The Slesinger Lab has developed an innovative technique for optically measuring in real-time the release of neurotransmitters in the brain.

Our technique is based on a new technology of cell-based neurotransmitter fluorescent engineered reporters, known as CNiFERs (pronounced “sniffers”). A CNiFER is a clonal cell engineered to express a specific G-protein coupled receptor, which when stimulated produces a Ca2+ transient that is detected by a fluorescence resonance energy transfer (FRET-based) Ca2+ indicator. CNiFERs detect nanoMolar concentrations of transmitter; have a temporal resolution of seconds, and a spatial resolution of < 100 mm.

The CNiFERs are physically implanted in the brain and can be monitored for up to one week in vivo for longitudinal studies. In collaboration with Dr. Kleinfeld at UCSD, our laboratory has created CNiFERs for detecting acetylcholine (M1-CNiFER), dopamine (D2-CNiFER) and norepinephrine (a1a-CNiFER), and has successfully measured volume transmission of these transmitters in vivo during learning. Recently, we simultaneously detected the release of dopamine and norepinephrine, two transmitters that are chemically very similar, in response to a sugar reward. This research was featured in Scientific American.

With the support of the NIH BRAIN Initiative, we are currently constructing CNiFERs for detecting the release of neuropeptides in vivo. Neuropeptides are genetically encoded molecules that are widely expressed in the brain. Neuropeptides diffuse over long distances and signal through G protein coupled neuropeptide receptors. Currently, it is not possible to monitor the release of peptides in real-time. Neuropeptide CNiFERs should make it possible to measure peptide release in real-time in awake animals as they perform complex behaviors, significantly advancing our understanding of the function of neuropeptides in regulating neural circuits in the brain.