Winter 2024/2025

bcs news

Learning from Machines:

How the interplay between biological and computational data drives new discoveries in both fields

brain+cognitive sciences

MIT

BCS Leadership

Laura Schultz, PhD
Professor of Cognitive Science
Associate Department Head for DEIJ

Josh McDermott, PhD
Associate Professor of Brain and Cognitive Sciences
Associate Department Head

From the Department Head

Dear Friends,

The last several months have brought many exciting developments to the Department of Brain and Cognitive Sciences. We welcomed our newest faculty member, Assistant Professor Linlin Fan. Her lab at The Picower Institute looks to identify the physical and neural processes underlying learning and memory.

We are continuing to build our department; as I write, we are deep into three faculty searches spanning a range of experimental, theoretical, and computational disciplines. We seek new faculty to augment our already broad faculty, and especially those who are interested in spanning multiple research areas in search of new breakthroughs.

Over the summer, several faculty received noteworthy recognition. Professor Nancy Kanwisher was selected as a shared winner of the Kavli Prize in Neuroscience for her identification of the fusiform facial area. We also celebrated the addition of Associate Professors Steven Flavell and Mehrdad Jazayeri to the ranks of Howard Hughes Medical Institute investigators in BCS.

In April, BCS hosted our Visiting Committee, an advisory group that convenes every two years to review the department. Faculty, staff, and students shared a range of information on academic programs, department finances, and culture and climate in Building 46. The meeting was engaging and productive, and the report from our committee to the MIT Corporation praised the strong scientific breadth and depth of the department and its programs while also highlighting the opportunities associated with increasing collaborations among disciplines.

Also in April, we celebrated our biannual Brains on Brains symposium, attended by approximately 140 alumni and friends. It was a day filled with stimulating discussions on the profound questions our faculty are exploring (for more coverage, see page 14. If you couldn't join us this year, be sure to mark your calendar for the next symposium in 2026.

Finally, I would like to thank Josh McDermott for serving as Interim Department Head while I was on medical leave for several months earlier this year. Among many other things, Josh led the department through the Visiting Committee process, and I deeply appreciate his work keeping the department on track.

I hope you enjoy this issue of BCS News, which is full of notable research, including our cover story on how the interplay between biological and computational data drives new discoveries in fields of both artificial intelligence and neuroscience.

Sincerely,

Michale Fee
Glen V. and Phyllis F. Dorflinger Professor of Neuroscience
Head, Department of Brain and Cognitive Sciences

Table of Contents

Awards and Honors

Faculty

Guoping Feng
National Academy of Sciences

Steve Flavell
Howard Hughes Medical Investigator

Mehrdad Jazayeri
Howard Hughes Medical Investigator

Nancy Kanwisher
Kavli Prize in Neuroscience

Fan Wang
Elected Member of National Academy of Medicine

Research Scientists

Sarthak Chandra
Infinite Expansion Award

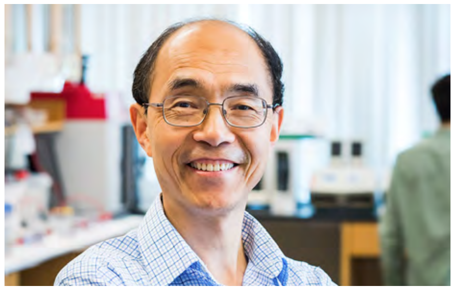
Michal Fux
Infinite Expansion Award

David Stoppel
Infinite Expansion Award

Graduate Students

Amani Maina-Kilaas
Hertz Foundation Fellowship

Building 46 Award winners were celebrated in a cermony last spring.



Guoping Feng

BCS Departmental Awards

Faculty Awards

Mehrdad Jazayeri
Faculty Award for Excellence in Graduate Teaching

Josh Tenenbaum
Faculty Award for Excellence in Undergraduate Teaching

Steve Flavell
Faculty Award for Excellence in Graduate Student Mentorship

John Gabrieli
Faculty Award for Excellence in Undergraduate Advising

Ed Boyden
Faculty Award for Excellence in Postdoctoral Mentorship

Teaching Assistant Awards

Minqing Jiang, David Stoppel, Moshe Poliak, Nicole Coates, Daniel Leible, Verna Peng
Angus MacDonald Awards for excellence in undergraduate teaching by a graduate student

Cheng Tang, Amanda Fath
Walle Nauta Awards for Excellence in Graduate Teaching

Fernanda De La Torre, Shannon Knight, Thomas Clark
Walle Nauta Continuing Dedication to Teaching Awards

Undergraduate Research Awards

Elizabeth Lee
Glushko Prize for Outstanding Research in Cognitive Science

Fan Wang

BCS Undergraduate Research Awards

Bianca Santi, Amy Wang, Jack Horgen, Kristine Zheng, Megan Eberts
BCS Diversity, Equity, Inclusion, and Justice Impact Awards

Quilee Simeon, Jamie Wiley
Building 46 Post-Doctoral Association

Staff Awards

Rhonda Valenti
Go-to Person Award

Alicia Evans
Problem Solver Award

Michelangelo Naim
Morale Booster Award

Kim DeMayo and Jamie Wiley
Special recognition for bringing back BCS Staff Awards

Faculty News

- Associate Professor Ev Fedorenko earned tenure, February 2024
- Associate Professor Steve Flavell earned tenure, May 2024
- Myriam Heiman named the John and Dorothy Wilson Associate Professor of Neuroscience, June 2024
- Laura Schulz named the John & Dorothy Wilson Professor Brain and Cognitive Sciences, June 2024
- Assistant Professor Robert Yang left the department in June 2024

Learning from machines

How the interplay between biological and computational data drives new discoveries in both fields

By Maura R. O'Connor

As far back as the 1940s, researchers studied neurons and the circuits they make – circuits that are involved in learning, object recognition, and information processing – as they sought to create computational models of the human brain.

During this era, the brain inspired the engineering of artificial neural networks and the creation of a science of intelligence. In 1951, Princeton graduate students Marvin Minsky and Dan Edmonds created the Stochastic Neural Analog Reinforcement Calculator – known as SNARC and considered the first artificial neural network – out of vacuum tubes. Minsky later joined MIT's faculty in 1958 and co-founded the Artificial Intelligence Laboratory – now known as the Computer Science and Artificial Intelligence Laboratory (CSAIL).

Whereas in the past the human brain inspired the engineering of artificial neural networks and creation of a science of intelligence, artificial neural networks today are leading neuroscientists to better models in pursuit of a deeper understanding of the brain. The descendants of such early experimentation in scientific models of intelligence are helping scientists at MIT's Department of Brain and Cognitive Sciences advance their understanding of neuroscience and ask new questions of cognition and the brain.

In the lab led by James DiCarlo, for instance, researchers are "reverse engineering" the neural mechanisms of human visual intelligence–our ability to complete feats of visual recognition of millions of objects in the course of daily life within milliseconds – by creating computational models of the neuroanatomy of the visual ventral stream. Meanwhile, a lab led by Ila Fiete is building simulations of neural circuits to ask questions about memory systems and spatial navigation. Within

James DiCarlo

Ila Fiete

Tomaso Poggio

Mark Harnett

the same building, the JazLab, led by Mehrdad Jazayeri, is focused on developing a mathematical framework for understanding how both biological and artificial neural systems create algorithms for things such as statistical, relational, and social inferences.

Artificial neural networks can identify patterns in enormous datasets and serve as useful hypotheses to be interrogated and tested against real data sets. The insights generated by these built systems are showing just how complex the brain's computational powers are and their central role in nearly every aspect of human learning and experience from how we see to how we learn language. By integrating artificial intelligence research into empirical research, scientists say both biology and engineering can reap benefits.

"If you have a digital model of a system, you can ask questions. 'What if I want to turn Neuron 12 of the Area X on and turn all the other neurons off?' Let's ask the model to design the image that would do that," explained DiCarlo, the Peter de Florez Professor of Neuroscience, Director of the MIT Quest for Intelligence, and an Investigator in the McGovern Institute for Brain Research. "You can do a lot with a digital twin. You can experiment on the digital twin. The field is kind of transferring what was in biology into digital systems that can then become the objects of study."

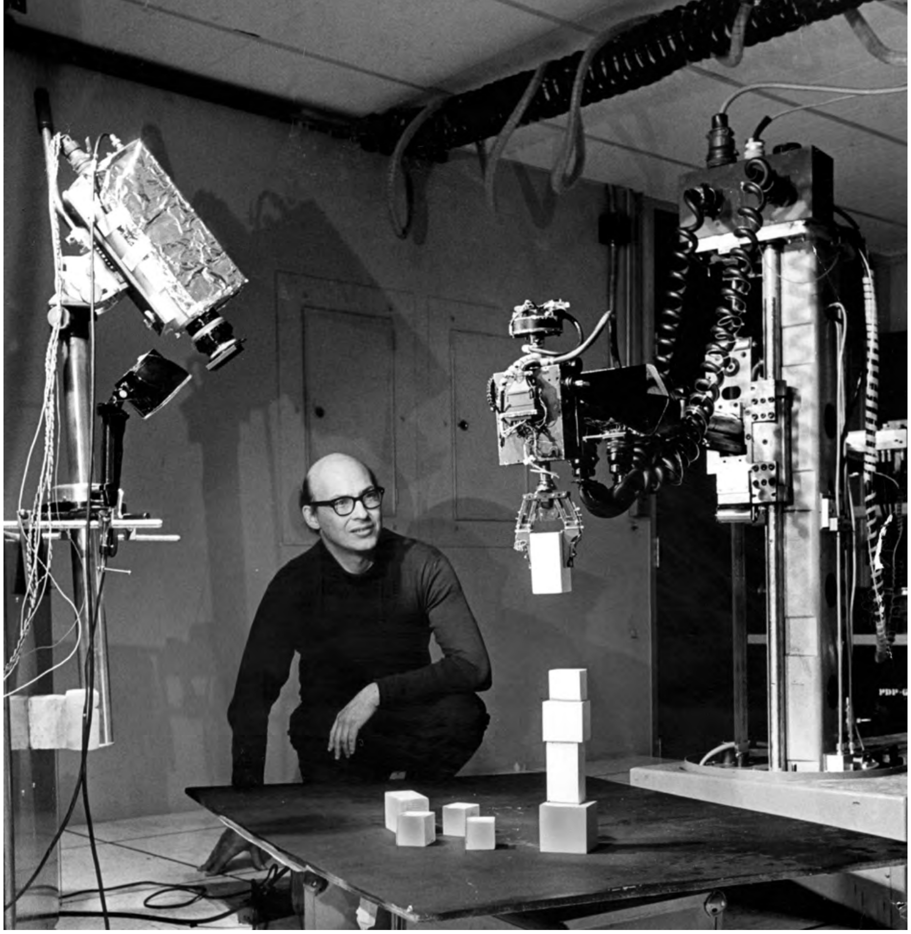
At a symposium held by the Center for Brains, Minds + Machines (CBMM) at MIT last fall, DiCarlo told the audience that when new artificial neural network models are accurate, they have the potential to illuminate elements of biology, creating a continuous loop that drives both scientific hypotheses and serve as drivers of new technologies.

At the same gathering, Tomaso Poggio, the Eugene McDermott Professor in the Brain Sciences and the director and co-founder of CBMM, said, "If you look at evolution, evolution went from probably very simple associative reflexes to language, to logic, eventually to large language models. And in a sense, these are back to association, so from programming to learning and associating things, so neuroscience to AI and back again."

As one of the founders of the field of computational neuroscience, which is focused on using mathematics and computer science to understand the brain, Poggio's work has been rooted in his belief that human intelligence is the greatest problem in science and that developing a computational understanding of human intelligence is a means to solving it. Today, said Poggio at the CBMM symposium, scientists have artificial intelligence systems that can be compared to human intelligence in order to look for similarities and differences. These comparisons help scientists come up with potential fundamental principles.

"I think developing some fundamental theory of learning and intelligence is a compelling and urgent need in the panorama of other intelligence appearing around us," he said.

> "You can do a lot with a digital twin. You can experiment on the digital twin. The field is kind of transferring what was in biology into digital systems that can then become the objects of study."



Marvin Minsky, shown above, joined MIT's faculty in 1958 and co-founded the Artificial Intelligence Laboratory – now known as the Computer Science and Artificial Intelligence Laboratory.

One important consideration is the ways that both genetics and evolution are critical forces in the development of human intelligence. Fiete, who also directs the recently established K. Lisa Yang Integrative and Computational Neuroscience (ICoN) Center, explained to the symposium's audience how she sees intelligence as a process of emergence.

"We can think about evolution as this bottleneck, this funnel that shapes your genes." Fiete and her co-investigators use mathematics, machine learning, and physics to try and understand how neural dynamics and connectivity constrain neural functions such as spatial navigation. By manipulating the parameters of convolutional neural models—a type of neural network in which information only flows in a single, forward direction—Fiete has found that one can approximate primate or mouse visual systems, or a visual processing hierarchy to a auditory processing hierarchy.

"My argument would be that development is the emergence process," she said. "Self-organization, over development, is the place where we might find a lot of fruitful ways to bridge those two areas."

Professor DiCarlo has described the ways that biological visual intelligence systems have inspired, formed, and directed the development of deep architectures underlying computer vision as a "successful interplay." But while our brains carry out information processing in a way that seems effortless, scientists only partially understand the mechanisms involved, including which capabilities are embedded in the cognitive architecture that we are born with, and which emerge through experience. "Part of our job as a field is that as we build with machine learning as a kind of engineered hypothesis space, [we also want] to figure out which parts [of learning] map to evolution, which parts map to postnatal development, which parts go back to adult learning," he said.

Graduate student Yena Han, an Electrical Engineering and Computer Science graduate student in Poggio's lab, was the primary author of a paper presented at the Proceedings of the 40th International Conference on Machine Learning last year that posed the question: Could functional similarity between artificial neural networks and brain neurons be a reliable predictor of architectural similarity? Along with co-authors Poggio and Brian Cheung, Han conducted experiments that trained different neural network architectures with neural recording data to explore whether they offer "reliable insights into the architectural building blocks of the brain."

The authors were also interested in whether one model architecture would be validated over another. "For instance, potential questions are whether recurrent connections are crucial in visual processing or," the authors wrote, "with the recent success of transformer models in deep learning, whether the brain similarly implements computations like attention layers in transformers." While their results were highly variable and could be interpreted in several different directions, they did prove the need for gathering more neuron recordings in the brain to better identify underlying architectures.

There are still levels of biology that artificial neural network models cannot engage, according to DiCarlo. "What does it mean to understand biology?" he asked. "If you asked, how could a CRISPR modification affect your visual intelligence, well, the models don't have molecules. So, it depends on the level of detail that you want out of the question." DiCarlo described the ability for scientists to reach beyond neurons to the molecular level as one of the "dreams" for those in the field of brain and cognitive sciences. "Then we would someday be able to modify how CRISPR modifications in your genetics could affect your visual cognition," he said.

Associate Professor Mark Harnett is focused on research that probes how the biophysical elements of neurons such as dendrites give rise to the computational power of the mind. Harnett pointed out that one of the difficulties of neuroscience is that the biology of the brain is so incredibly complicated that the field lacks a general theory for how brains compute, or an overarching framework that orients researchers collectively towards a shared

> "This is not a heart, a lung, or a spleen. It's us. We're studying ourselves in all our incredible grandeur and frailty. Everything that ever was. We're studying the invention of the human."

goal. "Neuroscience is kind of the inverse [of physics]," he said. "Nobody really knows how anything actually works or what the goal is. Somehow, some computation happens using algorithms that none of us understand, and this produces some interesting behavior like language or empathy or decision-making."

The result is a fractiousness that, in his opinion, is manifesting in ways that can hamper overall progress. But the complexity of the research is part of its allure and the ability to follow one's curiosity is what makes the job worth doing. "This is not a heart, a lung, or a spleen. It's us," said Harnett. "We're studying ourselves in all our incredible grandeur and frailty. Everything that ever was. We're studying the invention of the human. It's not surprising that we're having trouble agreeing."

The brain is still very much a black box: Peering inside to understand not just how human intelligence works but *why* it works the way it does could have implications for education, governance, and medicine.

"Actually taking the steps toward that world where the mechanisms of human intelligence are understood in [engineering] terms—that is hard," said DiCarlo, at the CBMM symposium. "This is very aspirational."

For BCS researchers, it is a moonshot worth taking.

Study: Deep neural networks don't see the world the way we do

Human sensory systems are very good at recognizing objects that we see or words that we hear, even if the object is upside down or the word is spoken by a voice we've never heard.
Computational models known as deep neural networks can be trained to do the same thing, correctly identifying an image of a dog regardless of what color its fur is, or a word regardless of the pitch of the speaker's voice.

A study from MIT neuroscientists has found that these models often also respond the same way to images or words that have no resemblance to the target.

When these neural networks were used to generate an image or a word that they responded to in the same way as a specific natural input, such as a picture of a bear, most of them generated images or sounds that were unrecognizable to human observers. This suggests that these models build up their own idiosyncratic "invariances" — meaning that they respond the same way to stimuli with very different features.

The findings offer a new way for researchers to evaluate how well these models mimic the organization of human sensory perception, says Josh McDermott, an associate professor of brain and cognitive sciences at MIT and a member of MIT's McGovern Institute for Brain Research and Center for Brains, Minds, and Machines.

"This paper shows that you can use these models to derive unnatural signals that end up being very diagnostic of the representations in the model," says McDermott, who is the senior author of the study.

Jenelle Feather PhD '22, who is now a research fellow at the Flatiron Institute Center for Computational Neuroscience, is the lead author of the open-access paper, which appeared in *Nature Neuroscience*. Guillaume Leclerc, an MIT graduate student, and Aleksander Mądry, the Cadence Design Systems Professor of Computing at MIT, are also authors of the paper.

Hearing and vision can build up their own idiosyncratic "invariances" — meaning that they respond the same way to stimuli with very different features.

Simple beginnings: Why the brain can robustly recognize images, even without color

Professor Pawan Sinha explores how the brain learns to recognize objects through visual experience

By Anne Trafton | MIT News

Even though the human visual system has sophisticated machinery for processing color, the brain has no problem recognizing objects in black-and-white images. A study from Professor Pawan Sinha's lab offers a possible explanation for how the brain comes to be so adept at identifying both color and color-degraded images.

Using experimental data and computational modeling, the researchers found evidence suggesting the roots of this ability may lie in development. Early in life, when newborns receive strongly limited color information, the brain is forced to learn to distinguish objects based on their luminance, or intensity of light they emit, rather than their color. Later in life, when the retina and cortex are better equipped to process colors, the brain incorporates color information as well but also maintains its previously acquired ability to recognize images without critical reliance on color cues.

The findings are consistent with previous work showing that initially degraded visual and auditory input can actually be beneficial to the early development of perceptual systems.

"This general idea, that there is something important about the initial limitations that we have in our perceptual system, transcends color vision and visual acuity. Some of the work that our lab has done in the context of audition also suggests that there's something important about placing limits on the richness of information that the neonatal system is initially exposed to," says Pawan Sinha, a professor of brain and cognitive sciences at MIT and the senior author of the study.

The findings also help to explain why children who are born blind but have their vision restored later in life, through the removal of congenital cataracts, have much more difficulty identifying objects presented in black and white. Those children, who receive rich color input as soon as their sight is restored, may develop an overreliance on color that makes them much less resilient to changes or removal of color information.

MIT postdocs Marin Vogelsang and Lukas Vogelsang, and research scientist Priti Gupta, are the lead authors of the study, which appeared in the journal *Science*. Sidney Diamond, a retired neurologist who is now an MIT research affiliate was also an author of the paper.

Seeing in black and white

The researchers' exploration of how early experience with color affects later object recognition grew out of a simple observation from a study of children who had their sight restored after being born with congenital cataracts. In 2005, Sinha launched Project Prakash (the Sanskrit word for "light"), an effort in India to identify and treat children with reversible forms of vision loss.

Many of those children suffer from blindness due to dense bilateral cataracts. This condition often goes untreated in India, which has the world's largest population of blind children, estimated between 200,000 and 700,000.

Children who received treatment through Project Prakash also participated in studies of their visual development, many of which have helped scientists learn more about how the brain's organization changes following restoration of sight, how the brain estimates brightness, and other phenomena related to vision.

In this study, Sinha and his colleagues gave children a simple test of object recognition, presenting both color and black-and-white images. For children born with normal sight, converting color images to grayscale had no effect at all on their ability to recognize the depicted object. However, when children who underwent cataract removal were presented with black-and-white images, their performance dropped significantly.

This led the researchers to hypothesize that the nature of visual inputs children are exposed to early in life may play a crucial role in shaping resilience to color changes and the ability to identify objects presented in black-and-white images. In normally sighted newborns, retinal cone cells are not well-developed at birth, resulting in babies having poor visual acuity and poor color vision. Over the first years of life, their vision improves markedly as the cone system develops.

Because the immature visual system receives significantly reduced color information, the researchers hypothesized that during this time, the baby brain is forced to gain proficiency at recognizing images with reduced color cues. Additionally, they proposed, children who are born with cataracts and have them removed later may learn to rely too much on color cues when identifying objects, because, as they experimentally demonstrated in the paper, with mature retinas, they commence their post-operative journeys with good color vision.

To rigorously test that hypothesis, the researchers used a standard convolutional neural network, AlexNet, as a computational model of vision. They trained the network to recognize objects, giving it different types of input during training. As part of one training regimen, they initially showed the model grayscale images only, then introduced color images later on. This roughly mimics the developmental progression of chromatic enrichment as babies' eyesight matures over the first years of life.

Another training regimen comprised only color images. This approximates the experience of the Project Prakash children, because they can process full color information as soon as their cataracts are removed.

In 2005, Pawan Sinha, pictured here, launched Project Prakash, an effort in India to identify and treat children with reversible forms of vision loss. Children who received treatment through Project Prakash also participate in studies of their visual development.

The researchers found that the developmentally inspired model could accurately recognize objects in either type of image and was also resilient to other color manipulations. However, the Prakash-proxy model trained only on color images did not show good generalization to grayscale or hue-manipulated images.

"What happens is that this Prakash-like model is very good with colored images, but it's very poor with anything else. When not starting out with initially color-degraded training, these models just don't generalize, perhaps because of their over-reliance on specific color cues," Lukas Vogelsang says.

The robust generalization of the developmentally inspired model is not merely a consequence of it having been trained on both color and grayscale images; the temporal ordering of these images makes a big difference. Another object-recognition model that was trained on color images first, followed by grayscale images, did not do as well at identifying black-and-white objects.

"It's not just the steps of the developmental choreography that are important, but also the order in which they are played out," Sinha says.

The advantages of limited sensory input

By analyzing the internal organization of the models, the researchers found that those that begin with grayscale inputs learn to rely on luminance to identify objects. Once they begin receiving color input, they don't change their approach very much, since they've already learned a strategy that works well. Models that began with color images did shift their approach once grayscale images were introduced, but could not shift enough to make them as accurate as the models that were given grayscale images first.

A similar phenomenon may occur in the human brain, which has more plasticity early in life, and can easily learn to identify objects based on their luminance alone. Early in life, the paucity of color information may in fact be beneficial to the developing brain, as it learns to identify objects based on sparse information.

"As a newborn, the normally sighted child is deprived, in a certain sense, of color vision. And that turns out to be an advantage," Diamond says.
Researchers in Sinha's lab have observed that limitations in early sensory input can also benefit other aspects of vision, as well as the auditory system. In 2022, they used computational models to show that early exposure to only low-frequency sounds, similar to those that babies hear in the womb, improves performance on auditory tasks that require analyzing sounds over a longer period of time, such as recognizing emotions. They now plan to explore whether this phenomenon extends to other aspects of development, such as language acquisition.

The research was funded by the National Eye Institute of NIH and the Intelligence Advanced Research Projects Activity.

How adults understand what kids are saying

By Anne Trafton | MIT News

When babies first begin to talk, their vocabulary is very limited. Often one of the first sounds they generate is "da," which may refer to dad, a dog, a dot, or nothing at all.

How does an adult listener make sense of this limited verbal repertoire? A study from MIT and Harvard University researchers has found that adults' understanding of conversational context and knowledge of mispronunciations that children commonly make are critical to the ability to understand children's early linguistic efforts.

Using thousands of hours of transcribed audio recordings of children and adults interacting, the research team created computational models that let them start to reverse engineer how adults interpret what small children are saying. Models based on only the actual sounds children produced in their speech did a relatively poor job predicting what adults thought children said. The most successful models made their predictions based on large swaths of preceding conversations that provided context for what the children were saying. The models also performed better when they were retrained on large datasets of adults and children interacting. The findings suggest that adults are highly skilled at making these context-based interpretations, which may provide crucial feedback that helps babies acquire language, the researchers say.

"An adult with lots of listening experience is bringing to bear extremely sophisticated mechanisms of language understanding, and that is clearly what underlies the ability to understand what young children say," says Roger Levy, a professor of brain and cognitive sciences at MIT. "At this point, we don't have direct evidence

that those mechanisms are directly facilitating the bootstrapping of language acquisition in young children, but I think it's plausible to hypothesize that they are making the bootstrapping more effective and smoothing the path to successful language acquisition by children."
Levy and Elika Bergelson, an associate professor of psychology at Harvard, are the senior authors of the study, which appeared in the journal *Nature Human Behavior*. MIT postdoc Stephan Meylan is the lead author of the paper.

Adult listening skills are critical

While many studies have investigated how children learn to speak, in this project, the researchers wanted to flip the question and study how adults interpret what children say.

"While people have looked historically at a number of features of the learner, and what is it about the child that allows them to learn things from the world, very little has been done to look at how they are understood and how that might influence the process of language acquisition," Meylan says.

Previous research has shown that when adults speak to each other, they use their beliefs about how other people are likely to talk, and what they're likely to talk about, to help them understand what their conversational partner is saying. This strategy, known as "noisy channel listening," makes it easier for adults to handle the complex task of deciphering the acoustic sounds they're hearing, especially in environments where voices are muffled or there is a lot of background noise, or when speakers have different accents.

In this study, the researchers explored whether adults can also apply this technique to parsing the often seemingly nonsensical utterances produced by children who are learning to talk. "This problem of interpreting what we hear is even harder for child language than ordinary adult language understanding, which is actually not that easy either, even though we're very good at it," Levy says.

For this study, the researchers made use of datasets originally generated at Brown University in the early 2000s, which

Roger Levy

contain hundreds of hours of transcribed conversations between children ages 1 to 3 and their caregivers. The data include both phonetic transcriptions of the sounds produced by the children and the text of what the transcriber believed the child was trying to say.

The researchers used other datasets of child language (which included about 18 million spoken words) to train computational language models to predict what words the children were saying in the original dataset, based on the phonetic transcription. Using neural networks, they created many different models, which varied in the sophistication of their knowledge of conversational topics, grammar, and children's mispronunciations. They also manipulated how much of the conversational context each model was allowed to analyze before making its predictions of what the children said. Some models took into account just one or two words spoken before the target word, while others were allowed to analyze up to 20 previous utterances in the exchange. The researchers found that using the acoustics of what the child said alone did not lead to models that were particularly accurate at predicting what adults thought children said. The models that did best used very rich representations of conversational topics, grammar, and beliefs about what words children are likely to say (ball, dog or baby, rather than mortgage, for example). And much like humans, the models' predictions improved as they were allowed to consider larger chunks of previous exchanges for context.

A feedback system

The findings suggest that when listening to children, adults base their interpretation of what a child is saying on previous exchanges that they have had. For example, if a dog had been mentioned earlier in the conversation, "da" was more likely to be interpreted by an adult listener as "dog."

This is an example of a strategy that humans often use in listening to other adults, which is to base their interpretation on "priors," or expectations based on prior experience. The findings also suggest that when listening to children, adult listeners incorporate expectations of how children commonly mispronounce words, such as "weed" for "read."

The researchers now plan to explore how adults' listening skills, and their subsequent responses to children, may help to facilitate children's ability to learn language.

"Most people prefer to talk to others, and I think babies are no exception to this, especially if there are things that they might want, either in a tangible way, like milk or to be picked up, but also in an intangible way in terms of just the spotlight of social attention," Bergelson says. "It's a feedback system that might push the kid, with their burgeoning social skills and cognitive skills and everything else, to continue down this path of trying to interact and communicate."
One way the researchers hope to study this interplay between child and adult is by combining computational models of how children learn language with the new model of how adults respond to what children say.

"We now have this model of an adult listener that we can plug into models of child learners, and then those learners can leverage the feedback provided by the adult model," Meylan says. "The next frontier is trying to understand how kids are taking the feedback that they get from these adults and build a model of what these children expect that an adult would understand."

The research was funded by the National Science Foundation, the National Institutes of Health, and a CONVO grant to MIT's Department of Brain and Cognitive Sciences from the Simons Center for the Social Brain.

Precision dosing for safer surgeries

New technology could allow for precise control of unconsciousness with anesthesia

By David Orenstein | Picower Institute

If anesthesiologists had a rigorous means to manage dosing, they could deliver less medicine, maintaining exactly the right depth of unconsciousness while reducing postoperative cognitive side effects in vulnerable groups like the elderly.

But with myriad responsibilities for keeping anesthetized patients alive and stable as well as maintaining their profoundly unconscious state, anesthesiologists don't have the time without the technology.

Emery N. Brown

To solve the problem, researchers at The Picower Institute for Learning and Memory at MIT and Massachusetts General Hospital (MGH) have invented a closed-loop system based on brain state monitoring that accurately controls unconsciousness by automating doses of the anesthetic drug propofol every 20 seconds.

The scientists detail the new system and its performance in animal testing in a paper in the journal *PNAS Nexus*.

"One of the ways to improve anesthesia care is to give just the right amount of drug that's needed," says corresponding author Emery N. Brown, an anesthesiologist and the Edward Hood Taplin Professor of Medical Engineering and Computational Neuroscience in the Department of Brain and Cognitive Sciences at MIT. "This opens up the opportunity to do that in a really controlled way."

In the operating room, Brown monitors the brain state of his patients using electroencephalograms (EEGs). He frequently adjusts dosing based on that feedback, which can cut the amount of drug he uses by as much as half compared to if he just picks a constant infusion rate and sticks with that. Nevertheless, the practice of maintaining dose, rather than consciousness level, is common because most anesthesiologists are not trained to track brain states and often don't take time in the operating room to precisely manage dosing.

"One of the ways to improve anesthesia care is to give just the right amount of drug that's needed," says corresponding author Emery N. Brown, an anesthesiologist and the Edward Hood Taplin Professor of Medical Engineering and Computational Neuroscience in the Department of Brain and Cognitive Sciences at MIT. "This opens up the opportunity to do that in a really controlled way."

The new system is not the first closed-loop anesthesia delivery (CLAD) system, Brown says, but it advances the young field in critical ways. Some prior systems merely automate a single, stable infusion rate based on general patient characteristics like height, weight, and age but gather no feedback about the actual effect on unconsciousness, says Brown, who is also a member of the Institute for Medical Engineering and Science at MIT and the Warren Zapol Professor in Harvard Medical School. Others use a proprietary control system that maintains "black box" markers of unconsciousness that vary within a wide range.

The new CLAD system, developed by Brown and his team at the MIT and MGH Brain Arousal State Control Innovation Center (BASCIC), enables very precise management of unconsciousness by making a customized estimate of how doses will affect the subject and by measuring unconsciousness based on brain state. The system uses those measures as feedback to constantly adjust the drug dose.

In the paper, the team demonstrates that the system enabled more than 18 hours of fine-grained consciousness control over the course of nine anesthesia sessions with two animal subjects. Brown Lab research affiliate Sourish Chakravarty and Jacob Donoghue, a former graduate student from the lab of co-senior author and Picower Professor Earl K. Miller, are the paper's co-lead authors.

Though there is more work to do, the authors write, "We are highly optimistic that the CLAD framework we have established … can be successfully extended to humans."

How it works

A foundation of the team's CLAD technology is that it employs a physiologically principled readout of unconsciousness from the brain (in the operating room, anesthesiologists typically rely on indirect markers such as heart

New statistical models to objectively quantify nociception can help anesthesiologists better manage it during surgery, improving management of drug dosing and post-operative pain.

rate, blood pressure, and immobility). The researchers established their brain-based marker by measuring changes in neural spiking activity amid unconsciousness in the animals and the larger-scale rhythms that spiking produces, called local field potentials (LFPs). By closely associating LFP power with spiking-based measures of unconsciousness in the animal subjects, they were able to determine that the total power of LFPs between 20 and 30 Hz is a reliable marker.

The researchers also built into the system a physiologically principled model of the pharmacokinetics (PK) and pharmacodynamics (PD) of propofol, which determines how much drug is needed to alter consciousness and how fast a given dose will have that effect. In the study they show that by coupling the model with the unconsciousness marker they could quickly tune the model for each subject.

"With a few basic recordings of the LFPs as drug is administered you can quickly learn how the subject is responding to the drug," Brown says.

To manage propofol dosing, every 20 seconds a "linear quadratic integral" controller determines the difference between the measured 20-30 Hz LFP power and the desired brain state (set by the anesthesiologist) and uses the PK/PD model to adjust the infusion of medicine to close the gap.

Initially the team ran computer simulations of how their CLAD system would work under realistic parameters, but then they performed nine 125-minute-long experiments with two animal subjects. They manually put the animals under and then let the CLAD system take over after about 30 minutes. In each case the CLAD had to bring the animals to a precise state of unconsciousness for 45 minutes, change to a different level for another 40 minutes, and then bring them back to the original level for 40 more minutes. In every session the system kept the marker very close to the goal levels throughout the duration of the testing.

In other words, rather than a system that automatically maintains the drug dose, the new system automatically maintains the desired level of unconsciousness by updating that dose every 20 seconds. "The common practice of using constant infusion rates can lead to overdosing," the researchers wrote. "This observation is particularly relevant for elderly patients who at standard propofol infusion rates readily drift into burst suppression, a profound level of unconsciousness associated with post-operative cognitive disorders."

Still to do

In the study the team acknowledges that they have more work to do to advance the technology for human use.

One needed step is basing the system on EEGs, which can be measured via the scalp. Along with that the team will need to determine a marker of unconsciousness based on EEG measurements of human brain rhythms, rather than animal LFPs. Finally, the team wants to extend the system's capabilities so that it not only maintains unconsciousness, but also helps induce it and helps bring patients back to wakefulness.

In addition to Brown, Chakravarty, Donoghue, and Miller, the paper's other authors are Ayan Waite, Meredith Mahnke, Indie Garwood, and Sebastian Gallo.

Funding for the study came from National Institutes of Health Awards, the JPB Foundation, and the Picower Institute for Learning and Memory. Support for BASCIC comes from George J. Elbaum '59, SM'63, PhD '67; Mimi Jensen; Diane B. Greene SM '78; Mendel Rosenblum; Bill Swanson; and Cheryl Swanson.

Brains on Brains: Celebrating achievement, exploring big questions

The Department of Brain and Cognitive Sciences celebrated its scientists and their discoveries, while exploring some of the most pressing questions in their fields at the biennial Brains on Brains symposium April 29.

More than 130 friends and alumni of the department gathered in Building 46 for a full day of lively presentations and engaging panel discussions with leading researchers from the Department of Brain and Cognitive Sciences, The Picower Institute for Learning and Memory and the McGovern Institute for Brain Research.

“Our community works together in pursuit of a deeper understanding of all aspects of the brain and mind, from the building blocks of neurons, to the algorithms and neural circuits that drive everything from rote behaviors to the representations of reality that we hold in our minds, to the nature of how human knowledge is used, processed, and acquired,” Interim Department Head for Brain and Cognitive Sciences Josh McDermott said in opening remarks. “You are joining us today for one of our signature events. The Brains on Brains symposium is held every two years to celebrate the accomplishments of our researchers and explore—together—some of the most profound questions in our fields.”

The morning session began with the panel discussion “Biological and Artificial Intelligence,” featuring Sherman Fairchild Professor of Neuroscience Matt Wilson, Associate Professor of Neuroscience Ev Fedorenko, and Professor of Brain and Cognitive Josh Tenenbaum Sciences. It was followed by a series of lightning talks by graduate students Eric Martínez and Talya Kramer, and postdoctoral fellow Sharmelee Selvaraji.

The morning concluded with two faculty talks: “Mindfulness, Brain, Education, & Mental Health” by Grover Hermann Professor of Health Sciences and Technology and Cognitive Neuroscience John Gabrieli; and a presentation by Professor of Cognitive Science Laura Schultz that highlighted research that included significant contributions by participants in BCS’s post-baccalaureate Research Scholars Program, which is designed to provide additional research and training to individuals from disadvantaged backgrounds, including first-generation college students, students with disabilities, and veterans preparing to apply to PhD programs.

Faculty joined symposium attendees for lively discussion during lunch.

Faculty members Ev Fedorenko, Joshua Tenenbaum, Matt Wilson and Josh McDermott discussed artificial and biological intelligence in a panel in Singleton Auditorium.

The afternoon session began with the faculty panel “Clinical Partnerships and Drug Development,” featuring Y. Eva Tan Professor in Neurotechnology Ed Boyden, James W. (1963) and Patricia T. Poitras Professor of Brain and Cognitive Sciences Guoping Feng, and Picower Professor of Neuroscience and Director of The Picower Institute for Learning and Memory Li-Huei Tsai. It was moderated by Edward Hood Taplin Professor of Medical Engineering Emery Brown.

The panel was followed by “Determinants of Neuronal Vulnerability in Neurodegenerative Disease: Insights from Molecular Profiling and Genetic Screening in the CNS,” a talk by Associate Professor of Brain and Cognitive Sciences and Picower Institute Investigator Myriam Heiman.

The afternoon session concluded with “Metaplasticity to the Rescue,” a talk by Picower Professor of Neuroscience Mark Bear, after which attendees and symposium participants were invited to the Building 46 Atrium for food, drinks and mingling.

The next Brains on Brains symposium is expected to be held in Spring 2026.

Professor Nancy Kanwisher wins Kavli Prize

Nancy Kanwisher, the Walter A. Rosenblith Professor of Brain and Cognitive Sciences and a McGovern Institute Investigator, was selected with her research partners as winners of the 2024 Kavli Prize in Neuroscience.

Kavli Prizes are among the most prestigious awards in scientific research. They are presented every two years to scientists who have made transformational discoveries in astrophysics, nanoscience and neuroscience.

Kanwisher was honored, along with research partners Doris Tsao of the University of California at Berkeley and Winrich Freiwald at the Rockefeller University, "for the discovery of a highly localized and specialized system for representation of faces in human and non-human primate neocortex."

"Their outstanding research will ultimately further our understanding of recognition not only of faces, but objects and scenes," says Kristine Walhovd, Chair of the Kavli Neuroscience Committee. "Their outstanding research will ultimately further our understanding of recognition not only of faces, but objects and scenes."

Together, the laureates, with their work on neocortical specialization for face recognition, have provided basic principles of neural organization which will further the understanding of how we perceive the world around us.

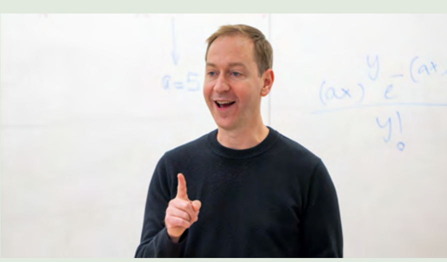
"Nancy and her students have identified neocortical subregions that differentially engage in the perception of faces, places, music and even what others think," says McGovern Institute Director Robert Desimone. "We are delighted that her groundbreaking work into the functional organization of the human brain is being honored this year with the Kavli Prize."

The Norwegian Academy of Science and Letters selects the laureates based on recommendations from three independent prize committees whose members are nominated by The Chinese Academy of Sciences, The French Academy of Sciences, The Max Planck Society of Germany, The U.S. National Academy of Sciences, and The Royal Society, UK. The 2024 Kavli Prize laureates were announced in June. Kanwisher, along with the other winners, formally received the prize from the King of Norway in a ceremony in Oslo in September.

BCS professors named HHMI Investigators

Two professors in the Department of Brain and Cognitive Sciences were appointed as investigators by the Howard Hughes Medical Institute in 2024.

Steven Flavell, associate professor of brain and cognitive sciences and investigator in the Picower Institute for Learning and Memory, seeks to uncover the neural mechanisms that generate the internal states of the brain, for example, different motivational and arousal states. Working in the model organism, the C. elegans worm, the lab has used genetic, systems, and computational approaches to relate neural activity across the brain to precise features of the animal's behavior.



Steven Flavell

Mehrdad Jazayeri

Mehrdad Jazayeri, a professor of brain and cognitive sciences and an investigator at the McGovern Institute for Brain Research, studies how physiological processes in the brain give rise to the abilities of the mind. Work in his lab brings together ideas from cognitive science, neuroscience, and machine learning with experimental data in humans, animals, and computer models to develop a computational understanding of how the brain creates internal representations, or models, of the external world.

Every three years, HHMI selects roughly two dozen new investigators who have significantly impacted their chosen disciplines to receive a substantial and completely discretionary grant. This funding can be reviewed and renewed indefinitely. The award, which totals roughly $11 million per investigator over seven years, enables scientists to continue working at their current institution, paying their full salary while providing financial support for researchers to be flexible enough to go wherever their scientific inquiries take them. The 2024 selections were announced in July.

Research In Brief

How the brain responds to reward is linked to socioeconomic background

The brain's sensitivity to rewarding experiences — a critical factor in motivation and attention — can be shaped by socioeconomic conditions, according to research by MIT neuroscientists.

In a study of 12 to 14-year-olds whose socioeconomic status varied widely, the researchers found that children from lower socioeconomic backgrounds showed less sensitivity to reward than those from more affluent backgrounds.

Using functional magnetic resonance imaging (fMRI), the research team measured brain activity as the children played a guessing game in which they earned extra money for each correct guess. When participants from higher socioeconomic backgrounds guessed correctly, a part of the brain called the striatum, which is linked to reward, lit up much more than in children from lower SES backgrounds.

The brain imaging results also coincided with behavioral differences in how participants from lower and higher socioeconomic backgrounds responded to correct guesses. The findings suggest that lower socioeconomic circumstances may prompt the brain to adapt to the environment by dampening its response to rewards, which are often scarcer in low SES environments.

"If you're in a highly resourced environment, with many rewards available, your brain gets tuned in a certain way. If you're in an environment in which rewards are more scarce, then your brain accommodates the environment in which you live," says John Gabrieli, the Grover Hermann Professor of Health Sciences and Technology, a professor of brain and cognitive sciences, and a member of MIT's McGovern Institute for Brain Research.

Gabrieli and Rachel Romeo, a former MIT postdoc, are the senior authors of the study. MIT postdoc Alexandra Decker is the lead author of the paper, which appeared in the *Journal of Neuroscience*.

Exposure to different kinds of music influences how the brain interprets rhythm

When listening to music, the human brain appears to be biased toward hearing and producing rhythms composed of simple integer ratios — for example, a series of four beats separated by equal time intervals.

However, the favored ratios can vary greatly between different societies, according to a large-scale study led by researchers at MIT and the Max Planck Institute for Empirical Aesthetics and carried out in 15 countries. The study included 39 groups of participants, many of whom came from societies whose traditional music contains distinctive patterns of rhythm not found in Western music.

"Our study provides the clearest evidence yet for some degree of universality in music perception and cognition, in the sense that every single group of participants that was tested exhibits biases for integer ratios," says Nori Jacoby, the study's lead author and a former MIT postdoc, who is now a research group leader at the Max Planck Institute for Empirical Aesthetics in Frankfurt, Germany.

The brain's bias toward simple integer ratios may have evolved as a natural error-correction system that makes it easier to maintain a consistent body of music, which human societies often use to transmit information.

"When people produce music, they often make small mistakes. Our results are consistent with the idea that our mental representation is somewhat robust to those mistakes, but it is robust in a way that pushes us toward our preexisting ideas of the structures that should be found in music," says Josh McDermott, an associate professor of brain and cognitive sciences at MIT and a member of MIT's McGovern Institute for Brain Research and Center for Brains, Minds, and Machines.

McDermott is the senior author of the study, which appeared in *Nature Human Behaviour*. The research team also included scientists from more than two dozen institutions around the world.

Study: Movement disorder ALS and cognitive disorder FTLD show strong molecular overlaps

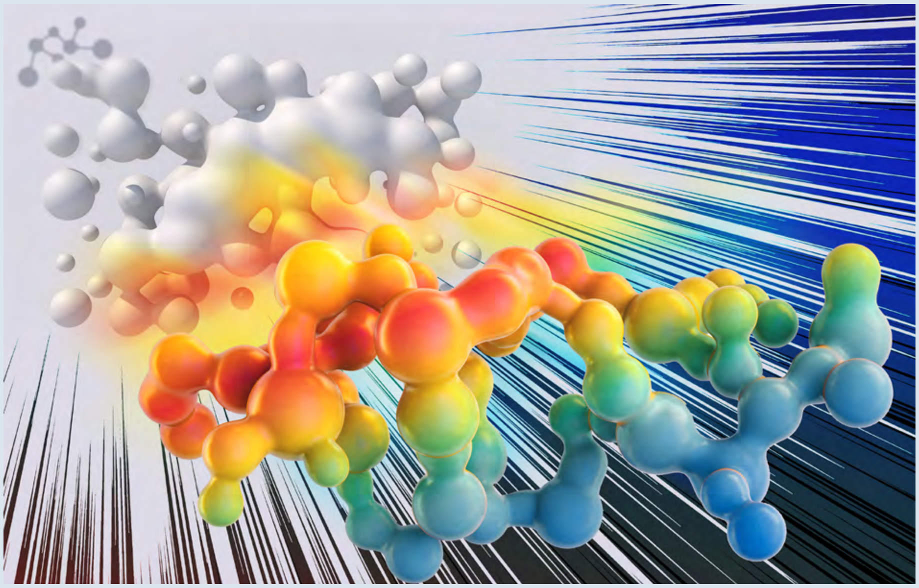
On the surface, the movement disorder amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, and the cognitive disorder frontotemporal lobar degeneration (FTLD), which underlies frontotemporal dementia, manifest in very different ways. In addition, they are known to primarily affect very different regions of the brain.

However, doctors and scientists have noted several similarities over the years, and a new study appearing in the journal *Cell* reveals that the diseases have remarkable overlaps at the cellular and molecular levels, offering potential targets that could yield therapies applicable to both disorders.

The paper, led by scientists at MIT and the Mayo Clinic, tracked RNA expression patterns in 620,000 cells spanning 44 different cell types across motor cortex and prefrontal cortex from postmortem brain samples of 73 donors diagnosed with ALS, FTLD, or who were neurologically unaffected.

One of the most prominent findings of the study revealed that in both diseases the most vulnerable neurons were almost identical both in the genes that they express, and in how these genes changed in expression in each disease.

"These similarities were quite striking, suggesting that therapeutics for ALS



MIT researchers have developed a computational approach that makes it easier to predict mutations that will lead to optimized proteins, based on a relatively small amount of data.

may also apply to FTLD and vice versa," says lead corresponding author Myriam Heiman, who is an associate professor of brain and cognitive sciences and an investigator in The Picower Institute for Learning and Memory at MIT. "Our study can help guide therapeutic programs that would likely be effective for both diseases." Heiman and Manolis Kellis, a professor of computer science at MIT, collaborated on the study with co-senior author Veronique Belzil, then associate professor of neuroscience at the Mayo Clinic Florida, now director of the ALS Research Center at Vanderbilt University.

A new computational technique could make it easier to engineer useful proteins

To engineer proteins with useful functions, researchers usually begin with a natural protein that has a desirable function, such as emitting fluorescent light, and put it through many rounds of random mutation that eventually generate an optimized version of the protein.

This process has yielded optimized versions of many important proteins, including green fluorescent protein (GFP). However, for other proteins, it has proven difficult to generate an optimized version. MIT researchers have now developed a computational approach that makes it easier to predict mutations that will lead to better proteins, based on a relatively small amount of data.

Using this model, the researchers generated proteins with mutations that were predicted to lead to improved versions of GFP and a protein from adeno-associated virus (AAV), which is used to deliver DNA for gene therapy. They hope it could also be used to develop additional tools for neuroscience research and medical applications.

"Protein design is a hard problem because the mapping from DNA sequence to protein structure and function is really complex. There might be a great protein 10 changes away in the sequence, but each intermediate change might correspond to a totally nonfunctional protein. It's like trying to find your way to the river basin in a mountain range, when there are craggy peaks along the way that block your view. The current work tries to make the riverbed easier to find," says Ila Fiete, a professor of brain and cognitive sciences at MIT, a member of MIT's McGovern Institute for Brain Research, director of the K. Lisa Yang Integrative Computational Neuroscience Center, and one of the senior authors of the study.

How humans continuously adapt while walking stably

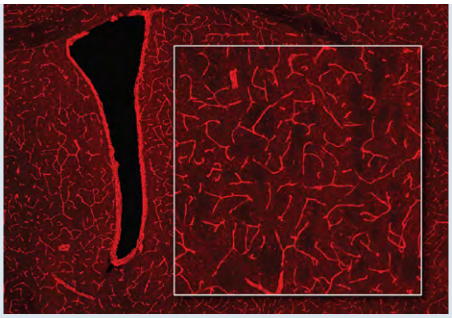
Researchers have developed a model that explains how humans adapt continuously during complex tasks, like walking, while remaining stable.

The findings were detailed in a paper published in the November 2024 edition of the journal *Nature Communications* authored by Nidhi Seethapathi, an assistant professor in MIT's Department of Brain and Cognitive Sciences; Barrett C. Clark, a robotics software engineer at Bright Minds Inc.; and Manoj Srinivasan an associate professor in the Department of Mechanical and Aerospace Engineering at Ohio State University.

In episodic tasks, like reaching for an object, errors during one episode do not affect the next episode. In tasks like locomotion, errors can have a cascade of short-term and long-term consequences to stability unless they are controlled. This makes the challenge of adapting locomotion in a new environment more complex.

"Much of our prior theoretical understanding of adaptation has been limited to episodic tasks, such as reaching for an object in a novel environment," Seethapathi says. "This new theoretical model captures adaptation phenomena in continuous long-horizon tasks in multiple locomotor settings."

To build the model, the researchers identified general principles of locomotor adaptation across a variety of task settings, and developed a unified modular and hierarchical model of locomotor adaptation, with each component having its own unique mathematical structure. The resulting model successfully encapsulates how humans adapt their walking in novel settings such as on a split-belt treadmill with each foot at a different speed, wearing asymmetric leg weights, and wearing an exoskeleton. The authors report that the model successfully reproduced human locomotor adaptation phenomena across novel settings in ten prior studies and correctly predicted the adaptation behavior observed in two new experiments conducted as part of the study.



A new MRI technique could enable researchers to explore the inner workings of the brain in more detail than previously possible. Pictured are blood vessels that now appear bright red after transduction with a gene that gives them photosensitivity.

Using MRI, engineers have found a way to detect light deep in the brain

Scientists often label cells with proteins that glow, allowing them to track the growth of a tumor, or measure changes in gene expression that occur as cells differentiate.

While this technique works well in cells and some tissues of the body, it has been difficult to apply this technique to image structures deep within the brain, because the light scatters too much before it can be detected.

MIT engineers have now come up with a novel way to detect this type of light, known as bioluminescence, in the brain: They engineered blood vessels of the brain to express a protein that causes them to dilate in the presence of light. That dilation can then be observed with magnetic resonance imaging (MRI), allowing researchers to pinpoint the source of light.

"A well-known problem that we face in neuroscience, as well as other fields, is that it's very difficult to use optical tools in deep tissue. One of the core objectives of our study was to come up with a way to image bioluminescent molecules in deep tissue with reasonably high resolution," says Alan Jasanoff, an MIT professor of biological engineering, brain and cognitive sciences, and nuclear science and engineering.

The new technique developed by Jasanoff and his colleagues could enable researchers to explore the inner workings of the brain in more detail than has previously been possible.

Jasanoff, who is also an associate investigator at MIT's McGovern Institute for Brain Research, is the senior author of the study, which appeared in *Nature Biomedical Engineering*. Former MIT postdocs Robert Ohlendorf and Nan Li are the lead authors of the paper.

To understand cognition — and its dysfunction — neuroscientists must learn its rhythms

It could be very informative to observe the pixels on your phone under a microscope, but not if your goal is to understand what a whole video on the screen shows. Cognition is much the same kind of emergent property in the brain. It can only be understood by observing how millions of cells act in coordination, argues a trio of MIT neuroscientists.

In an article published in the journal *Current Opinion in Behavioral Science*, they laid out a framework for understanding how thought arises from the coordination of neural activity driven by oscillating electric fields — also known as brain "waves" or "rhythms."

Historically dismissed solely as byproducts of neural activity, brain rhythms are actually critical for organizing it, write Picower Professor Earl Miller and research scientists Scott Brincat and Jefferson Roy. And while neuroscientists have gained tremendous knowledge from studying how individual brain cells connect and how and when they emit "spikes" to send impulses through specific circuits, there is also a need to appreciate and apply new concepts at the brain rhythm scale, which can span individual, or even multiple, brain regions.

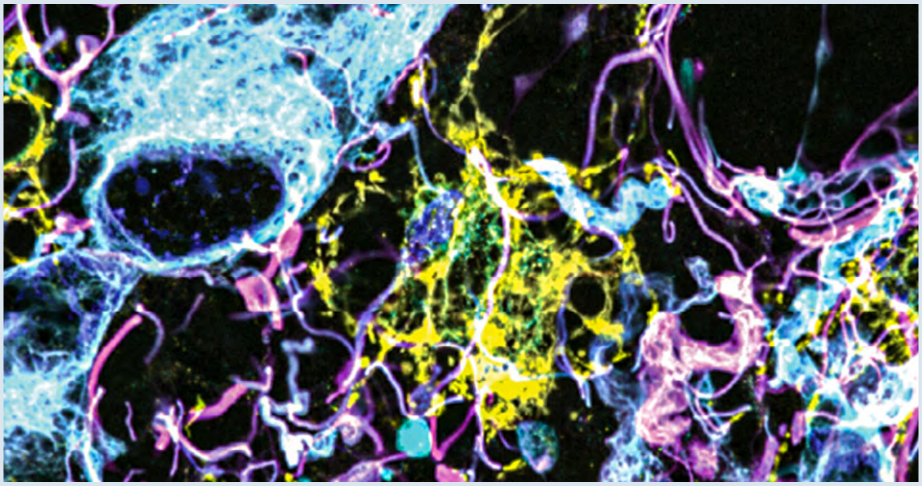
"Spiking and anatomy are important, but there is more going on in the brain above and beyond that," says senior author Miller, a faculty member in The Picower Institute for Learning and Memory and the Department of Brain and Cognitive Sciences at MIT. "There's a whole lot of functionality taking place at a higher level, especially cognition."

The stakes of studying the brain at that scale, the authors write, might not only include understanding healthy higher-level function but also how those functions become disrupted in disease.

Imaging method reveals new cells and structures in human brain tissue

Using a novel microscopy technique, MIT and Brigham and Women's Hospital/Harvard Medical School researchers have imaged human brain tissue in greater detail than ever before, revealing cells and structures that were not previously visible.

Among their findings, the researchers discovered that some "low-grade" brain tumors contain more putative aggressive



Using a novel microscopy technique, MIT and Harvard Medical School researchers have imaged human brain tissue in greater detail than ever before. In this image of a low-grade glioma, light blue and yellow represent different proteins associated with tumors. Pink indicates a protein used as a marker for astrocytes, and dark blue shows the location of cell nuclei.

tumor cells than expected, suggesting that some of these tumors may be more aggressive than previously thought.

The researchers hope that this technique could eventually be deployed to diagnose tumors, generate more accurate prognoses, and help doctors choose treatments.

"We're starting to see how important the interactions of neurons and synapses with the surrounding brain are to the growth and progression of tumors. A lot of those things we really couldn't see with conventional tools, but now we have a tool to look at those tissues at the nanoscale and try to understand these interactions," says Pablo Valdes, a former MIT postdoc who is now an assistant professor of neuroscience at the University of Texas Medical Branch and the lead author of the study.

Edward Boyden, the Y. Eva Tan Professor in Neurotechnology at MIT; a professor of biological engineering, media arts and sciences, and brain and cognitive sciences; a Howard Hughes Medical Institute investigator; and a member of MIT's McGovern Institute for Brain Research and Koch Institute for Integrative Cancer Research; and E. Antonio Chiocca, a professor of neurosurgery at Harvard Medical School and chair of neurosurgery at Brigham and Women's Hospital, are the senior authors of the study, which appeared in *Science Translational Medicine*.

Decoding the complexity of Alzheimer's disease

Alzheimer's disease affects more than 6 million people in the United States, and there are very few FDA-approved treatments that can slow the progression of the disease.

In hopes of discovering new targets for potential Alzheimer's treatments, MIT researchers have performed the broadest analysis yet of the genomic, epigenomic, and transcriptomic changes that occur in every cell type in the brains of Alzheimer's patients.

Using more than 2 million cells from more than 400 postmortem brain samples, the researchers analyzed how gene expression is disrupted as Alzheimer's progresses. They also tracked changes in cells' epigenomic modifications, which help to determine which genes are turned on or off in a particular cell. Together, these approaches offer the most detailed picture yet of the genetic and molecular underpinnings of Alzheimer's.

The researchers report their findings in a set of four papers that appeared in the journal *Cell*. The studies were led by Li-Huei Tsai, director of MIT's Picower Institute for Learning and Memory, and Manolis Kellis, a professor of computer science in MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL) and a member of the Broad Institute of MIT and Harvard.

The findings suggest that an interplay of genetic and epigenetic changes feed on each other to drive the pathological manifestations of the disease.

"It's a multifactorial process," Tsai says. "These papers together use different approaches that point to a converging picture of Alzheimer's disease where the affected neurons have defects in their 3D genome, and that is causal to a lot of the disease phenotypes we see."

For people who speak many languages, there's something special about their native tongue

A study of people who speak many languages found that there is something special about how the brain processes their native language.

In the brains of these polyglots — people who speak five or more languages — the same language regions light up when they listen to any of the languages that they speak. In general, this network responds more strongly to languages in which the speaker is more proficient, with one notable exception: the speaker's native language. When listening to one's native language, language network activity drops off significantly.

The findings suggest there is something unique about the first language one acquires, which allows the brain to process it with minimal effort, the researchers say.

"Something makes it a little bit easier to process — maybe it's that you've spent more time using that language — and you get a dip in activity for the native language compared to other languages that you speak proficiently," says Evelina Fedorenko, an associate professor of brain and cognitive sciences, a member of MIT's McGovern Institute for Brain Research, and the senior author of the study.

Saima Malik-Moraleda, a graduate student in the Speech and Hearing Bioscience and Technology Program at Harvard University, and Olessia Jouravlev, a former MIT postdoc who is now an associate professor at Carleton University, are the lead authors of the paper, which appeared in the journal *Cerebral Cortex*.

A study of polyglots found the brain's language network responds more strongly when hearing languages a speaker is more proficient in — and much more weakly to the speaker's native language.

brain+cognitive sciences

Massachusetts Institute of Technology
77 Massachusetts Ave
Cambridge, MA 02139

Summer 2023

bcs news

The mission of the MIT Department of Brain and Cognitive Sciences is to reverse engineer the brain in order to understand the mind. To do that we delve deeply into the mechanisms of the brain at all levels — from molecules to synapses to neurons to circuits to algorithms to human behavior and cognition, we build links between those levels. To sustain and advance this mission, we offer undergraduate programs in Brain and Cognitive Sciences and Computation and Cognition in order to train the next generation of scientific leaders.

***BCS News* is published twice a year and is distributed without charge to alumni, donors, and other BCS community members.**

Produced by BCS Communications
Design: Wing Ngan, Ink Design

Stay connected

@mitbrainandcog

MITBCS

mitbrainandcog

@mit_bcs

bcs-info@mit.edu

Support BCS

BCS is grateful for the generosity and support of our alumni and friends. Your philanthropy fuels our mission of reverse engineering the brain to understand the mind. To help support fellowships for tomorrow's neuroscience leaders, visit **giving.mit.edu/brain-cog** and select the BCS Graduate Fellowships Fund #2735856.

Donors are kept up to date with periodic reports, meetings, and invitations to departmental events. We welcome the chance to advance our work in alignment with your own philanthropic goals.

To discuss opportunities to make an impact in BCS, contact:

Devan Monroe
Senior Development Officer
monroed@mit.edu
617-324-6718