The Simons Center for the Social Brain Newsletter

Fall 2024

Simons Center for the Social Brain

Inside this issue

Massachusetts Institute of Technology

Upcoming Events: Fall 2024

Colloquium Series

September 11
Nancy Padilla-Coreano, Ph.D.
University of Florida

October 16
Michael Frank, Ph.D.
Brown University

October 30
Yang Zhou, Ph.D.
McGill University

November 13
Elizabeth Goldfarb, Ph.D.
Yale University

December 11
Katalin Gothard, Ph.D.
University of Arizona

General Info
Time: 4PM–5PM, *reception to follow*
Location: Singleton Auditorium, 46-3002
registration is not required

Lunch Series

September 13
Lio Wong, Ph.D.
Postdoctoral Researcher,
Computational Cognitive Science
group. BCS

September 27
Gabriel Stine, Ph.D.
SCSB Postdoctoral Fellow,
Mehrdad Jazayeri Laboratory, MIBR

October 11
Lace Riggs, Ph.D.
SCSB Postdoctoral Fellow,
Guoping Feng Laboratory, MIBR

November 8
Earl Miller, Ph.D.
Picower Professor of Neuroscience

December 6
Francisco Garcia, Ph.D.
Postdoctoral Associate,
Myriam Heiman Laboratory, PILM

General Info
Time: 12PM–1PM
Hybrid Location: Simons Center Conference Room,
46-6011 + Zoom Meeting, *registration is not required*

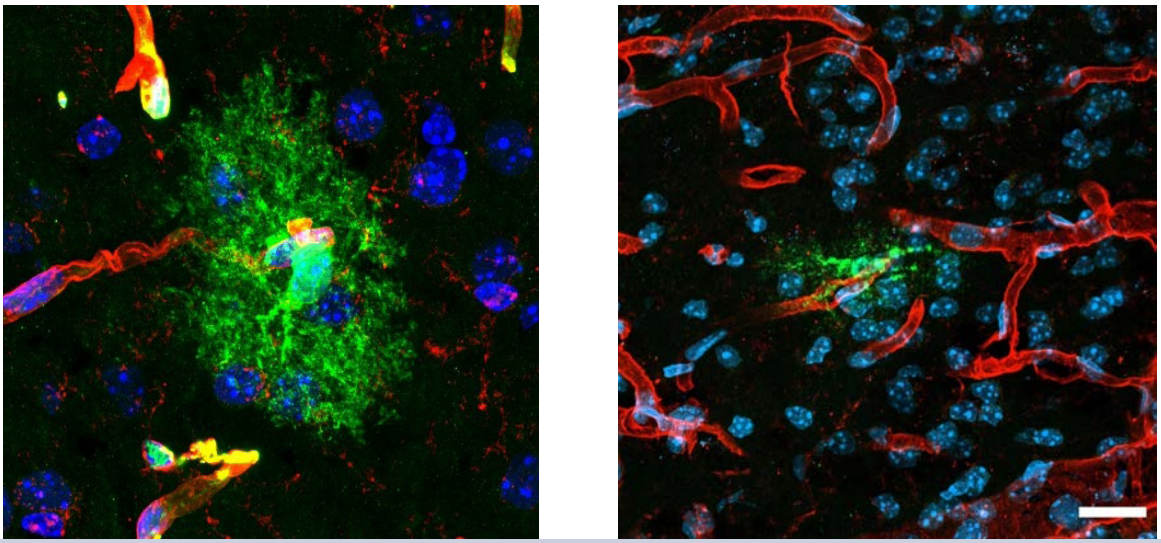
All events are open to public, please visit our website for all upcoming events: scsb.mit.edu/events

Targeted Projects: Updates

Meningeal immunity: a novel strategy for treating autism spectrum disorders

The SCSB targeted project entitled "Meningeal immunity: a novel strategy for treating autism spectrum disorders" involves four labs: Gloria Choi (Picower Institute), Jun Huh (Harvard Medical School), Myriam Heiman (Picower Institute), and Mriganka Sur (Picower Institute).

Gloria Choi's lab is investigating how immune cells in the meninges, the protective layers surrounding the brain, influence brain activity and behavior through cytokine release. They have uncovered that different IL-17 receptor subunits are expressed in distinct patterns across various brain regions, indicating that specific cytokines may modulate different aspects of brain function. This discovery is particularly relevant for understanding the role of immune signaling in social behaviors and how dysregulation of these pathways could contribute to autism. Moving forward, the Choi Lab will focus on experimentally controlling cytokine release from meningeal immune cells to modify brain activity.



(Left) a. GFP Labeling of vc-astrocytes in vivo using PHP.V1-CLDN5::EGFP. Note the close proximity of vc-astrocyte cell body (EGFP; green) to the vasculature (labeled by lectin in red). **(Right)** b. TRAP Labeling of vc-astrocytes in Aldh1l1::Cre expressing mice using PHP.V1-CLDN5::DiO-TRAP. Note the specific expression of the TRAP contruct (EGFP-L10a, green) in vc-astrocytes only and not the vasculature (labeled by lectin in red). Scale bar = 20um. Images courtesy of Heiman lab.

Jun Huh's lab is exploring the intriguing connection between the gut and the brain, specifically how immune cells migrate from the gut to the brain and affect behavior. Their recent findings show that several IL-17 ligands, including IL-17A, IL-17B, IL-17E, and IL-17F, can enhance social behaviors in mouse models of autism. This suggests a broader role for these cytokines in brain function than previously recognized. The lab's future research will aim to enhance the migratory potential of these immune cells to the meninges and unravel the mechanisms by which gut bacteria influence this process.

Myriam Heiman's lab is focused on mapping the glymphatic system and a particular subpopulation of astrocytes known as vascular-coupled astrocytes (vc-astrocytes). These cells, located near blood vessels, are thought to play a significant role in the brain's waste clearance system. By identifying specific molecular markers and developing new tools for targeting these astrocytes, the lab hopes to better understand their function and regulation. Additionally, they are investigating the roles of other cell types, such as pericytes and perivascular fibroblasts, in glymphatic flow.

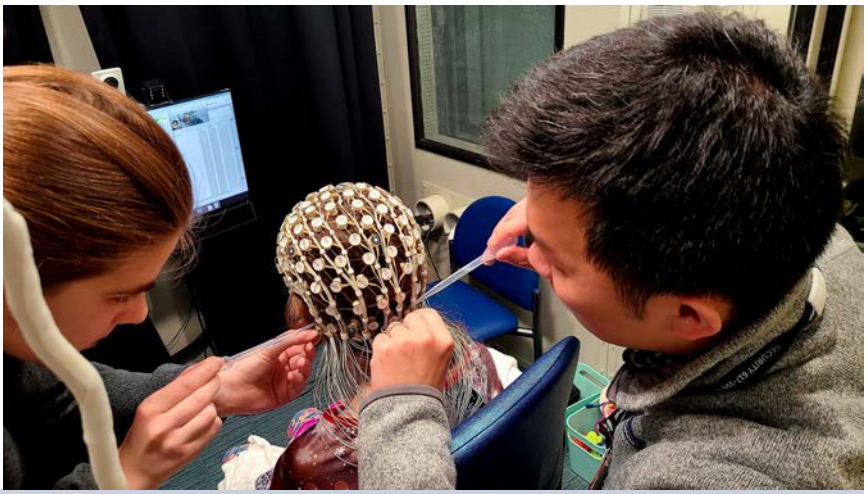
Mriganka Sur's lab has been delving into the complex role of astrocytes in regulating brain health. Using cutting-edge in vivo two-photon imaging, the team has developed sophisticated techniques to capture the dynamic interactions between astrocyte calcium signaling and blood vessel activity. These findings are crucial for understanding how astrocytes facilitate neurovascular and glymphatic coupling, processes that are essential for maintaining brain homeostasis and are also potentially implicated in neurodevelopmental disorders including autism.

Mitigating Sensory Overload with closed-loop stimulation

The SCSB targeted project titled "Mitigating Sensory Overload with Closed-Loop Stimulation" is led by Earl Miller (Picower Institute) and also involves Robert Desimone (McGovern Institute), and Charles Nelson (Boston Children's Hospital). The project aims to explore the mechanisms of predictive coding in the brain by manipulating alpha and beta rhythms. The research is particularly focused on understanding how these rhythms influence sensory processing and control, using both non-human primates and human subjects, including children with autism spectrum disorder (ASD) and Phelan-McDermid Syndrome (PMS).

Significant progress has been made toward the project's specific aims. One of the major accomplishments is the discovery of a consistent pattern of local field potential power across the primate cortex, which has been published recently in Nature Neuroscience with Diego Mendoza-Halliday, Alex Major, Noah Lee, Maxwell J. Lichtenfeld, Brock Carlson, Blake Mitchell, Patrick D. Meng, Yihan (Sophy) Xiong, Jacob A. Westerberg, Xiaoxuan Jia, Kevin D. Johnston, Janahan Selvanayagam, Stefan Everling, Alexander Maier, Robert Desimone, Earl K. Miller and André M. Bastos as authors. This discovery reveals that different layers of the cortex have distinct roles in managing sensory input and control. Specifically, the outer cortical layers are primarily responsible for processing sensory information through high-frequency gamma rhythms, while the deeper layers use slower alpha and beta rhythms to control the flow of this information. This pattern, observed in macaque monkeys and other primates, supports the theory of predictive coding, where the brain uses these rhythms to balance the processing of incoming sensory data and its internal control mechanisms.

In addition, a second paper currently in press at the Proceedings of the National Academy of Sciences with Yihan (Sophy) Xiong, Jacob Donoghue, Mikael Lundqvist, Meredith Mahnke, Alex Major, Emery Brown, Earl Miller, and André Bastos as authors, describes how propofol, a common anesthetic, disrupts this predictive coding process. The research shows that propofol eliminates the modulation of alpha and beta rhythms in the sensory cortex, impairing the brain's ability to respond to unexpected stimuli. These findings provide new insights into the neurophysiological basis of consciousness and suggest that disruptions in predictive coding could play a role in conditions such as sensory overload and impaired awareness.



A subject being prepared for EEG recording. Image courtesy of Virginia Rosenberger.

In the lab of Charles Nelson, parallel studies in children with ASD and PMS have also yielded promising results. The research team is conducting EEG studies to compare brain activity patterns among typically developing children, children with ASD, and those with PMS. Preliminary data show that children with PMS exhibit significantly lower alpha power and a reduced aperiodic exponent compared to both typically developing children and those with ASD. This suggests an increased excitation-to-inhibition ratio in their brain activity, indicating a possible imbalance in how their brains process and control sensory information. These findings, which will be presented at two upcoming symposiums, are the first to provide evidence of such altered neuronal activity in children with PMS.

Overall, the project's findings underscore the importance of rhythmic brain activity in sensory processing and highlight the potential for targeted interventions that could help individuals with sensory processing disorders.

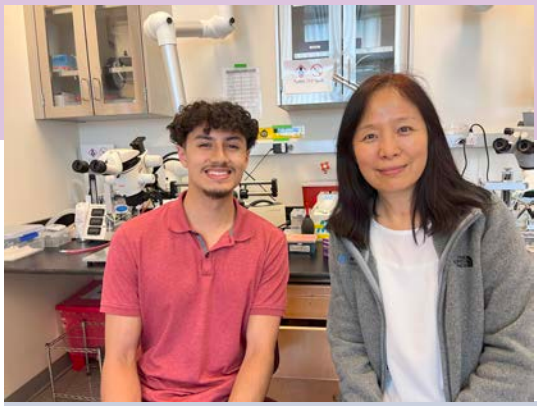
Simons Center MSRP 2024 Summer students

The 2024 MIT Summer Neuroscience Program brought together a diverse group of undergraduate students from across the nation for an intensive 10-week research experience. Hosted by the Department of Brain and Cognitive Sciences, the Center for Brains, Minds, and Machines, and the Department of Biology, the program offered non-MIT students an opportunity to engage in hands-on research in world-class facilities. Funded in part by MIT's School of Science, the National Science Foundation, and the Simons Center for the Social Brain, the program focused on inspiring students from underrepresented backgrounds to pursue graduate studies and careers in basic research. Participants worked closely with faculty and graduate mentors on a range of cutting-edge projects, from exploring the neural mechanisms underlying behavior to investigating brain development and disorders.

Raul Hernandez | Junior, Morgan Community College

Laboratory: Fan Wang, McGovern Institute for Brain Research, MIT

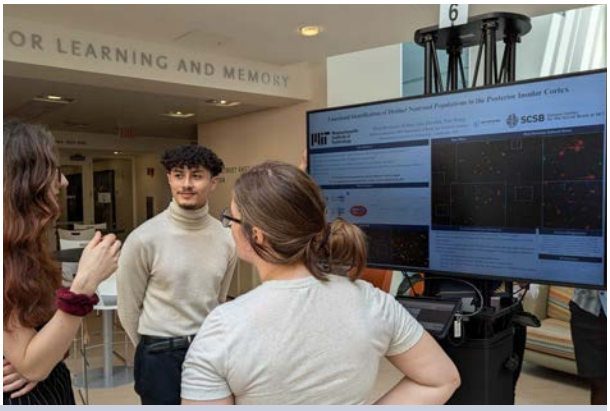
Project: Functional identification of distinct neuronal populations in the posterior insular cortex



Raul and Fan Wang.
Photo courtesy of Mandana Sassanfar

This summer I was an MSRP student in the lab of Fan Wang. My research was focused on understanding pain processing within the brain. We were specifically looking at one brain region, the posterior insular cortex (pIC). Previous studies have shown the pIC's unique role in processing pain, however pain processing is not the only function of the insular cortex. The insular cortex is also known to encode for other aversive states and behaviors such as hunger, thirst and stress. So our research was meant to answer the questions: what states/behaviors are encoded within the neuronal populations within the pIC? And how does the pIC process these different aversive stimuli? Our hypothesis is that distinct neuronal populations within the pIC encode for different aversive states.

In order to test our hypothesis we implemented the Fos-TRAP2 method in our experiments, a genetic tool that we can use to functionally identify active cells. Neurons responding to pain stimuli were labeled using TRAP2, and after two weeks, the same mice were either re-exposed to pain or subjected to hunger, thirst, or restraint-induced stress. Following perfusion and Fos staining, we analyzed whether the neuronal populations activated by the second condition overlapped with those initially TRAPed by the pain experience. We expect higher overlap in mice re-exposed to pain than in those exposed to different aversive conditions.



Raul presenting at the MSRP Poster Session.
Photo courtesy of Raul Hernandez

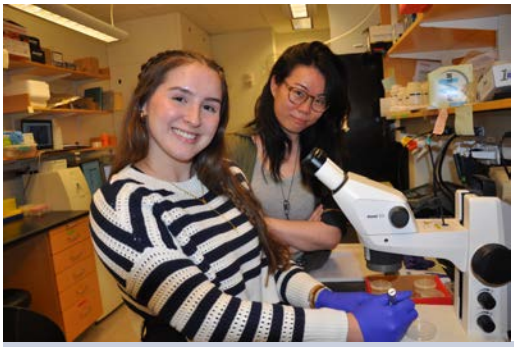
Due to time constraints we were unable to quantify the overlap between the TRAP'ed cells and Fos stained cells. Future plans would include quantifying the amount of overlap within these neuronal populations to determine if they encode for distinct or overlapping aversive states/behaviors, as well as optimizing the Fos-TRAP2 method to TRAP the most cells possible. Understanding these mechanisms in the pIC could inform targeted therapies for chronic pain and anxiety.

Carolina M. Rivera Méndez | Junior, University of Puerto Rico - Mayagüez

Laboratory: Steven W. Flavell, Picower Institute for Learning and Memory, MIT

Project: Improving the Multicolor Atlas for Neuronal Identification in C. elegans for Freely Moving Imaging

As an MSRP student in Steven Flavell's laboratory, my research focused on improving the multicolor atlas for neuronal identification in *C. elegans* for freely moving imaging. This project aimed to enhance our understanding of how neurons across the brain produce behavior and how this is influenced by an animal's internal state. While brain-wide calcium imaging in freely moving *C. elegans* is possible, there remains a need for a strain that combines naturalistic behavior with reliable neuronal identification. Using the innovative NeuroPAL strain (Yemini et al., 2021), neurons can be identified by their genetic expression using a color-coded system of 4 fluorophores: TagRFP-T panneuronally, as well as CyOFP1, mTagBFP2 and mNeptune2.5 in distinct subsets of neurons. However, annotating neuronal identity requires extensive manual curation, and not all neurons are identifiable in every animal. Additionally, the high number of transgenes expressed in the NeuroPAL strain hampers normal growth and behavior. To address these issues, we aimed to create a new tool by crossing two strains: a base strain that expresses brighter TagRFP-T panneuronally and CyOFP1 in a genetically defined subset of neurons, and an assistant strain that identifies the remaining neurons using mTagBFP2 and mNeptune2.5.



Carolina with her mentor, Di Kang (Candy).
Photo courtesy of Mandana Sassanfar

This summer, I worked on developing this two-color base strain, and characterized the growth rate and locomotion pattern of this base strain in comparison with wild-type animals. The identification of all neurons of this base strain based on their brightness, size, and spatial location during freely moving imaging can be achieved with an artificial neural network, which learns from human annotations of the four-color images of the crossed strain. This new approach will enable us to study the function of the *C. elegans* nervous system in a more accurate and high-throughput fashion.

Carolina presenting at the MSRP Poster Session.
Photo courtesy of David Orenstein

MSRP Poster Session, August 2024.
Photo courtesy of David Orenstein

UnrulyArt Program Fosters Creativity and Inclusion Across All Abilities

The UnrulyArt program, initiated by MIT Professor Pawan Sinha and now supported by the Simons Center for the Social Brain (SCSB), aims to provide children of all abilities with the opportunity to explore and create art in an inclusive environment. UnrulyArt empowers children, particularly those with developmental disabilities, to express themselves freely without the constraints often imposed by traditional art settings.

"Each child's artwork provides a window into their unique world. I was struck by the wide range of individual perceptions and actions, and I believe we have much to learn from this rich diversity."
- Lukas Vogelsang, SCSB Postdoctoral Fellow

SCSB co-hosted its first UnrulyArt event in April 2024 (see https://scsb.mit.edu/impact/unrulyart-creates-joy-and-engagement-regardless-of-ability/).

UnrulyArt MIT team with some of the artwork created at the event in July 2024. Photo by: Melanie Gonick

Building on its success, SCSB co-hosted a second UnrulyArt event on July 24, welcoming children from Cambridge Public Schools. This event brought together students of diverse abilities to collaborate and create art, reinforcing the program's mission of inclusion and engagement. The children explored multiple creative stations, experimenting with different materials and techniques to produce their own works of art. For many, it was a special opportunity to interact with peers in a supportive setting that celebrated their unique perspectives.

"Those creativities had no predetermined rules or restrictions, which essentially instilled an emotion of freedom and fulfillment in all of us who participated. Events like this inspire you to visualize the bigger picture of our research with ASD and the impact it can have on the betterment of society. Thanks to SCSB and Prof. Sinha for organizing this!"
- Sajal Sen, SCSB Postdoctoral Fellow

Plans are underway for additional UnrulyArt sessions in the coming months.

Simons Postdoctoral Fellows: Clinical Visit Experience

The Simons Center's Clinical Visit initiative enables postdoctoral fellows from basic science backgrounds to visit the Autism Spectrum Center at Boston Children's Hospital, offering them a unique opportunity to shadow clinicians diagnosing ASD patients. This interdisciplinary collaboration bridges the gap between laboratory research and clinical practice, providing fellows with hands-on experience in the complexities of diagnosing Autism Spectrum Disorder, a condition marked by challenges in social communication and behavior.

Through observing comprehensive assessments and interactions with patients and families, fellows gain valuable insights into the real-world implications of their research. The program fosters a deeper dialogue between scientists and clinicians, promoting collaborative efforts that can advance our understanding of ASD and lead to innovative diagnostic and therapeutic strategies.

Ruidong Chen, SCSB Fellow, Mehrdad Jazayeri Lab

"It was a valuable experience. As a new parent with a baby girl at home, I can see and better understand the concerns or anxieties from the parents who brought their child to visit the center. One thing I learned is the clinical center has a long family waiting list. I hope there will be more services provided, or new techniques to help speed up the process, so that more people can receive professional consulting at the early stage."
- Menglong Zeng, SCSB Postdoctoral Fellow

Alex Major, SCSB Fellow, Earl Miller Lab

This experience was both enlightening and humbling, underscoring the vital roles that researchers and clinicians play in advancing our understanding and treatment of ASD. Observing clinical realities made the real-world impact of our research much more tangible. For the first time, I grasped how early behavioral intervention can lead to significant therapeutic outcomes.
- Chenjie Shen, SCSB Postdoctoral Fellow

"This experience motivated me to delve deeper into the clinical aspects of autism research as well as basic science using mouse models, as I am interested in understanding human social behaviors in the future."
- Tomoe Ishikawa, SCSB Postdoctoral Fellow

Chenjie Shen and Menglong Zeng, SCSB Postdoctoral Fellows, Guoping Feng Lab

News & Announcements

Simons Postdoctoral Fellowship opportunities

The Simons Center has two rounds of funding annually for postdoctoral fellowships.

Fall 2024 deadline: Monday, September 30, 2024
Spring 2025 deadline: Friday, February 28, 2025

Postdoctoral Fellowships are intended for outstanding candidates with recent PhDs (please see eligibility criteria on our website) who wish to conduct autism-related research at MIT under the mentorship of MIT faculty researchers. Applicants currently completing their PhD outside MIT (external candidates), who wish to carry out postdoctoral research at MIT, are strongly encouraged to apply. *We strongly encourage applications from under-represented and under-served backgrounds.*

As part of the Brain & Cognitive Sciences complex at MIT, the Center offers supportive mentorship to postdoctoral researchers, an exceptional environment for scientific inquiry, and a strong commitment to an inclusive, welcoming culture. To learn more about our commitment to Diversity, Equity, Inclusion & Justice (DEIJ), visit here: https://bcs.mit.edu/diversity-equity-and-inclusion-bcs-and-building-46/outreach. To learn more about our postdoctoral resources that support personal, family, and community life here at MIT, visit here: https://postdocs.mit.edu/.

For information on how to apply, please visit our website at http://scsb.mit.edu/funding/postdoctoral-fellowship-funding/.

Support Our Research

We urge you to support the Simons Center for the Social Brain (SCSB) at MIT. Your gift will fund groundbreaking research into causes, mechanisms and treatments of neurodevelopmental disorders including autism spectrum disorders (ASD). The center supports laboratories that study the brain at multiple levels spanning molecular, circuit and computational mechanisms of brain function and cognition. Our programs include funding for innovative, collaborative team projects and postdoctoral fellowships, and events that reach a wide audience, as well as outreach efforts within the larger community.

Please consider making a gift: Simons Center for the Social Brain - **Autism Research Fund 3836050**

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