Brain Tsunamis

PROJECT SUMMARY
The last decade of research has established that Cortical Spreading Depolarizations (CSDs), or “Brain Tsunamis,” play an important role in many disorders, including Traumatic Brain Injury (TBI), stroke, hemorrhage, and migraine, that collectively affect more than a billion people worldwide and are major causes of death and disability. CSDs are waves of neurochemical changes that propagate across the brain surface and are thought to mediate secondary brain damage following an injury or event.

The only reliable way to measure CSDs now is an invasive method using electrodes; it is costly, risky, and inappropriate for patients with certain contraindications. In addition, detection is slow and requires a physician to visually inspect the data. Diagnosis and treatment in real-time thus is not realistic in most clinical settings.

Our solution is a Noninvasive Platform for Automated CSD Detection and Suppression. Our multidisciplinary team will develop algorithms and techniques to noninvasively suppress CSDs by using online detection and ensuing stimulation. This is the critical first step for discovery of novel therapeutic strategies and would eliminate the need for invasive monitoring. Real-time detection would allow rapidly iterated, individualized care, timely intervention, and enhanced patient outcomes.

Clinical Genomics Modeling Platform

PROJECT SUMMARY
The Clinical Genomics Modeling Platform is an engine for easily building precision-medicine models for various diseases and populations. Triage algorithms, for instance, might help to determine if patients with a certain disease should be sent home with monitoring or sent to the intensive care unit.

Their project focuses on the understanding of the relationship between genetic variation and medical outcomes in a large population, which is key to realizing the vision of personalized medicine. Efforts are now underway to obtain the genome sequences of thousands of individuals, and as the cost of sequencing continues to drop, it will become routine to sequence patients in a medical setting. However, a number of computational and practical challenges remain in the way of using genomic sequencing for clinical decision making. (continued)
In this project, Dr. Carl Kingsford and Dr. Christopher Langmead are aiming to increase the usage of predictive systems based on machine learning techniques and genomics through the development and commercialization of a computational system that will:

- Make predictive models easy to build for clinical researchers
- Make predictive models easy to share (sell) and apply
- Make results of models easy to understand

**PROJECT SUMMARY**

Readmission after complex cancer surgery is common, with studies reporting between 15% and 50% of patients being readmitted within 30 days of discharge from the hospital. Readmissions are associated with increased healthcare costs, poor clinical outcomes including increased risk of infection and early mortality, and patient and family stress and suffering. Prior research has identified demographic and clinical predictors of readmission, but the role of patient-centered behavioral processes remains relatively unexplored. Identifying behavioral factors associated with readmission, which might include physical activity levels, sleep habits, and social contacts, could highlight ways to prevent readmissions and empower patients to take a more active role in their recovery.

The project team is collaborating to take a generalizable and scalable approach that holistically looks at patients’ behavior before and after surgery and identifies routines in this behavior. These routines will form the basis of their understanding of the predictive factors for readmissions, particularly while patients are still in the hospital after surgery or other treatments.

Harnessing technology to monitor these and other behavioral risks before surgery, during inpatient recovery, and during the critical transition from hospital to home will advance the field in a number of ways:

- Reliably assessing and computationally modeling behavioral risks associated with readmissions to improve risk stratification
- Identifying optimal targets and timing for behavioral intervention to reduce preventable readmissions
- Providing data that may be helpful and motivating for patients and that could inform clinical decision making to improve quality of care

**RESEARCHERS**

**Carl Kingsford, PhD**
Carnegie Mellon University’s Computational Biology Department

**Christopher Langmead, PhD**
Carnegie Mellon University’s Computational Biology Department

**Anind Dey, PhD**
Director of the Human-Computer Interaction Institute at Carnegie Mellon University

**Charles M. Geschke, PhD**
Assistant Professor of Medicine and Psychology, Biobehavioral Oncology Program, University of Pittsburgh Cancer Institute
Detecting Intestinal Activity by Analyzing Gut Sounds

PROJECT SUMMARY
A noninvasive device that analyzes sounds from the intestinal tract could become a powerful new tool to help physicians diagnose and monitor a variety of gastric illnesses, such as acute pancreatitis, bowel obstructions, irritable bowel syndrome, inflammatory bowel disease, and Crohn’s disease.

Carnegie Mellon researchers, collaborating with UPMC gastroenterologists, will be developing, testing, and performing clinical research on a wearable sensor array to detect intestinal sounds – a new vital sign for the “gut.” Its impact could be substantial: In the U.S. alone, digestive diseases afflict 60-70 million people annually with treatment costs totaling more than $100 billion.

Using machine learning techniques, the researchers will develop a means of interpreting the acoustic signals to examine the determinants of gut activity and activity suppression, the ability to identify gastric disorders on the basis of sounds, and the device’s therapeutic potential for enabling gut regulation via biofeedback. The project will also develop classification procedures that use these features to distinguish between the various types of gastrointestinal activity.

RESEARCHERS
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Rich Stern, PhD
Professor Electrical & Computer Engineering

Max Gsell, PhD
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Valerie Ventura, PhD
Associate Professor, Department of Statistics.
**Developing a Biomarker for Alzheimer’s Disease Using Machine Learning and Immune Cell Epigenomics**

**PROJECT SUMMARY**
Researchers from Carnegie Mellon University’s School of Computer Science and the University of Pittsburgh School of Medicine are combining areas of expertise and techniques that span machine learning, immunology, and genomics to develop new methods of diagnosing Alzheimer’s disease (AD) that are less expensive than current standards and that may help researchers discover possible treatments.

Currently 5.7 million Americans have AD dementia, including approximately one out of every 10 people over the age of 65. As the population ages, it is projected that 13.8 million Americans will have the disease by 2050. The estimated cost of Alzheimer’s disease is $277 billion annually. Unfortunately, there are still no highly effective treatments or cures for AD.

This team is developing biomarkers that would enable AD to be diagnosed with a blood test, rather than by use of expensive brain imaging techniques. CMU’s Andreas Pfenning has proposed a solution that leverages research in epigenetics and knowledge of the immune mechanisms underlying AD predisposition to develop a novel biomarker. The team will also continue to investigate the impact of genetic changes on AD predisposition and progression of the disease. They hope to leverage these models to inform future research and the design of effective therapeutics for the treatment of AD.

**RESEARCHERS**

Andreas R. Pfenning  
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Department, School of Computer Science

Joshua C. Cyktor  
Research Assistant Professor, Associate Director, Virology Specialty Laboratory, Division of Infectious Diseases, University of Pittsburgh

John W. Mellors  
Endowed Professor and Chief, Department of Medicine, Division of Infectious Diseases, University of Pittsburgh Alzheimer’s Disease Research Center

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**Diagnosis Coding Engine for Electronic Health Records**

**PROJECT SUMMARY**
Medical diagnostic errors impact 12 million adults each year in the U.S. The number of deaths due to medical diagnostic errors is the third leading cause of death, equivalent to the crash of a large aircraft every day, based on estimates in the U.S. alone. A key reason why diagnostic errors are made – even by the best clinicians in highly reliable organizations – is the increasing complexity of the diagnostic process, with over 10,000 diseases and 5,000 laboratory tests to choose from.

This project focuses specifically on preventing coding and billing errors. To address this cognitively complex problem, the team is developing an engine that will predict likely diagnosis codes based on information available in a patient’s electronic health record. Specifically, the solution will review both structured and unstructured data, such as clinical notes, and apply a machine learning-based mapping from these data to specific diagnosis codes.

When the diagnosis code suggestions are acknowledged and accepted, these can then also flow into billing codes through electronic medical records or other systems. The solution will thus aid clinicians in their medical management, decision support, accurate documentation, billing, and quality improvement.

**RESEARCHERS**

Pradeep Ravikumar, PhD  
Associate Professor of Machine Learning at Carnegie Mellon University

Jeremy Weiss, MD  
Heinz College at Carnegie Mellon University and the Department of Biomedical Informatics at University of Pittsburgh.
Healthcare Trials and Care Coordination Using Admissions, Discharges, and Transfers Data

**PROJECT SUMMARY**

This project is determining if coordinated care decisions could be improved by analyzing and monitoring how patients move through the healthcare system.

They will be focusing on healthcare trials – time-ordered sequences in which a patient obtains services such as dialysis, blood work, or psychological counseling. These trials will be analyzed to identify those that are commonly used by patients with similar conditions and those that most often improve patient conditions. Factors such as a patient’s age, healthcare coverage, and medical condition can affect the flow of these services, and differences in flow can be associated with different patient outcomes.

The goal is to develop, test, and assess algorithms and interfaces for analyzing hospital admissions data and for providing feedback to doctors and caregivers through automated patient tracking and notification systems. By analyzing the timing of admits, discharges, and transfers, the application could help inform caregivers about how a patient’s care is being managed and detect when a patient might be at risk because of the healthcare trial they are on.

**RESEARCHERS**

Kathleen M. Carley, PhD  
Institute for Software Research  
L. Richard Carley, PhD  
Electrical and Computer Engineering Department

Evaluating the Predictive Capability of Machine Learning Algorithms in Adult Cardiac Surgery

**PROJECT SUMMARY**

A team from the University of Pittsburgh Medical Center and Carnegie Mellon University is investigating the application of machine learning to clinical cardiac surgery in ways that could have profound implications in clinical trials, therapy selection, patient prognostication and counseling, and surgeon and hospital evaluations.

According to the American Heart Association, one in three Americans have heart disease. The cost of treating heart disease is expected to triple from $273 billion in 2010 to $818 billion in 2030. This is largely attributable to the aging population. In addition, a shortage of cardiac surgeons may be at hand, with the number of active cardiothoracic surgeons expected to decline from 3,708 to 3,411 between 2010 and 2025. Taken together, these trends have profound implications for cardiac surgery as a field. The increased demand coupled with decreased supply will underscore the need for cost-effective, personalized care that optimizes outcomes for patients with surgical heart disease.

Risk modeling has played a vital role for many years in adult cardiac surgery, with the Society of Thoracic Surgeons (STS) database created in 1989 as an initiative for quality improvement and patient safety. This team of researchers from Pitt/UPMC and CMU is investigating how machine learning might enhance risk modeling. There are opportunities to apply machine learning to data that is already used for risk modeling, and to incorporate vast amounts of additional data that are routinely collected but not used in current models. The ultimate goals of this research are to improve the accuracy of risk models in adult cardiac surgery, introduce new and potentially predictive data, and develop clinical platforms and technology that can provide real-time guidance to physicians in clinical management of cardiac surgery patients to improve outcomes.

**RESEARCHERS**

Arman Kilic, MD  
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Director, Surgical Quality and Analytics for Cardiac Surgery  
Co-Director, Center for Cardiovascular Outcomes and Innovation, University of Pittsburgh Medical Center

James Miller  
Project Scientist, Chemical Engineering Department, Carnegie Mellon University

Artur Dubrawski, PhD  
Research Professor, Robotics Institute, Carnegie Mellon University
Ingestible Impedance Sensors to Acquire Large-Scale Data Sets from Patients with Eosinophilic Esophagitis

**PROJECT SUMMARY**

An ingestible sensor may provide a faster, more convenient alternative to biopsies for diagnosing esophageal disorders, such as eosinophilic esophagitis (EoE). EoE is an inflammatory disorder of the gastrointestinal tract that can cause persistent feeding problems, vomiting, and abdominal pain.

Christopher J. Bettinger of Carnegie Mellon University’s Biomedical Engineering Department is developing an ingestible, flexible sensor that could be used to detect and monitor EoE and other esophageal disorders. EoE affects more than 150,000 Americans each year and the incidence of EoE is increasing rapidly, especially in Western Pennsylvania. It is thought to arise from the patient’s immune response to specific foods and, when properly diagnosed, can be treated by identifying and eliminating those foods. But timely diagnosis is challenging because it now relies on biopsies, which are slow, expensive, and highly invasive.

If EoE could be reliably monitored on a more frequent basis, the resulting data could be analyzed in conjunction with a patient’s diet using machine-learning algorithms to identify and eliminate specific foods that may be responsible for causing EoE on a case-by-case basis.

**RESEARCHERS**

Christopher J. Bettinger  
Associate Professor, Biomedical Engineering Department

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In-Home Movement Therapy Data Collection

**PROJECT SUMMARY**

A team from Carnegie Mellon, the University of Pittsburgh, and UPMC is working on a project to evaluate the ability of cameras, inertial measurement units, and other sensors, in combination with machine learning (ML) algorithms, to assess patients’ movement therapy exercises in the home. The long-term goal is to increase the quality and efficacy of physical therapy by providing patients with automated, in-home monitoring, near real-time feedback on exercise performance, and feedback to providers when issues arise outside of the PT setting. This will enable providers to prioritize clinic time for patients whose recovery has stalled while avoiding unnecessary appointments for those who are progressing satisfactorily.

**RESEARCHERS**

Jessica Hodgins, PhD  
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Carnegie Mellon’s School of Computer Science

Asim Smailagic, PhD  
Carnegie Mellon’s School of Computer Science

Andrew Whitford, PhD  
UPMC Center for Rehab Services

Keelan Enseki  
UPMC Center for Rehab Services

Adam Popchak, PhD  
University of Pittsburgh’s Department of Physical Therapy
Integrating Deep Learning with High Throughput Materials Engineering for Detecting Noroviruses

PROJECT SUMMARY
Researchers from Carnegie Mellon University’s Mechanical Engineering Department are developing technologies for rapidly detecting if surfaces are contaminated with norovirus, a major cause of epidemic gastroenteritis.

Norovirus, sometimes referred to as the winter vomiting bug, results in about 685 million cases of disease and 200,000 deaths globally each year. About half of food-borne disease outbreaks in the United States is caused by norovirus.

Noroviruses are very contagious, and less than 20 virus particles can cause an infection. One of the challenges faced by healthcare facilities like hospitals is preventing contamination by and transmission of noroviruses. The spread of the virus is of particular concern during winter, when ventilation of buildings may be reduced.

Mechanical Engineering’s B. Reeja Jayan and Amir Barati Farimani are introducing highly sensitive and specific sensors that can rapidly detect noroviruses and significantly reduce the chance of these infections and epidemics, especially in healthcare facilities. Their research combines deep learning techniques with molecular-scale materials engineering to allow for quick, sensitive detection of norovirus.

RESEARCHERS
B. Reeja Jayan
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Amir Barati Farimani
Assistant Professor, Mechanical Engineering, CIT

Machine Learning Algorithms for Advanced Manufacturing of High-Fidelity 3D Printed Biomaterials

PROJECT SUMMARY
Carnegie Mellon University’s Newell Washburn, Philip R. LeDuc, and Jennifer Bone are designing a tool that would enable the 3D printing of biomaterials, removing one of the obstacles to using additive manufacturing to produce surgical implants and organ transplants.

The need for bioprinted implants and organs is significant. At any given time, nearly 3,500 – 4,000 people are waiting for a heart or heart-lung transplant, and every 10 minutes a new person is added to the national transplant waiting list. Furthermore, the prevalence of rejection and immunosuppression currently impact the success of transplantation and highlight the need for patient-specific implants that will increase the rate of survival. Due to this high demand, the market for patient-specific implants is projected to reach $1 billion by 2020.

Based on hierarchical machine learning (HML), this work will enable the manufacturing of high-fidelity 3D constructs from various starting materials, including biological components. The tool will be used by designers, manufacturers, and others who require the ability to integrate information from various models in order to leverage 3D bioprinting for efficient and accurate manufacturing.

RESEARCHERS
Newell Washburn
Associate Professor, Department of Chemistry, Department of Biomedical Engineering
Philip R. LeDuc
William J. Brown Professor Mechanical Engineering, Biomedical Engineering, Computational Biology, and Biological Sciences
Jennifer Bone
PhD candidate, Biomedical Engineering
**Noninvasive Intracranial Pressure Monitoring**

**PROJECT SUMMARY**

The healthy brain maintains a relatively constant blood flow to the brain even when there are changes in blood pressure or intracranial pressure (ICP). The mechanism preserving blood flow is called cerebral autoregulation (CA), which is known to be impaired in a variety of diseases, such as diabetes, Parkinson’s disease, stroke, and traumatic brain injury (TBI). ICP now can only be measured by placing an invasive pressure sensor inside the brain.

This project seeks to establish an optical technique called near-infrared spectroscopy (NIRS) as a noninvasive method to monitor ICP in humans. Development of a noninvasive ICP sensor would optimize patient treatment in cases where invasive ICP is not possible or could be dangerous to the patient.

**RESEARCHERS**

Jana Kainerstorfer, PhD
Assistant Professor of Biomedical Engineering at Carnegie Mellon University

Elizabeth Tyler-Kabara, MD
Neurological Surgery at UPMC Children’s Hospital of Pittsburgh

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**My Healthy Pregnancy**

**PROJECT SUMMARY**

The costs of preterm births to the healthcare system and society are exceedingly large, and the incidence of preterm births is on the rise despite medical advances. This has created a need to provide reliable, personalized information to pregnant women about how they can reduce their risk of premature births. In response, researchers have created the “MyHealthyPregnancy” smartphone app.

The app applies statistical machine learning techniques to comprehensive pregnancy data sets to improve the app’s patient-specific risk predictions of adverse pregnancy outcomes. It also employs decision science techniques to extend the app to provide postpartum education and behavioral feedback to minimize infant mortality outcomes. The team, which has performed pilot studies of the concept, expects this work will result in a product that can be tailored to both the UPMC health system and developed into an off-the-shelf application for the general population of pregnant women.

**RESEARCHERS**

Hyagriv Simhan, MD
Magee-Women’s Hospital

Tamar Krishnamurti, PhD
Carnegie Mellon University

Alexander Davis, PhD
Carnegie Mellon University
**Phylogenetic Models for Predicting Cancer Progression**

**PROJECT SUMMARY**

Despite screening technologies and public health efforts that have improved the detection of early-stage cancers, methods to reliably predict which of these cancers will progress to more aggressive stages, metastasis, and ultimately patient mortality are lacking.

The project team is working on a suite of software tools that clinicians will use to improve cancer diagnosis and therapeutics based on the molecular signatures of the patient’s tumor genome.

The goal of the project is to develop novel models, algorithms, and software tools to better understand the origin and evolution of tumor cells and how a patient’s tumors are likely to progress. This information would contribute to personalized, precision treatment of cancer.

**RESEARCHERS**

Russell Schwartz, PhD  
Professor of Biological Sciences and Computational Biology  
Jian Ma, PhD  
Associate Professor of Computational Biology, the School of Computer Science

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**Programming Framework for Managing Patient Privacy**

**PROJECT SUMMARY**

As health data is increasingly digitized, the need to protect patient privacy is unprecedented. The Programming Framework for Managing Patient Privacy team is collaborating on an approach to protect patients’ health records and computations involving sensitive patient data from being leaked in a breach.

Project researchers propose a programming model and software framework for managing the privacy of health data. The programming model allows programs to attach privacy policies directly to the data, rather than requiring the programmer to implement the correct privacy checks across code that uses the data. Attaching privacy policies to the data enables programs to be policy-agnostic and to be updated independently of the specification and implementation of privacy policies. The system tracks the flow of data, as well as the policies, so the programmer need not do so. This approach facilitates auditing, as policies may now be centralized and to be implemented only once, instead of as checks across the program. Auditors may also leverage the fact that the framework, rather than the programmer, is now responsible for correctly implementing the checks.

This project is the first step in a long-term plan to improve patient care and promote scientific discovery by allowing sensitive health data to be shared safely. This plan involves 1) applying prior work on policy-agnostic programming for information flow policies in the context of patient health records, 2) extending and combining prior work to support more expressive policies, and 3) building a practical framework that can be used to safely share sensitive data.

**RESEARCHERS**

Jean Yang, PhD  
Carnegie Mellon’s School of Computer Science  
Matt Fredrikson, PhD  
Carnegie Mellon’s School of Computer Science  
Jian Ma, PhD  
Carnegie Mellon’s School of Computer Science
**Sepsis Phenotyping from Electronic Health Records**

**PROJECT SUMMARY**
Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection that has a high mortality rate and is a large burden on the healthcare industry, constituting over $24 billion annually. This team will use machine learning and artificial intelligence methods to develop analytic tools to identify sepsis earlier and define subgroups of patients who are at high risk for sepsis and share other traits. Successful completion of this research will advance efforts to identify subgroups with sepsis for whom particular treatments are more effective, thereby reducing morbidity and mortality. It will also support the development of physician-competitive, health records-based risk scores that can be used for risk stratification and for early warning clinical decision support. This proposal leverages an established collaboration between experts in machine learning and sepsis at CMU, Pitt, and UPMC.

**RESEARCHERS**
- **Jeremy Weiss, PhD**
  Heinz College and Machine Learning at Carnegie Mellon University and the Department of Biomedical Informatics at University of Pittsburgh
- **Christopher Seymour, MD**
  Critical Care and Emergency Medicine at University of Pittsburgh

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**Towards Automated Multimodal Behavioral Screening for Depression**

**PROJECT SUMMARY**
Depression is a leading cause of disability worldwide. Effective, evidence-based treatments for depression exist but many individuals suffering from depression go undetected and therefore untreated. Efforts to increase the accuracy, efficiency, and adoption of depression screening thus have the potential to minimize human suffering and even save lives. Recent advances in computer sensing technologies provide exciting new opportunities to improve depression screening, especially in terms of their objectivity, scalability, and accessibility. Professor Morency and Dr. Szigethy are collaborating to develop sensing technologies to automatically measure subtle changes in individuals’ behavior that are related to affective, cognitive, and psychosocial functioning. Their goal is to develop and refine computational tools that automatically measure depression-related behavioral biomarkers and to evaluate the clinical utility of these measurements.

**RESEARCHERS**
- **Louis-Philippe Morency, PhD**
  Finmeccanica Associate Professor of Language Technologies at Carnegie Mellon University
- **Eva Szigethy, MD**
  Professor of Psychiatry and Director of Behavioral Health with the Chief Medical and Scientific Office at the University of Pittsburgh

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**Real-Time Tool to Predict Clinical Outcomes After Cardiac Arrest**

**PROJECT SUMMARY**
Over 150,000 Americans are treated in hospitals each year after cardiac arrest, virtually all of whom are initially comatose. Once their hearts are revived, most such patients eventually die in the hospital from brain injury, but a sizable minority will awaken and have a good neurological recovery. With current technology, no sign, symptom, or test result in the first 72 hours after cardiac arrest is sufficient to preclude a favorable recovery. Prognosis often remains uncertain for days or even weeks thereafter. The project team is developing technology that will use advanced signal processing and modeling methods to allow accurate neurological prognostication sooner than currently possible.

**RESEARCHERS**
- **Daniel Nagin, PhD**
  Carnegie Mellon University’s Heinz College, and Physicians
- **Jonathan Elmer, PhD** and **Cliff Callaway, MD**
  University of Pittsburgh Medical School