

## Spying on neuromodulation by constructing new genetically encoded fluorescent sensors

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Monoamine transmitters, e.g. dopamine (DA), norepinephrine (NE) and serotonin (5-HT), are playing important roles in a plethora of physiological processes, including reward, attention and mood regulation. Malfunction of the monoaminergic signaling is implicated in diseases such as addiction, stress and depression. Take the DA as an example, a longstanding yet largely unmet goal is to measure DA changes reliably and specifically with high spatiotemporal precision, particularly in animals executing complex behaviors. We developed the new genetically encoded GPCR-activation-based-DA (GRAB<sub>DA</sub>) sensors that enable these measurements. GRAB<sub>DA</sub> sensors can resolve a single-electrical-stimulus-evoked DA release in mouse brain slices and detect endogenous DA release in living flies, fish, and mice. We have further expanded the repertoire of GRAB sensors for detecting monoamines, purinergic transmitters (e.g. adenosine, ADP and ATP) and neuropeptides (e.g. cholecystinin, somatostatin and vasoactive intestinal peptide). In sum, these newly developed GRAB sensors provide powerful tools for understanding the regulation and malfunction of monoaminergic and purinergic systems and neuropeptides in both physiological and pathological processes.