Imaging Striatal Dopamine Release With a Non-Genetically Encoded Near-Infrared Fluorescent Nanosensor

Abraham Beyene[1], Jackson Travis O'Donnell[1], Linda Wilbrecht[2], Markita Landry[1,3,4]
landry@berkeley.edu

[1] Department of Chemical and Biomolecular Engineering, University of California Berkeley
[2] Department of Psychology, University of California Berkeley
[3] Quantitative Biosciences Institute (qb3), University of California Berkeley
[4] Chan-Zuckerberg Biohub, San Francisco, CA

Neurons communicate through chemical neurotransmitter signals that either terminate at the postsynaptic process ("wired transmission") or diffuse beyond the synaptic cleft to modulate the activity of larger neuronal networks ("volume transmission"). Molecules such as dopamine belong to the latter class of neurotransmitters, and have been the pharmacological targets of antidepressants and antipsychotics for decades. Owing to the central role of dopamine over a range of behaviors and psychiatric disorders, real-time imaging of the signal's spatial propagation would constitute a valuable advance in neurochemical imaging. To this end, we present a nanoscale near-infrared fluorescent nanosensor for dopamine and demonstrate its efficacy for imaging dopamine volume transmission in the extracellular space of the brain striatum and prefrontal cortex (Beyene *et al. ACS Chem. Neuro.* 2017). The sensor is developed from polymers pinned to the surface of single wall carbon nanotubes (SWNT) in which the surface-adsorbed polymer is the recognition moiety and the carbon nanotube the fluorescence transduction element. Excitonic transitions in functionalized SWNT yield up to $\Delta F/F = 4500\%$ near-infrared fluorescence emission in the presence of dopamine (Beyene *et al. Nano Letters* 2018). We next demonstrate imaging of evoked dopamine release in acute striatal slices, and show altered dopamine reuptake kinetics when brain tissue is exposed to dopamine agonist and antagonist drugs (Beyene *et al. Science Advances* 2019). We characterize our findings in the context of their utility for high spatial and temporal neuromodulator imaging in the brain, describe nanosensor exciton behavior from a molecular dynamics (MD) perspective, and validate nanosensor for use to elucidate dopaminergic signaling variability with disease or pharmacological perturbations at a synaptic scale.