Docket #: S22-228

Apparatus for sensitive fluorescence optical measurement of biological parameters in freely behaving animals

Brief Description: Inventors at Stanford have developed a novel fiber-optic technology to achieve unprecedented sensitivity and immunity to motion artifacts that can be used in freely moving animals. The uSMAART (ultra-Sensitive Measurement of Aggregated Activity in Restricted cell-Types) technology enables the study of small dynamic variation of one or more biological process in the healthy and pathological brain from animal undergoing ecologically relevant behavior.

More Details: Fiber photometry, a measurement technique that aggregates fluorescence signal using a fiber optic, is a highly pervasive approach in the field of systems neuroscience to study in vivo brain tissue dynamics during ecologically relevant behavior. Despite its common usage by researchers and companies alike, none of the state-of-the art fiber photometry device is capable of detecting small and fast signal changes in a low-light regime in freely behaving animals. Current technologies are benchmarked against cytosolic calcium indicators whose dynamic ranges far exceed that of the instrument and biological noises. Therefore, when used outside of this original configuration, i.e. with other fluorescent indicators (voltage, neuromodulator sensors…) with much weaker dynamic ranges, these instruments do not protect against unwanted noise sources which can lead to biological confounds, especially when the instrumental noise correlates with the animal motion.

Inventors at Stanford have developed a novel fiber-optic technology that achieve ~10 fold greater sensitivity than prior fiber photometry systems and is immune to optical artefacts induced by animal motions. The uSMAART (ultra-Sensitive Measurement of Aggregated Activity in Restricted cell-Types) technology tracks signals from up to 2 reporters from up to 2 different brain regions concurrently, with high sensitivity. The uSMAART system outperforms similar fiber photometry implementations in at least one of the three following aspects: (1) stability of illumination source, (2) immunity to fiber motion-induced illumination artefacts, and (3) detection sensitivity in the visible range. The novel technology offers a low-cost, flexible, and highly sensitive tool to decipher the precise temporal relationship of multiple physiological processes from multiple brain regions simultaneously.

Stage of Development:
Research – in vivo – working prototype and proof-of-concept in mice

Applications

- Neuroscience research
- Medical Diagnostics and Treatment Monitoring
- Pharmaceutical Development, Drug discovery platform
- Analytic chemistry

Advantages

- Can be used in freely moving animals
- Measurements are immune to instrumental and biological artefacts.
- High bandwidth, high sensitivity detection of biological parameter dynamics
- Simultaneous dual biological parameters with identical performance, such as quadruple processes recordings from two brain regions (two per region) with identical performance
- Experimental flexibility to combine multiple fluorescence sensors and monitor signals from multiple, deep brain areas.
- Universally applicable to any fluorescent reporters, from genetically encoded fluorescent proteins to synthetic dyes and nanoparticles.

Publications

- Haziza S. et. al., "Imaging high frequency voltage dynamics in multiple neuron classes of behaving mammals". (under revision).

- Haziza S. et. al., "Cutting edged tools for Neuroscience", Symposium, Stanford (2024)
- Haziza S. et. al., "Optical sensing of high-frequency voltage dynamics in multiple neuron classes
- of behaving mammals", ref. #7976, *Society for Neuroscience* (Washington DC-2023).

Innovators

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