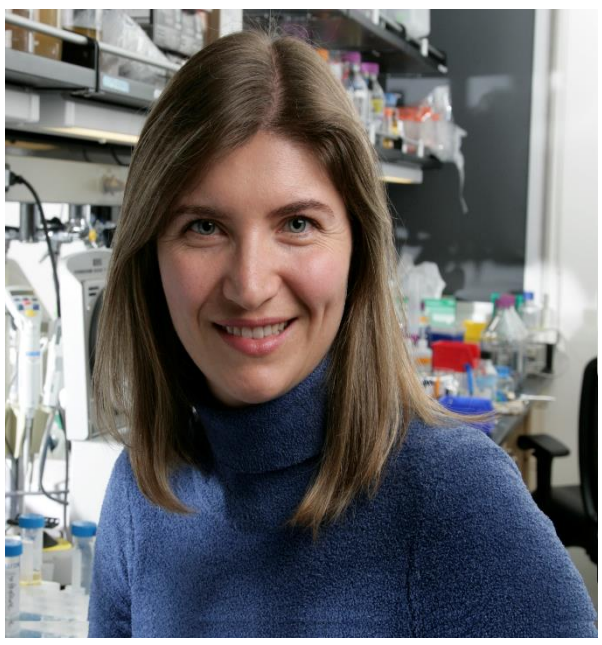
Electrical & Computer ENGINEERING

JUDITH RESNIK YEAR OF WOMEN IN ECE

Graduate Seminar



Optogenetic and tissue clearing approaches to understand and influence whole-animal physiology and behavior

Viviana Gradinaru

Assistant Professor
Biology and Biological Engineering
Heritage Principal Investigator
Caltech University

Thursday, March 23rd **3:00 pm** **Scaife Hall 125**

Abstract:
Our research group at Caltech employs optogenetics, chemogenetics, tissue clearing, and viral vectors to gain new insights on circuits underlying locomotion, reward, and sleep. In particular we will discuss how bidirectional manipulation of mesopontine cholinergic cell bodies exerted opposing effects on locomotor behavior and reinforcement learning and how these effects were separable via limiting photostimulation to PPN cholinergic terminals in the ventral substantia nigra pars compacta or to the ventral tegmental area, respectively (Xiao et al, Neuron, 2016). In addition to control of neuronal activity we need feedback on how exactly the tissue is responding to modulation. We have worked on two related topics: optical voltage sensors and imaging of single molecule RNA in cleared tissue. My group used directed evolution of opsins to make them better at reporting action potentials (Flytzanis et al, Nature Communications, 2014). Changes in RNA transcripts can also report on activity history of brain circuits. Preserving spatial relationships while accessing the transcriptome of selected cells is a crucial feature for advancing many biological areas, from developmental biology to neuroscience. Collaborators and us recently reported on methods for multi-color, multi-RNA, imaging in deep tissues. By using single-molecule hybridization chain reaction (smHCR), PACT tissue hydrogel embedding and clearing and light-sheet microscopy we detected single-molecule mRNAs in ~mm-thick brain tissue samples (Shah et al, Development, 2016) and by rRNA labeling we mapped the identity and growth rate of pathogens in clinical samples (DePas et al, mBio, 2016). Together these technologies can enable high content anatomical and functional mapping to define changes that affect cell function and health body-wide.

Bio:
Viviana Gradinaru completed her BS at Caltech (2005) and did her PhD research at Stanford University (2010). She is now an assistant professor of biology and biological engineering and Heritage Principal Investigator at Caltech. Gradinaru's research focuses on investigating the mechanisms underlying neurodegeneration, its affected behaviors, and relevant interventions such as deep brain stimulation. Her group also develops tools and methods for use in neuroscience, such as optogenetic actuators and sensors, tissue clearing and imaging, and gene-delivery vehicles.

Since 2012, Viviana Gradinaru with her research group at Caltech made breakthroughs in both viral vector engineering and tissue clearing by tissue-binding size-adjustable polymeric scaffolding. She reported the first case of whole-body clearing – transparent rodents that can be used to obtain detailed maps of both central and peripheral nerves at their target organs throughout the body (*Cell, 2014*). Viviana's group also bypassed the challenge of crossing the blood brain barrier by engineering viruses to deliver cargo, such as fluorescent labels, efficiently and (with appropriate regulatory elements) with cell specificity to the entire central nervous system (*Nature Biotechnology 2016*). Most recent publications from her group also show methods for RNA labeling in cleared samples to map cell identities in brain tissue and infections agents in challenging clinical samples such as sputum from cystic fibrosis patients.

She has received the NIH Director's New Innovator Award and a Presidential Early Career Award for Scientists and Engineers, and has been honored as a World Economic Forum Young Scientist and as one of *Cell*'s 40 under 40. Gradinaru is also a Sloan Fellow, Pew Scholar, and Allen Brain Institute NGL Council Member, and received the inaugural Peter Gruss Young Investigator Award by the Max Planck Florida Institute for Neuroscience.

SEMINAR NOTES: (REFRESHMENTS SERVED AT 3:00 PM)

ECE Seminar Committee

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