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Mriganka Sur, Ph.D., FRS Newton Professor of Neuroscience

Department of Brain and Cognitive Sciences Building: 46-6237 Lab: Sur Lab Email: msur@mit.edu

Cortical Plasticity and Dynamics

Mriganka Sur' s laboratory studies cortical development and plasticity. The developing brain requires a genetic blueprint but is also acutely sensitive to the environment. The adult brain constantly adapts to changes in stimuli, and this plasticity is manifest not only as learning and memory but also as dynamic changes in information transmission and processing. The goal of the laboratory is to understand long-term plasticity and short-term dynamics in networks of the developing and adult visual cortex. A related goal is to discover mechanisms underlying disorders of brain development.

Cortical development starts with genes that demarcate different areas, and subsequently genes that lay a scaffold of connections between neurons in each area. The lab uses microarrays and proteomics analyses to discover genes that underlie cortical patterning and plasticity, followed by molecular and physiological tools to examine the function of these genes and the interactions between them and the environment.

The Sur lab uses several model systems for studying developmental plasticity and its mechanisms. The first, which they pioneered, involves rewiring the brain: they induce projections from the eye to innervate nonvisual centers, such as the auditory thalamus, early in life. Visual inputs cause the auditory pathway to develop with a very different pattern of activity than normal. Sur and his colleagues have demonstrated that this profoundly alters neuronal networks and connectivity in the rewired auditory cortex.

The second model system involves the formation and maintenance of ocular dominance columns in visual cortex. Here, the lab examines molecular mechanisms and dynamics of rapid structural and functional changes in

synapses. Specific molecules, such as Arc, CaMKII, and actin, are key players that link feedforward and feedback changes in neuronal connectivity due to changes in electrical activity.

Cortical circuits are comprised of specific cell-types that each have unique patterns of connections and contribute in specific ways to function. The lab uses cell-specific markers combined with two-photon measurements of single-cell responses, to analyze the role of inhibitory interneuron and excitatory neuron subtypes, along with astrocytes, in visual cortex circuits.

Many disorders of brain development arise from dysfunction in cortical synapses and circuits. The Sur laboratory uses animal models of subsets of autism, such as Rett Syndrome, to discover mechanisms by which the underlying genes influence synaptic function and plasticity. Novel therapeutics arising from these insights have entered clinical trials.

The laboratory uses state-of-the-art techniques. These include imaging of single cells, synapses and molecules *in vivo* and *in vitro* using two-photon microscopy, high resolution optical imaging of activity, whole-cell intracellular recording, novel genetically engineered proteins, and genomic and proteomic analyses combined with computational tools to identify genes in specific tissues.

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Additional publications



MASSACHUSETTS INSTITUTE OF TECHNOLOGY 77 Massachusetts Ave Cambridge, MA 02139 (tel) 617.258.9344