Chemical & Physical Sciences
UNIVERSITY OF TORONTO
MISSISSAUGA

Colloquium Seminar Series
Wednesday, October 16, 2024
3:15PM in CC3150

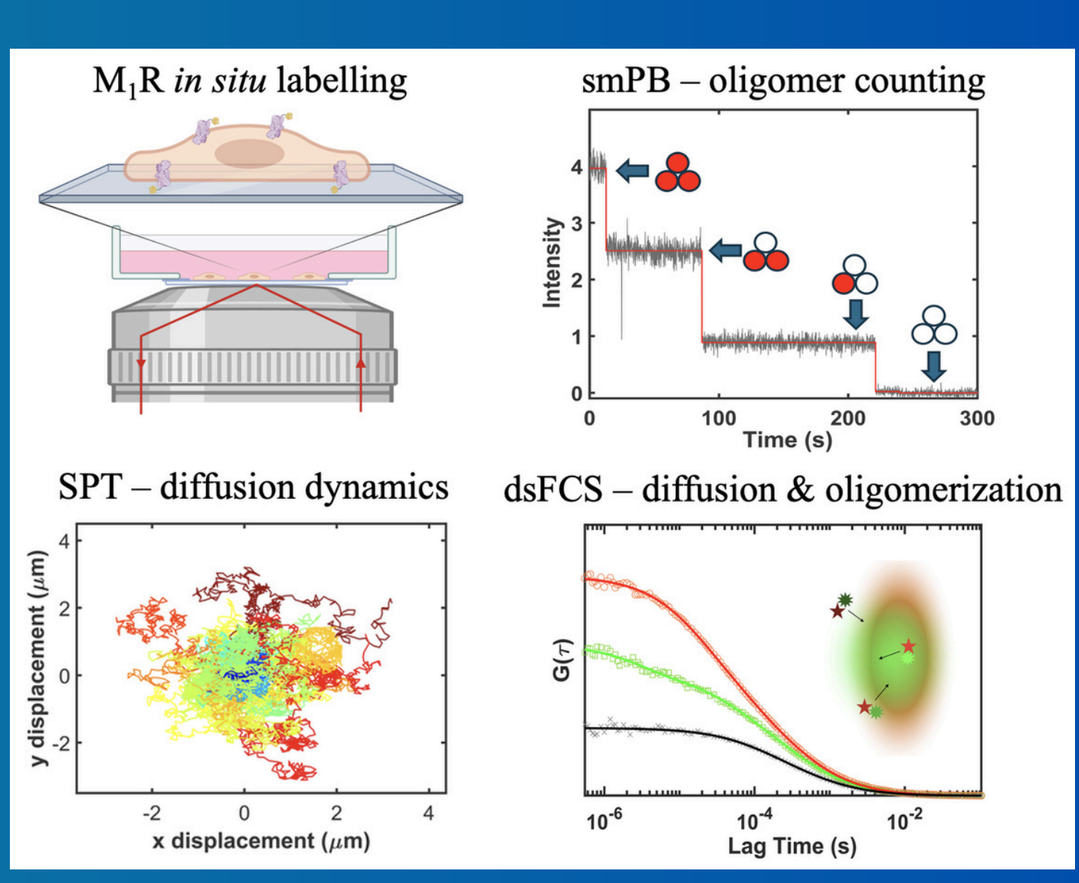
Towards Dissecting in vivo GPCR Signalling in Space and Time using Single-Molecule Fluorescence

featuring

Xiaohan Zhou

PhD Student | Physics | Gradinaru Lab

University of Toronto



G protein-coupled receptors (GPCRs) are major gateways to cellular signaling, which respond to ligands binding at extracellular sites through allosteric conformational changes that modulate their interactions with G proteins at intracellular sites.

While significant evidence from recent structural and spectroscopic studies suggests GPCRs exist in a dynamic equilibrium between multiple conformational states, their spatial organization in the plasma membrane is also important for downstream signalling. Using single-molecule fluorescence techniques, I studied the diffusion behavior and the quaternary structure of M1 muscarinic receptor (M1R) in living cells in different activation states and cellular nano-environments. M1Rs exhibit heterogenous diffusion characterized by three diffusion constants, whose populations were found to be modulated by both orthosteric ligands and membrane disruptors. By incorporating an internal ribosome entry site (IRES), M1R and the cognate G11 protein will be simultaneously expressed at stable, controlled levels in the same cell line, and bio-orthogonally labelled using click chemistry, a bi-arsenic moiety or unnatural amino acids. Co-diffusion events of M1R and G11 in the absence of any ligand will be obtained by dual-color tracking and used to shed light into the mechanisms of basal signaling. This study is an important step towards defining "when", "where" and "how" GPCRs and G proteins diffuse, activate and interact with each other within the cell membrane, and can lead to new in vivo screening assays for novel therapeutic drug design.

CPS Teaching Fellowship for CHM242

featuring

Rebeca Lopez-Miranda

PhD Student | Biological Chemistry | Beharry Lab

University of Toronto