Picower Institute Holiday Party

(*Clockwise from below*) Matt Wilson & Li-Huei Tsai; Earl Miller & Elly Nedivi; Kelly Murray, David Vaughn, Najat Kessler; Najat Kessler & Barbara Vejvoda; Trevor Clement, Mriganka Sur, Monica Linden.

Photos/Najat Kessler

The Picower Institute
for learning and memory at MIT

Massachusetts Institute of Technology
77 Massachusetts Avenue Building 46 Room 1303
Cambridge, MA 02139-4307

Neuroscience News
Winter/Spring 2011 | Volume 5, Number 1

TOP ROW: Mark F. Bear, Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences, Investigator, Howard Hughes Medical Institute (HHMI); Myriam Heiman, Assistant Professor of Neuroscience, Department of Brain and Cognitive Sciences, Broad Institute core member; Troy Littleton, Associate Professor with Tenure, Departments of Biology and Brain and Cognitive Sciences; Earl Miller, Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences.
MIDDLE ROW: Elly Nedivi, Associate Professor with tenure , Departments of Brain and Cognitive Sciences and Biology; Mriganka Sur, Paul E. Newton Professor of Neuroscience; Head, Department of Brain and Cognitive Sciences; Susumu Tonegawa, Picower Professor of Biology and Neuroscience, Departments of Brain and Cognitive Sciences and Biology, Alumni Investigator, Howard Hughes Medical Institute, Alumni Investigator and Director of the RIKEN-MIT Center for Neural Circuit Genetics; Li-Huei Tsai, Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences, Director, The Picower Institute for Learning and Memory, Investigator, Howard Hughes Medical Institute.
BOTTOM ROW: Matthew Wilson, Sherman Fairchild Professor in Neurobiology, Departments of Brain and Cognitive Sciences and Biology, Associate Director, The Picower Institute for Learning and Memory; Weifeng Xu, Assistant Professor of Neuroscience, Department of Brain and Cognitive Sciences.

How to Subscribe

Subscriptions to *Neuroscience News*, the quarterly newsletter of the Picower Institute for Learning and Memory, are available at no charge in print or PDF form. To subscribe, send your mailing or email address to:

Neuroscience News
najatk@mit.edu

How to Submit

News, story ideas and comments from readers are welcome. Please contact Najat Kessler, at najatk@mit.edu.

Support the Picower Institute

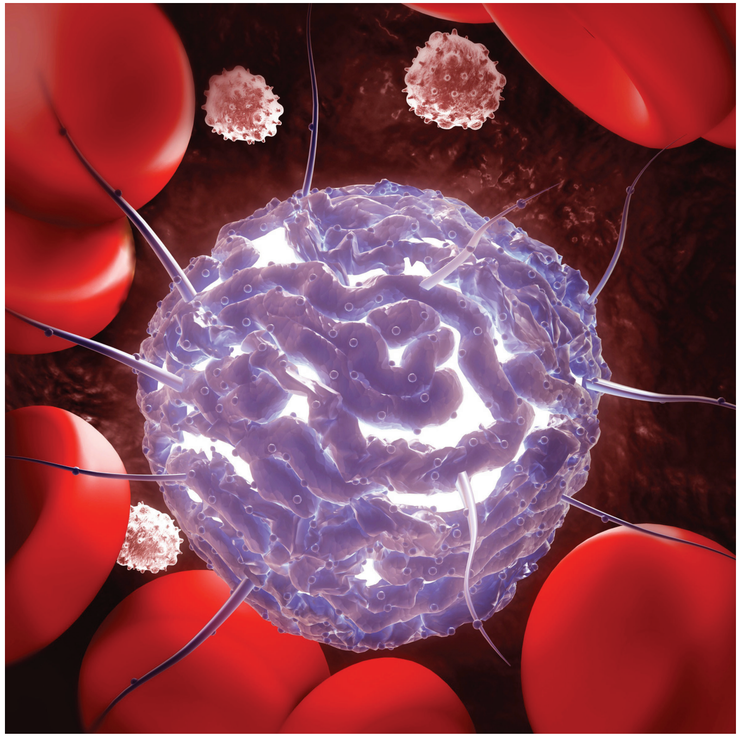
For more information on our research or how to make a gift to the Picower Institute for Learning and Memory, please contact:

Office of the Director
Tel: 617-324-1660
Email: lhtsai@mit.edu

Contact the Picower Institute

MIT
The Picower Institute for Learning and Memory
Massachusetts Institute of Technology
77 Massachusetts Avenue, Building 46, Room 1303
Cambridge, MA 02139-4307

Tel: 617-324-0305



Neuroscience News

Winter/Spring 2011
Volume 5, Number 1

The Picower Institute
for learning and memory at MIT

Li-Huei Tsai
Director, Picower Institute for Learning and Memory

Photo / Len Rubenstein

COVER: A visualization of a stem cell which is an unspecialized cell that gives rise to differentiated cells. These are important in cell development.

Credit: 3D4 Medical / Photo Researchers, Inc.

FROM THE DIRECTOR
LI-HUEI TSAI

Recruiting talented junior faculty members who work on fundamental mechanisms underlying cognitive and neurological disorders is a crucial component of the Picower Institute's ongoing mission of assembling a contingent of innovative world-class researchers.

We welcome Myriam Heiman to our ranks as the latest addition to the Picower Institute. Heiman received a Ph.D. in biology from The Johns Hopkins University and completed postdoctoral training in the Rockefeller University laboratory of Nobel laureate Paul Greengard. Heiman aims to elucidate the molecular mechanisms that make certain types of cells particularly vulnerable in Huntington's and Parkinson's disease by using a novel methodology she helped develop. The technique allows translated messenger RNAs to be isolated from precise, genetically defined cell types in mouse models of neurological disease.

We are also excited to announce the completion and opening of the iPS core facility in the Brain and Cognitive Sciences complex. The advent of human induced pluripotent stem (iPS) cells has heralded a new generation of clinical and basic research into human disorders. iPS cells have remarkable therapeutic potential; they can be differentiated into multiple cell types, including neurons, and transplanted back into the donor without the risk of an immune response. Cells derived from patients can also be used to screen novel therapeutic compounds, and can be used to study the mechanisms of epigenetic disorders such as Rett's Syndrome. The iPS core facility will bridge the gap between basic mechanisms and potential therapeutics for human neurological diseases.

Expanding the use of iPS cells to studies of cognitive disorders and brain disease is part of MIT's commitment to multidisciplinary, cutting-edge approaches to neurological research. These approaches afford our researchers invaluable new tools to uncover the innermost secrets of the brain in ways never before possible.

The Dendritic Branch Is the Preferred Integrative Unit for Protein Synthesis-Dependent LTP

CAMBRIDGE, Mass. – Researchers have long believed that minor details associated with emotional memories—like the color of the shirt you were wearing when you were in a car accident--are scattered throughout the brain. Neuroscientists at MIT's Picower Institute for Learning and Memory report that, on the contrary, these details are stored close to the site of the memory itself on a single neuron.

The work, published in the 69th issue of Neuron, explains for the first time on a molecular level why relatively minor details are sometimes inextricably linked to long-term memories.

"Our work demonstrates that the neuron's dendritic branch is a key organizer—namely, these long-term engrams are stored as a set of synapses along a branch, as opposed to scattered," said study co-author Arvind Govindarajan, assistant director of the RIKEN/MIT Center for Neural Circuit Genetics. "This allows the memories to be easier to recall." Given the fact that a neuron could be connected to as many as 15,000 other neurons, this is an efficient way for the brain to keep track of which details are tied to which events.

"Also, this storage method limits the amount of less-important information being stored as part of the memory. This is important because it allows organisms to not get confused between similar events," he said.

The data also showed that peripheral information that follows rather than precedes the relevant event is more likely to be integrated into long-term memory. Nevertheless, details from both before and after emotionally charged memories can be linked.

Shaping a memory

One theory holds that memory traces or fragments are distributed throughout the brain as biophysical or biochemical changes called engrams. Just as one fragment of a hologram can create the entire holographic image, one engram can launch a more extensive memory of a place, event or scene. The exact mechanism underlying engrams is not well understood.

MIT neuroscientists Susumu Tonegawa, Picower Professor of Biology and Neuroscience and Howard Hughes Medical Institute Investigator; Arvind Govindarajan; Picower Institute postdoctoral associate Inbal Israely; and technical associate Shu-Ying Huang looked at single neurons to explore how memories are created and stored in the brain.

Previous research has focused on the role of synapses—the connections through which neurons communicate. An individual synapse is thought to be the minimum unit necessary to establish a memory engram.

Instead of looking at individual synapses, the MIT study explored neurons' branch-like networks of dendrites and the multiple synapses within them.

Boosting the signal

Neurons sprout dendrites that transmit incoming electrochemical stimulation to the cell body. Synapses located at various points throughout the dendritic arbor act as signal amplifiers for the dendrites, which play a critical role in integrating these synaptic inputs and determining the extent to which the neuron acts on incoming signals.

When we experience an emotionally powerful event or reap a big reward like finding a long-lost Picasso, a flood of neurotransmitters are released and proteins are activated. Details associated with the main event get recorded by piggybacking on the protein boost that lasts for a short time after the initial burst. These secondary memories are filed on the dendrite in close proximity to the main event, the researchers believe.

The MIT study found that a less-significant detail—the kind of detail that would normally be relegated to a short-term memory and fade away over time--may get permanently hitched to a long-term memory if two synapses on a single dendritic arbor are stimulated within an hour and a half of each other. "Every active synapse is a timer," Govindarajan said. "Proteins arrive for a certain amount of time, and given enough time in the presence of the proteins, the memory becomes strong. If there's not enough time and proteins, the memory goes away."

"A synapse that received a weak stimulation, the kind that would normally accompany a short-term memory, will express a correlate of a long-term memory if two synapses on a single dendritic branch were involved in a similar time frame," he said.

This work was supported by RIKEN, Howard Hughes Medical Institute and the National Institutes of Health.

Preplay of future place cell sequences by hippocampal cellular assemblies

CAMBRIDGE, Mass.—Researchers at MIT's Picower Institute for Learning and Memory report for the first time how animals' knowledge obtained through past experiences can subconsciously influence their behavior in new situations.

The work, which sheds light on how our past experiences inform our future choices, was reported on Dec. 22 in an online publication of Nature.

Previous work has shown that when a mouse explores a new space, neurons in its hippocampus, the center of learning and memory, fire sequentially like gunpowder igniting a makeshift fuse. Individual neurons called place cells fire in a specific pattern that mirrors the animal's movement through space. By looking at the time-specific patterns and sequences recorded from the firing cells, researchers can tell which part of the maze the animal was running at the time.

In the current work, research scientist George Dragoi and Susumu Tonegawa, Picower Professor of Biology and Neuroscience and director of the RIKEN-MIT Center for Neural Circuit Genetics, found that some of the sequences of place cells in mice' brains that fired during a novel spatial experience such as running a new maze had already occurred while the animals rested before the experience.

"These findings explain at the neuronal circuit level the phenomenon through which prior knowledge influences our decisions when we encounter a new situation," Dragoi said. "This explains in part why different individuals form different representations and respond differently when faced with the same situation."

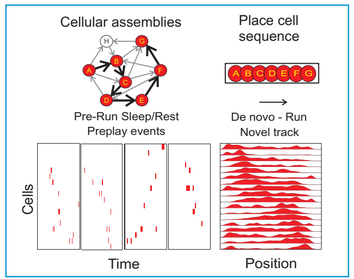
Thinking ahead

When a mouse pauses and rests while running a maze, it mentally replays its experience. Its neurons fire in the same pattern of activity that occurred while it was running. Unlike this version of mental replay, the phenomenon found by the MIT researchers is called preplay. It occurred before the animal even started the new maze.

"These results suggest that internal neuronal dynamics during resting organize cells within the hippocampus into time-based sequences that help encode a related experience occurring in the future," Tonegawa said.

"Previous work largely ignored internal neuronal activities representing prior knowledge that occurred before a new event, space or situation. Our work shows that an individual's access to prior knowledge can help predict a response to a new but similar experience," he said.

This work is supported by the National Institutes of Health.



In The News

The Picower Institute staff members were recently featured and recognized for their achievements on national and international media outlets:

- Li-Huei Tsai has been elected as a Fellow of the American Association for the Advancement of Science, for "studies of cellular mechanisms of learning and of learning disruptions in Alzheimer's disease."
- Both Time and Forbes Magazine recently featured Mark Bear's work on Autism, that suggests how a specific class of drug, which is already on shelves, could help with a disease called Fragile X Syndrome.
- Jason Shepherd, Ph.D. was recently presented with The Peter and Patricia Gruber International Research Award in Neuroscience, from The Society for Neuroscience; for his work investigating the role of Arc in the physiology of the visual system.