Room 103C: Sunday, February 11

1:30 PM – 3:00 PM
Mad City Labs Inc

Looking to the Future – Enabling Single Molecule Methods for Improved Health Outcomes
This session features researchers employing single molecule methods aimed at improving medical diagnosis or health outcomes. The emphasis is on the challenges facing scientists to develop improved methods and sensors to achieve these outcomes.

Interfacing Coherent Qubits with Biological Targets
Speaker: *Uri Zvi, Pritzker School of Molecular Engineering, University of Chicago*
Prof. Peter Maurer's lab at the University of Chicago investigates new quantum sensing techniques and their application to probe physical properties of biological processes with nanoscale resolution. The scientific challenges our lab addresses fall roughly into two distinct yet synergetic areas: (1) What are the sensitivity limits of nanoscale quantum sensors in a noisy environment and can we engineer qubit sensors and sensing protocols that overcome these limitations? (2) How can we interface these qubit sensors with biological systems and what are the specific biological questions that we can address with quantum sensing?

Single Molecule Pharmacology Reveals the Kinetic Mechanism of Action of Splicing Modulators
Speaker: *Aaron Hoskins, Wasson Professor of Biochemistry, University of Wisconsin-Madison*
Therapeutics targeting pre-mRNA splicing are a promising avenue to treat human diseases, including spinal muscular atrophy and Huntington's disease. Here, we use single molecule colocalization spectroscopy (CoSMoS) to directly measure modulation of 5' splice site recognition by human U1 snRNP. By leveraging large single molecule data sets with >50,000 immobilized molecules and >33 million video frames, we show that a modulator enhances the binding of targeted splice sites by changing the off-, but not on-, rates. The magnitude of the changes in binding kinetics in vitro mirror those measured in vivo for changes in mRNA isoform generation, suggesting that U1 lifetime could be at least partially limiting for splicing in cells. Our results demonstrate the power of single molecule fluorescence for revealing complex RNA pharmacology.

PIP2 is a Negative Regulator of $Na_V1.4$ Channels Gating
Speaker: *Kirin Gada, Jordie Kamuene & Leigh Plant, Department of Pharmaceutical Sciences and the Center for Drug Discovery, Northeastern University*
Voltage-gated sodium (Na_V) channels activate in response to depolarization, causing the rapid influx of Na^+ ions that initiates action potentials in excitable cells. Na_V channel gating is tightly controlled, with perturbations leading to a range of diseases. Recently, we reported that the ubiquitous signaling phospholipid, $PI(4,5)P_2$ is a negative regulator of $Na_V1.4$ channels gating. Combining patch-clamp with optogenetic activation of specific, membrane associated phosphoinositide phosphatases we showed that dephosphorylating $PI(4,5)P_2$ left-shifts the voltage-dependence of $Na_V1.4$ channels to more hyperpolarized potentials, slows the rate of fast inactivation, augments the persistent late current, and speeds recovery from fast inactivation. Using TIRF microscopy, we show that the changes to $Na_V1.4$ gating coincide with decoupling of a fluorescent $PI(4,5)P_2$-biosensor from the plasma membrane.