

NEURO TIMES



UCI CNLM
Ayala School of Biological Sciences

Center for the Neurobiology
of Learning & Memory

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FALL 2017

A Grand Quest - The Promise of Neuroscience

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Storms of electrical activity and tidal waves of chemicals weave the very fabric of our minds. Our brains are made up of close to a hundred billion cells, intricately connected and ever pulsating over some quadrillion synapses. This communication is not random or haphazard. It is subtle, yet influential. It is efficient, yet vulnerable. It is what makes up our complex thought processes – a feat of evolution that we are still a long way from fully understanding.

Perhaps the most transformative discoveries to date were made at the wake of the 20th century by the Spanish anatomist Santiago Ramón y Cajal, the “Father of Modern Neuroscience”, whose work paved the path to systematic investigation of brain structure and function. Motivated by a metacognitive desire to understand what makes us understand, the last seventy years saw the birth and rapid maturation of neuroscience as a field unlike any of its predecessors. Combining knowledge and approaches across physics, chemistry, biology, pharmacology, psychology, computer science, and mathematics to name a few, neuroscience surfaced as perhaps the most interdisciplinary science

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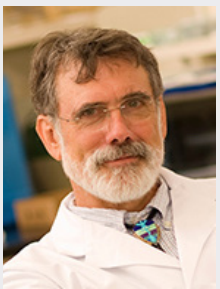
New Research Funding

Benca - New Center for Sleep Research



Congratulations to CNLM Fellow and Chair of Psychiatry **Dr. Ruth Benca** on being awarded seed funding from the UCI Office of Research to set up the Sleep and Circadian Neuroscience (SCN) Center. The SCN will develop collaborative teams and put research programs in place over the next two years to examine links between sleep loss and neurological illness.

McNaughton - DARPA L2M Program



Congratulations to CNLM Fellow and Distinguished Professor of Neurobiology and Behavior **Dr. Bruce McNaughton** who was recently awarded a contract by DARPA for over \$5.2M to set up an infrastructure to study the mechanisms by which the brain is able to continuously learn and update information using cutting-edge in vivo imaging and recording techniques.

Piomelli - New Center for Cannabis Research



Congratulations to CNLM Fellow and Professor of Anatomy and Neurobiology **Dr. Daniele Piomelli** for receiving Office of Research seed funding to set up a new institute for interdisciplinary cannabis research engaging biology, law, and politics. The goal is to study how cannabis intersects with every facet of life, from the environment to criminal justice to culture.

Yassa - New award for Studying Preclinical Alzheimer's



Congratulations to CNLM Director and UCI Chancellor's Fellow **Dr. Michael Yassa** for being awarded a \$3.8M grant from the National Institute on Aging to study the mechanisms by which Alzheimer's pathology manifests in the brain prior to onset of symptoms. The project is a highly collaborative effort with the UCI Alzheimer's Disease Research Center.



humanity has ever encountered. The 1960's saw a major growth of freestanding neuroscience departments around the world, starting with the department of "Psychobiology" at the new Irvine campus of the University of California in 1964, and culminating in the founding of the Society for Neuroscience (SFN) in 1969. Since then, SFN's membership has grown steadily to reach over 40,000 in 2016.

The enormous popularity of neuroscience as a field is in no small part due to the significance of its mission. After all, what could be more exciting than understanding a thing of such beauty and complexity? The impact of such a feat will transform humanity as we know it. It will empower a new generation of innovative neurotechnology mimicking and augmenting human intelligence. It will transform how we learn and educate by unlocking the formidable potential of the human mind. It will empower scientists and clinicians to eradicate brain diseases and promote brain health. It will have countless legal applications from understanding criminal behavior to novel therapies for drug addiction and abuse. It will impact economic growth and development as we better understand the basis of human decision making. It will elucidate the basis of social relationships and the underpinnings of ethics, morality, and religion. It will open up new dialogues to understand radical and extremist behavior, military conflict, bias, discrimination, and other social phenomena that have shaped our civilization over thousands of years.

Neuroscience gives scholars a rare chance to remain perpetual students – never ceasing to surprise us, constantly humbling us, and motivating us to work together to solve humanity's biggest challenges.

To read more about the CNLM Fellows' research programs and read their most recent work, please visit

<http://cnlm.uci.edu/fellows>

#brain #neuroscience #grandchallenge

Director's Message

Welcome to the Fall 2017 edition of NeuroTimes!

I hope you enjoyed your summer. It has been a busy year for us at the CNLM. Our Fellows' research programs have secured considerable financial support from the NIH, NSF, DARPA, and more. These funded studies will make inroads into understanding memory mechanisms in the brain, how the brain deteriorates in Alzheimer's disease and other disorders, among many other important topics.

The CNLM's work in various research areas including neurodegenerative disease, psychiatric disorders, highly superior autobiographical memory, and brain imaging continue to be featured in the media, gaining national and international prominence and recognition. We are now ramping up faculty recruitment programs, and building new core facilities for shared resources to accommodate our growth and support collaborative research.

Our outreach programs have also made significant strides over the last year. We have launched the "CNLM Ambassadors" program, which is planning and implementing outreach programs both on campus and in the community.

Finally, we are gearing up to host the 2018 UCI International Conference on Learning and Memory (#LEARNMEM2018) in April 2018. The conference is a major landmark event, held in celebration of the 35th anniversary of the Center. The 5-day event, packed with scientific as well as public engagement sessions, is the largest scientific conference to have ever been held at UCI. We hope you can join us!

I hope you have a wonderful holiday season this fall and winter and I look forward to seeing you at one of our events.



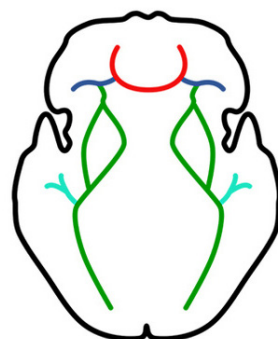
A handwritten signature in blue ink, reading "Michael A. Yassa".

Michael A. Yassa, Ph.D.
Center Director

Cutting-Edge Brain Imaging

UCI is committed to bringing cutting-edge imaging resources to our research community. In 2017, a partnership between the Office of Research, the School of Medicine, the School of Social Sciences, and the School of Biological Sciences was formed to further develop and integrate neuroimaging across campus. The Campus Center for Neuroimaging (CCNI) includes two human 3T MRI facilities, a PET facility, and a small animal preclinical and translational MRI facility. Led by the CNLM's former director, Dr. Craig Stark, Professor of Neurobiology and Behavior and James L. McGaugh Chair in the Neurobiology of Learning and Memory, the CCNI has recently celebrated the opening of its newest resource, the **Facility for Imaging Brain Research (FIBRE)**. The FIBRE's flagship research-

dedicated MRI machine (pictured on the left) is a state-of-the-art Siemens Prisma scanner, which will enable the most cutting edge neuroscience research on topics including cognition, aging, dementia, depression, schizophrenia, and autism. The Prisma scanner is the outcome of a tremendous effort by both Siemens and the National Institutes of Health to develop an MRI machine that is a generation above the current technology. This was done in the service of the Human Connectome Project which aims to provide far greater resolution and detail when mapping connectivity within the human brain.



FIBRE

The resource is also a great example of how all of UCI can partner effectively to bring a resource to the campus that will significantly enhance the collective quality of our research. For more information about the CCNI and UCI's new imaging facilities, please visit:

<http://imaging.uci.edu>



Navigating Brain Oscillations

By Manuella Yassa

Fellow Spotlight: Kei Igarashi



Space, the final frontier. Uncharted and unexplored, it remains a mystery to us. But aside from the common cliché – apologies to all Trekkies – space is much more than the enigmatic celestial void we contemplate with wonder and awe. It is everything around us, from our personal space to traversing the planet. Navigating successfully

around space is essential to our survival as a species. Some may be better than others. There's even a gender difference, but I'll let you guess what it is. As we get older, all of us begin to struggle a little with navigating around new as well as familiar spaces. But for a patient with Alzheimer's disease, this ability can be severely compromised. Enter Kei Igarashi, assistant professor of Anatomy and Neurobiology and Fellow of the CNLM at UC Irvine. His work is making strides in understanding how spatial navigation and spatial memory mechanisms deteriorate in Alzheimer's disease, potentially paving the way to improved diagnosis and treatment.

I arrived at Igarashi's newly established lab in Irvine Hall on the medical school campus ready to pepper him with questions about his most recent paper. He welcomed me into his no frills office looking out onto Irvine's expanse of undeveloped desert.

On one side stood a wooden chair etched with the University of California letters. "I bought this for 30 bucks!" he commented with pride. On the other side stood a bookcase where one book in particular was placed prominently in front – a pristine copy of *The Cognitive Neuroscience of Memory* by Howard Eichenbaum, a memory pioneer who had passed away suddenly only a few days before our interview. Eichenbaum visited the Irvine CNLM just a few months before and Igarashi made sure to get his copy of the book signed by the distinguished author. "His early studies on olfaction informed my work a great deal. Such a tragic loss to us all..." he soberly remarked.

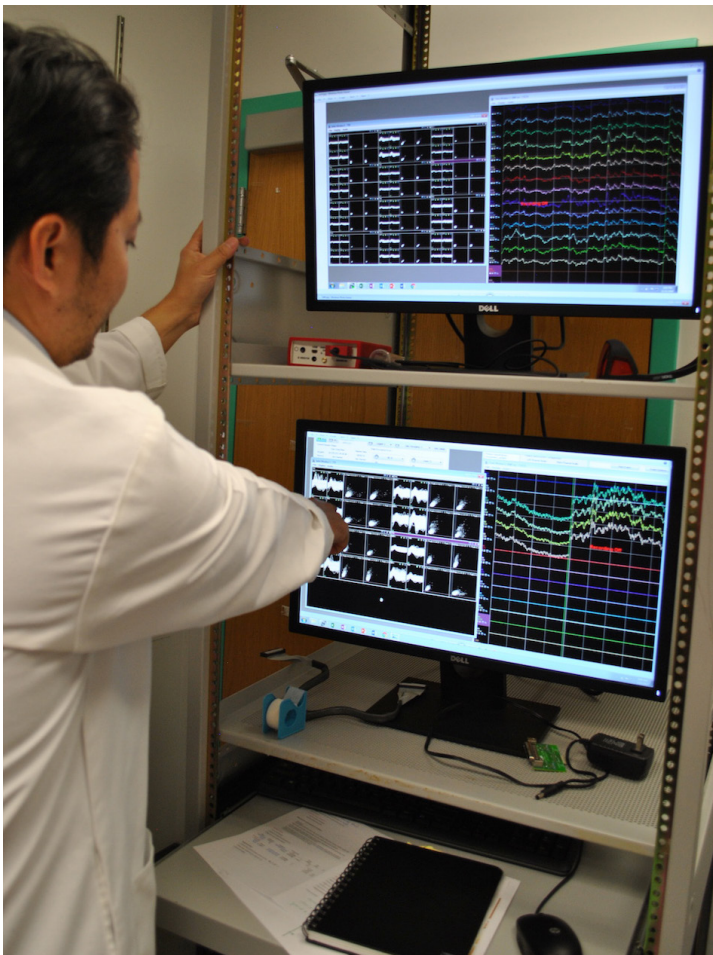
He asked me to sit down on a cushioned chair next to his desk, as I pulled out my camera, pen, and notepad. Igarashi arrived at Irvine in the spring of 2016 after completing a highly coveted postdoctoral fellowship with Edvard and May-Britt Moser. The Mosers were

awarded the 2014 Nobel Prize in Physiology or Medicine, an award they shared with University College London's John O'Keefe for their collective discoveries related to the brain mechanisms of spatial navigation. The Mosers direct the Kavli Institute for Systems Neuroscience in Trondheim, Norway. "I could not have asked for better mentors in fundamental science", he said.



Since arriving at Irvine, Igarashi's lab has focused on making new inroads into understanding the role of brain oscillations in spatial processing and how these mechanisms are disrupted in Alzheimer's disease. Spatial navigation involves a set of interconnected circuits nestled in regions deep in the brain, the hippocampus and the entorhinal cortex. The same two regions are among the earliest sites to deteriorate in Alzheimer's. A coincidence? Likely not. Igarashi is studying this intricate system in detail to identify why it fails.

His lab is recording electrical activity directly from these regions in a novel Alzheimer's mouse model. The amyloid precursor protein (APP) knock-in model developed by Japanese researchers in 2014, he explained, offers several advantages over transgenic models. This particular model exhibits typical age-related pathology without overproduction of other APP fragments. His findings, published in June of this year, show impairments in the synchrony or coupling of brain waves in these mice. In the normal brain, two different types of brain waves (gamma and theta) synchronize to allow for information transfer from one brain region to another. In the Alzheimer's mouse, however, gamma oscillations in the entorhinal cortex were impaired. It was Igarashi's postdoctoral advisors, the Mosers, who first identified cells in the entorhinal cortex that represent space using a grid pattern (dubbed grid cells).



Disruption of the gamma rhythm in the same region could be a possible mechanism for spatial navigation deficits in Alzheimer's patients. Next, he intends to stimulate the region to determine if the gamma rhythm can be restored. He hopes to accomplish these experiments in the coming months.

Just a synapse away from the entorhinal cortex is another region that is of particular interest to Igarashi. The piriform cortex, the olfactory center in the brain, has direct and privileged access to the entorhinal-hippocampal memory system. All other senses must funnel through the thalamus, traditionally thought to be a relay station (although admittedly it's more complicated). Olfactory information, however, passes directly to the memory centers of the brain. Igarashi has his eye on this system as well, one that is known to be vulnerable in the early stages of Alzheimer's disease. Using olfactory tasks with precisely timed odor delivery, he hopes to use a combination of electrophysiological recordings and optogenetics to better understand how this system operates and what features may be compromised in Alzheimer's.

We walked across the hall to his lab where he took me on a quick tour. Immediately visible were two large computer monitors showing raw traces from the electrodes connected to his physiological recording equipment. Around the lab he had organized a surgical station, a T-shaped maze for behavioral tests in rodents, as well as an olfactory chamber. We then sat at his

fabrication station, complete with tools and gadgets for building electrodes and machining electrical components.

"When you're setting up a lab, no one gives you a shopping list," he shrugged his shoulders. It was clear that he rose to the challenge quickly and set up his lab with state-of-the-art equipment. "And then of course, some things you have to make", he demonstrated to me how to make a tetrode – four wires twisted around each other.

I marveled at the simplicity and asked "what does it do?" He laughed, "Everything!" He explained that this simple technology transformed the field by allowing investigators to identify individual cells firing by recording electrical activity in their vicinity. The tetrode was invented by another CNLM Fellow, distinguished professor Bruce McNaughton, one of the key reasons why Igarashi was motivated to come to Irvine. "It's remarkable to be at the same institution with a pioneer like Bruce."



As I watched him work the forceps deliberately and carefully under the microscope, I couldn't help but notice the precision and fine motor skill needed for such work. I asked if this came naturally or took years of practice. "Both" he said, "but I played with Legos quite a bit as a kid." I suspect it took a bit more than Legos to acquire these skills. Despite having students and postdoctoral fellows in the lab, Igarashi still spends considerable amounts of time in the lab himself, doing experiments, setting up rigs, building tetrodes, testing animals, and teaching his growing team how to use these techniques to address their scientific questions.

Igarashi's work on spatial processing in Alzheimer's disease is clearly poised to transform the field and is gaining steady support. Most recently, he received a highly competitive seed grant to support his innovative work from the Brain Research Foundation, a nonprofit supporting neuroscience research. The first of many, he hopes. We hope so too. Uncharted and unexplored as it may be, work by Igarashi and others stands to make the fundamental and translational neuroscience of space a little less of a mystery.

Meet the CNLM Staff



Manuella Yassa | Director of Outreach and Education

Manuella was born in Brazil and raised in the Bay Area. She completed undergraduate studies in neuroscience at the Johns Hopkins University, followed by advanced training at JHU's School of Education. She then worked as a middle school science teacher in Baltimore's impoverished inner city public school system. This experience was a major influence that motivated Manuella to take on the role of leading the CNLM's outreach and education programs.



Michael Gomez | Undergraduate Assistant

Michael was raised in Guatemala and transferred to UCI in the fall of 2016 after attending El Camino Community College in the city of Torrance. As a biological sciences major he is interested in pursuing a career in understanding the brain, a path of insatiable curiosity for him. Michael enjoys reading, dance, nature, sports, and conversations. He teaches Latin Dance, directs a beach exercise group, and tutors Spanish and science. Michael is excited to be part of the CNLM team, especially its outreach and education efforts.



Lena Nguyen | Undergraduate Assistant

Lena is a third year undergraduate in the school of Biological Sciences. She is currently involved in research with Prof. John Guzowski investigating the impact of neuroinflammation on the neurobiological pathways that support memory. She is active in the Tennis Club and is involved with the Medical, Educational Missions and Outreach (M.E.M.O.) club, which is a student-run, non-profit organization that serves the underprivileged in their medical and educational needs.

CNLM Ambassadors

Education and outreach where it matters most. Join to make a difference!

November 30th 2017 marks the formal launch of the CNLM Ambassadors, a group of dedicated individuals who strive to shape neuroscience education and outreach both on campus and off-campus. The group, which includes over twenty five students, staff, postdoctoral fellows and community volunteers has already been working hard over the last year with our director of outreach and education, Manuella Yassa. With the formal launch of the Ambassadors, greater emphasis will be placed on formalizing the programs and offering volunteerism opportunities to anyone who is interested in making a difference.

The programs developed and implemented by the Ambassadors are diverse and multidisciplinary in nature. From in-school programs to public lectures to brain demos and illustrations to community workshops to on-campus tours, the list of activities continues to grow. In October, the Ambassadors hosted Project Kinship for an on-campus tour. Established in 2014, [Project Kinship](http://projectkinship.org) (projectkinship.org) is an organization devoted to providing opportunities for formerly incarcerated youth in the Los Angeles area and helping individuals successfully re-enter the community. Working with community partners like Project Kinship ensures that our efforts are focused where they are needed the most and can make the greatest impact. To learn more about the Ambassadors or volunteer, please contact Manuella Yassa at 949-824-5193 or memory@uci.edu.



cnlm.uci.edu/ambassadors

Supporting CNLM Research and Scholars

The CNLM would not exist if it were not for the dedicated community of supporters who share our vision. We have a long history of scientific discovery and a global reputation for advancing the field. More discoveries are around the corner. But we need your help!

Donations, memorials, and honorary gifts: All donations are fully tax-deductible. You can make a donation in any amount in someone's honor or memory. No amount is ever too small. Gifts can be made online at <http://cnlm.uci.edu/gifts>

Memory Lane Dedications: Create a memory that will last forever. The CNLM courtyard is home to cherished memories inscribed on the bricks of our courtyard's Memory Lane and on the benches in our Memorial garden. With donations ranging from \$500 to \$2500 you can memorialize a loved one, honor a friend or colleague, celebrate a special occasion, or champion a cause.

Become a Friend of the CNLM: Friends of the CNLM are community patrons who generously support and sustain the CNLM and its research, education, and service programs through commitments to annual giving. Friends receive access to our newsletter and are invited to join us for special events including our Evenings to Remember lecture series, the annual Distinguished Lectures in Brain, Learning, and Memory, as well as other special interdisciplinary scientific symposia and community lectures. Opportunities to invite CNLM Fellows to give lectures or salons at Friends' homes are also available.

Join the CNLM Legacy Society: The Legacy Society honors supporters who designate the CNLM as a beneficiary of a planned gift. Legacy Society members receive special benefits including invitations to all of our events and seminars including the annual Barclay lectures and our Evenings to Remember series, an invitation to an annual luncheon at the UCI Chancellor's home, as well as exclusive Legacy Society mailings. Gifts include charitable bequests, charitable lead trusts and remainder trusts, charitable gift annuities, as well as retirement accounts. If you wish you could do more for our mission and cause, please consider naming the CNLM in your will. Your bequest will go a long way to supporting our work. For more information on how to join the legacy society please contact Mr. Roland Ho at 949-824-6454 or roland.ho@uci.edu.

Help spread the word: One of the best ways to support the CNLM's activities is by spreading the word about our research mission and our outreach activities. By being an advocate for the CNLM, you can multiply our efforts and educate others passionate about brain science. You can contribute by referring friends and family to learn more about the CNLM, hosting a salon or dinner at your home, or taking part in other fundraising activities including dinners and silent auctions. Show your friends and colleagues why you are passionate about brain science. Invite them to an event!

Please contact Manuella Yassa at memory@uci.edu or (949) 824-5193 to learn more.



The Lasting Legacy of Mrs. Kathleen Burke



We are deeply saddened by the loss of our long-time friend and supporter Mrs. Kathleen Burke in January of 2017. Mrs. Burke believed strongly in the mission of the CNLM and the critical importance of the research conducted by its faculty. We are honored and grateful that she designated the CNLM as a beneficiary of her charitable remainder trust. The fund will set up a perpetual endowment, the income from which will be used for the CNLM's highest research priorities. Mrs. Burke's generous legacy gift will go a long way to enabling high impact research at the CNLM. Charitable Remainder Trusts have numerous benefits. In addition to providing a fixed income stream to the donor and spouse for the remainder of their lives, there are numerous tax benefits and exemptions including being able to sell a highly appreciated asset and avoid capital gains tax. Trust assets transfer, estate and income tax free, to the CNLM after donor's and spouse's passing. For information on estate planning and legacy gifts, please contact Mr. Roland Ho at 949-824-6454 or roland.ho@uci.edu.



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University of California, Irvine

Save the Dates!

For more info or to RSVP please contact memory@uci.edu or 949.824.5193

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|-------------------------------|--|
| Wednesday, November 8th, 2017 | 6:00 PM Evenings to Remember Lecture Series Herklotz Conference Center
Enriching the Brain: A Lifespan Approach
Prof. Susanne Jaeggi, Associate Professor of Education and Cognitive Science, UC Irvine |
| Wednesday, February 7th, 2018 | 6:00 PM Evenings to Remember Lecture Series Herklotz Conference Center
Huntington's Disease: A Race Against Time
Prof. Leslie Thompson, Professor of Psychiatry and Neurobiology & Behavior, UC Irvine |
| Tuesday, February 27th, 2018 | 7:30 PM The 24th Distinguished Lecture on Brain, Learning and Memory Irvine Barclay Theatre
Linking Brains to Machines: From Basic Science to Neurological Neurorehabilitation
Prof. Miguel Nicolelis, Distinguished Professor of Neuroscience, Duke University |
| Wednesday April 18th, 2018 | 5:30 PM LEARNMEM2018 Keynote Public Lecture The Waterfront Beach Resort
The Brain's GPS: Grid Cells and the Entorhinal Map of Space
Prof. Edvard Moser, Director, Kavli Institute, Trondheim, Norway and 2014 Nobel Prize Laureate |
| Wednesday May 9th, 2018 | 6:00 PM Evenings to Remember Lecture Series Herklotz Conference Center
The Flow of the Brain: How Stroke Affects the Brain and How We Can Treat it
Prof. Steve Cramer, Professor of Neurology and Anatomy & Neurobiology, UC Irvine |