"Smart nanoshuttles and implantable array AFM for biophysical studies of synapses and brain activity"

Ratnesh Lal
UCSD

Neural networks, a population of highly interconnected neural elements through synapses carry out a specific activity through a complex spatial and temporal dynamics, helped us to understand human behavior and neural disorders. Recent advances in high throughput techniques including automated electrophysiology, optogenetics, functional medical imaging and computational models lack nanoscale information regarding cells' biophysical mechanisms, anatomical connections, and their interaction with the surrounding environment at molecular resolutions. We have developed a prototypic multi-probe AFM (array-AFM) to map neural network structure-activity relationship of individual synapses at high resolutions. We are planning to design the first implantable array-AFM device as a fully integrated brain-machine interfaces-on-chip for ultra-low noise and power electrical recording and stimulation in vivo, as well as integrated microsystems for high bandwidth adaptive control. Brain functions are mediated by a constellation of neurotransmitters (NTs) through activation of their cognate receptors. Unfortunately, their brain administration is inefficient and non-specific. Systemically delivered drugs to the entire brain fail to address major challenges: individual NTs may play distinct or opposing roles in different brain region, individual NTs activate multiple and distinct NT receptor subtypes (hence, synapse subtypes) that may be present on the cell body, axon and dendrite of a neuron and mediate different modes of neurotransmission depending on the synapse locations and subtypes, and NTs are released in both phasic (pulsed and fast) and non-phasic (passive and slow) fashions to mediate primary (synaptic) function and secondary (non-synaptic) tuning roles, respectively. We have developed a smart magnetically-guided nano-delivery vesicles which can be targeted to specific brain regions. I will describe our effort in combining two platform technologies and prospects.