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

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Neuromodulation plays a critical role in brain function in both health and disease. New optical tools are needed that can image neuromodulation with high spatial and temporal resolution, which will add an important new dimension of information to neuroscience research. Here, we demonstrate the use of a catecholamine nanosensor (nIRCat) with fluorescence modulation ΔF/F of up to 2400% in the 1000-1300 nm near-infrared window[1] to measure dopamine transmission in *ex vivo* brain slices. We show that nIRCats can be used to detect catecholamine efflux in brain tissue driven by both electrical or optogenetic stimulation.[2] Spatial analysis of electrically evoked signals revealed dynamic regions of interest approximately 2 microns in size in which transients scaled with simulation intensity. Optogenetic stimulation of dopaminergic terminals produced similar transients, while optogenetic stimulation of glutamatergic terminals showed no effect on nIRCat signal. Furthermore, bath application of nomifensine, a dopamine reuptake inhibitor, prolonged nIRCat fluorescence signal as expected. Bath application of dopamine receptor agonist quinpirole decreased nIRCat signal, whereas bath application of dopamine receptor antagonists sulpiride or haloperidol increased nIRCat signal. We discuss insights gained from computational work to rationalize experimental findings.[1,3] These nanosensors may be advantageous for future use because they i) do not require virus delivery, gene delivery, or protein expression, ii) their near-infrared fluorescence facilitates imaging in optically scattering brain tissue and is compatible for use in conjunction with other optical neuroscience tool sets, and iii) the broad availability of unique near-infrared colors have the potential for simultaneous detection of multiple neurochemical signals.

Abraham Beyene is a Ph.D. candidate in chemical and biomolecular engineering at University of California, Berkeley. Abraham received his undergraduate degree in chemical engineering from the University of Maryland, Baltimore County, where he was a Meyerhoff and MARC scholar. Abraham was a research engineering at ExxonMobil and worked on algal biofuel research before returning to graduate school. Abraham's current research interests focus on the development of optical probes for applications in neurobiology. His graduate thesis work with Professor Landry is focused on developing a near-infrared fluorescent non-genetically encoded nanosensor for a critical neurotransmitter molecule, dopamine. Abraham is the recipient of a UC Berkeley Chancellor's fellowship, the NSF Graduate Research Fellowship, the HHMI Gilliam Fellowship, and is a recent awardee of the NIH F99/K00 from NINDS.