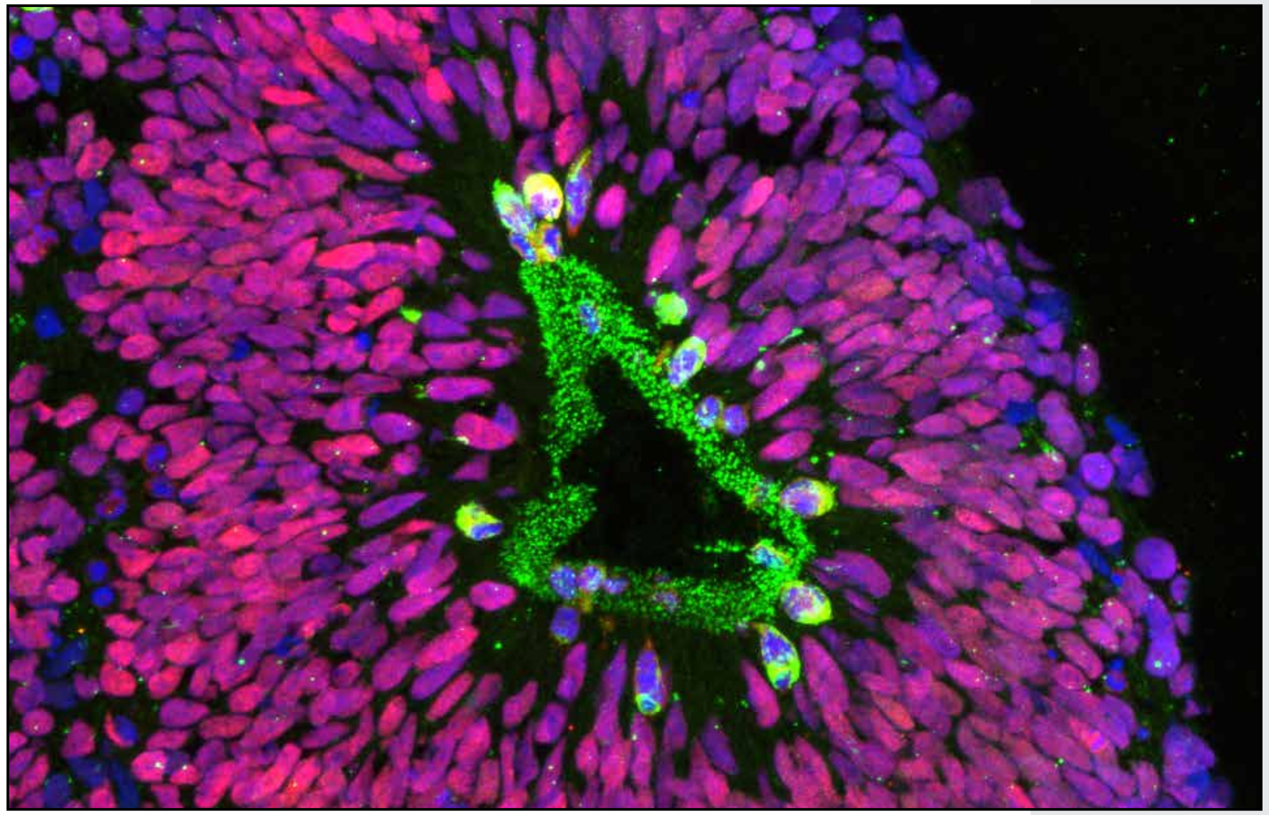
Stanford Neurosciences Institute

Annual Report

September 2016
Through August 2017

Stanford | Neurosciences Institute



Our Mission

The Stanford Neurosciences Institute is dedicated to understanding how the brain gives rise to mental life and behavior, both in health and in disease. Our research community draws from and informs multiple disciplines, including neuroscience, medicine, engineering, psychology, education and law. The discoveries that arise from these collaborations will transform our understanding of the human brain, provide novel treatments for brain disorders, and promote brain health throughout the lifespan.

Message From the Director

Dec 20, 2017

2017 was an exhilarating year for the Stanford Neurosciences Institute. We advanced interdisciplinary neuroscience through three major emphases: supporting outstanding people, catalyzing innovative research, and commencing construction on a new state-of-the-art research facility.

Our emphasis on people resulted in recruitment of Guosong Hong, an outstanding junior faculty member (jointly with the Department of Materials Science Engineering), and we have initiated a new faculty search in statistical and computational neuroscience in collaboration with the departments of Statistics and Electrical Engineering. In addition, we awarded five postdoctoral Interdisciplinary Scholar Fellowships and two Stanford Interdisciplinary Graduate Fellowships, involving three schools and six departments.

In the research arena, our Big Ideas in Neuroscience program announced three winning teams of researchers who will receive five years of phase 2 support for novel interdisciplinary research in the broad fields of NeuroDiscovery, NeuroHealth, and NeuroEngineering. In addition, we recently announced six winning teams for our 2017 Seed Grant competition, ranging from basic science discovery (sex hormone interaction proteins) to tool development (sonomagnetic neurostimulation) to clinically relevant science (NGF and TrkA in chronic pain; Tau and cognitive aging). We are very pleased to announce that a new phase 1 Big Ideas competition will take place over the next several months; winners will be announced in the early autumn of 2018.

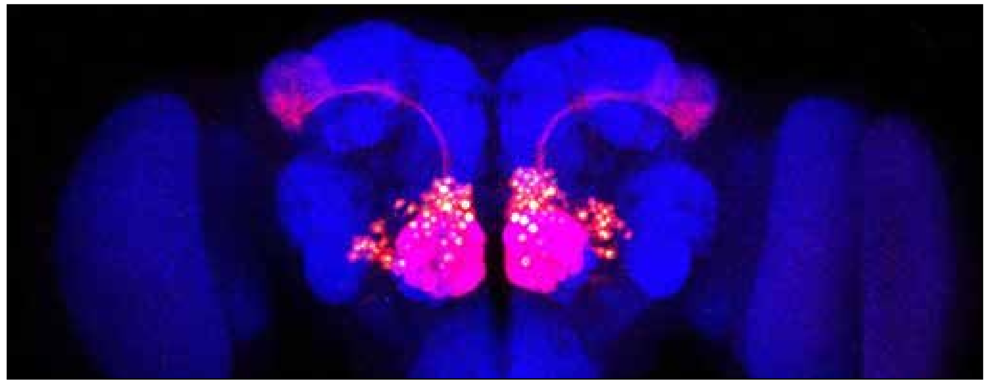
A quick look at the corner of Campus Drive and Via Ortega will confirm that construction has begun on the new research facility for Stanford Neurosciences & ChEM-H, which will serve as a focal point for our community. It will be a uniquely beautiful and functional space—an expression of the values and intellectual goals of both institutes. That this building is becoming real reflects a great deal of dedicated work by numerous members of our community. As I write, faculty planning committees are actively conceiving and designing four new community resource laboratories in addition to the four core laboratories already functioning under the auspices of the Institute. With occupation of the new facility in Spring 2019, tangible benefits will soon flow to the entire community.

In all these efforts, our overarching goals are to enable all members of the Stanford neuroscience community to do their very best research, and to enable interdisciplinary neuroscience training of the very highest caliber.

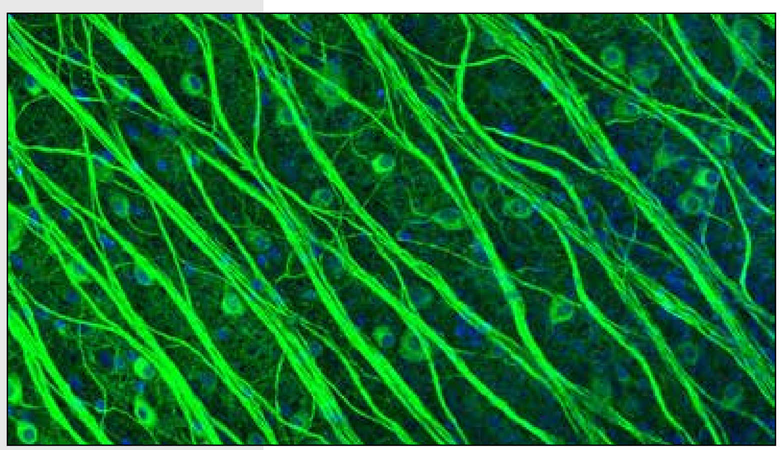
We look forward to all that we will accomplish together in 2018!

Sincerely,
William T. Newsome, PhD
Vincent V.C. Woo Director, Stanford Neurosciences Institute
Harman Family Provostial Professor
Professor of Neurobiology, HHMI Investigator

Stanford Interdisciplinary Neurosciences



The Stanford Neurosciences Institute fosters interdisciplinary research furthering our knowledge of the brain and behavior in health and disease. Understanding the human brain, the most complex entity in the known universe, is no longer a problem for biology or psychology alone. We are therefore building bridges between the traditional neurosciences (both clinical and basic) and a diverse array of disciplines ranging from chemistry, physics and engineering to communications and education, bringing a broad set of ideas and techniques to bear on unraveling the mysteries of the brain. The fourth year of the Stanford Neurosciences Institute was one of continuing growth and evolution as we pursue our goals to build community, to accelerate groundbreaking research, and to create key infrastructures for neuroscience.



The research emphases of the Stanford Neurosciences Institute fall into three broad categories:

- **NeuroDiscovery** - question-driven discovery about how the brain works
- **NeuroEngineering** - tools for making novel measurements of brain structure and function
- **NeuroHealth** - translating neuroscience discoveries into treatments

Big Ideas in Neuroscience is the institute's flagship research effort. Major cross-disciplinary teams of faculty are currently tackling big challenges in brain science. These large-scale research endeavors have the potential to revolutionize neuroscience research, technologies, and treatments. In 2017, three Big Ideas projects advanced to Phase 2 status:

- **Brain Rejuvenation**, an interdisciplinary initiative to understand the basis of brain aging and rejuvenation
- **NeuroChoice**, a far-reaching collaboration on the neural mechanisms supporting addictive choices, linking basic biology, psychology and policy initiatives
- **NeuroTechnology**, developing a new generation of brain-machine interfaces that match the intrinsic resolution and performance of the biological circuitry

In 2017, the institute awarded its second round of **Seed Grants** to six interdisciplinary teams. Each team is piloting a novel idea that could develop into significant advances in the future. In addition, the Institute funded three **Research Accelerator** awards that have substantial potential for high impact advances in understanding brain biology and improving brain health.

The essence of the Neurosciences Institute is our community of remarkable researchers. Partnering with the School of Engineering, the institute successfully recruited Dr. Guosong Hong, who will become an assistant professor in materials science and engineering in Fall 2018. Dr. Hong, who is developing tools to probe and stimulate neurons, joins our group of institute Faculty Scholars, each driving research programs that span traditional disciplinary boundaries. Dedicated to training the next generation of neuroscientists, in 2017, the Institute awarded five Interdisciplinary Scholar Awards to outstanding postdoctoral scientists and two Stanford Interdisciplinary Graduate Fellowships to remarkable graduate students. Five Neurosciences Institute researchers participated in international exchanges with École Polytechnique Fédérale de Lausanne through the EPFL-Stanford Exchange Program, funded by the Firmenich Foundation.

The Institute community gathered at our Fourth Annual Symposium held on October 19, 2017. Top neuroscientists from around the world presented their work: Carlos Brody (Princeton University) Martha Farah (University of Pennsylvania), Maiken Nedergaard (University of Copenhagen), Matthew State (University of California San Francisco) and Barbara Webb (University of Edinburgh). A highlight of the symposium was the annual presentation of the Sammy Kuo Awards to students and postdocs for outstanding neuroscience research papers.

Our weekly seminar series hosted thirty top neuroscientists from around the country and across the globe. Four seminars were hosted in partnership with psychiatry and behavioral sciences or the Alzheimer's disease research center. Speakers are nominated by members of our community, and represent a wide diversity of disciplines. Eminent speakers this past year included Arnold Kriegstein (UCSF), Joshua Gordon (director of NIMH), Sheena Josselyn (University of Toronto), Yang Dan (HHMI and UC Berkeley), Zayd Khaliq (NINDS) and Bradley Hyman (Harvard). In the spring quarter, we held a special seminar series focused on theoretical and computational neuroscience.

After years of planning, construction began on the new research complex for the Neurosciences Institute and ChEM-H. Most of the activity was below ground level: excavating the site, building utilities and preparing the foundations for the structure. In January 2017, the institute selected 18 faculty who will be the first neuroscience occupants of the complex. When complete, a total of 24 neuroscience labs, along with shared community laboratories will reside in this new programmatic hub for the institute.

The Dean of Research convened a new advisory council for interdisciplinary biosciences in 2017, composed of prominent leaders from the private sector and trusted friends of Stanford with serious interest in the biosciences. The council advises the Neurosciences Institute, Bio-X and ChEM-H, which have in common the overarching goal of promoting interdisciplinary approaches to complex problems in biomedical science. Input from the council has already been valuable to the leadership of the three institutes as we plan the future of interdisciplinary bioscience research at Stanford University. We look forward to deepening relationships with this special group of advisors in the coming years.

New Faculty

The Institute held a successful joint faculty search with the school of engineering. Guosong Hong will join the Institute as an assistant professor of materials science and engineering in Fall 2018. Dr. Hong has a deeply interdisciplinary training background in chemistry, optics, electronics and neuroscience. He is a tool builder who is developing transformative technologies to interface with the central nervous system using injectable mesh electronics. Tools developed by Dr. Hong have the promise of providing long-term stable interfaces at single-neuron spatio-temporal resolution, and will be used in studies of learning/memory, aging and neurodegenerative diseases.

Faculty Awards and Honors

Several faculty affiliates of the Stanford Neurosciences Institute were awarded major prizes or were appointed to preeminent academies.

Stanford University honored **Ben Barres** (neurobiology, developmental biology, neurology) with a President's Award for Excellence Through Diversity. Barres was honored "for blazing trails as a brilliant scholar and researcher, exceptional teacher, academic leader, and as the first transgender man elected to the National Academy of Sciences."

Marion Buckwalter (neurosurgery, neurology) received the Award for Excellence in Mentoring and Service from Stanford Medicine. This award recognizes faculty who make distinguished contributions toward enhancing the quality of training and the educational experience for biosciences graduate students.

Karl Deisseroth (D.H. Chen Professor in bioengineering and psychiatry) won the 2017 Fresenius Research Prize for his pioneering work in two distinct biomedical technologies — optogenetics and hydrogel-tissue chemistry — and for exploring his clinical specialty, depression, at the level of its underlying neural circuitry.

Amit Etkin (psychiatry) was awarded a 2017 NIH Director's Pioneer Award to develop a "circuits-first" platform focused on understanding the brain circuits of individual patients as a means for personalized diagnosis and treating patients using individually-tailored, plasticity-inducing neurostimulation.

Andrea Goldsmith (Stephen Harris Professor in electrical engineering) received the 2017 Women in Communications Engineering Mentorship Award from the IEEE Communications Society in recognition of her efforts to bring diversity to her field and opportunity to her students.

Keith Humphreys (psychiatry) was named the Esther Ting Memorial Professor. The professorship is intended to support efforts to increase understanding and treatment of addiction, particularly among adolescents. Humphreys' research focuses on treatment and public policy affecting addiction and psychiatric disorders.

Jennifer Raymond (neurobiology) received the Award for Excellence in Graduate Teaching from Stanford Medicine. The award recognizes faculty whose teaching of graduate students is distinguished and especially valued by the Stanford biosciences community.

Sergiu Pasca (psychiatry) and **Gregory Scherrer** (anesthesia, neurosurgery) became 2017 Robertson investigators of the New York Stem Cell Foundation. Pasca, a Roberston Stem Cell Investigator, develops new approaches for studying human brain development and uncovering the mechanisms of neuropsychiatric disorders. Scherrer is a Robertson Neuroscience Investigator, and works to alter the brain's interpretation of pain signals to eliminate the unpleasantness associated with pain and restore patients' quality of life with a goal of finding new pain relief solutions.

Andrea Goldsmith (Stephen Harris Professor in electrical engineering) was elected into the National Academy of Engineering for her work on adaptive and multi-antenna wireless communications.

Tirin Moore (neurobiology) was elected into the National Academy of Medicine. His research focuses on neural mechanisms of sensory-motor integration and the neural basis of cognitive functions, such as attention.

2017 Interdisciplinary Scholars

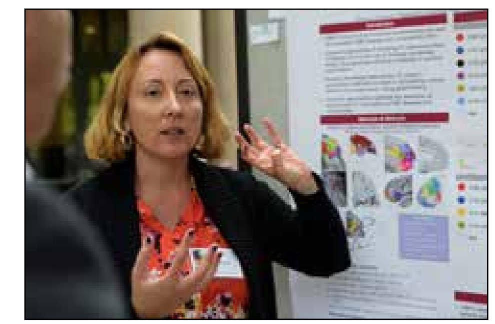
We presented five outstanding postdoctoral scholars with Interdisciplinary Scholar Awards. The award includes a two-year fellowship and participation in a program for career development and network-building.

Kyle Brewer *(neurology)*
Sponsors: Carolyn Bertozzi (chemistry) and Tony Wyss-Coray (neurology)

Recently, blood from young mice has been found to rejuvenate several tissues of old mice, including the brain. Seeking to identify the protein factors that produce youthful effects, Dr. Brewer is developing a mouse model to label proteins secreted into the bloodstream from the liver to determine if these factors can interact with or enter the brain.

Hongjie Li (biology)
Sponsors: Liqun Luo (biology) and Stephen Quake (bioengineering)

Dr. Li wants to explore how specific neural circuit connections are established during development. He is working to systematically identify wiring specificity molecules for Drosophila olfactory neurons using single cell RNA-sequencing.



Zoi (Zoe) Samara (psychiatry)
Sponsors: Leanne Williams (psychiatry) and Robert Malenka (psychiatry)

Dr. Samara seeks to understand the reward circuit activity of patients with anhedonia. She aims to elucidate the dysfunction of the reward network in anhedonia and use this knowledge to improve treatment efficacy.

Mariapaola Sidoli
(developmental biology)
Sponsor: William Talbot (developmental biology)

Dr. Sidoli seeks to understand the role of an important intracellular messenger molecule in the development of the nervous system. She is combining fluorescent imaging and gene expression analyses in zebrafish to probe the messenger molecule role and dynamics.

Corianne van den Akker (chemistry)
Sponsor: Steven Boxer (chemistry) and Justin Du Bois (chemistry)

Ion channels in the membranes of neuronal cells are the key regulators of neuronal signaling. Dr. van den Akker's goal is to understand the mechanism of activation and blocking of ion channels by toxins and drugs. She developed a chip in which she can perform both ultra-high resolution fluorescence microscopy and electrical measurements on single, functional ion channels in a well-controlled environment.

2017 Stanford Interdisciplinary Graduate Fellows

Two extraordinary graduate students were awarded fellowships affiliated with Stanford Neurosciences Institute.

Kevin Feigelis (physics) was named the David L. Sze and Kathleen Donohue Interdisciplinary Fellow for his project titled *Engineering versatile deep neural networks that model cortical flexibility*.

Xulu Sun (biology) was named a Stanford Interdisciplinary Graduate Fellow (Anonymous Donor) for her project titled *Neural mechanisms of learning multiple motor skills and implications for motor rehabilitation*.

Interdisciplinary Research

The research emphases of the Stanford Neurosciences Institute fall into three broad categories:

NeuroDiscovery Question-driven discovery about how the brain works

NeuroEngineering Tools for making novel measurements of brain structure and function

NeuroHealth Translating neuroscience discoveries into treatments

Below, we describe the research projects and the teams pursuing them that belong to each category.

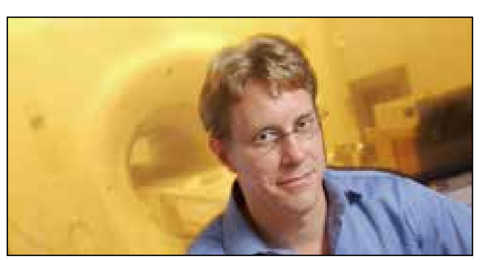
NeuroDiscovery

NeuroDiscovery

Question-driven investigation of how the brain works

NeuroDiscovery applies cutting-edge techniques to make fundamental discoveries in brain science — discoveries that could unlock new medical treatments, transform education, inform public policy, and help us understand who we are. Our scientists peer at individual molecules at synapses, trace networks of interconnected neurons responsible for specific brain functions, and obtain dynamic views of the human brain in action through noninvasive neuroimaging. We tap into those circuits via causal manipulations of specific neural systems to understand how our brains detect, integrate and transform stimuli into action.

Big Idea in Neuroscience

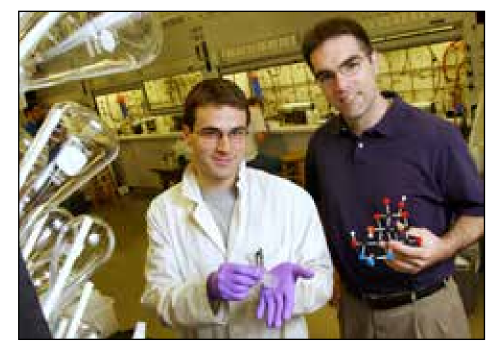


NeuroChoice – Understanding and treating addictive behavior - from circuits to policy

Team Leaders: Brian Knutson (psychology), Keith Humphreys (psychiatry), Robert Malenka (psychiatry)

Our decisions define the quality of our lives as well as those of future generations. In response to changing environmental conditions, organisms ranging from rodents to humans must continually adjust their choices to exploit environmental resources effectively, thus ensuring their procreation and survival. Key neural mechanisms supporting choice have been evolutionarily conserved and can be examined across species at multiple levels of analysis. Establishing strong conceptual and experimental links that bridge these levels of analysis – from neural circuits to individual choice to group choices – could spark major advances both in basic neuroscience research as well as the application of neuroscience findings to enduring societal problems. Addiction (e.g., to substances, gambling, overeating) can be framed as a pathological choice problem ripe for interdisciplinary multilevel solutions. Our team continues to connect diverse faculty to deepen interdisciplinary understanding of the neural mechanisms supporting healthy and addictive choices by combining conceptual, experimental, and clinical approaches that bridge historically disparate fields of inquiry. The team engages with policymakers whose work on addiction might be informed by neuroscience evidence, and who might reciprocally help us to identify promising new issues poised to benefit from transformative research advances.

Seed Grants



Identification of sex hormone interacting proteins

Nirao Shah (psychiatry) and Justin Du Bois (chemistry)

These collaborators aim to elucidate the multiple roles that sex hormones play in development of the nervous system and in regulating brain functions that influence gender identity, puberty, and reproduction. Understanding how these potent small molecules influence neural development and physiology should reveal new mechanisms for treating human diseases, including illnesses such as autism, PTSD, and Alzheimer's disease. There is a common misperception that the action of sex hormones, namely estrogen and testosterone, is well established, when in fact quite the opposite is true. Answers to questions regarding how these molecules traffic into and within cells and regulate cellular functions remain largely unknown. To gain deeper insight into the pharmacology of sex hormones, the team is developing selective chemical probes that mimic sex hormones to enable labeling and identification of proteins that interact with these molecules. Subsequent studies will determine the consequences of these molecular interactions for physiology and behavior. This collaboration will combine chemical synthesis, biochemistry, and neuroscience to advance this multidisciplinary research program.

TrkA-ing the chronic pain

Bianxiao Cui (chemistry) and Gregory Scherrer (anesthesia)

Although acute pain serves an essential protective function, many types of chronic pain including inflammatory, neuropathic, and cancer pain cause disabilities and significantly impact life quality. Nerve growth factor (NGF) and its membrane receptor, TrkA, are potent mediators of chronic pain. Despite their vast potential as therapeutic targets, the question of how NGF/TrkA plays a role in pain remains unanswered. In particular, how NGF differentially sensitizes pain in sensory neurons versus in the central nervous system (CNS) is unknown. To fill this gap in knowledge, this team proposes to develop a novel approach: to activate TrkA directly with light, in the absence of NGF. This light-inducible approach allows high spatial and temporal control of TrkA activation. These new light-inducible TrkA systems will permit analysis of how TrkA activation influences the excitability of sensory neurons detecting painful stimuli, on neurotransmission between these sensory neurons and CNS pain circuits, and on acute and chronic pain perception with in vivo behavioral pain tests. By bridging scientific disciplines, this project will significantly broaden our understanding of TrkA function in pain sensation, and in the longer term, of other neurological disorders influenced by TrkA and/or other neurotrophin receptors.

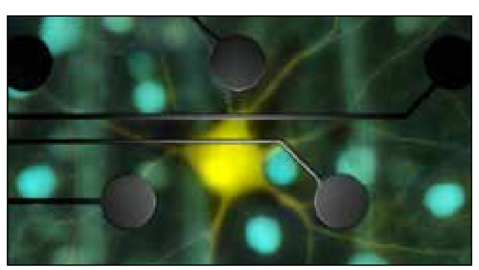
NEUROENGINEERING

NeuroEngineering

Tools for making novel measurements of brain structure and function

The human brain has 100 billion nerve cells and trillions of connections between them. Understanding the workings of such a complex and dynamic organ requires new tools and technologies. Materials scientists are developing probes to form gentle but sensitive and reliable interfaces to stimulate and record signals from thousands of individual neurons at once. Our engineers are developing ways to manipulate neural circuits with electricity, light, ultrasound and magnetic fields, and others are listening to the brain, interpreting the language of neural signals and using that language to drive robotic arms or to type on a computer. New tools will enable as yet unimagined discoveries and will allow us to repair and even to augment the human brain.

Big Idea in Neuroscience



Stanford neurotechnology initiative

Team Leaders: Nicholas Melosh (materials science and engineering) and E.J. Chichilnisky (neurosurgery and ophthalmology)

Neural interfaces of the future will be used to treat a wide range of diseases for which there is no cure, ranging from sensory and motor degeneration to psychiatric disorders. Yet, present-day neural interfaces remain crude compared to the neural circuits in which they are embedded. The project goal is to develop the next generation of neural interfaces that match the resolution and performance of the biological circuitry. The team will focus on two signature efforts to spearhead the necessary advances: high-density wire bundles for electrical recording and stimulation, and analog and digital bi-directional retinal prostheses for restoration of vision. In the process of assembling the people to achieve these goals, the initiative will develop an interdisciplinary research and training environment to place Stanford as a global leader in neurotechnology. The core team spans Humanities & Sciences, the School of Medicine, and the School of Engineering, and includes expertise in neuroscience, biomaterials engineering, nanofabrication, and integrated circuit design.

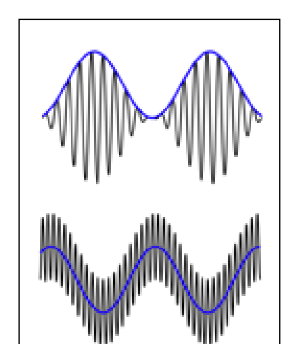
Seed Grants

Enabling faster and more responsive voltage imaging through computational biophysics

Ron Dror (computer science) and Michael Lin (neurobiology, bioengineering)

Our brains process information and make decisions by means of electrical and chemical interactions between many millions of neurons. The primary form of information transmission within the nervous system is the action potential, or electrical 'impulse', which can travel long distances between brain structures. Being able to measure when neurons fire electrical impulses (at scale, from many thousands of neurons simultaneously) would allow us to better understand how the brain carries out critical functions, such as encoding sensations, recalling thoughts, or making decisions. Neuroscientists thus have long sought reliable ways to visualize electrical activity in neurons in real time. In this project, a computational biophysicist (Dror) and a protein engineer (Lin) are teaming up to improve voltage-sensing fluorescent proteins, proteins that can report electrical activity by changing their production of light. They are beginning with ASAPs, a family of voltage indicators recently created by the Lin Lab. Dr. Dror has expertise in using physics-based computer simulations to understand how proteins move, including voltage-induced motions in voltage-sensing protein domains similar to the one that drives responses in ASAPs. The team is using these simulations to study voltage-induced movements of ASAPs. By identifying what parts of the protein limit speed and responsiveness, new ideas for improving ASAP responses will be generated that can be tested immediately. If successful, this collaborative interdisciplinary work can lead to dramatic improvements in voltage sensor performance, enabling the detection of faster or smaller electrical impulses than previously possible.

Remote and localized neural activation using sonomagnetic stimulation



Amin Arbabian (electrical engineering) and Stephen Baccus (neurobiology)

Neurostimulation plays a critical role in the understanding of neural circuits and treating disease. Brain stimulation therapies now treat Parkinson's disease, depression, dystonia, and epilepsy and hold promise for Alzheimer's, anxiety, schizophrenia, and stroke. Neurostimulation methods that generate electrical currents, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), have strong effects on neural activity. Yet, noninvasive stimulation of structures deep in the brain has a fundamental barrier in that electromagnetic waves cannot be focused deeply into the brain. Consequently, TMS and tDCS can only reach shallow brain structures or larger target volumes. As an alternative approach, ultrasonic neurostimulation is a promising technology that can reach deep into the brain, but current in vivo results in humans have shown effects that are much weaker than those from TMS. This team is developing a new modality of noninvasive neural stimulation, sonomagnetic stimulation (SMS), that can generate an electrical current focused in a small volume deep in neural tissue, a goal not possible with any existing method of neurostimulation. The proposed method combines ultrasonic and magnetic field interactions to enable remote neural activation. If successful, this approach will introduce a fundamentally new tool for the basic study of neural function and treatment of neural disease.

Research Accelerator

The neural prosthetics translational laboratory

Krishna Shenoy (electrical engineering) and Jaimie Henderson (neurosurgery)

The research of this team focuses on the twin goals of investigating fundamental principles of human neuroscience and translating laboratory insights into clinically viable assistive devices for people with paralysis. Using small, surgically implantable sensors, the lab decodes nerve cell activity from the areas of the brain that control movement, allowing research participants with paralysis to move computer cursors, robotic limbs, and other assistive devices. The team recently demonstrated the highest typing performance ever reported by people with paralysis using a brain-computer interface, allowing our participants to type up to 8 words per minute using an on-screen computer keyboard. The laboratory has active research projects in a number of areas, including improving the performance of brain-controlled robotics, investigating the use of a fully-implantable wireless brain-computer interface system, restoring communication capabilities for people with paralysis, and understanding the basis of volitional movement in human research participants.

NeuroHealth

Translating neuroscience discoveries into treatments

Understanding the brain in health and disease will improve treatments for ourselves and our loved ones. Our clinical scientists not only treat patients, but are also working with basic scientists to pioneer novel treatments for psychiatric and neurological disease. Ongoing research aims to reverse brain aging, ease the devastating consequences of stroke, and develop non-invasive treatments to modulate brain activity associated with epilepsy and other neurological diseases. Breakthrough improvements in brain and mental health benefit not just individuals, but society as a whole.

Big Idea in Neuroscience

Brain rejuvenation

Team Leaders: Tony Wyss-Coray (neurology) and Aaron Gitler (genetics)

Aging leads to a precipitous loss of cognitive faculties and it is the key risk factor for dementia and neurodegenerative diseases. Many new genetic factors causing neurodegeneration have now been identified but how they cause disease and how aging modulates disease is unknown. The Stanford Brain Rejuvenation Project assembles leading aging researchers, neuroscientists, chemists, and engineers to understand the basis of brain aging and rejuvenation and how they relate to neurodegeneration. The missions of the Project are to slow or reverse aging to maintain brain function and extend health span, to rejuvenate brains for the treatment of neurodegenerative and other neurological diseases, and to elucidate novel mechanisms of human neurodegenerative diseases to develop innovative therapeutic strategies based on this new concept of rejuvenation. We have assembled a highly collaborative and multi-disciplinary team focused on harnessing a powerful new approach to discover, characterize, and utilize brain rejuvenation factors harbored in the blood to improve human health and to combat neurodegenerative diseases. The team brings together a neurologist, geneticists, a chemist, stem cell biologists and neuroscientists all with distinct and complementary expertise and technologies.

Seed Grants

The impact of early medial temporal lobe Tau in human cognitive aging

Elizabeth Mormino (neurology) and Anthony Wagner (psychology)

Memory decline is a common complaint among older individuals. Interestingly, the pathological changes of Alzheimer's disease (AD) begin years before clinical symptoms of dementia are noticeable, and may contribute to decline in memory among putatively 'healthy' older individuals that have performance in the normal range. Positron emission tomography (PET) allows the visualization of early AD pathology. In particular, the abnormal aggregation of the Tau protein is a hallmark pathological feature of AD dementia, and is also common among older normal adults. Interestingly, the accumulation of the Tau protein begins in the medial temporal lobe, a brain region that is essential for the formation of new memories. By combining PET imaging with high-resolution magnetic resonance imaging (MRI) to measure the structure and function of the medial temporal lobe, we can understand how this early AD pathology influences memory in healthy older individuals and whether these early changes can predict who is most at risk for AD dementia in the future. Given the failure of multiple clinical trials in symptomatic AD dementia patients, there is hope that targeting the disease as early as possible, even before symptoms are present, will be a successful strategy against AD.

A novel sigma-1 receptor PET radioligand as a probe of ketamine's rapid therapeutic action in disorders of human brain and behavior

Carolyn Rodriguez (psychiatry), Frederick Chin (radiology), David Lyons (psychiatry), Alan Schatzberg (psychiatry) and Pamela Flood (anesthesia)

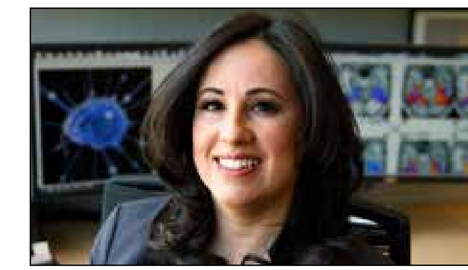
Major Depressive Disorder (MDD) and Obsessive Compulsive Disorder (OCD) are among the top-ten leading causes of disability worldwide, but standard medications provide only minimal relief. A recent discovery by Dr. Rodriguez shows that ketamine, perhaps best known as an anesthetic, could treat symptoms of MDD and OCD within hours. Current OCD treatments often take months to bring only partial symptom relief. Coincidentally, ketamine is also a powerful dissociative, a class of hallucinogenic drugs. Interestingly, the degree of dissociation strongly predicts a more robust clinical response, raising the question of whether the troublesome side effect may hold a clue to how ketamine acts to reduce psychiatric symptoms. This interdisciplinary collaboration across psychiatry and radiology is developing and validating a new method to study the mechanisms underlying ketamine's biochemical action and its effects on dissociation and treatment effectiveness.

Research Accelerator

New tools, analytic methods and conceptual approaches for harnessing plasticity in the human brain

Amit Etkin (psychiatry), Gary Glover (radiology), James Gross (psychology), Manish Saggar (psychiatry), Surya Ganguli (applied physics), Brian Knutson (psychology)

Human cognition arises from the activity and interactions of brain regions within well-defined circuits and that psychiatric disease results from dysfunction of these circuits. However, our ability to non-invasively manipulate human neural activity – both for gaining a more causal understanding of normal brain function and to therapeutically remediate dysfunctional circuits – remains very limited. Critical to advancing these capacities, and with it the availability of novel psychiatric treatments, are a more robust understanding of which patient-relevant brain circuits are most important for which cognitive operations, how these circuits can be best modulated through repetitive transcranial magnetic stimulation (rTMS) and how the broader societal understanding of the brain basis of mental illness can be advanced so that new technologies best impact the lives of individuals in need of treatment. This team is addressing these challenges by bringing expertise from neuroscience, psychiatry, psychology, engineering, physics and computational modeling to bear. The research project ranges from tool development and experimental work in healthy individuals to complex data analysis and computational modeling, and ultimately to a larger-scale engagement with societal attitudes through educational interventions. Through these efforts and the interdisciplinary collaborations involved, we hope to establish a new intellectual, scientific and clinical paradigm for understanding and manipulating human brain circuits in healthy individuals and for treating psychiatric disease.



StrokeCog

Marion Buckwalter (neurology) and Maarten Lansberg (neurology)

StrokeCog is an extension of the Stroke Collaborative Action Network (SCAN) Big Idea project and is a key component of the Stanford Stroke Recovery Program. StrokeCog is focused on cognitive problems after stroke. While common, the exact mechanisms of post stroke cognitive decline are not well understood. StrokeCog funds a large prospective cohort study aimed at identifying if neuroinflammation plays an important role in the development of post-stroke cognitive decline. In addition, we continue to support SCAN investigators with their clinical pilot studies via a clinical core. The core helps investigators with study design, stroke subject recruitment, and regulatory requirements for human research such as institutional review board applications and compliance.

A New Research Center

In 2017 construction began on a new research center that will serve as the hub for the Neurosciences Institute and Stanford ChEM-H. In January, 18 faculty were identified as the first neuroscience occupants of the facility, 3 new hires and 15 existing faculty selected from the schools of Humanities & Sciences, Medicine, and Engineering. The occupants were grouped into lab neighborhoods of 3-5 faculty, and spent months planning the details of their shared lab spaces. Simultaneously, construction began, mostly below ground level, as the site was excavated, utilities constructed and foundations prepared.

When complete, the 235,000 square foot facility will be home to 24 interdisciplinary neuroscience laboratories, critical neuroscience core facilities, and

vibrant meeting and interaction spaces. By bringing building residents together and drawing in researchers and students from many disciplines across campus, we will create an intellectual collaboration zone where serendipitous encounters could lead to breakthrough neuroscience discoveries. “This building is a physical manifestation of Stanford’s commitment to breaking down barriers between disciplines,” says Ann Arvin, Vice Provost and Dean of Research.

Embracing a light-filled courtyard, the Neuroscience wing of the center will provide state-of-the-art laboratories with bright, open shared spaces as well as customized zones for specialized equipment and techniques. Within a neighborhood, trainees will work side-by-side with colleagues from different schools and departments. The second floor has a large, bright, two-story open space – the living room – with comfortable furniture, tables and whiteboards where researchers will mingle and interact.

Another unique space is the neuro-theory center. Surrounded with glass and embedded in the living room, this three-story structure within the building places theorists, who often work tucked away from view, front and center physically and intellectually. Reaching the important goal of understanding how the brain computes will require development of novel theoretical and analytical approaches, and the Institute hopes to recruit the best and brightest quantitative minds to this center.

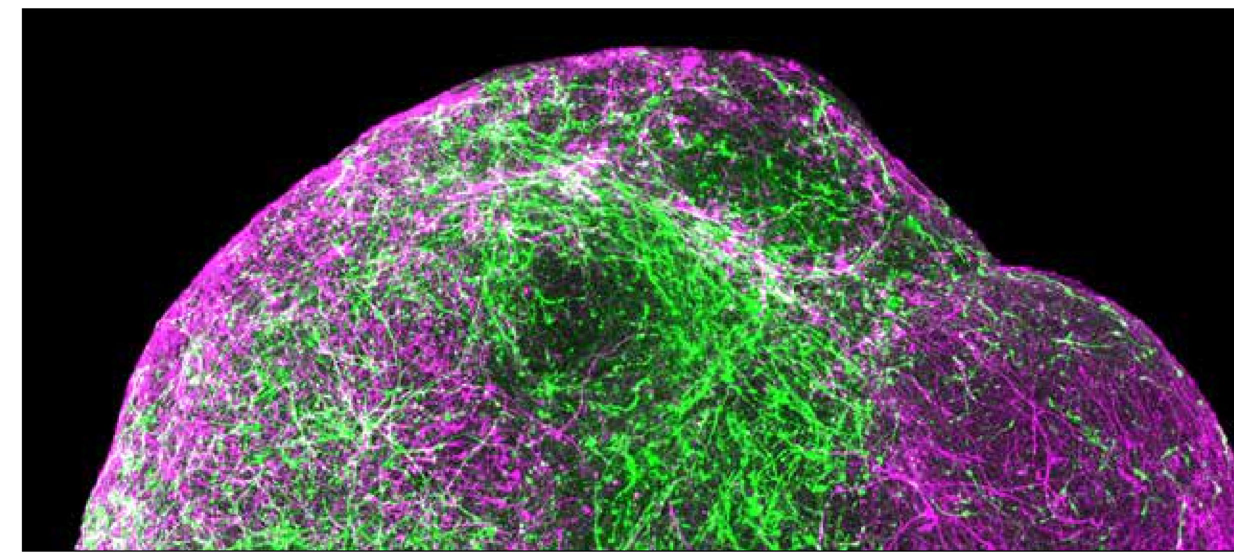
Co-localization of the Neurosciences Institute and ChEM-H in the same building will pay intellectual dividends in the future. New collaborations between neuroscience and ChEM-H faculty have been initiated simply in the course of planning the building; more will certainly ensue when research groups are *in situ* and ‘collisions’ begin occurring the building common spaces. “I really do believe the future of neuroscience is going to be collaborative,” Institute director Bill Newsome says. “Being co-located with ChEM-H will bring neuroscientists in contact with chemists who are interested in biological applications.”

Neuroscience Community Labs

Stanford Neurosciences Institute facilitates the efforts and productivity of a broad array of neuroscientists by providing core facilities and services. These cores allow researchers to access tools, techniques and expertise that would be costly or impractical to replicate many times over in individual laboratories.

Gary Steinberg (neurosurgery) and Mehrdad Shamloo (neurosurgery) direct a trio of neuroscience cores. The Stanford Behavioral and Functional Neuroscience Laboratory is a preclinical discovery platform providing expertise in all aspects of design and implementation of rodent behavioral experiments, including data analysis and interpretation. The Neuroscience Microscopy Service provides access to high-end, capital-intensive microscopy equipment that is often not available to individual labs. The Gene Viral Vector Core creates vectors for virally mediated molecular manipulations that allow unprecedented experimental control over synapses, cells and circuits in model systems, both in vitro and in vivo. Together, the three cores have supported more than 200 laboratories throughout Stanford and nationwide with more than 13,000 hours of services in the past year. The cores provide services that are well-matched to the faculty’s funded research aims, as demonstrated by 40 peer-reviewed publications.

Joachim Hallmayer (psychiatry), Richard Reimer (neurology) and Sergiu Pasca (psychiatry) direct the Neuroscience Induced Pluripotent Stem Cell (iPSC) Core in collaboration with Psychiatry and the Neurosciences Institute. Technology for generating iPSCs allows the derivation of neural tissues directly from patients with neurologic or psychiatric disorders and healthy individuals alike, and has tremendous potential for research in individualized medicine.



We will introduce new cores when the research center opens in 2019, including a human neuroscience core, a small animal imaging facility, a data visualization core, and a sandbox laboratory for training the next generation of interdisciplinary neuroscientists.

Development Activities at the Stanford Neurosciences Institute

The Stanford Neurosciences Institute is thrilled to have received a generous anonymous leadership gift providing a strong foundation for the future of the institute and its ability to foster collaborative brain research and generate new discoveries. This remarkable gift will help fuel bold interdisciplinary initiatives including Big Ideas, support innovative faculty and students, and help provide programs in benefit of scientists across campus.

Additionally, the future home of the Stanford Neurosciences Institute is under construction and set to open in Spring 2019, thanks to wonderful lead gifts for the interdisciplinary research complex, which will also house Stanford ChEM-H. Friends of the institutes have made gifts to name spaces and core facilities in the complex, including the Sandbox, the prime meeting area, other key spaces, and multiple conference rooms.

Ongoing fundraising priorities for the Stanford Neurosciences Institute include long-term support for collaborative brain research, shared facilities and interdisciplinary faculty and students. One notable activity is the institute's efforts to engage philanthropic partners to establish a collective endowed fund in support of highly promising major collaborative neuroscience research endeavors that would otherwise not get funded through traditional grants. Stanford has dedicated presidential matching funds to help inspire individuals to make gifts in support of this priority, and also to encourage gifts that will create named professorships. The Stanford Neurosciences Institute is grateful for the remarkable philanthropic support from alumni, parents and friends that benefits hundreds of faculty and students campus-wide. The institute also is actively involved in meaningful activities to steward its community of donors.

Under the leadership of the Dean of Research, the Stanford Neurosciences Institute, Bio-X and ChEM-H established a new advisory council this year. The Council is made up of nearly 40 members, including many those who were formerly Bio-X Council and/or ChEM-H/Neuro Task Force members. While these three institutes have different areas of focus, they have incredible synergies, shared interests, and many faculty members in common. All three strive to foster collaborative research and create new knowledge at the intersections of disciplines. The Council is committed to serving as a sounding board and providing guidance and leadership support to help all three institutes advance their individual and collective missions.

Our Team

Stanford Neurosciences Institute owes the success of its fourth year to its leadership and to the dedicated team that makes our events and programs happen.

Executive Committee

William Newsome (Neurobiology), Vincent V.C. Woo Director and Harman Family Provostial Professor

Marion Buckwalter (Neurology and Neurosurgery), Deputy Director

Scott Delp (Bioengineering and Mechanical Engineering), Deputy Director and James H. Clark Professor

Miriam Goodman (Molecular and Cellular Physiology), Deputy Director

Robert Malenka (Psychiatry), Deputy Director and Nancy Friend Pritzker Professor

Brian Wandell (Psychology), Deputy Director and Isaac and Madeline Stein Family Professor

Tanya Raschke, Associate Director for Planning and Operations

Staff

Tanya Raschke, Associate Director for Planning and Operations

Roula El-Asmar, Program Manager

Cathy Lau, Financial Analyst

Daisy Ramirez, Administrative Associate

Maura McGinnity, Development Director

Patrick Gutteridge, Development Director

Nathan Collins, Communications Director

“The Big Ideas initiative promises to have a powerful effect on the field – creating an environment where radical ideas will yield remarkable advances, and where pioneers can transform our understanding and treatment of the brain.”

–Stanford Provost Persis Drell

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