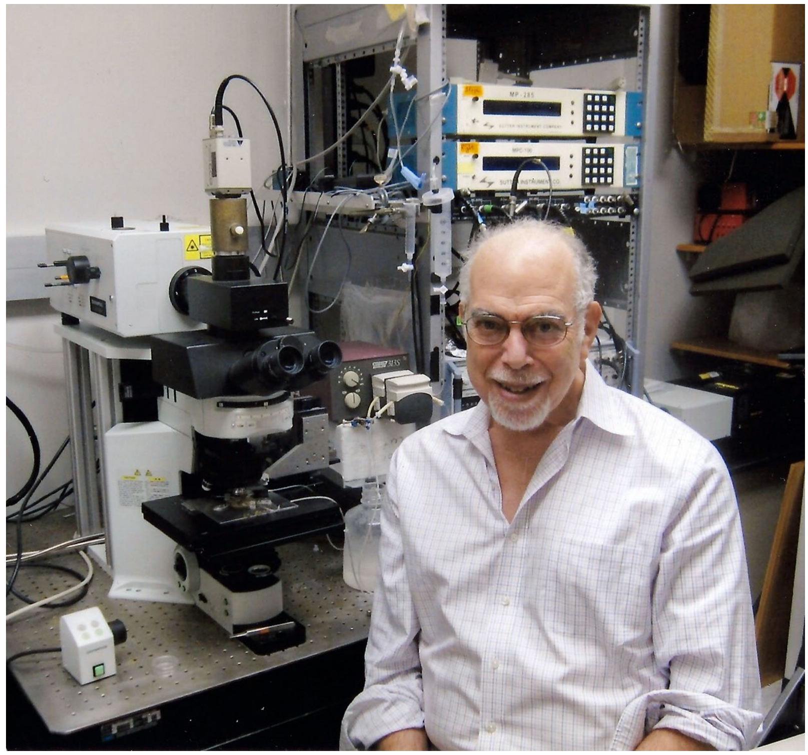
obituary

John Lisman 1944–2017

On 20 October 2017, John Lisman passed away at the age of 73. Neuroscience lost a great luminary.



Credit: Lisman family

John Lisman was a passionate scientist, a generous and inspirational mentor and an endless source of surprising ideas. His scientific oeuvre was remarkably broad, ranging from the biochemistry of photoreception to the systems biology of schizophrenia to the computational basis of memory. His research has strongly shaped many fields of neuroscience while his infectious appetite for science, big ideas and warm, irreverent humor touched the lives of his many friends, students and collaborators.

John received his BA in physics in 1966 at Brandeis University. He went on to obtain a PhD in physiology at MIT, and then worked as a postdoctoral fellow under Nobel laureate George Wald at Harvard. He returned to Brandeis as an assistant professor in 1974, where he remained for his entire career, most recently as the Zalman Abraham Kekst Chair in Neuroscience.

John was an iconoclast, with a penchant for bold and original theories that crossed scientific fields. He began his career studying photoreceptors in the horseshoe crab *Limulus*. John made seminal contributions in this field, identifying second messenger cascades and principles underlying amplification and noise reduction in invertebrate photoreceptors. Fortunately for systems neuroscience, the NIH was not keen on funding this research area, and so in the late 1980s John changed his focus to the study of memory. His initial insight was that the secret of memory might be a molecular switch within individual synapses. He proposed an ingenious model in which individual molecules phosphorylate each other, forming a positive feedback system whereby a group of molecules can sustain a bit of information, even if individual proteins degrade over time. Soon after, Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) was discovered—a multisubunit kinase that could by itself implement this switch and that is highly enriched in dendritic spines. John then proposed a model for how synaptic plasticity could rely on CaMKII for the maintenance of memories. These models heralded his life-long journey to understanding the molecular basis of long-term information storage at synapses.

Despite his strong theoretical disposition, John deeply cared about getting the answer right and was not afraid when experimental data—including those from his own lab—proved his initial models were incorrect. Rather, such setbacks spurred him to update the model, and with Sridhar Raghavachari he proposed additional structural roles for CaMKII as a master controller of a synaptic switch complex. This led him to devise important memory erasure experiments, published as his capstone paper shortly before his death. This last work, performed by a coterie of undergraduates in his lab, added critical evidence showing that CaMKII is required for the storage of memories supporting a hippocampus-dependent behavior.

To honor John's contributions to our understanding of the molecular basis of memory, his colleagues at Brandeis organized a retreat recently. Not being able to attend this in person, John delivered a talk over video from the intensive care unit, with hospital beeps humming in the background. He began, "It's really exciting for me to give this talk because it's a quest of over 30 years; I don't think that's very common these days, to have such a long quest. In any case, that's how long it took to almost settle this question: what is the molecular basis of memory?" It was a masterful presentation, delivered in his usual captivating voice. Assembling evidence across 30 years, from his lab and many others, John made a persuasive case that the CaMKII complex is a basis for synaptic memory storage—and his quest for the holy grail of memory succeeded.

Another favorite topic of John's was brain oscillations. He noticed that the amplitude of fast gamma oscillations in rodent hippocampus is modulated by the slower theta oscillations. This suggested to him that each theta cycle could serve as a temporal frame for four to eight gamma cycles. In an extraordinary intellectual jump, John connected these observations to working memory processing in humans. Psychology experiments had shown that humans have a limited working memory capacity of 7 ± 2 items; when searching for an item stored in this memory, it is serially scanned.

John together with Marco Idiart proposed a model based on nested theta/gamma oscillations that quantitatively explained these phenomena, with individual gamma cycles each representing an item in a defined order within each cycle of theta oscillation. Remarkably, this model has received much experimental support, from studies of the firing of hippocampal neurons in rodents to electroencephalogram recordings in humans during working memory tasks.

The unexpectedness and sheer audacity of this model may be less obvious in hindsight: the use of rat neurophysiological observations to explain classic psychological constraints in human working memory! Indeed, it was initially met with amusement, but John indefatigably and productively pursued the model's implications through numerous collaborations. Nested theta/gamma oscillations have since been observed outside the hippocampus as well, from sensory areas to motor cortex. This led John and Ole Jensen to expand the model, proposing that such nested oscillations provide a neural code for sending multi-item messages across brain regions.

Beyond a passion for science, John also had artistic inclinations. He loved digital arts and photography. He carried a camera when visiting labs and would suddenly snap a picture of a colleague in the middle of a conversation—capturing the essence of their character. Pictures from his fabled gallery of neuroscientists decorate the walls of his lab and can be found online at https://johnlisman.smugmug.com/.

I was privileged to study with John as a graduate student. Working with him was challenging, inspiring and full of surprises; he would regularly start a day with a new outlandish idea and grab some of us from the lab for a walk around campus with his dog while we helped him scrutinize the idea. For me, these morning discussions epitomized John's unique style: he could suspend disbelief at will to make imaginative connections, then move on to deliberating whether the idea is even theoretically feasible and finally jump into examining the finer points of experimental evidence, rapidly shifting back and forth among these. His friend and collaborator Gordon Fain playfully called his approach Lisman's law: "You have to believe it in order to see it!" What John meant was that scientific discovery begins with an idea, an expectation, which we hope to prove or disprove. He expected a lot from his students and provided daily inspiration with big ideas to guide our day-to-day research and a personal example of dedication to rigor and to science. After I graduated from Brandeis and established my own lab, John transitioned from advisor and mentor to becoming a colleague and a dear friend. I think of him often. And when I do research, teach and mentor students, his way of accomplishing these tasks with intelligence, creativity and humor continues to guide me. I will sorely miss John, as will the rest of the neuroscience community, his many friends and students and his family. ❐

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