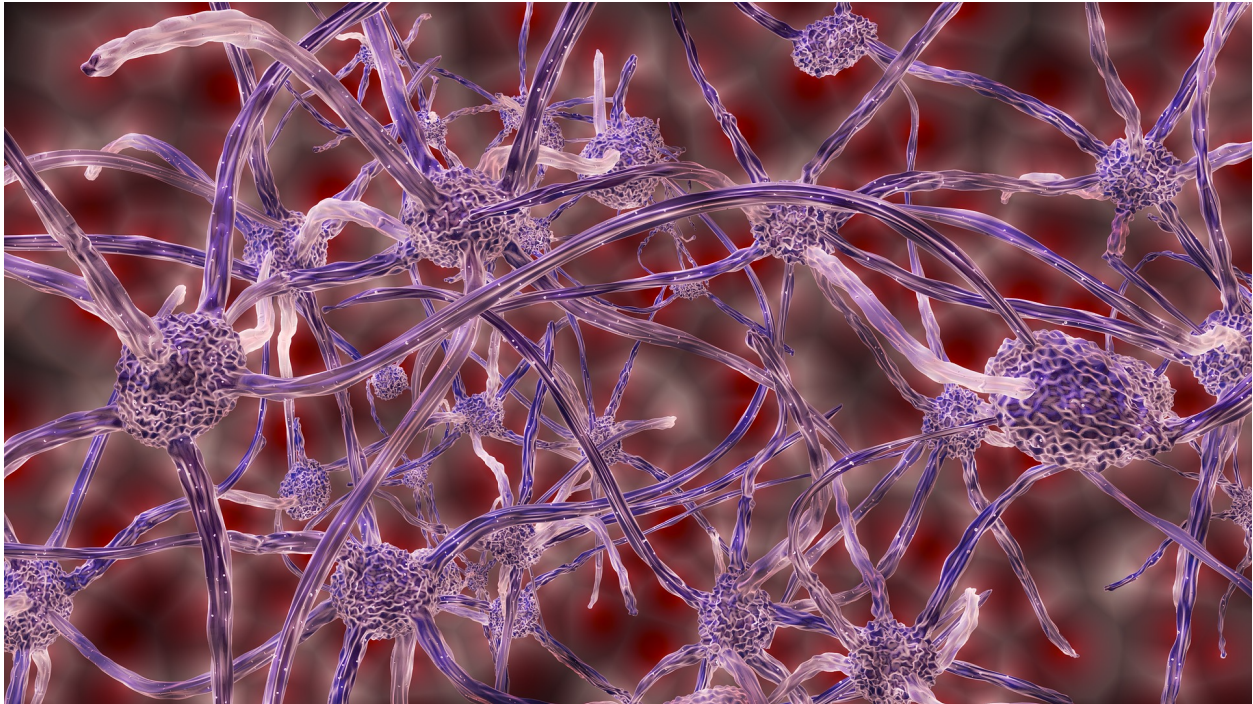


Neuronal Ensembles TCCI Meeting Report

By [Lux Steinberg](#), Lab Manager & Research Scientist, Yuste Lab, Columbia University



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On Wednesday, May 4th, 2022, a group of esteemed scientists and an audience of hundreds gathered on Zoom to attend [Neuronal Ensembles 2022](#) – a symposium put on by the NeuroTechnology Center at Columbia University and generously sponsored by the Tianqiao & Chrissy Chen Institute. Neuronal Ensembles 2022 was the 15th meeting the NeuroTechnology Center has presented, and the second Neuronal Ensembles meeting (the first was in 2021). The NeuroTechnology Center at Columbia is less a physical place than it is a combination of ideology and mission. Founded in response to President Obama’s BRAIN initiative, the NeuroTechnology Center was created by Columbia University in 2014. The NTC itself is a bit of a renaissance group, as it includes scientists and academics alike from a variety of disciplines, such as the Columbia School of Arts and Sciences (A&S), the School of Engineering and Applied Sciences (SEAS), the Zuckerman Mind, Brain, and Behavior Institute (Z-MBBI), and the Kavli Institute for Brain Science. This group includes biologists, chemists, neuroscientists, engineers, computer scientists, and physicists among others. However, the NTC is united around a common goal – to better understand how the brain works. Thus, the NTC understands that the best way to comprehend something as massive and complex as the brain is to include as many perspectives as possible. Neuronal Ensembles 2022 was evidence of this mission made manifest. Scientists from universities and research groups all around the world presented on topics as different as understanding zebrafish spatial reasoning using VR and utilizing new microscopy techniques to better visualize neuronal activity.

Why was this conference called Neuronal Ensembles? [Dr. Rafael Yuste](#) of the NeuroTechnology Center at Columbia University explained that neuroscience is “an exercise in cryptography, and we’re trying to break the neural code.” He continued that neuronal ensembles, groups of neurons which act together, are effectively the “codons” of this system, as they are the simplest functional unit within the brain. Ensembles function as modules and are used by the brain to symbolize concepts, behaviors, and more.

Thus, they are an excellent starting point for understanding how the brain works. Various attendees had their own takes on what a neuronal ensemble was. Symposium facilitator [Dr. Emre Yaksi](#) of NTNU defined ensembles as “groups of locally and internally correlated neurons that make a functional unit, which is reactivated for brain function.” Meanwhile, Dr. Rafael Yuste described an ensemble as a group of neurons that fire together (i.e. are coactive) in a window of time. According to Yuste, – this group fires together spontaneously. Thus, each ensemble is a “functional unit” and has a behavioral or functional purpose.

In fact, the idea of neurons connecting in ensembles is over one hundred years old. In the lab of Santiago Ramón y Cajal, the neuroscientist who first identified neurons as the basic unit of the nervous system, discussions of “chains” of neurons were common. Next, it was Hebb who introduced the idea of a neuronal assembly. Importantly, however, ensembles are non-Hebbian – they don’t rely on plasticity to form.



Ramón y Cajal

[Dr. Misha Ahrens](#) of HHMI’s Janelia Research Campus began the conference with a talk on his current line of research, which explores how zebrafish use neuronal ensembles to create a sense of place while swimming. It is known that zebrafish swim against the current of water when they would like to stay in place. Ahrens posited that zebrafish have neuronal ensembles that function as positional integrators to ensure that a fish remains in the same area of water. When Ahrens looked for cellular representations of where a zebrafish was in space, he observed a correlation between fish location and neuronal activity. In fact, he found two encoding cells which correlate and work together to produce this movement. If these backward movement neurons or forward movement neurons Ahrens identified are activated, this spiking activity directly maps onto what spiking activity looks like when a zebrafish actually moves forward or backward. This line of research demonstrates that ensembles are functional units which underlie behavior and can serve to coordinate behavior and activity.



Zebrafish. Source: News-Medical

Meanwhile, [Dr. Valentina Emiliani](#) from The Institut de la Vision approached the topic of ensembles from another fascinating angle – optogenetics. Emiliani investigates the use of circuit optogenetics for manipulation of single and multiple targets independently in space and time. The goal of this work is to reach as many desired imaging areas as possible, and to perform sequential light-patterning quickly. Both of these would dramatically improve the way neuronal ensembles can be imaged, and therefore understood. The means for achieving this, Emiliani reported, is to replace wide-field single-photon with focused two-photon excitation and holographic light shaping, in addition to using low-repetition lasers.

Another key line of investigation on neuronal ensembles is being pioneered by [Dr. Carsen Stringer](#), also of the Janelia Research Campus. Stringer's research focuses on determining how deep learning can lead to better interpretations of data from neuronal ensembles. According to Dr. Stringer, unsupervised dimensionality reduction is the best approach to produce clear and accurate representations of neuronal data. A method called principal component analysis finds the areas with the most variance in principal components. However, this approach also compresses neural data into just a few dimensions, and thus dimensions are lost, as demonstrated by power law decay. Dr. Stringer posited that other unsupervised approaches such as non-linear dimensionality reduction and clustering may better interpret and visualize data, and that the Raster map is a better way of viewing these results as opposed to two other methods: t-sne and UMAP.

[Dr. David Anderson](#) of Caltech gave a talk which commented on a fundamental question in animal research: is animal behavior driven by genuine internal states, or simply by external stimuli? Dr. Anderson suggested that animals could simply be living Braitenberg vehicles – machines that respond to stimuli in such a way that it appears they are driven by complex motives. In order to investigate this possibility, Dr. Anderson and his lab chose to utilize jellyfish as a model organism. Jellyfish exhibit many key behaviors such as laying eggs, eating, defensive activity, and two distinct swimming modes. Jellyfish are also unique since they do not have any central ganglion, or a brain. Instead, all responses are mediated by a disperse network of neurons. When Dr. Anderson and collaborators observed jellyfish feeding behavior, they noticed that the steps necessary for eating occur repeatedly and synchronously in the umbrella structure of the jellyfish body, and folding of the umbrella occurs spontaneously. A

picture of modular organization became clear, where the rings and net in the jellyfish umbrella all coordinate to create a flow of information to the mouth. Thus, it is possible that jellyfish may be highly sophisticated Braitenberg machines, in that they respond in a rich and complex manner to outside stimuli, yet they don't have the central anatomical structures necessary to produce an internal state.



Left to right: John Dabiri, Lea Goentoro, and David Anderson. Image: Caltech

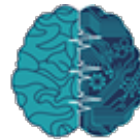
Neuronal Ensembles 2022 was also pleased to welcome [Dr. Raoul-Martin Memmesheimer](#) of University of Bonn as a speaker. Dr. Memmesheimer explained that he sought to examine dynamics of neuronal ensembles by modeling the jellyfish nervous system through examining changes in the shape of its umbrella. The general idea of the model was to assemble a layer of ensemble processes in response to input, which then initiate action. Dr. Memmesheimer found that these neuronal ensembles change when stimulated, with certain assemblies being reactivated, and new inputs & outputs being generated.

[Dr. Vivek Jayaraman](#) of Janelia was also an honored guest of Neuronal Ensembles 2022, and spoke about his research on how flies can perform flexible navigation. Dr. Jayaraman noted that when flies are placed in a heated environment with one "cool" spot, they are reliably able to locate this spot. Flies usually use one cue to drive navigational reasoning, such as cues from visual surroundings. However, if this cue is absent, then flies may use various inputs to understand their environment. There is a specific type of neuron, called an EPG neuron, which maps onto fly motion. EPG neurons and PEN neurons, which are phase-shifted off the EPGs of the ellipsoid body, function together as an ensemble to create fly head-turning and velocity during flight.

Finally, [Dr. Lisa Giocomo](#) of Stanford University gave an exciting talk on memory and navigation, specifically discussing how neurons in the entorhinal cortex influence senses of space. It is known that neurons in the entorhinal cortex called grid cells are found to be important in navigation. In fact, no matter where an animal is in space, some grid cells are active as they map location and create a neural representation. Grid cells vary in their spatial resolutions, and work together with border cells, landmark cells, and speed cells to provide information to hippocampal place cells. These cells all work together in various ensembles. Thus, these entorhinal codes are quite sensitive to changes in animal behavior. Key stimuli can be integrated by the network and change the mental representation of space that is encoded in place cells.

In closing, the NeuroTechnology Center at Columbia University would like to extend our deepest gratitude to the Tianqiao & Chrissy Chen Foundation for generously sponsoring this groundbreaking event and allowing for key cross-communication across related but diverse scientific disciplines to occur. A special thanks to Yan Li from the TCCI Foundation for providing some illuminating closing remarks. We look forward to future NTC events which the Chen Institute will be sponsoring, [NanoNeuro 2022](#) in July and Neuronal Ensembles 2023 next year.

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[Lux Steinberg](#) earned a B.A. in Neuroscience from Reed College in 2021, and subsequently joined the Yuste Lab at Columbia University's NeuroTechnology Center, where they are the lab manager & research scientist. They wrote this meeting report as part of the Tianqiao and Chrissy Chen Institute Science Writers Fellowship which aims to extend the conversation beyond the meeting with the hopes of sparking new ideas and collaborations.