance the quality of healthcare, the understanding of cyber arms races and the delivery of online education... Scalable machine learning technology, evolutionary algorithms, and data science frameworks for large-scale knowledge mining, prediction, analytics and optimization with projects in clinical medicine knowledge discovery, cyber security and MOOC technology.

### ***GIGABEATS: Data science for medical sensor data***

<https://www.csail.mit.edu/research/gigabeats-data-science-medical-sensor-data>

Our projects tap into machine learning to interpret and exploit repositories holding waveform data e.g. arterial blood pressure, ECG and EEG. They include “BeatDB” where we are developing a fast and scalable framework for compiling machine learning data sets from waveform repositories and “Trajectories Like Mine” where we are developing a sub-linear time method called Locality Sensitive Hashing to find approximate nearest neighbors in waveform space....

### **BeatDB v3: A Framework for the Creation of Predictive Datasets from Physiological Signals**

Master's Thesis by Steven Anthony Rivera, 2017

Thesis Supervisor: Una-May O'Reilly

[http://alfagroup.csail.mit.edu/12.x/tiki-download\\_file.php?fileId=165&display](http://alfagroup.csail.mit.edu/12.x/tiki-download_file.php?fileId=165&display)

BeatDB is a framework for fast processing and analysis of physiological data, such as arterial blood pressure (ABP) or electrocardiograms (ECG). BeatDB takes such data as input and processes it for machine learning analytics in multiple stages. It offers both beat and onset detection, feature extraction for beats and groups of beats over one or more signal channels and over the time domain, and an extraction step focused on finding condition windows and aggregate features within them. BeatDB has gone through multiple iterations, with its initial version running as a collection of single-use MATLAB and Python scripts run on VM instances in OpenStack and its second version (known as PhysioMiner) acting as a cohesive and modular cloud system on Amazon Web Services in Java. The goal of this project is primarily to modify BeatDB to support multi-channel waveform

data like EEG and accelerometer data and to make the project more flexible to modification by researchers. Major software development tasks included rewriting condition detection to find windows in valid beat groups only, refactoring and writing new code to extract features and prepare training data for multi-channel signals, and fully redesigning and reimplementing BeatDB within Python, focusing on optimization and simplicity based on probable use cases of BeatDB. BeatDB v3 has become more accurate in the datasets it generates, usable for both developer and non-developer users, and efficient in both performance and design than previous iterations, achieving an average AUROC increase of over 4% when comparing specific iterations.

### **Analysis of locality-sensitive hashing for fast critical event prediction on physiological time series**

Kim, Y.B., O'Reilly, U.-M., Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS, Volume 2016-October, 13 October 2016, Article number 7590818, Pages 783-787, <http://doi.org/10.1109/EMBC.2016.7590818>

We apply the sublinear time, scalable locality-sensitive hashing (LSH) and majority discrimination to the problem of predicting critical events based on physiological waveform time series. Compared to using the linear exhaustive k-nearest neighbor search, our proposed method vastly speeds up prediction time up to 25 times while sacrificing only 1% of accuracy when demonstrated on an arterial blood pressure dataset extracted from the MIMIC2 database. We compare two widely used variants of LSH, the bit sampling based (L1LSH) and the random projection based (E2LSH) methods to measure their direct impact on retrieval and prediction accuracy. We experimentally show that the more sophisticated E2LSH performs worse than L1LSH in terms of accuracy, correlation, and the ability to detect false negatives. We attribute this to E2LSH's simultaneous integration of all dimensions when hashing the data, which actually makes it more impotent against common noise sources such as data misalignment. We also demonstrate that the deterioration of accuracy due to approximation at the retrieval step of LSH has a diminishing impact on the prediction accuracy as the speed up gain accelerates.

### **ROSALIND W. PICARD**

Professor of Media Arts and Sciences, <http://web.media.mit.edu/~picard/index.php>,  
<https://www.media.mit.edu/people/picard/overview/>

Co-Director, Advancing Wellbeing Initiative, <https://www.media.mit.edu/groups/advancing-wellbeing/overview/>

Director, Affective Computing Group, <https://www.media.mit.edu/groups/affective-computing/overview/>

Publications: <https://www.media.mit.edu/groups/affective-computing/publications-list/>

Professor Rosalind W. Picard, Sc.D. is founder and director of the Affective Computing Research Group at the MIT Media Lab, co-director of the Media Lab's Advancing Wellbeing Initiative, and faculty chair of MIT's Mind+Hand+Heart Initiative. She has co-founded Empatica, Inc. creating wearable sensors and analytics to improve health, and Affectiva, Inc. delivering technology to help measure and communicate emotion. Picard also served as a founding member of the IEEE Technical Committee on Wearable Information Systems in 1998, helping launch the field of wearable computing. Picard has authored or co-authored over two hundred scientific articles and chapters spanning computer vision, pattern recognition, machine learning, human-computer interaction, wearable sensors and affective computing.

### **Affective Computing Research Group**

<https://www.media.mit.edu/groups/affective-computing/overview/>, <http://affect.media.mit.edu/>

The Affective Computing Research Group aims to bridge the gap between human emotions and computational technology. Current research addresses machine recognition and modeling of human emotional expression, including the invention of new software and hardware tools to help people gather, communicate, and express emotional information, together with tools to help people better manage and understand the ways emotion impacts health, social interaction, learning, memory, and behavior.

### **Machine Learning for Pain Measurement**

<https://www.media.mit.edu/projects/pain-measurement/overview/>

Pain is a subjective experience commonly measured through patient's self report. Unfortunately, self-report measures only work when the subject is sufficiently alert and cooperative, and hence they lack utility in multiple situations (e.g. during drowsiness) and patient populations (e.g. patients with dementia or paralysis). To circumvent the limitations of pain self-reports, in this project we are developing automatic methods for pain estimation based on physiological signals, and/or facial expressions.

### **Behavioral Indications of Depression Severity**

<https://www.media.mit.edu/projects/behavioral-indications-of-depression-severity/overview/>

In collaboration with Massachusetts General Hospital, we are conducting a clinical trial exploring objective methods for assessing depression and its severity. We are challenging the assessment methods that were created decades ago and which rely mostly on self-reported measures. We are including information from wearable sensors and regular sensors in mobile phones to collect information about sleep, social interaction, and location changes to find behavioral patterns that are associated with depressive symptoms.

### **Automated Tongue Analysis**

<https://www.media.mit.edu/projects/automated-tongue-analysis/overview/>

A common practice in Traditional Chinese Medicine (TCM) is visual examination of the patient's tongue. This study will examine ways to make this process more objective and to test its efficacy for understanding stress- and health-related changes in people over time. We start by developing an app that makes it comfortable and easy for people to collect tongue data in daily life together with other stress- and health-related information. We will obtain assessment from expert practitioners of TCM, and also use pattern analysis and machine learning to attempt to create state-of-the-art algorithms able to help provide better insights for health and prevention of sickness.

### **Personalized Multitask Learning for Predicting Tomorrow's Mood, Stress, and Health**

Taylor, S.A., Jaques, N., Nosakhare, E., Sano, A., Picard, R., IEEE Transactions on Affective Computing, 18 December 2017, <https://doi.org/10.1109/TAFFC.2017.2784832>

While accurately predicting mood and wellbeing could have a number of important clinical benefits, traditional machine learning (ML) methods frequently yield low performance in this domain. We posit that this is because a one-size-fits-all machine learning model is inherently ill-suited to predicting outcomes like mood and stress, which vary greatly due to individual differences.

Therefore, we employ Multitask Learning (MTL) techniques to train personalized ML models which are customized to the needs of each individual, but still leverage data from across the population. Three formulations of MTL are compared: i) MTL deep neural networks, which share several hidden layers but have final layers unique to each task; ii) Multi-task Multi-Kernel learning, which feeds information across tasks through kernel weights on feature types; and iii) a Hierarchical Bayesian model in which tasks share a common Dirichlet Process prior. We offer the code for this work in open source. These techniques are investigated in the context of predicting future mood, stress, and health using data collected from surveys, wearable sensors, smartphone logs, and the weather. Empirical results demonstrate that using MTL to account for individual differences provides large performance improvements over traditional machine learning methods and provides personalized, actionable insights.

### **Personalized Automatic Estimation of Self-Reported Pain Intensity from Facial Expressions**

Martinez, D.L., Rudovic, O., Picard, R., IEEE Computer Society Conference on Computer Vision and Pattern Recognition Workshops, Volume 2017-July, 22 August 2017, Article number 8015020, Pages 2318-2327, <https://doi.org/10.1109/CVPRW.2017.286>

Pain is a personal, subjective experience that is commonly evaluated through visual analog scales (VAS). While this is often convenient and useful, automatic pain detection systems can reduce pain score acquisition efforts in large-scale studies by estimating it directly from the participants' facial expressions. In this paper, we propose a novel two-stage learning approach for VAS estimation: first, our algorithm employs Recurrent Neural Networks (RNNs) to automatically estimate Prkachin and Solomon Pain Intensity (PSPI) levels from face images. The estimated scores are then fed into the personalized Hidden Conditional Random Fields (HCRFs), used to estimate the VAS, provided by each person. Personalization of the model is performed using a newly introduced facial expressiveness score, unique for each person. To the best of our knowledge, this is the first approach to automatically estimate VAS from face images. We show the benefits of the proposed personalized over traditional non-personalized approach on a benchmark dataset for pain analysis from face images.

### **Multicenter clinical assessment of improved wearable multimodal convulsive seizure detectors**

Onorati, F., Regalia, G., Caborni, C., Migliorini, M., Bender, D., Poh, M.-Z., Frazier, C., Kovitch Thropp, E., Mynatt, E.D., Bidwell, J., Mai, R., LaFrance, W.C., Jr., Blum, A.S., Friedman, D., Loddenkemper, T., Mohammadpour-Touserani, F., Reinsberger, C.I., Tognetti, S., Picard, R.W. Epilepsia, Vol 58, Iss 11, November 2017, Pages 1870-1879, <https://doi.org/10.1111/epi.13899>

Objective: New devices are needed for monitoring seizures, especially those associated with sudden unexpected death in epilepsy (SUDEP). They must be unobtrusive and automated, and provide false alarm rates (FARs) bearable in everyday life. This study quantifies the performance of new multimodal wrist-worn convulsive seizure detectors. Methods: Hand-annotated video-electroencephalographic seizure events were collected from 69 patients at six clinical sites. Three different wristbands were used to record electrodermal activity (EDA) and accelerometer (ACM) signals, obtaining 5,928 h of data, including 55 convulsive epileptic seizures (six focal tonic-clonic seizures and 49 focal to bilateral tonic-clonic seizures) from 22 patients. Recordings were analyzed offline to train and test two new machine learning classifiers and a published classifier based on EDA and ACM. Moreover, wristband data were analyzed to estimate seizure-motion duration and autonomic responses. Results: The two novel classifiers consistently outperformed the previous detector. The most efficient (Classifier III) yielded sensitivity of 94.55%, and an FAR of 0.2

events/day. No nocturnal seizures were missed. Most patients had <1 false alarm every 4 days, with an FAR below their seizure frequency. When increasing the sensitivity to 100% (no missed seizures), the FAR is up to 13 times lower than with the previous detector. Furthermore, all detections occurred before the seizure ended, providing reasonable latency (median = 29.3 s, range = 14.8–151 s). Automatically estimated seizure durations were correlated with true durations, enabling reliable annotations. Finally, EDA measurements confirmed the presence of postictal autonomic dysfunction, exhibiting a significant rise in 73% of the convulsive seizures. Significance: The proposed multimodal wrist-worn convulsive seizure detectors provide seizure counts that are more accurate than previous automated detectors and typical patient self-reports, while maintaining a tolerable FAR for ambulatory monitoring. Furthermore, the multimodal system provides an objective description of motor behavior and autonomic dysfunction, aimed at enriching seizure characterization, with potential utility for SUDEP warning.

### **Wrist sensor reveals sympathetic hyperactivity and hypoventilation before probable SUDEP**

Rosalind W. Picard, ScD, Matteo Migliorini, PhD, Chiara Caborni, MSc, Francesco Onorati, PhD, Giulia Regalia, PhD, Daniel Friedman, MD and Orrin Devinsky, MD, Neurology 2017 Jul  
<https://doi.org/10.1212/WNL.0000000000004208>

We report a probable sudden unexpected death in epilepsy (SUDEP) in a 20-year-old man wearing a smartwatch that recorded wrist motion via 3-axis accelerometer (ACC) and electrodermal activity (EDA). EDA reflects sympathetic activity without parasympathetic antagonism. The smartwatch (Empatica [Milan, Italy] Embrace, with CE Medical clearance from the European Union for seizure detection) issued an alert, received by the caregiver at 8:50 AM, indicating a probable convulsive seizure. An adult trained in cardiopulmonary resuscitation (CPR) arrived at 9:05 AM, found the patient pulseless, prone, face in pillow with mucus in his mouth, and commenced CPR for 15 minutes without recovery. The family declined autopsy.

### **BrightBeat: Effortlessly influencing breathing for cultivating calmness and focus**

Ghandeharioun, A., Picard, R., Conference on Human Factors in Computing Systems—Proceedings, Volume Part F127655, 6 May 2017, Pages 1624-1631,  
<https://doi.org/10.1145/3027063.3053164>

While technology is usually associated with causing stress, technology also has the potential to bring about calm. In particular, breathing usually speeds up with higher stress, but it can be slowed through a manipulation, and in so doing, it can help the person lower their stress and improve their focus. This paper introduces BrightBeat, a set of seamless visual and auditory interventions that look like respiratory biofeedback, rhythmically oscillating, but that are tuned to appear with a slower speed, with the aim of slowing a stressed computer user's breathing and, consequently, bringing a sense of focus and calmness. These interventions were designed to run easily on commonplace personal electronic devices and to not require any focused attention in order to be effective. We have run a randomized placebo-controlled trial and examined both objective and subjective measures of impact with N=32 users undergoing work tasks. BrightBeat significantly influenced slower breathing, had a lasting effect, improved self-reported calmness and focus, and was highly preferred for future use.

### **DAVID SONTAG**

Hermann L. F. von Helmholtz Career Development Professor of Medical Engineering,  
<http://imes.mit.edu/people/faculty/david-sontag/>



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Lab: <http://clinicalml.org>  
Publications: [http://people.csail.mit.edu/dsontag/papers/biblio\\_year.html](http://people.csail.mit.edu/dsontag/papers/biblio_year.html)

David Sontag joined the MIT faculty in 2017 as Hermann L. F. von Helmholtz Career Development Professor in the Institute for Medical Engineering and Science (IMES) and as Assistant Professor in the Department of Electrical Engineering and Computer Science (EECS). He is also a principal investigator in the Computer Science and Artificial Intelligence Laboratory (CSAIL). Professor Sontag's research interests are in machine learning and artificial intelligence. As part of IMES, he leads a research group that aims to transform healthcare through the use of machine learning.

Prior to joining MIT, Dr. Sontag was an Assistant Professor in Computer Science and Data Science at New York University's Courant Institute of Mathematical Sciences from 2011 to 2016, and postdoctoral researcher at Microsoft Research New England from 2010 to 2011. Dr. Sontag received the Sprowls award for outstanding doctoral thesis in Computer Science at MIT in 2010, best paper awards at the conferences Empirical Methods in Natural Language Processing (EMNLP), Uncertainty in Artificial Intelligence (UAI), and Neural Information Processing Systems (NIPS), faculty awards from Google, Facebook, and Adobe, and a NSF CAREER Award. Dr. Sontag received a B.A. from the University of California, Berkeley.

### **Clinical Machine Learning Group**

Research: <http://clinicalml.org/research.html>

Publications: <http://clinicalml.org/publications.html>

Our lab is broadly interested in advancing machine learning and artificial intelligence, and using these to transform health care. We currently have three main focus areas:

- Theoretical machine learning
- Precision medicine
- Intelligent electronic health records

### ***Precision Medicine***

<http://clinicalml.org/research.html>

These are exciting times for the practice of medicine. The rapid adoption of electronic health records has created a wealth of new data about patients, which is a goldmine for improving our understanding of human health. Our lab develops algorithms that use this data to better understand disease progression and to facilitate new, precise treatment strategies for a wide range of diseases and conditions such as Type 2 diabetes, which affects tens of millions of people worldwide every year, and multiple myeloma, a rare blood cancer. In pursuit of these aims, a major methodological focus has been on developing novel approaches to modeling high-dimensional time-series data, particularly approaches that bring together probabilistic modeling and deep learning, and causal inference from observational data.

### ***Intelligent Electronic Health Records***

<http://clinicalml.org/research.html>

Today's electronic health records are predominately a place for recording a patient's health data. We aim to develop the foundation for the next-generation of intelligent electronic health records, where machine learning and artificial intelligence is built-in to help with medical diagnosis, automatically trigger clinical decision support, personalize treatment suggestions, autonomously retrieve relevant past medical history, make documentation faster and higher quality, and predict adverse events before they happen. A major challenge is the need for robust machine learning algorithms that are safe, interpretable, can learn from little labeled training data, understand natural language, and generalize well across medical settings and institutions.

### Learning a Health Knowledge Graph from Electronic Medical Records

Rotmensch, M., Halpern, Y., Tlimat, A., Horng, S., Sontag, D., Scientific Reports, Volume 7, Issue 1, December 2017, Article number 5994, <https://doi.org/10.1038/s41598-017-05778-z>

Demand for clinical decision support systems in medicine and self-diagnostic symptom checkers has substantially increased in recent years. Existing platforms rely on knowledge bases manually compiled through a labor-intensive process or automatically derived using simple pairwise statistics. This study explored an automated process to learn high quality knowledge bases linking diseases and symptoms directly from electronic medical records. Medical concepts were extracted from 273,174 de-identified patient records and maximum likelihood estimation of three probabilistic models was used to automatically construct knowledge graphs: logistic regression, naive Bayes classifier and a Bayesian network using noisy OR gates. A graph of disease-symptom relationships was elicited from the learned parameters and the constructed knowledge graphs were evaluated and validated, with permission, against Google's manually-constructed knowledge graph and against expert physician opinions. Our study shows that direct and automated construction of high quality health knowledge graphs from medical records using rudimentary concept extraction is feasible. The noisy OR model produces a high quality knowledge graph reaching precision of 0.85 for a recall of 0.6 in the clinical evaluation. Noisy OR significantly outperforms all tested models across evaluation frameworks ( $p < 0.01$ ).

### Creating an automated trigger for sepsis clinical decision support at emergency department triage using machine learning

Horng, S., Sontag, D.A., Halpern, Y., Jernite, Y., Shapiro, N.I., Nathanson, L.A., PLoS ONE, Vol 12, Iss 4, April 2017, Article number e0174708, <https://doi.org/10.1371/journal.pone.0174708>

**Objective:** To demonstrate the incremental benefit of using free text data in addition to vital sign and demographic data to identify patients with suspected infection in the emergency department. **Methods:** This was a retrospective, observational cohort study performed at a tertiary academic teaching hospital. All consecutive ED patient visits between 12/17/08 and 2/17/13 were included. No patients were excluded. The primary outcome measure was infection diagnosed in the emergency department defined as a patient having an infection related ED ICD-9-CM discharge diagnosis. Patients were randomly allocated to train (64%), validate (20%), and test (16%) data sets. After preprocessing the free text using bigram and negation detection, we built four models to predict infection, incrementally adding vital signs, chief complaint, and free text nursing assessment. We used two different methods to represent free text: a bag of words model and a topic model. We then used a support vector machine to build the prediction model. We calculated the area under the receiver operating characteristic curve to compare the discriminatory power of each model. **Results:** A total of 230,936 patient visits were included in the study. Approximately 14% of patients had the primary outcome of diagnosed infection. The area under the ROC curve (AUC) for the vitals model, which used only vital signs and demographic data, was 0.67 for the training data

set, 0.67 for the validation data set, and 0.67 (95% CI 0.65-0.69) for the test data set. The AUC for the chief complaint model which also included demographic and vital sign data was 0.84 for the training data set, 0.83 for the validation data set, and 0.83 (95% CI 0.81-0.84) for the test data set. The best performing methods made use of all of the free text. In particular, the AUC for the bag-of-words model was 0.89 for training data set, 0.86 for the validation data set, and 0.86 (95% CI 0.85-0.87) for the test data set. The AUC for the topic model was 0.86 for the training data set, 0.86 for the validation data set, and 0.85 (95% CI 0.84-0.86) for the test data set. Conclusion: Compared to previous work that only used structured data such as vital signs and demographic information, utilizing free text drastically improves the discriminatory ability (increase in AUC from 0.67 to 0.86) of identifying infection.

### Early Identification of Patients With Acute Decompensated Heart Failure

Blecker, S., Sontag, D., Horwitz, L.I., Kuperman, G., Park, H., Reventovich, A., Katz, S.D.  
Journal of Cardiac Failure, 2017, <https://doi.org/10.1016/j.cardfail.2017.08.458>

Background: Interventions to reduce readmissions after acute heart failure hospitalization require early identification of patients. The purpose of this study was to develop and test accuracies of various approaches to identify patients with acute decompensated heart failure (ADHF) with the use of data derived from the electronic health record. Methods and Results: We included 37,229 hospitalizations of adult patients at a single hospital during 2013-2015. We developed 4 algorithms to identify hospitalization with a principal discharge diagnosis of ADHF: 1) presence of 1 of 3 clinical characteristics, 2) logistic regression of 31 structured data elements, 3) machine learning with unstructured data, and 4) machine learning with the use of both structured and unstructured data. In data validation, algorithm 1 had a sensitivity of 0.98 and positive predictive value (PPV) of 0.14 for ADHF. Algorithm 2 had an area under the receiver operating characteristic curve (AUC) of 0.96, and both machine learning algorithms had AUCs of 0.99. Based on a brief survey of 3 providers who perform chart review for ADHF, we estimated that providers spent 8.6 minutes per chart review; using this parameter, we estimated that providers would spend 61.4, 57.3, 28.7, and 25.3 minutes on secondary chart review for each case of ADHF if initial screening were done with algorithms 1, 2, 3, and 4, respectively. Conclusions: Machine learning algorithms with unstructured notes had the best performance for identification of ADHF and can improve provider efficiency for delivery of quality improvement interventions.

### COLLIN M. STULTZ

Professor of Electrical Engineering and Computer Science, and Professor of Health Sciences and Technology, <http://www.rle.mit.edu/people/directory/collin-stultz/>,  
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Professor Stultz conducts research to understand conformational changes in macromolecules and the effect of structural transitions on common human diseases. His research group employs an interdisciplinary approach that uses techniques drawn from computational chemistry, signal processing, machine-learning and basic biochemistry.

### The Computational Biophysics Group

Research: <http://www.rle.mit.edu/cbg/research.htm>  
Publications: <http://www.rle.mit.edu/cbg/publications.htm>

Research in Professor Stultz's group revolves around two general themes. Firstly, a major thrust of the group is to use computational methods to understand conformational changes in macromolecules and the effect of structural transitions on common human diseases. Secondly, his group draws upon concepts in signal processing and machine learning to develop computational biomarkers that identify patients at high risk of adverse cardiovascular events. His research group employs an interdisciplinary approach that utilizes techniques drawn from computational chemistry, signal processing, and basic biochemistry.

### ***Risk Stratification for Patients with Cardiovascular Disease***

<http://www.rle.mit.edu/cbg/research.htm>

We are interested in developing automated methods that can identify patients with cardiovascular disease who are at high risk of adverse outcomes. To do this we employ a variety of different methods grounded in signal processing and machine learning. Our methods combine disparate types of clinical information (e.g., medical history, genetic information, physiologic signals) to arrive at models that can guide clinical decision making.

### **Machine Learning Improves Risk Stratification after Acute Coronary Syndrome**

Myers, P.D., Scirica, B.M., Stultz, C.M., *Scientific Reports*, Volume 7, Issue 1, 1 December 2017, Article number 12692, <https://doi.org/10.1038/s41598-017-12951-x>

The accurate assessment of a patient's risk of adverse events remains a mainstay of clinical care. Commonly used risk metrics have been based on logistic regression models that incorporate aspects of the medical history, presenting signs and symptoms, and lab values. More sophisticated methods, such as Artificial Neural Networks (ANN), form an attractive platform to build risk metrics because they can easily incorporate disparate pieces of data, yielding classifiers with improved performance. Using two cohorts consisting of patients admitted with a non-ST-segment elevation acute coronary syndrome, we constructed an ANN that identifies patients at high risk of cardiovascular death (CVD). The ANN was trained and tested using patient subsets derived from a cohort containing 4395 patients (Area Under the Curve (AUC) 0.743) and validated on an independent holdout set containing 861 patients (AUC 0.767). The ANN 1-year Hazard Ratio for CVD was 3.72 (95% confidence interval 1.04-14.3) after adjusting for the TIMI Risk Score, left ventricular ejection fraction, and B-type natriuretic peptide. A unique feature of our approach is that it captures small changes in the ST segment over time that cannot be detected by visual inspection. These findings highlight the important role that ANNs can play in risk stratification.

### **Beatquency domain and machine learning improve prediction of cardiovascular death after acute coronary syndrome**

Liu, Y., Scirica, B.M., Stultz, C.M., Gutttag, J.V., *Scientific Reports*, Volume 6, 6 October 2016, Article number 34540, <https://dx.doi.org/10.1038/srep34540>

Frequency domain measures of heart rate variability (HRV) are associated with adverse events after a myocardial infarction. However, patterns in the traditional frequency domain (measured in Hz, or cycles per second) may capture different cardiac phenomena at different heart rates. An alternative is to consider frequency with respect to heartbeats, or beatquency. We compared the use of frequency and beatquency domains to predict patient risk after an acute coronary syndrome. We then determined whether machine learning could further improve the predictive performance. We first evaluated the use of pre-defined frequency and beatquency bands in a clinical trial dataset (N = 2302) for the HRV risk measure LF/HF (the ratio of low frequency to high frequency power).

Relative to frequency, beatquency improved the ability of LF/HF to predict cardiovascular death within one year (Area Under the Curve, or AUC, of 0.730 vs. 0.704,  $p < 0.001$ ). Next, we used machine learning to learn frequency and beatquency bands with optimal predictive power, which further improved the AUC for beatquency to 0.753 ( $p < 0.001$ ), but not for frequency. Results in additional validation datasets ( $N = 2255$  and  $N = 765$ ) were similar. Our results suggest that beatquency and machine learning provide valuable tools in physiological studies of HRV.

### **PETER SZOLOVITS**

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Peter Szolovits is Professor of Computer Science and Engineering in the MIT Department of Electrical Engineering and Computer Science (EECS) and an associate faculty member in the MIT Institute of Medical Engineering and Science (IMES) and its Harvard/MIT Health Sciences and Technology (HST) program. Professor Szolovits' interests in artificial intelligence and medical computing include: knowledge representation; qualitative reasoning; and probabilistic inference; Web-based heterogeneous medical record systems; life-long personal health information systems; and design of cryptographic schemes for health identifiers. He teaches classes in artificial intelligence, programming languages, medical computing, medical decision-making, knowledge-based systems and probabilistic inference.

### **The Clinical Decision-Making Group**

[http://people.csail.mit.edu/psz/home/Pete\\_MEDG\\_site/Home.html](http://people.csail.mit.edu/psz/home/Pete_MEDG_site/Home.html),

<http://groups.csail.mit.edu/medg/?#>

Research: [http://people.csail.mit.edu/psz/home/Pete\\_MEDG\\_site/Research.html](http://people.csail.mit.edu/psz/home/Pete_MEDG_site/Research.html)

Publications: [http://people.csail.mit.edu/psz/home/Pete\\_MEDG\\_site/Publications.html](http://people.csail.mit.edu/psz/home/Pete_MEDG_site/Publications.html)

The Clinical Decision Making Group at the MIT Laboratory for Computer Science is a research group dedicated to exploring and furthering the application of technology and artificial intelligence to clinical situations. Because of the vital and crucial nature of medical practice, and the need for accurate and timely information to support clinical decisions, the group is also focused on the gathering, availability, security and use of medical information throughout the human "life cycle" and beyond.

### **Segment convolutional neural networks (Seg-CNNs) for classifying relations in clinical notes**

Luo, Y., Cheng, Y., Uzuner, Ö., Szolovits, P., Starren, J., Journal of the American Medical Informatics Association, Volume 25, Issue 1, 1 January 2018, Article number ocx090, Pages 93-98, <https://doi.org/10.1093/jamia/ocx090>

We propose Segment Convolutional Neural Networks (Seg-CNNs) for classifying relations from clinical notes. Seg-CNNs use only word-embedding features without manual feature engineering. Unlike typical CNN models, relations between 2 concepts are identified by simultaneously learning separate representations for text segments in a sentence: preceding, concept1, middle, concept2, and succeeding. We evaluate Seg-CNN on the i2b2/VA relation classification challenge dataset. We show that Seg-CNN achieves a state-of-the-art micro-average F-measure of 0.742 for overall evaluation, 0.686 for classifying medical problem-treatment relations, 0.820 for medical problem-



test relations, and 0.702 for medical problem-medical problem relations. We demonstrate the benefits of learning segment-level representations. We show that medical domain word embeddings help improve relation classification. Seg-CNNs can be trained quickly for the i2b2/VA dataset on a graphics processing unit (GPU) platform. These results support the use of CNNs computed over segments of text for classifying medical relations, as they show state-of-the-art performance while requiring no manual feature engineering.

### Enabling phenotypic big data with PheNorm

Yu, S., Ma, Y., Gronsbell, J., Cai, T., Ananthakrishnan, A.N., Gainer, V.S., Churchill, S.E., Szolovits, P., Murphy, S.N., Kohane, I.S., Liao, K.P., Cai, T., *Journal of the American Medical Informatics Association*, Volume 25, Issue 1, 1 January 2018, Article number ocx111, Pages 54-60, <https://doi.org/10.1093/jamia/ocx111>

**Objective:** Electronic health record (EHR)-based phenotyping infers whether a patient has a disease based on the information in his or her EHR. A human-annotated training set with gold-standard disease status labels is usually required to build an algorithm for phenotyping based on a set of predictive features. The time intensiveness of annotation and feature curation severely limits the ability to achieve high-throughput phenotyping. While previous studies have successfully automated feature curation, annotation remains a major bottleneck. In this paper, we present PheNorm, a phenotyping algorithm that does not require expert-labeled samples for training. **Methods:** The most predictive features, such as the number of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes or mentions of the target phenotype, are normalized to resemble a normal mixture distribution with high area under the receiver operating curve (AUC) for prediction. The transformed features are then denoised and combined into a score for accurate disease classification. **Results:** We validated the accuracy of PheNorm with 4 phenotypes: coronary artery disease, rheumatoid arthritis, Crohn's disease, and ulcerative colitis. The AUCs of the PheNorm score reached 0.90, 0.94, 0.95, and 0.94 for the 4 phenotypes, respectively, which were comparable to the accuracy of supervised algorithms trained with sample sizes of 100-300, with no statistically significant difference. **Conclusion:** The accuracy of the PheNorm algorithms is on par with algorithms trained with annotated samples. PheNorm fully automates the generation of accurate phenotyping algorithms and demonstrates the capacity for EHR-driven annotations to scale to the next level - phenotypic big data.

### Medical subdomain classification of clinical notes using a machine learning-based natural language processing approach

Weng, W.-H., Waghlikar, K.B., McCray, A.T., Szolovits, P., Chueh, H.C., *BMC Medical Informatics and Decision Making*, Volume 17, Issue 1, 1 December 2017, Article number 155, <https://doi.org/10.1186/s12911-017-0556-8>

**Background:** The medical subdomain of a clinical note, such as cardiology or neurology, is useful content-derived metadata for developing machine learning downstream applications. To classify the medical subdomain of a note accurately, we have constructed a machine learning-based natural language processing (NLP) pipeline and developed medical subdomain classifiers based on the content of the note. **Methods:** We constructed the pipeline using the clinical NLP system, clinical Text Analysis and Knowledge Extraction System (cTAKES), the Unified Medical Language System (UMLS) Metathesaurus, Semantic Network, and learning algorithms to extract features from two datasets - clinical notes from Integrating Data for Analysis, Anonymization, and Sharing (iDASH) data repository (n = 431) and Massachusetts General Hospital (MGH) (n = 91,237), and built medical subdomain classifiers with different combinations of data representation methods and

supervised learning algorithms. We evaluated the performance of classifiers and their portability across the two datasets. Results: The convolutional recurrent neural network with neural word embeddings trained-medical subdomain classifier yielded the best performance measurement on iDASH and MGH datasets with area under receiver operating characteristic curve (AUC) of 0.975 and 0.991, and F1 scores of 0.845 and 0.870, respectively. Considering better clinical interpretability, linear support vector machine-trained medical subdomain classifier using hybrid bag-of-words and clinically relevant UMLS concepts as the feature representation, with term frequency-inverse document frequency (tf-idf)-weighting, outperformed other shallow learning classifiers on iDASH and MGH datasets with AUC of 0.957 and 0.964, and F1 scores of 0.932 and 0.934 respectively. We trained classifiers on one dataset, applied to the other dataset and yielded the threshold of F1 score of 0.7 in classifiers for half of the medical subdomains we studied. Conclusion: Our study shows that a supervised learning-based NLP approach is useful to develop medical subdomain classifiers. The deep learning algorithm with distributed word representation yields better performance yet shallow learning algorithms with the word and concept representation achieves comparable performance with better clinical interpretability. Portable classifiers may also be used across datasets from different institutions.

### **Understanding vasopressor intervention and weaning: Risk prediction in a public heterogeneous clinical time series database**

Wu, M., Ghassemi, M., Feng, M., Celi, L.A., Szolovits, P., Doshi-Velez, F., Journal of the American Medical Informatics Association, Volume 24, Issue 3, 2017, Pages 488-495, <https://doi.org/10.1093/jamia/ocw138>

Background: The widespread adoption of electronic health records allows us to ask evidence-based questions about the need for and benefits of specific clinical interventions in critical-care settings across large populations. Objective: We investigated the prediction of vasopressor administration and weaning in the intensive care unit. Vasopressors are commonly used to control hypotension, and changes in timing and dosage can have a large impact on patient outcomes. Materials and Methods: We considered a cohort of 15 695 intensive care unit patients without orders for reduced care who were alive 30 days post-discharge. A switching-state autoregressive model (SSAM) was trained to predict the multidimensional physiological time series of patients before, during, and after vasopressor administration. The latent states from the SSAM were used as predictors of vasopressor administration and weaning. Results: The unsupervised SSAM features were able to predict patient vasopressor administration and successful patient weaning. Features derived from the SSAM achieved areas under the receiver operating curve of 0.92, 0.88, and 0.71 for predicting ungapped vasopressor administration, gapped vasopressor administration, and vasopressor weaning, respectively. We also demonstrated many cases where our model predicted weaning well in advance of a successful wean. Conclusion: Models that used SSAM features increased performance on both predictive tasks. These improvements may reflect an underlying, and ultimately predictive, latent state detectable from the physiological time series.

## **MOBILE DIAGNOSTIC TOOLS, IMPLANTABLE, INGESTIBLE, WEARABLE, WIRELESS DEVICES, SENSORS**

### **DR. LEO CELI**

Principal Research Scientist, MIT Institute for Medical Engineering & Science (IMES); Clinical Research Director, MIT Laboratory of Computational Physiology; Co-Director, MIT Sana

Staff Physician, Division of Pulmonary, Critical Care and Sleep Medicine, Beth Israel Deaconess Medical Center; Assistant Professor, Part-time, <http://imes.mit.edu/research-staff-prof/leo-anthony-celi/> ; PUBS: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Celi+L>

Leo Anthony Celi has practiced medicine in three continents, giving him broad perspectives in healthcare delivery. As clinical research director and principal research scientist at the MIT Laboratory of Computational Physiology (LCP), he brings together clinicians and data scientists to support research using data routinely collected in the intensive care unit (ICU). His group built and maintains the Medical Information Mart for Intensive Care (MIMIC) database. This public-access database has been meticulously de-identified and is freely shared online with the research community. It is an unparalleled research resource; over 2000 investigators from more than 30 countries have free access to the clinical data under a data use agreement. In 2016, LCP partnered with Philips eICU Research Institute to host the eICU database with more than 2 million ICU patients admitted across the United States. The goal is to scale the database globally and build an international collaborative research community around health data analytics.

Leo founded and co-directs Sana, a cross-disciplinary organization based at the Institute for Medical Engineering and Science at MIT, whose objective is to leverage information technology to improve health outcomes in low- and middle-income countries. At its core is an open-source mobile tele-health platform that allows for capture, transmission and archiving of complex medical data (e.g. images, videos, physiologic signals such as ECG, EEG and oto-acoustic emission responses), in addition to patient demographic and clinical information. Sana is the inaugural recipient of both the mHealth (Mobile Health) Alliance Award from the United Nations Foundation and the Wireless Innovation Award from the Vodafone Foundation in 2010. The software has since been implemented around the globe including India, Kenya, Lebanon, Haiti, Mongolia, Uganda, Brazil, Ethiopia, Argentina, and South Africa...

### Sana

<http://sana.mit.edu/about>

Sana is a cross-disciplinary organization, including clinicians, engineers, policy, public health, and business experts along the entire healthcare value chain. Hosted at the Laboratory for Computational Physiology at MIT's Institute for Medical Engineering & Science.

Technology alone is not enough to transform global health and too often resources are indiscriminately thrown at problems without understanding what actually works. Furthermore, technology can't simply be transferred from developed countries to resource-limited settings, as solutions that work in one context, usually needs to be adapted to be sustainable in another locale.

We leverage a multidisciplinary team of Harvard and MIT trained clinicians and engineers, working together with public health professionals and researchers on the ground, to adapt the latest technologies to build sustainable practical solutions to global health problems.

~Sana promotes open source technologies and licenses to promote rapid and widespread adoption, expanding global access to mobile technologies. Sana Mobile is a highly customizable end-to-end mobile telehealth platform that accelerates the development of mHealth solutions to greatly improve access to quality care.

### ***mHealth***

~Sana actively contributes to the development and implementation of mHealth projects around the world, applying our extensive knowledge in informatics and leveraging our global network of experts and collaborators. The projects range from clinical research studies to social ventures, with a common focus on quality improvement and sustainable scaling.

### **CANAN DAGDEVIREN**

Assistant Professor of Media Arts and Sciences,

<https://www.media.mit.edu/people/canand/overview/>

Lab: <http://conformabledecoders.media.mit.edu/index.html>

Publications: <http://conformabledecoders.media.mit.edu/publications.html>

Dr. Canan Dagdeviren is an Assistant Professor in the Program in Media Arts and Sciences, where she leads the Conformable Decoders research group. The group aims to convert the patterns of nature and the human body into beneficial signals and energy.

Born in Istanbul, Turkey, Dagdeviren earned her PhD in Materials Science and Engineering from the University of Illinois at Urbana-Champaign, where she focused on exploring patterning techniques and creating piezoelectric biomedical systems. Her collective PhD research involved flexible mechanical energy harvesters, multi-functional cardiac vessel stents, wearable blood pressure sensors, and stretchable skin modulus sensing bio-patches.

### **Conformable Decoders**

<http://conformabledecoders.media.mit.edu/index.html>,

<https://www.media.mit.edu/groups/conformable-decoders/overview/>

Projects: <http://conformabledecoders.media.mit.edu/projects.html>

Publications: <http://conformabledecoders.media.mit.edu/publications.html>

The Conformable Decoders group explores novel materials, device designs, and fabrication strategies to create micro- and nanoscale electromechanical systems with mechanically adaptive features, which allow intimate integration with the objects of interest. These systems enable us to collect and convert essential patterns into beneficial forms in order to gain insights into our world, and enhance interactions with nature and each other.

### ***Conformal Piezoelectric Mechanical Energy Harvesters: Mechanically Invisible Human Dynamos***

<http://conformabledecoders.media.mit.edu/project1.html>

Nearly all classes of wearable and implantable biomedical devices depend on battery power for continuous operation. However, the life span of batteries is limited, rarely exceeding a few hours for wearables and a few years for implants. Consequently, battery replacements and, often times, surgical procedures are required to change the depleted batteries of implants, exposing people to high risks of surgical complications and/or high financial costs. This project seeks to develop conformal piezoelectric patches integrated to personal garments to extract energy from body movements such as motion of arms, fingers, and legs. The completion of this project could improve quality life for people and potentially provide environmentally friendly power.

***Conformal, Implantable Viscosity and Electrochemical Sensors: For Continuous Localized Tissue Monitoring and Disease Treatment***

<http://conformabledecoders.media.mit.edu/project2.html>

The continuous monitoring of physical patterns such as viscoelasticity and pH in the immediate environment of tissues is vitally important to do precise assessment and ensuing required treatment. Despite recent advances in understanding the pathological changes associated with specific diseases formation and progression, there is a deficit of suitable technology that can integrate a miniaturized sensory interface with a treatment platform. Our proposal aims to develop a new class of interfaces that can access the tissue through direct intimate contact and provide continuous monitoring of the changes in local viscoelasticity and pH. In addition, this interface will provide means for infusion of therapeutics for localized treatment. Successful execution of this proposal will provide continuous monitoring of physical pattern variations inside the human body and guidance for physicians to understand disease progression, and therefore, a future personalized treatment to increase survival rate of individuals.

***Flexible Piezoelectric Devices for Gastrointestinal Motility Sensing***

<http://conformabledecoders.media.mit.edu/project3.html>

Improvements in ingestible electronics with the capacity to sense physiological and pathophysiological states have transformed the standard of care for patients. Yet, despite advances in device development, significant risks associated with solid, non-flexible gastrointestinal transiting systems remain. Here, we report the design and use of an ingestible, flexible piezoelectric device that senses mechanical deformation within the gastric cavity. We demonstrate the capabilities of the sensor in both in vitro and ex vivo simulated gastric models, quantify its key behaviours in the gastrointestinal tract using computational modelling and validate its functionality in awake and ambulating swine. Our proof-of-concept device may lead to the development of ingestible piezoelectric devices that might safely sense mechanical variations and harvest mechanical energy inside the gastrointestinal tract for the diagnosis and treatment of motility disorders, as well as for monitoring ingestion in bariatric applications.

***Flexible piezoelectric devices for gastrointestinal motility sensing***

Canan Dagdeviren, Farhad Javid, Pauline Joe, Thomas von Erlach, Taylor Bensel, Zijun Wei, Sarah Saxton, Cody Cleveland, Lucas Booth, Shane McDonnell, Joy Collins, Alison Hayward, Robert Langer, Giovanni Traverso, Nature Biomedical Engineering, Vol 1, October 2017, 807–817, <https://doi.org/10.1038/s41551-017-0140-7>

Improvements in ingestible electronics with the capacity to sense physiological and pathophysiological states have transformed the standard of care for patients. Yet, despite advances in device development, significant risks associated with solid, non-flexible gastrointestinal transiting systems remain. Here, we report the design and use of an ingestible, flexible piezoelectric device that senses mechanical deformation within the gastric cavity. We demonstrate the capabilities of the sensor in both in vitro and ex vivo simulated gastric models, quantify its key behaviours in the gastrointestinal tract using computational modelling and validate its functionality in awake and ambulating swine. Our proof-of-concept device may lead to the development of ingestible piezoelectric devices that might safely sense mechanical variations and harvest mechanical energy inside the gastrointestinal tract for the diagnosis and treatment of motility disorders, as well as for monitoring ingestion in bariatric applications.



### *Flexible sensors can detect movement in GI tract*

#### **Ingestible devices could diagnose gastrointestinal slowdown or monitor food intake.**

Anne Trafton, MIT News Office, October 10, 2017, <http://news.mit.edu/2017/flexible-sensors-can-detect-movement-gi-tract-1010>

Researchers at MIT and Brigham and Women's Hospital have built a flexible sensor that can be rolled up and swallowed. Upon ingestion, the sensor adheres to the stomach wall or intestinal lining, where it can measure the rhythmic contractions of the digestive tract.

Such sensors could help doctors to diagnose gastrointestinal disorders that slow down the passage of food through the digestive tract. They could also be used to detect food pressing on the stomach, helping doctors to monitor food intake by patients being treated for obesity.

The flexible devices are based on piezoelectric materials, which generate a current and voltage when they are mechanically deformed. They also incorporate polymers with elasticity similar to that of human skin, so that they can conform to the skin and stretch when the skin stretches.

In a study appearing in the Oct. 10 issue of *Nature Biomedical Engineering*, the researchers demonstrated that the sensor remains active in the stomachs of pigs for up to two days. The flexibility of the device could offer improved safety over more rigid ingestible devices, the researchers say.

"Having flexibility has the potential to impart significantly improved safety, simply because it makes it easier to transit through the GI tract," says Giovanni Traverso, a research affiliate at MIT's Koch Institute for Integrative Cancer Research, a gastroenterologist and biomedical engineer at Brigham and Women's Hospital, and one of the senior authors of the paper.

Canan Dagdeviren, an assistant professor in MIT's Media Lab and the director of the Conformable Decoders research group, is the paper's lead author and one of the corresponding authors. Robert Langer, the David H. Koch Institute Professor and a member of the Koch Institute, is also an author of the paper....

### **Energy Harvesting from the Animal-Human Body for Self-Powered Electronics**

Dagdeviren, C., Li, Z., Wang, Z.L., *Annual Review of Biomedical Engineering*, Volume 19, 21 June 2017, Pages 85-108, <https://doi.org/10.1146/annurev-bioeng-071516-044517>

Living subjects (i.e., humans and animals) have abundant sources of energy in chemical, thermal, and mechanical forms. The use of these energies presents a viable way to overcome the battery capacity limitation that constrains the long-term operation of wearable-implantable devices. The intersection of novel materials and fabrication techniques offers boundless possibilities for the benefit of human health and well-being via various types of energy harvesters. This review summarizes the existing approaches that have been demonstrated to harvest energy from the bodies of living subjects for self-powered electronics. We present material choices, device layouts, and operation principles of these energy harvesters with a focus on in vivo applications. We discuss a broad range of energy harvesters placed in or on various body parts of human and animal models. We conclude with an outlook of future research in which the integration of various energy harvesters with advanced electronics can provide a new platform for the development of novel technologies for disease diagnostics, treatment, and prevention.

**RICHARD FLETCHER**

Research Scientist, MIT D-Lab and MIT Tata Center for Technology + Design,  
<http://tatacenter.mit.edu/portfolio/richard-fletcher/>, [http://d-lab.mit.edu/staff/rich\\_fletcher](http://d-lab.mit.edu/staff/rich_fletcher)  
<http://web.media.mit.edu/~fletcher/bio.html>

Assistant Professor, UMass Medical School, Department of Psychiatry; Research Scientist, Massachusetts General Hospital (MGH); Instructor, Harvard Medical School (HMS);  
Lab: <http://www.mobiletechnologylab.org/>  
Publications: <http://www.mobiletechnologylab.org/publications>

Dr. Fletcher has degrees in physics and electrical engineering from MIT, including graduate work in low-cost wireless sensors. Dr. Fletcher spent 5 years as research scientist in the US Air Force, designing microwave devices, antennas, and sensors for military applications, and holds more than 15 patents in the area of wireless sensors. Dr. Fletcher has founded multiple small companies, including TagSense, Inc., ([tagsense.com](http://tagsense.com)) which sells a variety of both active and passive RFID readers, tags and sensors – all designed by Dr. Fletcher – and provided custom sensor design for larger clients such as Motorola, US Postal Service, and NASA. Dr. Fletcher has created a variety of wearable sensors and systems to support mobile health research, some of which are sold commercially ([ashametrics.com](http://ashametrics.com)). Dr. Fletcher also builds wearable sensors for non-human primate animal studies at MIT, and also leads sensor efforts for living plants and agriculture at the MIT Media Lab ([www.mitcityfarm.com](http://www.mitcityfarm.com)) as well as D-Lab.

**Mobile Technology Lab**

<http://www.mobiletechnologylab.org>  
Projects: <https://mobilehealthlab.com/portfolio/>  
Publications: <https://mobilehealthlab.com/publications/>

The Mobile Technology group was established in 2012 by Dr. Rich Fletcher and is based at the MIT D-Lab and MIT SUTD-IDC Program. We develop new mobile technologies for a wide range of applications that have social impact, including: mHealth, global health, mobile psychiatry, and intelligent agriculture. We are particularly motivated by the needs of the poor and marginalized segments of the world's population, such as people living in poor villages in India or the homeless and mentally ill here in the US. To the extent that it can make a difference, we use technology as a tool to help improve the existing health disparities and economic disparities. Our research spans the areas of electronics / sensor design, advanced signal processing algorithms, machine learning, and user interface design; and we partner with clinical organizations and NGOs around the world to validate these technologies and create a sustainable long-term implementation.

***Thermography for Health Diagnostics and Monitoring***

<https://mobilehealthlab.com/portfolio/thermography-for-health-diagnostics-and-monitoring/>

The availability of small affordable thermal camera modules now make it possible to perform thermal analysis on mobile phones and in the spaces where we live and work. Thermography is routinely used to measure blood flow and microvasculature, as well as to measure breathing patterns. By combining thermal imaging with machine vision and machine learning, it is possible to create simple tools that can diagnose disease and monitor our health.

Our group collaborates with several clinical organizations to explore several different applications of thermal imaging, ranging from the diagnosis of infectious diseases, such as pneumonia and

tuberculosis, to creating early-warning systems for hospital ICU wards to automatically detect signs of sepsis and circulatory shock.

### ***Games for Mental Health Screening***

<https://mobilehealthlab.com/portfolio/games-for-mental-health-screening/>

While a variety of mobile apps exist to screen or monitor mental health conditions, few apps have been successful because: 1) they lack validation; and 2) they cannot maintain engagement with the user/patient. Our group is developing a mobile video game which addresses both of these issues. Each module in the game is derived from traditional clinically validated psychology assessments, and the design of the game provides greater enjoyment and engagement over longer periods of time.

### ***Algorithms for Autonomic Assessment***

<https://mobilehealthlab.com/portfolio/algorithms-for-autonomic-assessment/>

Autonomic Nervous System function is a fundamental part of psychophysiology, and the ability to analyze autonomic function is essential to many areas of medicine and clinical research. Our group is particularly interested in signatures of autonomic function that can be applied to the study of stress and also substance abuse. Our group develops algorithms that can be embedded in a variety of tools including commercial wearable sensors and non-contact sensors to monitor autonomic activity. By monitoring autonomic activity in real-time, it is also then possible to create real-time or just-in-time Interventions for a variety of mental health disorders.

### ***Mobile Tools for Community Health Workers***

<https://mobilehealthlab.com/portfolio/mobile-tools-for-community-health-workers/>

Community Health Workers (CHW) are a critical part of the health care system in many developing countries. They provide health education and perform basic tasks such as maternal and child health screening. These workers do not have formal medical training and carry out their job with very meager tools and paper-based records. Our group has developed a variety of smart-phone-based tools that automatically digitize the readings, improve data quality, and also provide the health workers with increased confidence and increased credibility with families to perform better screening and referrals.

### ***Low Cost Mobile Platform for Pulmonary Disease Screening***

Principal Investigator: Richard Fletcher

Project Dates: September 23, 2016 – August 31, 2018

[https://projectreporter.nih.gov/project\\_info\\_description.cfm?aid=9018346&icde=35225321](https://projectreporter.nih.gov/project_info_description.cfm?aid=9018346&icde=35225321)

Pulmonary disease is a very large public health concern in India, as well as in most developing countries. Relatively few general practitioner (GP) doctors are trained to properly diagnose pulmonary disease, and affordable tools for diagnostic support simply do not exist. This proposal seeks to validate and test the use of low-cost mobile phone-based diagnostic tools for pulmonary disease.

**Leveraging thermal patterns in children for telemedicine: Role of affordable imagers, smartphones and data-analytics**

Bhatnagar, A., Nagori, A., Fletcher, R., Lodha, R., Sethi, T., ACM International Conference Proceeding Series, Volume Part F128003, 7 March 2017, Pages 588-589, <https://doi.org/10.1145/3047273.3047376>

Smartphones combined with affordable technologies has a huge potential in Telemedicine and for better delivery of healthcare. We have used an affordable thermal camera combined with intensive patient monitoring and analytics to successfully enable digitization of whole body, non-contact sensing of temperature patterns. The utility of relative and absolute temperature patterns was tested for early diagnosis of various ailments such as circulatory shock. Image analytics combined with the development of computer algorithms enabled us to validate these patterns which can be deployed for remote community based care in the absence of adequate clinical staff and scarcity of resources. The use of this approach can help health workers such as ASHA workers to visualize, record and share whole body temperature patterns with the specialists via telemedicine helping them to make an informed decision. These techniques can be extended for use in adults and we plan to validate these for early detection of severe conditions eventually saving more lives through telemedicine.

**Validating the tele-diagnostic potential of affordable thermography in a big-data data-enabled ICU**

Sethi, T., Nagori, A., Bhatnagar, A., Gupta, P., Fletcher, R., Lodha, R., ACM International Conference Proceeding Series, Volume Part F127653, 7 March 2017, Pages 64-69, <https://doi.org/10.1145/3055219.3055234>

The potential for whole body thermal patterns in diagnosis of hemodynamic perfusion disturbances in critical care as well as community settings is unexplored. In this study we have combined an in-house digitized Big-data resource from ICU settings with Infra-red thermography to derive novel inferences about the tele-diagnostic potential of IR thermography in diagnosis of shock and perfusion disturbances. While Data-science and Big-data are expected to revolutionize the next generation medicine and healthcare, the scientific efforts towards building Big-data resources for enhancing patient safety and healthcare governance are missing, especially in developing countries. We addressed this challenge and describe our experience on deployment of Big-data warehousing and data-analytics software using lean pipelines developed using open-source technologies and their utility in deriving knowledge and high utility patterns from Affordable Infra-red Thermography. These knowledge frameworks and potentially translatable technology were developed in the Pediatric Intensive Care environment through extensive cross-talk between expert clinicians and data-scientists. In this work, we first demonstrate the successful creation of a unique Pediatric ICU resource of over 60,000 hours of continuous multivariate monitoring data followed by validation of the potential of whole body IR thermography in diagnosis of hemodynamic compromise. These patterns were validated through linear mixed models, a state-of-the-art statistical method for longitudinal data. The validated technology is affordable, and can be coupled to smartphones thus providing a huge potential in tele-medicine and electronic governance in healthcare and has the potential to be deployed in a tele-medicine setting with capturing of whole body temperature patterns by Accredited Social Health Activist (ASHA) workers. Therefore, this can enable early diagnosis of critical conditions such as sepsis and shock that are commonly associated with epidemics such as Dengue hemorrhagic fever in developing countries such as India. These images can be remotely shared with expert physicians and data-analysts via telemedicine thus aiding decisions in the Critical Care as well as Community settings.

### **Wearable sensor and algorithm for automated measurement of screen time**

Fletcher, R.R., Chamberlain, D., Richman, D., Oreskovic, N., Taveras, E., 2016 IEEE Wireless Health, WH 2016, 1 December 2016, Article number 7764564, Pages 109-116, <https://doi.org/10.1109/WH.2016.7764564>

The human use of electronic displays (television or computers), also known as "screen time", is currently a topic of great interest within behavior medicine and general clinical research. This behavior has been linked with a wide variety of pathologies, including obesity, circadian disruption, sleeping disorders, cardiometabolic disease, and socio-emotional behavior disorders in children. As an alternative to conventional data collection methods, such as self-reported questionnaires or interviews, we present an automated objective method for estimating screen time that makes use of a wearable wrist band containing an optical color sensor. By applying a machine learning model, and using data collected from a custom designed sensor band, we present results from a small study to demonstrate that it is possible to measure screen time exposure using the color sensor alone without the use of an accelerometer. Using data from two users in two different homes under a variety of activities and lighting conditions, we achieved a classification score of AUC=0.90 for television alone, 0.89 for computer alone, and 0.83 for the combination of both devices. As an additional test, we also present sample results from an experiment in a natural environment. These preliminary results are encouraging and are comparable to the accuracy of conventional self-reported methods. Limitations of this method and potential improvements are also discussed.

### **Revolutionizing Global Health**

**In more than 20 years working on wireless sensors and radio frequency identification (RFID), Richard Fletcher has produced several startups and over a dozen patents.**

Daniel de Wolff, MIT Industrial Liaison Program, April 26, 2017, <http://news.mit.edu/2017/revolutionizing-global-health-rich-fletcher-0426>

MIT research scientist Richard Fletcher directs the Mobile Technology Group at MIT D-Lab, which develops a variety of mobile sensors, analytic tools, and diagnostic algorithms to study problems in global health and behavior medicine. Utilizing mobile technologies — which include smartphones, wearable sensors, and the so-called internet of things — his group applies these technologies to real-world social problems with global implications. These issues involve a variety of areas, such as environmental monitoring and air pollution, agriculture, farming, and global health.

Fletcher notes that public health is of enormous importance and includes a wide range of diseases and conditions. His work at D-Lab has a myriad of applications: Sometimes this means simply doing better point-of-care diagnosis of acute or chronic diseases; other times, the focus is on screening and identifying those who are sick but don't realize it. "For example, consider the fact that every two minutes around the world a woman dies in childbirth. This is something that is for the most part preventable if problems can be detected ahead of time," Fletcher says.

Fletcher's group also creates tools that promote healthier behaviors and lifestyles. In addition to cardiometabolic diseases, such as diabetes, he points to the multitude of mental health disorders, like depression, anxiety disorders, sleep disorders, and the crisis of substance abuse, which negatively impact millions of lives, as areas that are in severe need of better solutions. His work seeks to apply technology to address many of these fundamental social problems affecting people on a daily basis.



“Mobile technology is a double-edged sword,” says Fletcher. “Addiction to smartphones and social media are emerging as serious problems, and most mobile health apps on the market have never been validated or tested clinically. But our group is trying to change that, and demonstrate that mobile technology can be a powerful tool to positively impact people’s health...”

### **DINA KATABI**

Andrew (1956) and Erna Viterbi Professor of Computer Science and Engineering,  
<https://www.csail.mit.edu/person/dina-katabi>, <http://nms.lcs.mit.edu/~dina/>  
Director, Center for Wireless Networks and Mobile Computing (Wireless@MIT),  
<http://wireless.csail.mit.edu/index>  
Director, Networks@MIT, <http://groups.csail.mit.edu/netmit/wordpress/>  
Publications: <http://groups.csail.mit.edu/netmit/wordpress/publications/publications/>

Professor Katabi’s research interests are in computer networks and data communication; these areas encompass congestion control, network measurements, scalability and robustness of communication systems, differentiated services, Internet pricing, routing, content distribution, peer-to-peer systems, self-configurable and wireless networks, and network security. Professor Katabi is particularly interested in adapting tools from various fields of applied mathematics such as control theory, coding theory, and artificial intelligence to solve problems in computer networks.

### **Networks@MIT**

<http://groups.csail.mit.edu/netmit/wordpress/>  
Projects: <http://groups.csail.mit.edu/netmit/wordpress/projects/projects/>  
Publications: <http://groups.csail.mit.edu/netmit/wordpress/publications/publications/>

Professor Katabi leads the Networks@MIT research group, which builds new protocols and architectures that improve the robustness and performance of computer networks. The group also works on wireless networks, network security, traffic engineering, congestion control, and routing. The group draws on advanced mathematical models to deliver practical network solutions and focuses. The group has a particular interest in adapting tools from various fields of applied mathematics such as control theory, coding theory, and machine learning to solve problems in computer networks.

### **Learning Sleep Stages from Radio Signals: A Conditional Adversarial Architecture**

Mingmin Zhao, Shichao Yue, Dina Katabi, Tommi Jaakkola, Matt Bianchi, Proceedings of the 34<sup>th</sup> International Conference on Machine Learning, Sydney, Australia, 2017, See:  
<http://sleep.csail.mit.edu/>  
Paper: <http://sleep.csail.mit.edu/files/rfsleep-paper.pdf>

RF-Sleep learns to predict sleep stages from radio measurements without any attached sensors on subjects. We introduce a new predictive model that combines convolutional and recurrent neural networks to extract sleep-specific subject-invariant features from RF signals and capture the temporal progression of sleep. A key innovation underlying our approach is a modified adversarial training regime that discards extraneous information specific to individuals or measurement conditions, while retaining all information relevant to the predictive task.

### ***New AI algorithm monitors sleep with radio waves***

**Patients with sleep disorders could be studied nonintrusively at home using wireless signals.**

Anne Trafton, MIT News Office, August 6, 2017, <http://news.mit.edu/2017/new-ai-algorithm-monitors-sleep-radio-waves-0807>

More than 50 million Americans suffer from sleep disorders, and diseases including Parkinson's and Alzheimer's can also disrupt sleep. Diagnosing and monitoring these conditions usually requires attaching electrodes and a variety of other sensors to patients, which can further disrupt their sleep.

To make it easier to diagnose and study sleep problems, researchers at MIT and Massachusetts General Hospital have devised a new way to monitor sleep stages without sensors attached to the body. Their device uses an advanced artificial intelligence algorithm to analyze the radio signals around the person and translate those measurements into sleep stages: light, deep, or rapid eye movement (REM).

"Imagine if your Wi-Fi router knows when you are dreaming, and can monitor whether you are having enough deep sleep, which is necessary for memory consolidation," says Dina Katabi, the Andrew and Erna Viterbi Professor of Electrical Engineering and Computer Science, who led the study. "Our vision is developing health sensors that will disappear into the background and capture physiological signals and important health metrics, without asking the user to change her behavior in any way."

Katabi worked on the study with Matt Bianchi, chief of the Division of Sleep Medicine at MGH, and Tommi Jaakkola, the Thomas Siebel Professor of Electrical Engineering and Computer Science and a member of the Institute for Data, Systems, and Society at MIT. Mingmin Zhao, an MIT graduate student, is the paper's first author, and Shichao Yue, another MIT graduate student, is also a co-author....

### **Extracting Gait Velocity and Stride Length from Surrounding Radio Signals**

Chen-Yu Hsu, Yuchen Liu, Zachary Kabelac, Rumen Hristov, Dina Katabi, Christine Liu, 2017 ACM, <http://dx.doi.org/10.1145/3025453.3025937>  
[https://people.csail.mit.edu/cyhsu/papers/wigait\\_chi17.pdf](https://people.csail.mit.edu/cyhsu/papers/wigait_chi17.pdf)

Gait velocity and stride length are critical health indicators for older adults. A decade of medical research shows that they provide a predictor of future falls, hospitalization, and functional decline among seniors. However, currently these metrics are measured only occasionally during medical visits. Such infrequent measurements hamper the opportunity to detect changes and intervene early in the impairment process. In this paper, we develop a sensor that uses radio signals to continuously measure gait velocity and stride length at home. Our sensor hangs on a wall like a picture frame. It does not require the monitored person to wear or carry a device on her body. Our approach builds on recent advances in wireless systems which have shown that one can locate people based on how their bodies impact the surrounding radio signals. We demonstrate the accuracy of our method by comparing it to the gold standard in clinical tests, and the VICON motion tracking system. Our experience from deploying the sensor in 14 homes indicates comfort with the technology and a high acceptance rate.

### ***Detecting walking speed with wireless signals***

**By measuring this emerging vital sign, CSAIL system could help monitor and diagnose health issues like cognitive decline and cardiac disease.**

Adam Conner-Simons, Rachel Gordon, CSAIL, May 1, 2017, <http://news.mit.edu/2017/dina-katabi-csail-team-develop-wireless-system-to-detect-walking-speeds-0501>

We've long known that blood pressure, breathing, body temperature and pulse provide an important window into the complexities of human health. But a growing body of research suggests that another vital sign – how fast you walk – could be a better predictor of health issues like cognitive decline, falls, and even certain cardiac or pulmonary diseases.

Unfortunately, it's hard to accurately monitor walking speed in a way that's both continuous and unobtrusive. Professor Dina Katabi's group at MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL) has been working on the problem, and believes that the answer is to go wireless.

In a new paper, the team presents "WiGait," a device that can measure the walking speed of multiple people with 95 to 99 percent accuracy using wireless signals.

The size of a small painting, the device can be placed on the wall of a person's house and its signals emit roughly one-hundredth the amount of radiation of a standard cellphone. It builds on Katabi's previous work on WiTrack, which analyzes wireless signals reflected off people's bodies to measure a range of behaviors from breathing and falling to specific emotions.

"By using in-home sensors, we can see trends in how walking speed changes over longer periods of time," says lead author and PhD student Chen-Yu Hsu. "This can provide insight into whether someone should adjust their health regimen, whether that's doing physical therapy or altering their medications."

WiGait is also 85 to 99 percent accurate at measuring a person's stride length, which could allow researchers to better understand conditions like Parkinson's disease that are characterized by reduced step size....

### **ROBERT S. LANGER**

David H Koch Institute Professor; <https://ki.mit.edu/people/faculty/langer>

Professor of Mechanical, Chemical and Biomedical Engineering and Health Sciences and Technology, <http://cheme.mit.edu/profile/robert-s-langer/>, <http://hst.mit.edu/users/rlangermitedu>, <http://be.mit.edu/directory/robert-langer>, <http://imes.mit.edu/people/faculty/langer-robert/>;  
Lab: <http://web.mit.edu/langerlab/>, <http://langer-lab.mit.edu/>

Publications: <http://langer-lab.mit.edu/publications>

Professor Langer's research interests include: drug delivery; biomaterials; tissue engineering; biotechnology; immobilized enzymes; and biomedical engineering. His research group works at the interface of biotechnology and materials science. A major focus is the study and development of polymers to deliver drugs, particularly genetically engineered proteins, DNA and RNAi, continuously at controlled rates for prolonged periods of time. Work is in progress in the following areas:

- Investigating the mechanism of release from polymeric delivery systems with concomitant microstructural analysis and mathematical modeling

- Studying applications of these systems including the development of effective long-term delivery systems for insulin, anti-cancer drugs, growth factors, gene therapy agents and vaccines
- Developing controlled release systems that can be magnetically, ultrasonically, or enzymatically triggered to increase release rates
- Synthesizing new biodegradable polymeric delivery systems which will ultimately be absorbed by the body
- Creating new approaches for delivering drugs such as proteins and genes across complex barriers in the body such as the blood-brain barrier, the intestine, the lung and the skin
- Researching new ways to create tissue and organs including creating new polymer systems for tissue engineering
- Stem cell research including controlling growth and differentiation
- Creating new biomaterials with shape memory or surface switching properties
- Angiogenesis inhibition

### Langer Lab

Research: <http://langer-lab.mit.edu/research>

Publications: <http://langer-lab.mit.edu/publications>

Our work is at the interface of biotechnology and materials science. A major focus is the study and development of polymers to deliver drugs, particularly genetically engineered proteins, DNA and RNAi, continuously at controlled rates for prolonged periods of time. Work is in progress in the following areas:

- Investigating the mechanism of release from polymeric delivery systems with concomitant microstructural analysis and mathematical modeling.
- Studying applications of these systems including the development of effective long-term delivery systems for insulin, anti-cancer drugs, growth factors, gene therapy agents and vaccines.
- Developing controlled release systems that can be magnetically, ultrasonically, or enzymatically triggered to increase release rates.

### **Langer Lab: Medical devices**

[http://langer-lab.mit.edu/research/medical\\_devices](http://langer-lab.mit.edu/research/medical_devices)

In addition to internal regulation (degradation of polymers or enzymatic trigger) for drug controlled release, we are also interested in developing novel approaches for drug delivery responding to external stimuli such as magnetic or ultrasound signals. We investigate microtech devices for treating traumatic brain injury, transdermal delivery systems, photo-triggered Intravitreal implants and injectable gastrointestinal delivery devices for minimally invasive drug delivery routes. Our lab includes a highly multidisciplinary team of chemists, biologists, engineers and physicians to develop and rapidly translate new nanotechnologies to better diagnose and treat cancers and other diseases.

### **Miniaturized neural system for chronic, local intracerebral drug delivery**

Dagdeviren, C., Ramadi, K.B., Joe, P., Spencer, K., Schwerdt, H.N., Shimazu, H., Delcasso, S., Amemori, K.-I., Nunez-Lopez, C., Graybiel, A.M., Cima, M.J., Langer, R., *Science Translational Medicine*, Volume 10, Issue 425, 24 January 2018, Article number eaan2742, <https://doi.org/10.1126/scitranslmed.aan2742>

Recent advances in medications for neurodegenerative disorders are expanding opportunities for improving the debilitating symptoms suffered by patients. Existing pharmacologic treatments, however, often rely on systemic drug administration, which result in broad drug distribution and consequent increased risk for toxicity. Given that many key neural circuitries have sub-cubic millimeter volumes and cell-specific characteristics, small-volume drug administration into affected brain areas with minimal diffusion and leakage is essential. We report the development of an implantable, remotely controllable, miniaturized neural drug delivery system permitting dynamic adjustment of therapy with pinpoint spatial accuracy. We demonstrate that this device can chemically modulate local neuronal activity in small (rodent) and large (nonhuman primate) animal models, while simultaneously allowing the recording of neural activity to enable feedback control.

### **Wireless power transfer to millimeter-sized gastrointestinal electronics validated in a swine model**

Abid, A., O'Brien, J.M., Bense, T., Cleveland, C., Booth, L., Smith, B.R., Langer, R. Traverso, G., *Scientific Reports*, Volume 7, 2017, Article number 46745, <https://doi.org/10.1038/srep46745>

Electronic devices placed in the gastrointestinal (GI) tract for prolonged periods have the potential to transform clinical evaluation and treatment. One challenge to the deployment of such gastroresident electronics is the difficulty in powering millimeter-sized electronics devices without using batteries, which compromise biocompatibility and long-term residence. We examined the feasibility of leveraging mid-field wireless powering to transfer power from outside of the body to electronics at various locations along the GI tract. Using simulations and *ex vivo* measurements, we designed mid-field antennas capable of operating efficiently in tissue at 1.2 GHz. These antennas were then characterized *in vivo* in five anesthetized pigs, by placing one antenna outside the body, and the other antenna inside the body endoscopically, at the esophagus, stomach, and colon. Across the animals tested, mean transmission efficiencies of -41.2, -36.1, and -34.6 dB were achieved *in vivo* while coupling power from outside the body to the esophagus, stomach, and colon, respectively. This corresponds to power levels of 37.5  $\mu$ W, 123  $\mu$ W and 173  $\mu$ W received by antennas in the respective locations, while keeping radiation exposure levels below safety thresholds. These power levels are sufficient to wirelessly power a range of medical devices from outside of the body.

### **Wireless power could enable ingestible electronics**

#### **Small sensors or drug delivery devices could reside in the GI tract indefinitely.**

Anne Trafton, MIT News Office, April 27, 2017, <http://news.mit.edu/2017/wireless-power-ingestible-electronics-0427>

Researchers at MIT, Brigham and Women's Hospital, and the Charles Stark Draper Laboratory have devised a way to wirelessly power small electronic devices that can linger in the digestive tract indefinitely after being swallowed. Such devices could be used to sense conditions in the gastrointestinal tract or carry small reservoirs of drugs to be delivered over an extended period.

Finding a safe and efficient power source is a critical step in the development of such ingestible electronic devices, says Giovanni Traverso, a research affiliate at MIT's Koch Institute for Integrative Cancer Research and a gastroenterologist and biomedical engineer at Brigham and Women's Hospital.



“If we’re proposing to have systems reside in the body for a long time, power becomes crucial,” says Traverso, one of the senior authors of the study. “Having the ability to transmit power wirelessly opens up new possibilities as we start to approach this problem.”

The new strategy, described in the April 27 issue of the journal *Scientific Reports*, is based on the wireless transfer of power from an antenna outside the body to another one inside the digestive tract. This method yields enough power to run sensors that could monitor heart rate, temperature, or levels of particular nutrients or gases in the stomach.

“Right now we have no way of measuring things like core body temperature or concentration of micronutrients over an extended period of time, and with these devices you could start to do that kind of thing,” says Abubakar Abid, a former MIT graduate student who is the paper’s first author.

Robert Langer, the David H. Koch Institute Professor at MIT, is also a senior author of the paper. Other authors are Koch Institute technical associates Taylor Benseal and Cody Cleveland, former Koch Institute research technician Lucas Booth, and Draper researchers Brian Smith and Jonathan O’Brien....

### **Prolonged energy harvesting for ingestible devices**

Nadeau P, El-Damak D, Glettig D, Kong YL, Mo S, Cleveland C, Booth L, Roxhed N, Langer R, Chandrakasan AP, Traverso G, *Nat Biomed Eng.* 2017;1. pii: 0022. doi: 10.1038/s41551-016-0022. Epub 2017 Feb 6., <https://doi.org/10.1038/s41551-016-0022>

Ingestible electronics have revolutionized the standard of care for a variety of health conditions. Extending the capacity and safety of these devices, and reducing the costs of powering them, could enable broad deployment of prolonged monitoring systems for patients. Although prior biocompatible power harvesting systems for in vivo use have demonstrated short minute-long bursts of power from the stomach, not much is known about the capacity to power electronics in the longer term and throughout the gastrointestinal tract. Here, we report the design and operation of an energy-harvesting galvanic cell for continuous in vivo temperature sensing and wireless communication. The device delivered an average power of 0.23  $\mu\text{W}$  per  $\text{mm}^2$  of electrode area for an average of 6.1 days of temperature measurements in the gastrointestinal tract of pigs. This power-harvesting cell has the capacity to provide power for prolonged periods of time to the next generation of ingestible electronic devices located in the gastrointestinal tract.

### **Engineers harness stomach acid to power tiny sensors**

**Ingestible electronic devices could monitor physiological conditions or deliver drugs.**

Anne Trafton, MIT News Office, February 6, 2017, <http://news.mit.edu/2017/engineers-harness-stomach-acid-power-tiny-sensors-0206>

Researchers at MIT and Brigham and Women’s Hospital have designed and demonstrated a small voltaic cell that is sustained by the acidic fluids in the stomach. The system can generate enough power to run small sensors or drug delivery devices that can reside in the gastrointestinal tract for extended periods of time.

This type of power could offer a safer and lower-cost alternative to the traditional batteries now used to power such devices, the researchers say.

“We need to come up with ways to power these ingestible systems for a long time,” says Giovanni Traverso, a research affiliate at the Koch Institute for Integrative Cancer Research. “We see the GI tract as providing a really unique opportunity to house new systems for drug delivery and sensing, and fundamental to these systems is how they are powered.”

Traverso, who is also a gastroenterologist and biomedical engineer at Brigham and Women’s Hospital, is one of the senior authors of the study. The others are Robert Langer, the David H. Koch Institute Professor at MIT; and Anantha Chandrakasan, head of MIT’s Department of Electrical Engineering and Computer Science and the Vannevar Bush Professor of Electrical Engineering and Computer Science. MIT postdoc Phillip Nadeau is the lead author of the paper, which appears in the Feb. 6 issue of Nature Biomedical Engineering....

### **RAMESH RASKAR**

Associate Professor of Media Arts and Sciences,

<https://www.media.mit.edu/people/raskar/overview/>, <http://web.media.mit.edu/~raskar/>;

Co-Director, Center for Future Storytelling, <http://cfs.media.mit.edu/research.html>

Head, Camera Culture Group, <http://cameraculture.media.mit.edu/>

Publications: <https://www.media.mit.edu/people/raskar/publications/>

Ramesh Raskar joined the Media Lab from Mitsubishi Electric Research Laboratories in 2008 as head of the Lab's Camera Culture research group. His research interests span the fields of computational photography, inverse problems in imaging, and human-computer interaction. Recent inventions include transient imaging to look around a corner, a next-generation CAT-scan machine, imperceptible markers for motion capture (Prakash), long-distance barcodes (Bokode), touch + hover 3D interaction displays (BiDi screen), low-cost eye care devices (NETRA) and new theoretical models to augment light fields (ALF) to represent wave phenomena.

### **Camera Culture Group**

<http://cameraculture.media.mit.edu/>

Research: <http://cameraculture.media.mit.edu/research/>

Publications: <http://cameraculture.media.mit.edu/publications/>

MIT Media Lab’s Camera Culture Group focuses on making the invisible visible—inside our bodies, around us, and beyond—for health, work, and connection. The goal is to create an entirely new class of imaging platforms that have an understanding of the world that far exceeds human ability and produce meaningful abstractions that are well within human comprehensibility. The group conducts multi-disciplinary research in modern optics, sensors, illumination, actuators, probes and software processing. This work ranges from creating novel feature-revealing computational cameras and new lightweight medical imaging mechanisms, to facilitating positive social impact via the next billion personalized cameras.

### ***Skin Perfusion Photography***

<http://cameraculture.media.mit.edu/research/#cbp=/cubepportfolio/skin-perfusion-photography>

Perfusion is the process of delivering blood into tissue. Measuring skin perfusion is important for wound and burn estimation, and for monitoring plastic and reconstructive surgeries. Here, we integrate computational photography with skin perfusion measurements via laser speckle contrast imaging (LSCI). By recording multiple images, we compute the direct scattering of laser light from

the skin and eliminate unwanted scattering from the underlying tissue. Our method holds promise for many applications of precise analysis of in vivo blood flow.

### ***Identi-Wheez: A Device for In-home Diagnosis of Asthma***

<https://www.media.mit.edu/projects/identi-wheez-a-device-for-in-home-diagnosis-of-asthma/overview/>

Asthma is the most common chronic illness among children. The skills required to diagnose it make it an even greater concern. Our solution is a child-friendly wearable device that allows in-home diagnosis of asthma. The device acquires simultaneous measurements from multiple stethoscopes. The recordings are then sent to a specialist who uses assistive diagnosis algorithms that enable auscultation (listening to lung sounds with a stethoscope). Sound refocusing algorithms enable the specialist to listen to any location in the lungs. The specialist also has access to a sound "heat map" that shows the location of sound sources in the lungs.

### ***Portable Retinal Imaging***

<https://www.media.mit.edu/projects/portable-retinal-imaging/overview/>

The major challenge in preventing blindness is identifying patients and bringing them to specialty care. Diseases that affect the retina, the image sensor in the human eye, are particularly challenging to address, because they require highly trained eye specialists (ophthalmologists) who use expensive equipment to visualize the inner parts of the eye. Diabetic retinopathy, HIV/AIDS-related retinitis, and age-related macular degeneration are three conditions that can be screened and diagnosed to prevent blindness caused by damage to retina. We exploit a combination of two novel ideas to simplify the constraints of traditional devices, with simplified optics and clever illumination in order to capture and visualize images of the retina in a standalone device easily operated by the user. Prototypes are conveniently embedded in either a mobile hand-held retinal camera, or wearable eyeglasses.

### ***Automated retinal imaging and trend analysis - a tool for health monitoring***

Roesch, K., Swedish, T., Raskar, R., *Clinical Ophthalmology*, Volume 11, 23 May 2017, Pages 1015-1020, <https://doi.org/10.2147/OPHTH.S116265>

Most current diagnostic devices are expensive, require trained specialists to operate and gather static images with sparse data points. This leads to preventable diseases going undetected until late stage, resulting in greatly narrowed treatment options. This is especially true for retinal imaging. Future solutions are low cost, portable, self-administered by the patient, and capable of providing multiple data points, population analysis, and trending. This enables preventative interventions through mass accessibility, constant monitoring, and predictive modeling.

### ***Real-Time Physiological Measurement and Visualization Using a Synchronized Multi-camera System***

Gupta, O., McDuff, D., Raskar, R., *IEEE Computer Society Conference on Computer Vision and Pattern Recognition Workshops*, 16 December 2016, Article number 7789536, Pages 312-319, <https://doi.org/10.1109/CVPRW.2016.46>

Remote physiological measurement has widespread implications in healthcare and affective computing. This paper presents an efficient system for remotely measuring heart rate and heart rate variability using multiple low-cost digital cameras in real-time. We combine an RGB camera,

monochrome camera with color filter and a thermal camera to recover the blood volume pulse (BVP). We show that using multiple cameras in synchrony yields the most accurate recovery of the BVP signal. The RGB combination is not optimal. We show that the thermal camera improves performance of measurement under dynamic ambient lighting but the thermal camera alone is not enough and accuracy can be improved by adding more spectral channels. We present a real-time prototype that allows accurate physiological measurement combined with a novel user interface to visualize changes in heart rate and heart rate variability. Finally, we propose how this system might be used for applications such as patient monitoring.

### **Identi-wheez - A device for in-home diagnosis of asthma**

Satat, G., Ramchander, K., Raskar, R., Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS, Volume 2016-October, 13 October 2016, Article number 7591696, Pages 4375-4378, <https://doi.org/10.1109/EMBC.2016.7591696>

Asthma is the most common chronic illness among children. The skills required to diagnose it make it an even greater concern. In this work, we present a child-friendly wearable device, which allows in-home diagnosis of asthma. The device acquires simultaneous measurements from multiple stethoscopes. The recordings are then sent to a specialist who uses assistive diagnosis algorithms that enable auscultation (listening to lung sounds with a stethoscope) at any location in the lungs volume by sound refocusing. The specialist is also presented with a sound 'heat map' which shows the location of sound sources in the lungs. We present design considerations of our device, as well as the algorithms for assistive diagnosis and their analysis which demonstrate reduction of ambient and measurement noise by over 10dB.

## **RELATED**

### **ZEN CHU**

Senior Lecturer, <http://mitsloan.mit.edu/faculty-and-research/faculty-directory/detail/?id=53473>  
Co-Founder, MIT Hacking Medicine, <http://hackingmedicine.mit.edu/>

Zen Chu serves as Senior Lecturer in Healthcare Innovation at the MIT Sloan School of Management and Harvard-MIT Health Sciences & Technology program. With Professors Martha Gray and Bill Aulet, he created and directs HST.978 MIT Healthcare Ventures graduate course and serves as faculty director for the HackingMedicine.MIT.edu healthcare technology innovation initiative. Zen actively consults health tech companies and healthcare systems adapting to global digital healthcare transformation and emerging markets.

### **A Systems Approach to Healthcare Innovation Using the MIT Hacking Medicine Model**

Gubin, T.A., Iyer, H.P., Liew, S.N., Sarma, A., Revelos, A., Ribas, J., Movassaghi, B., **Chu, Z.M.**, Khalid, A.N., Majmudar, M.D., Lee, C.X., Cell Systems, Volume 5, Issue 1, 26 July 2017, Pages 6-10, <https://doi.org/10.1016/j.cels.2017.02.012>

MIT Hacking Medicine is a student, academic, and community-led organization that uses systems-oriented “healthcare hacking” to address challenges around innovation in healthcare. The group has organized more than 80 events around the world that attract participants with diverse backgrounds. These participants are trained to address clinical needs from the perspective of multiple stakeholders and emphasize utility and implementation viability of proposed solutions. We describe the MIT Hacking Medicine model as a potential method to integrate collaboration and training in rapid innovation techniques into academic medical centers. Built upon a systems

approach to healthcare innovation, the time-compressed but expertly guided nature of the events could enable more widely accessible preliminary training in systems-level innovation methodology, as well as creating a structured opportunity for interdisciplinary congregation and collaboration.

### **Video: Moving from Hype to Impact with Digital Health**

ILP Video, April 12, 2017, <http://ilp.mit.edu/videodetail.jsp?confid=163&ilp-videos=Y&id=2004#>

Digital Health mobile apps and connected medical devices are rapidly changing how patients learn, monitor, diagnose and treat disease. Even in these early days of the digital transformation of healthcare, connected medical devices and digital services are winning reimbursement as digiceuticals by payors and insurers. However, the critical need going forward is how to measure, compare and prove these new tools and digital biomarkers are safe, effective and valuable at scale, not just in the USA but globally, across geographies, cultures and health systems.

### **Digital Health Scales Medicine**

#### **Zen Chu leverages digital technology to improve healthcare access, cost, and quality across the globe.**

Alice McCarthy, ILP Institute Insider, <http://ilp.mit.edu/newsstory.jsp?id=21964>

“Now is the best time in the history of the world to be an entrepreneur and a technologist focused on healthcare,” says Zen Chu, of MIT Health Sciences and Technology Program and the Sloan School of Management. “Fundamental shifts in technology and business models have created immense new opportunities that only startups and innovative companies can capture.”

As a serial entrepreneur and MIT researcher, Chu embraces what he calls tectonic shifts in healthcare, not just the changing incentives in the United States but also consumer healthcare in emerging markets where smartphones and connectivity are increasingly ubiquitous. As the co-founder and lead faculty director of MIT Hacking Medicine, a program focused on healthcare transformation through technology, Chu convenes technologists, entrepreneurs, clinicians, and life scientists to review and assess new models and new ventures in digital healthcare at the core of these shifts....

### **Data into Action**

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

Kara Baskin, Spectrum, Fall 2016, <https://spectrum.mit.edu/fall-2016/data-into-action/>

“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)....



## LABS, CENTERS, PROGRAMS

### AI AND DIGITAL HEALTH IN TRANSLATIONAL MEDICINE AND CLINICAL TRIALS

March 30, 2018, <http://aibiotech.csail.mit.edu>

The summit brings together the top leaders and visionaries in three domains: technology, biotech, and regulatory agencies. The technology leaders will explain cutting edge technologies and how they can deliver new biomarkers, improve safety, and reduce the cost and duration of clinical trials. The biotech visionaries will talk about the key opportunities in biotech and the challenges of integrating AI and digital technologies in clinical trials. The leaders in regulatory agencies will speak about new regulations regarding digital technologies and AI, and the requirements for registering new digital biomarkers and endpoints.

### MEDICAL ELECTRONIC DEVICE REALIZATION CENTER

Co-Directors: Charles Sodini, Brian Anthony, Joel Voldman, Thomas Heldt

Projects: <http://medrc.mit.edu/projects/>

Publications: <http://medrc.mit.edu/publications/>

The MEDRC will serve as a focal point for large business, for venture-funded startups, and for the medical community. The Center will foster the creation of prototype devices and intellectual property and aims to serve as the catalyst for the deployment of innovative healthcare technology that will reduce the cost of healthcare in both the developed and developing world.

### An Electronically Steered, Wearable Transcranial Doppler (TCD) Ultrasound

Authors: Sabino Pietrangelo, Charles Sodini, Hae-Sung Lee

<http://medrc.mit.edu/services/an-electronically-steered-wearable-transcranial-doppler-tcd-ultrasound/>

The central objective of critical care for patients affected by neurotrauma, cerebrovascular accident (i.e., stroke), and other neurovascular pathologies is to monitor patient state and provide suitable medical intervention to mitigate secondary injury and aid in recovery. While several non-invasive cerebrovascular diagnostic modalities exist, the use of transcranial Doppler (TCD) sonography is highly compelling for certain diagnostic needs due to its safety in prolonged studies, high temporal resolution, and relative portability. Despite a growing list of potential diagnostic applications, several constraints – notably operator dependent measurement results and the need for manual vessel location – have generally confined the use of TCD ultrasound to highly-specific clinical environments (e.g., neurocritical care units and vascular laboratories).

### Long-Term, Subdermal Implantable EEG Recorder and Seizure Detector

Authors: Bruno Do Valle, Jason Yang, Charles Sodini

<http://medrc.mit.edu/services/long-term-subdermal-implantable-ee-recorder-and-seizure-detector/>

Epilepsy is a common neurological disorder that affects about 1% of world population. It is characterized by repeated seizures, which are caused by an abnormal neuronal firing at the affected brain area. Although EEG has been the chief modality in the diagnosis and treatment of epileptic disorders for more than half a century, long term recordings (days to weeks) still can only be obtained in the hospital setting. Many patients, however, have intermittent seizures occurring far

less often. Patients cannot come into the hospital for weeks on end in order for an event to be captured on EEG – a necessary prerequisite for making a definitive diagnosis, tailoring therapy, or even affixing the true rate of events. This work aims to solve this need by proposing a subdermal implantable 8-channel EEG monitor and seizure detector. The system will be implanted behind the patient's ear in order to guarantee continuous monitoring of the brain's activity. An ASIC containing a novel seizure detector and all the circuits required to record 8 channels of EEG has been designed. The system is expected to be implanted in a pig.

### **Predicting Death After Acute Coronary Syndrome**

Authors: Yun Liu, John Guttag, Collin Stultz

<http://medrc.mit.edu/services/predicting-death-after-acute-coronary-syndrome/>

Frequency domain measures of heart rate variability (HRV) are associated with adverse events after a myocardial infarction. However, because of natural variability in heart rate over time and across patients, patterns in the traditional “time-frequency” domain (measured in Hz) may capture different cardiac phenomena at different heart rates. An alternative is to consider frequency with respect to heartbeats, or “beat-frequency”. We compared the use of both types of frequency domains to risk stratify patients after a non-ST-elevation acute coronary syndrome (NSTEMI). We then determined whether machine learning could be used to further improve the ability of HRV metrics to identify high-risk patient subgroups. Our results on a dataset of 2,302 patients indicate that applying beat-frequency to a current HRV metric, low frequency high frequency (LFHF) improves the area under receiver operating characteristic curve (AUC) from 0.704 for time-frequency LFHF to 0.730 for beat-frequency LFHF. Use of machine learning to learn the predictive frequency bands further increased the AUC to 0.753 for beat-frequency, but not time-frequency. These improvements were statistically significant ( $p < 0.001$ ). We conclude that beat-frequency and machine learning improve our ability to risk stratify patients after NSTEMI, and more generally, we have presented a novel data-driven method to select frequency bands for analysis of HRV.

### **Calibration-Free Blood Pressure Estimation Using Ultrasound**

Authors: Aaron M. Zakrzewski, Brian Anthony

<http://medrc.mit.edu/services/calibration-free-blood-pressure-estimation-using-ultrasound/>

Current non-invasive blood pressure estimation technology suffers from many inconveniences; for example, some techniques cut off blood flow, are hard to use, might be inaccurate, and require external calibration. In this poster, an algorithm is developed to estimate blood pressure at the carotid artery in a way that is non-invasive, potentially continuous, easy-to-use, and calibration-free. Inspired by quantitative compression-based elastography methods, this optimization algorithm solves an inverse problem using the Levenberg-Marquardt method. It takes an ultrasound image sequence and applied force as an input and estimates blood pressure, artery hyperelastic stiffness, average background tissue linear stiffness, and artery thickness. By considering the zero pressure condition of the artery, the blood pressure estimation does not require any external calibration. To test the algorithm, a Terason 3000t system is used to acquire ultrasound data at the carotid artery as the applied force slowly increases from 2 N to 8 N. The carotid artery is segmented from the image sequence using an algorithm based on the Kalman Filter. This data is used as input into the blood pressure estimation algorithm, and the resulting percent errors of the algorithm when estimating systole and diastole blood pressures are 6.7 and 7.4 percent, respectively, compared to blood pressure estimated by an automatic blood pressure cuff. The results of the algorithm suggest that ultrasound can be used in a clinical setting to estimate blood pressure.

**MIT DESIGN LAB**

Founder: Federico Casalegno; Director: Yihun Lim

Projects: <https://design.mit.edu/projects>

Publications: <https://design.mit.edu/articles>

At MIT, the Design Laboratory exists within a context of broad-based technological innovation and builds upon the unique advantages offered by this setting. It pursues research, executes practical design and art projects, and engages in scholarship and criticism.

The Laboratory is organized as a collection of multidisciplinary research and project teams unconstrained by the traditional boundaries between the design, planning, and engineering professions and disciplines.

Generally, the Laboratory's projects engage new technologies and their potential to enable fresh and highly effective solutions to problems of significant social, economic, and cultural importance. The Laboratory is particularly interested in the emerging possibilities afforded by: new information technologies; new material, fabrication, and construction technologies; new ways of providing functionality at micro- and nano-scales; new techniques for engineering biological materials and structures; and new planning and management strategies. We are concerned not only with the design of individual products, systems, buildings, and urban areas, but also with the roles these elements play in larger urban, regional, and global systems and their long-term sustainability.

**Augmented Health and Safety. Future vision**

<https://design.mit.edu/projects/advanced-health-and-safety>

We investigate emerging technologies such as Artificial Intelligence, Internet of Things, Augmented Reality and Advanced robotics in relation to health and safety issues in the energy industry. The goal is to create a vision of the future through the design of a number of concepts that will radically improve health and safety practices and will have an impact on workers' everyday lives. The MIT Design Lab and Eni have been collaborating over the last five years on a number of projects concerning the use of emerging technologies to design new solutions for the energy industry.

**Connected chair embedding smartness**

<https://design.mit.edu/projects/buddy-chair>

Vibration motors, embedded in the arm rests, provide alerts and feedback to users. They vibrate in different patterns depending on the type of feedback notification. Infrared sensors (IR), embedded in the seatback, measure the user's spinal curvature and provide feedback to help users achieve neutral spinal alignment. Force sensitive resistors (FSRs), embedded in the seating surface, measure differences in pressure as the users leans to the left or right. These measurements help Buddy Chair determine a user's posture.

**Healthcare for millennials**

<https://design.mit.edu/projects/healthcare-for-millennials>

Redesigning the digital strategy and digital interfaces for the healthcare business for “Bradesco Saude”. Understanding Millennials behavior and designing services and technologies, specifically based on innovative UI and UX.

**MIT HACKING MEDICINE**

<http://hackingmedicine.mit.edu/>

MIT Hacking Medicine is a group founded at MIT in 2011, comprising of MIT students and community members, aimed at energizing the healthcare community and accelerating medical innovation. We accomplish this by carrying out health hackathons, design thinking workshops, and networking gatherings to teach healthcare entrepreneurship. The group has organized to date more than 150 events across 15 countries and 5 continents. Over 40 companies have been created, raising over \$150M in venture funding.

**2018 Grand Hack**

April 13-15, 2018, <http://hackingmedicine.mit.edu/grandhack2018/>

Join MIT Hacking Medicine for one of the largest health hackathons in the world! This is the weekend to brainstorm and build innovative solutions with hundreds of like-minded engineers, clinicians, designers, developers and business people. Within our three hackathon tracks, there is sure to be a healthcare challenge for everyone!

**MIT SLOAN INITIATIVE FOR HEALTH SYSTEMS INNOVATION**

Faculty: Joseph Doyle, Retsef Levi

Director: Anne Quaadgras

Research: <http://hsi.mit.edu/faculty-and-research/ongoing-research>

The MIT Sloan Initiative for Health Systems Innovation (HSI) identifies high-quality, cost effective health systems as essential to individual and societal wellbeing. HSI plays a pivotal role in the transformation of health care systems through industry-based research. HSI brings together faculty, researchers, and practitioners from across MIT and around the world to advance health management and delivery through applied research.

**MIT Sloan: Innovating Health Systems, Digital Health Transformations**

November 29, 2017, <http://mitsloan.mit.edu/alumni/events/2017-cambridge-health-conference/>

The health care industry is in flux, facing shifting economic, regulatory, and societal demands. Yet a vision is emerging: an affordable system that consumers can rely on – not only to diagnose and cure disease, but to help them achieve and maintain health. This transformation from “Health Care” to “Health Management” will require integrating the social determinants of health – how people live, learn, work, and play – into new models of care that leverage analytics and technology. It also requires input from YOU. Together, we can create an ecosystem that nurtures system innovation and new management practices. This discussion is an important step and you can help point the way forward.

**TATA CENTER FOR TECHNOLOGY AND DESIGN**

Director: Robert Stoner, <https://tatacenter.mit.edu/>

Publications: <https://tatacenter.mit.edu/theses-publications/>

The Tata Center for Technology and Design trains and supports MIT researchers working to solve challenges facing communities in India and the developing world. Working with collaborators throughout India, and with our sister-centre at the Indian Institute of Technology, Bombay, the

Tata Center creates solutions designed to serve human needs. Our work spans six overlapping areas: agriculture, energy, environment, health, housing, and water.

### Health Projects

<https://tatacenter.mit.edu/healthcare/>

Developing cost-effective healthcare solutions is a global challenge, and of paramount importance to long-term economic stability. India faces specific challenges in delivering care to the majority of its population, which lives in rural or informal communities with poor public health facilities, creating a healthcare environment characterized by very high demand and low margins...

#### ***Development of mobile technology tools for cardiovascular disease screening in resource-constrained environments***

Dr. Richard Fletcher

<https://tatacenter.mit.edu/portfolio/development-of-mobile-technology-tools-for-cardiovascular-disease-screening-in-resource-constrained-environments/>

India is living through a Cardiovascular Disease (CVD) epidemic due to the increase in risk factor prevalence as well as the South Asian genetic predisposition to CVD's. In 2000 CVD's caused the loss of 9.2 million years of life in India. Moreover, the incidence of CVD's may well be underestimated, especially in rural areas; a study in 53 villages in the Godavari region of Andhra Pradesh showed mortality rates due to CVD's were north of 30%. This issue has to be tackled by both mitigating the consequences and developing strategies to reduce its future incidence....

...On the technology front, we are developing non-invasive and affordable Mobile Tools that will enable a healthworker to screen for CVD risk in people within her village, to refer people at high risk to secondary points of care and keep track of patient progress.

There are three devices which we are working on which when combined will give a holistic assessment of CVD risk: (1) A digital Stethoscope which listens for abnormal hearts sounds, (2) An external pulse detector which measures Pulse Wave Velocity, a key indicator of Cardiovascular health, (3) A Microwave Doppler Probe which may illicit information about heart muscle function.

I am mostly working on the external pulse detector that measures Pulse Wave Velocity. A recent medical study involving 42 subjects performed at our partner hospital Sengupta Hospitals and Research Institute will help us show how well our devices work. After we have assessed the clinical significance of the results from our devices we will move on to running a pilot study to assess how well healthworkers are able to use our devices.

#### ***Scale-up and deployment of pulmonary disease diagnostic tools***

Dr. Richard Fletcher, <https://tatacenter.mit.edu/portfolio/scale-up-and-deployment-of-pulmonary-disease-diagnostic-tools/>

...This research project aims to create affordable tools to screen for pulmonary disease in rural settings. Building off of previous research using machine learning to diagnose pulmonary disease, our group has developed a low-cost mobile kit to diagnose several pulmonary diseases. Diagnostic tools for asthma and COPD have been completed and validated, and we are now expanding the range of diseases to include pneumonia, tuberculosis, lung cancer, and ILD (Interstitial Lung Disease).



While the diagnostic kit works well for primary health clinics and doctors, there remains a need to create an even simpler set of tools that can be used by a frontline health worker with a phone and no peripherals. With this motivation, we will be developing diagnostic tools that are based on the analysis of a person's voluntary cough sounds, in addition to a standard questionnaire. Integrating cough analysis into our application will allow us to target key populations which might not be able to complete some parts of our screening kit, such as children.

The main outcome of this work will be to produce two versions of the pulmonary diagnostic kit – a version that can be used by general practitioner doctors and primary care clinics, and a simpler version that is intended to be used by frontline health workers, such as ASHA workers in India.

#### ***Mobile child health toolkit for community health workers***

Dr. Richard Fletcher, <https://tatacenter.mit.edu/portfolio/mobile-child-health-toolkit/>

In India, there are more than 700,000 accredited social health activists (ASHAs), part of a government initiative to tackle the challenge of lack of medical access in rural zones. Each ASHA worker is nominated from her neighborhood and go door-to-door providing health information and screening services to the families in her neighborhood. ASHAs receive performance-based compensation for facilitating immunizations and providing referral services.

...This project is focused on NCH (Neonatal and Child Health), which is a core function of the ASHA workers. We are developing a series of smartphone-enabled apps to empower ASHAs to screen children and infants for multiple conditions, and to collect basic epidemiological health data, such as a baby's height and weight.

These mobile apps make use of the smartphone camera combined with computer vision and augmented reality (AR) to extract, collect, and analyze data from the image of the child, and provide the ASHA with relevant feedback about the health of the baby. The end goal is to encapsulate all of the apps into a comprehensive smartphone enabled mobile toolkit. Currently, we have a prototypes for AR apps to measure baby's height, weight, and middle upper arm circumference (MUAC), as well as other apps that capture essential physiological measurements, such as heart rate variability and pulse oximetry. We are also exploring multi-spectral sensing as a means of collecting additional physiological information.

For deployment and field testing of the technology, we are partnering with the Public Health Foundation of India (PHFI), which implements much of the training for ASHA workers. Since the ASHA health worker program is a government program, we have obtained approval from the Government of India to conduct a pilot study with ~20 ASHA workers in the New Delhi slums using our technology, which will be conducted during first half of 2017.

#### ***Rapid diagnostic tests for Zika, Dengue, and Chikungunya viruses in India***

Prof. Lee Gehrke, <https://tatacenter.mit.edu/portfolio/rapid-diagnostic-tests-for-zika-dengue-and-chikungunya-viruses-in-india/>

The dengue, zika and chikungunya viruses require special attention for public health preparedness due to their rapid spread in recent decades and cause of serious illness. They are transmitted by the mosquitos *Aedes aegypti* and *Aedes albopictus* and are a major international health concern since their dissemination has increased greatly in urban areas due to travel and globalization. The WHO

estimates that there are 3.2 billion people living in endemic areas where the mosquitoes thrive, and that collectively these diseases account for more than 150 million infections every year.

The three diseases have similar initial symptoms, but the potential disease outcomes are life threatening and distinct for each disease, thus the need for an accurate diagnosis.

Lateral flow strips are widely used in point of care (POC) devices, such as pregnancy tests, disease diagnostics, etc. because they can be operated by non-experts, they are inexpensive, portable, and do not require electric power to be operated. By enabling mobile phone readability of the diagnosis results, we will be able to obtain real-time epidemiologic data on the spread of the disease.

These effective, fast, reliable and inexpensive lateral flow devices, together with our new techniques for data analysis and reporting and methods to screen and identify antibodies for lateral flow assays, will represent significant improvements to field detection of dengue, zika, and chikungunya epidemiology in situations where there is a lack of specialized personnel or materials. Current work is being done in Mumbai, in collaboration with an industry partner, testing the devices with PCR-confirmed serum samples from patients affected by dengue and chikungunya.

#### ***Automated histopathological analyses at scale***

Prof. Ramesh Raskar, <https://tatacenter.mit.edu/portfolio/automated-histopathological-analyses-at-scale/>

The cytological and histological assessment of human tissues has emerged as a key challenge for detection and treatment of multiple clinical conditions, including cancer. Experts analyze slide images in order to characterize samples by performing tasks like whole-slide classification, patch-wise classification, tumor localization, region segmentation etc. The results of these tasks inform the diagnosis. But a mismatch between demand and supply of experts, especially in the Indian setting and the rural context, has led to suboptimal quality and turnaround times for these analyses.

An automated histopathological analysis platform could help the lives of millions in resource-constrained communities who require screening and diagnostic services every year, by enabling a reduction in reliance on hard-to-acquire experts, increase in throughput, and improvement in efficiencies. It could be effectively deployed into the diagnostic pipeline of existing organized pathology lab chains, recuperating initial costs effectively over time while simultaneously getting better in terms of accuracy as access to more continuous data is made available.

This research aims to build a platform for automated histopathological analysis, powered by machine learning, in order to significantly reduce reliance on experts, price and time, and provide a cloud-based image analysis solution targeted at hospitals, usable by operators requiring much lower level of expertise, especially in resource and data constrained contexts.

#### ***OpenEye: A platform for scalable diabetic retinopathy screening***

Ramesh Raskar, <https://tatacenter.mit.edu/portfolio/low-cost-retinal-health-screening/>

Incidence of diabetes in India has reached epidemic level; some studies indicate as many as 15% of all Indians already have diabetes. When diabetes is well managed, many people are able to live a healthy life with few complications. However, poorly managed diabetes can lead to health complications such as blindness, neurological disorders, and cardiovascular problems.

The aim of this research is to develop a scalable system to screen for a complication of diabetes that can lead to blindness: diabetic retinopathy. If diabetic retinopathy can be identified early, vision can be saved and intervention can lead to better management of diabetes.

Our solution consists of an imaging device and software for automatic classification of measurements that will indicate if an individual has diabetic retinopathy, even when operated by a non-expert. The hardware and software is designed to be released as part of an open platform to encourage manufacturers to reduce cost and maximize potential impact. Our automatic classification system is based on state of the art methods and has the potential to provide super-human classification performance while running locally on the device without an internet connection.

We are designing the second generation of hardware which is being developed in collaboration with our partners at LV Prasad Eye Institute in Hyderabad, India. This design will be used to test scalability of our solution in a rural screening program.

### ***Smartphone-Based Skin Imaging***

Prof. Ramesh Raskar, <http://tatacenter.mit.edu/portfolio/smartphone-based-skin-imaging/>

This project utilizes the power of the smartphone coupled with a highly sensitive compact spectrometer to image skin in a rapid, non-invasive manner. Earlier versions of low-cost spectrometers utilize the camera of the mobile phone to image the field after moving through a diffraction grating. These approaches are inherently limited by the closed nature of mobile phone image sensors and built in optical elements. The system presented uses a novel integrated grating and sensor that is compact, accurate and calibrated. Additionally, UV and visible LED excitation sources are built into the device. Data collection and analysis is simplified using the wireless interfaces and logical control on the smart phone. Furthermore, by utilizing an external sensor, the mobile phone camera can be used in conjunction with spectral measurements. We are exploring ways to use this device to measure endogenous fluorescence of skin in order to distinguish cancerous from non-cancerous lesions with a mobile phone based dermatoscope.

### ***Mobile-enabled diabetic foot analyzer (m-DFA)***

Prof. Mandayam Srinivasan, <https://tatacenter.mit.edu/portfolio/mobile-enabled-diabetic-foot-analyzer-m-dfa/>

India has the highest number of diabetics in the world. A frequent complication of diabetes is nerve damage leading to distal symmetric neuropathy, which clinically manifests as loss of sensation in the feet, a major cause of foot ulcers and leg amputations in India.

The commonly used neuropathy diagnostic technology is the biothesiometer, which measures vibration perception threshold (VPT). The VPT is defined as the lowest intensity of vibration that a patient can feel in the sole of the foot. As opposed to stimuli that could potentially cause pain such as pin prick or heat, vibration is a harmless and painless stimulus that can be used to evaluate a person's sensation. Unfortunately, existing biothesiometers are large and heavy, mechanically and electrically inefficient, and require trained technicians to operate. These drawbacks make the biothesiometer impractical for low-resource settings in most parts of the world. Consequently, the majority of the Indian population with diabetes in rural areas is currently not being tested for neuropathy.

The aim of the m-DFA project is to design and manufacture a biothesiometer-like device that is portable, rugged, battery powered, mobile-connected, and can easily be operated by minimally trained allied medical personnel or community health workers; and to develop a quantitative, objective standard of VPT measurement.

Over the last two years we have developed a device that provides quantitative information about a diabetic patient's foot sensation by stimulating the sole of the foot with vibration at a fixed frequency and varying amplitude. The m-DFA connects wirelessly to a mobile phone or tablet, which records and tracks data on a periodic, per-person and per-visit basis. A clinical validation study to compare the performance of the m-DFA with commercial biothesiometers and nerve conduction studies is ongoing at MIT and Agada Hospital (Chennai, India).

## MIT-RELATED STARTUPS

### MIT STARTUP EXCHANGE

<http://startupexchange.mit.edu/startupexchange/html/index.html>

MIT Startup Exchange is a web community for the MIT innovation ecosystem, particularly MIT ILP's members, MIT-connected startups and all MIT employees or alumni who have active startup engagements.

### ASHAMETRICS

MIT Relationships: Richard Redemske (Co-Founder, Developer, MIT Alumnus), Olufemi Omojola (Co-Founder, CTO, MIT Alumnus), Richard Fletcher (Co-Founder, Advisor, MIT Faculty)  
Cambridge, MA, <http://www.ashametrics.com>

Founded in 2011, Ashametrics was formed as a spin off company from the MIT Media Lab with wireless technology from another MIT spin-off company, TagSense, Inc. Ashametrics designs and manufactures wireless wearable sensors and mobile phone applications for collecting physiological data. These mobile health tools are available to researchers as well as individuals that are interested in monitoring parameters such as physical activity or emotional arousal. Ashametrics specializes in mobile data collection, which is of interest in Global Health as well as behavior monitoring and outpatient ambulatory monitoring in domestic health applications.

### ATLAS5D

MIT Relationships: Zeb Kimmel (Co-Founder, CEO, MIT Alumnus), Jon Varsanik (CTO, MIT Alumnus)  
Cambridge, MA, <http://www.atlas5d.com/>

Atlas5D provides real world evidence of patient function and mobility. Our Echo5D technology is an Ambient Measurement System (AMS) that accurately identifies and monitors patients in any setting, including the home. As a result, clinicians and researchers can better personalize interventions and understand disease progression. Our technology easily integrates with patients' daily lives; nothing is worn and no video or photos are collected.

### **BLOOMER TECH**

MIT Relationships: Alicia Chong R. (Co-Founder, MIT Student), Aceil Halaby (Co-Founder, MIT Alumna)  
Cambridge, MA, <https://www.bloomertech.com/>

Bloomer Tech is transforming how people understand their bodies using ordinary clothing to collect extraordinary data. Bloomer Tech provides the tools to build a reliable and vast data set on women's heart health. Through integrated healthcare practices in monitoring and treatment, we accelerate progress on solving cardiovascular global health problems. Through biometric sensors in every day clothing, meaningful data is collected, analyzed and made accessible to users, doctors and medical professionals for real-time personalized healthcare.

### **CARDIIO**

MIT Relationship: Ming-Zher Poh (Co-Founder, CEO, MIT Alumnus)  
Cambridge, MA, <https://www.cardiio.com>

Cardiio is a health technology company born out of MIT and works on solutions to make physiological sensing frictionless. We provide mobile and cloud-based software that turns ordinary cameras into biosensors, allowing people to use the devices they already own to gain insight and take charge of their wellbeing.

#### **App screens for arrhythmia using smartphone camera**

##### **Startup develops app to detect irregular heartbeats that can cause strokes.**

Rob Matheson, MIT News Office, March 29, 2017, <http://news.mit.edu/2017/cardiio-app-screens-arrhythmia-smartphone-camera-0329>

... MIT Media Lab spinout Cardiio has developed a mobile app that uses a smartphone camera to detect facial signs of a heart arrhythmia associated with strokes. It does so by measuring and analyzing minute changes of light reflected on the skin as the result of the underlying pulse.

Cardiio is the startup behind the popular fitness app of the same name, launched in 2012, that calculates heart rate based off facial light reflection. It works because each heartbeat increases the volume of blood in the user's vessels. Blood's hemoglobin absorbs light, which decreases the light reflected by the skin. The Cardiio app tracks those tiny changes in reflected light, not visible to the human eye, to accurately calculate a heartbeat.

Recently, however, the startup has started using that light-reflection data to make a new app that can detect irregular heartbeat patterns of atrial fibrillation (AF), a common type of heart arrhythmia that can lead to strokes. Called Cardiio Rhythm, the clinical app is currently being used for research only and has been validated by several academic papers. In the near future, Cardiio hopes to make the app available to consumers for early heart-arrhythmia screening.

"We aim to develop algorithms that unlock clinical insights from [biometric] data collected from commonly available devices such as smartphones and wearables," says Cardiio co-founder and CEO Ming-Zher Poh PhD '11, a former Media Lab research affiliate who co-developed the app. "That enables people to learn more about their health and ... take more control of their health..."



### COMMON SENSING

MIT Relationships: James White (Co-Founder, President, MIT Alumnus), Richard Whalley (Co-Founder, CEO, MIT Alumnus)  
Cambridge, MA, <http://common-sensing.com/>

The company is building the next generation of smart health technology and design through user-oriented, ultraportable devices and experiences. Gocap is the smart cap for insulin pens. It's small enough to fit in a pocket and has a USB-rechargeable battery that lasts a week. Gocap automatically generates an insulin logbook that can be wirelessly shared with care providers and family.

#### Data-driven diabetes management

##### Smart insulin-pen cap lets patients and doctors track dosage data to better manage treatment.

Rob Matheson, MIT News Office, November 16, 2016, <http://news.mit.edu/2016/startup-common-sensing-data-driven-diabetes-insulin-management-1116>

...Now MIT spinout Common Sensing aims to solve the nation's diabetes-management issues by going digital. The startup's smart insulin-pen cap logs insulin intake data on an app and in the cloud, to help patients better manage their regimen. Moreover, the cap gives doctors a detailed view into patients' insulin habits and how they affect blood-glucose levels, for more targeted care.

Invented by co-founders James White '10, SM '12 and Richard Whalley '10, the Gocap is now going through clinical studies to test its viability. Most recently, Common Sensing, headquartered in Cambridge, Massachusetts, has partnered with the Joslin Diabetes Center in Boston, where it will collect data on 125 patients using the cap over the next year.

When Gocap finally hits the market, it will be provided to insurers, pharmaceutical companies, and provider and clinician networks, and be free for end users. "We really want these to be available, free of charge, to people that need them," White says....

### CONSTELLATION

MIT Relationships: Ramesh Raskar (Co-Founder, Chief Scientist, MIT Faculty), Christian Bailey (Founder, CEO, MIT Alumnus), Sanjay Sarma (Advisor, MIT Faculty), Ed Boyden (Advisor, MIT Faculty)  
Cambridge, MA, <http://constellation.io>

Constellation is an imaging system that empowers patients to conduct quick, cost-effective, full body scans every month in the privacy of their homes, or in health clubs, doctors' offices and other commercial settings. Signs of skin cancer are detected as early as possible, dramatically increasing patient survival rates. Unlike applications currently on the market, Constellation is the only solution that detects changes in moles over time — which is critical to early detection.

### EMPATICA

MIT Relationships: Rosalind Picard (Co-Founder, Chief Scientist, MIT Faculty), Matteo Lai (Co-Founder, CEO, MIT Alumnus)  
Cambridge, MA, <https://www.empatica.com/>

We develop groundbreaking wearable devices with clinical quality sensing. We are a super passionate team, from diverse engineering fields, such as sensor design, electrical, DSP, data science, biomedical, and software development and wearable.

We design and develop the world's smallest and most accurate wearable device for medical research of human behavior in daily life. Our E4 is used in 30 countries around the world, its clients are the most respected hospitals, universities, and companies that use it for advanced research on human behavior. The E4 provides the most sophisticated way to monitor autonomic nervous system disruption and heart rate variability, among a set of 5 sensors. We are launching the Embrace watch, a wearable device designed to improve lives, that has just completed a very successful crowdfunding campaign.

### **From Stress to Seizures and Personalized Health: The launch of Embrace by Empatica**

ILP Video, September 7, 2016, <http://ilp.mit.edu/videodetail.jsp?confid=null&ilp-videos=Y&id=1779#>

### **EYENETRA INC.**

MIT Relationships: Vitor Pamplona (Founder, CEO, Former MIT Affiliate), Ramesh Raskar (Founder, Advisor, MIT Faculty)  
Somerville, MA, <https://eyenetra.com>

EyeNETRA grew out of collaborative research at the MIT Media Labs Camera Culture Group. Innovations in computational ophthalmology to increase accessibility to high-quality eye care are applied. The mission is to exploit mobile phones as scientific instruments to provide accessible health diagnostics to underserved areas of the world.

...EyeNETRA's mission is to give everyone access to the vision correction they need to see the world. Using advanced eye measurement technology developed by the team, we're creating tools that enable anyone, anywhere to gain access to the best eye test possible. The mobile network will connect people to a personalized eye testing experience, where individuals and their care providers can collaborate around accurate data, and make better-informed choices, facilitated by technology.

### **HEALTH[AT]SCALE**

MIT Relationships: Zeeshan Syed (Co-Founder, CEO, MIT Alumnus), John Guttag (Co-Founder, CTO, MIT Faculty), Mohammed Saeed (Co-Founder, CMO, MIT Alumnus), David Guttag (Co-Founder, CBO, MIT Alumnus)  
Palo Alto, CA, <http://www.healthatscale.com/>

HEALTH[at]SCALE's Analytical Engine and Application Suites are based on new approaches to machine learning and artificial intelligence with specialized technologies by placing importance on a variety of challenges (e.g., issues of sample size, event rates, poor or inconsistent data quality, fragmented datasets, multi-modal parameters, time-varying changes, integration of knowledge bases, workflow constraints etc.) that are often restrictive in real-world settings.

### **HUMON**

MIT Relationships: Alessandro Babini (Co-Founder, CEO, MIT Alumnus), Daniel Wiese (Co-Founder, CTO, MIT Alumnus)  
Cambridge, MA, <https://humon.io>

Humon started as a research project at MIT Sloan on the premise that technology and biology were on a collision course. The result of this intersection would create the next generation of sensors and products allowing users to understand more about their own bodies and as a result, be their better selves. ...we came to the conclusion that the people who were ready to adopt and embrace these new technologies were the athletes. More specifically we could help them solve their biggest problem: understand how hard to push themselves but without ever exceeding their limits. That day, we started developing Humon's first product.

The Humon Hex uses near-infrared spectroscopy to measure the hemoglobin saturation in muscles (also referred to as SmO<sub>2</sub>). LEDs emit light into the tissue and detectors measure the intensity of light that propagates through the muscle. Since oxyhemoglobin (HbO<sub>2</sub>) and deoxyhemoglobin (Hb) have different absorption spectra in the near-infrared wavelength range, the SmO<sub>2</sub> can be calculated.

#### **MICROCHIPS BIOTECH, INC.**

MIT Relationships: Robert Langer (Co-Founder, Director, MIT Faculty), Michael Cima (Co-Founder, Director, MIT Faculty)  
Lexington, MA, <http://microchipsbiotech.com/>

Microchips Biotech, Inc. is dedicated to improving the lives of patients by revolutionizing drug delivery. Our proprietary microchip-based implant can store and release precise doses of drugs over months and years. The implant, which is placed under the skin by a trained physician during a simple office procedure using local anesthesia, can be wirelessly activated or deactivated by a physician or patient, without requiring removal. In addition, physicians can wirelessly modify the frequency or dose of the drug to meet the individual needs of each patient.

#### **PISON TECHNOLOGY**

MIT Relationships: David Ang (CEO, MIT Alumnus), John Leonard (Advisor, MIT Faculty) Tyler Clites (Advisor, MIT Student)  
Brookline, MA, <http://pisontechnology.com/>

Pison Technology is creating a micromovement communication and control system to help people with ALS and other neuromuscular conditions who cannot speak or move their body. Our device is an EMG-based wearable sensor to control a laptop, phone and wheelchair. Even if a person has no ability to move, the nerves in the arms and legs are preserved and generate electrical signals. We capture the peak of that signal and translate it to a mouse click or keyboard press. Our device can help a person from initial diagnosis through progression of the condition. A person can wear 2-6 sensors for multiple channels of input to control the on-screen keyboard and mouse. The on-screen software will be customizable according to user preferences and level of tech savvy. It will be fully compatible with existing communication technologies like eye gaze. We have successfully tested prototypes on people who have lost arm and leg movement years ago and provided demonstrations to the X Prize, MIT, and MGH.

#### **PLENOPTIKA**

MIT Relationship: MIT Spinout from MIT LinQ (formerly Madrid-MIT M+ Visión Consortium)  
Boston, MA, <http://plenoptika.com>

PlenOptika is a company that spun out from MIT and the Madrid–MIT M+Visión Consortium. The founders were research fellows in a biomedical technology innovation initiative who felt compelled to solve the problem of low vision suffered by more than 1 billion people worldwide. Our mission is to make eye care easy for anyone who needs it in the United States, and accessible to underserved and low-resource communities worldwide. PlenOptika was formed to respond to the problem of low vision suffered by more than a billion people worldwide. QuickSee by PlenOptika enables accurate autorefractometry anywhere, at the touch of a button.

### Startup aims to make vision care more accessible in developing world

#### Portable device can generate corrective lens prescriptions in areas with no optometry care.

Rob Matheson, MIT News Office, January 10, 2018, <http://news.mit.edu/2018/startup-plenoptika-vision-care-developing-world-0111>

Vision impairment is a major global issue. More than 2 billion people worldwide don't have access to corrective lenses. Getting eyeglasses prescriptions is especially difficult in developing countries. Optometrists are generally located in urban centers and rarely see patients from rural areas, so many people suffer from uncorrected impairments. According to the World Health Organization, this can lead to impaired quality of life, learning difficulties, and lost employment opportunities and finances.

Now MIT spinout PlenOptika aims to correct this issue with a highly accurate, portable autorefractometer that measures refractive errors of the eye and produces estimated prescriptions in 10 seconds. Moreover, it's more affordable than the current technology, with the potential to reach patients in previously inaccessible areas of developing countries. After six years of development, eight product iterations, and several clinical studies with a total of 1,500 patients across five countries, the device, called QuickSee, has hit the market in India.

"People at the bottom of the pyramid have poor vision, because they don't have glasses or aren't aware of how to get glasses. It's a big unmet medical need we're trying to address," says Shivang Dave, one of four former postdocs at the Madrid-MIT M+Visión Consortium (now MIT LinQ), along with Daryl Lim, Eduardo Lage, and Nicholas Durr...

### SQZ BIOTECH

MIT Relationships: Armon Sharei (CEO, MIT Alumnus), Klavs Jensen (MIT Faculty), Robert Langer (MIT Faculty)

Watertown, MA, <http://sqzbiotech.com/>

Access to the cytoplasm of a cell enables scientists to study the intricacies of disease pathways as well as expands the potential for therapeutic intervention in many diseases. Current methods to access the intracellular space include viral vectors, chemical or electric pulses to deliver the material into the cytoplasm. However, these existing methods are often highly specific to a particular material and/or cell type and thus are limited in their efficacy. There is thus an urgent need for more robust and precise intracellular delivery techniques. SQZ's technology is a microfluidic device capable of facilitating high throughput, robust intracellular delivery for a range of applications. This method was developed at MIT in 2013 and has demonstrated substantial improvements relative to current intracellular delivery methods: it is more efficient, less toxic and capable of addressing previously challenging cell types.