NEUROSCIENCE

Optoacoustic imaging of neural activity

Gottschalk, S. et al. *Nat. Biomed. Eng.* https://doi.org/10.1038/s41551-019-0372-9 (2019).

Optoacoustics, which is also called photoacoustics, has been used to image hemodynamic activity in the brain. For this, the tissue is illuminated, and the light is then absorbed and converted into ultrasound waves, which can be recorded with acoustic transducers. In hemodynamic imaging, contrast is provided by hemoglobin, but alternative contrast agents can be used. In a recent paper, Gottschalk et al. extend previous work on optoacoustic imaging of the calcium sensor GCaMP5G in zebrafish. The researchers demonstrate that GCaMP6s and GCaMP6f can be imaged in the mouse despite potentially confounding hemodynamic contrast. In particular, calcium transients can be visualized when brief stimuli are used to elicit neural activity. Under these conditions, detectable hemodynamic responses are not evoked. In contrast, when longer stimuli are applied to the mouse, hemodynamic signals are dominant. The researchers demonstrate these findings in the context of electrical stimulation of the hind paw in anesthetized mice. *NV*

https://doi.org/10.1038/s41592-019-0415-x

MICROSCOPY

Polarization-varying anisotropic terahertz microscopy

Niessen, K. A. et al. *Nat. Commun.* **10**, 1026 (2019).

Anisotropic terahertz microscopy (ATM) offers a spectroscopic signature for measuring intramolecular protein vibrations in the terahertz (THz) frequency range that may be associated with protein functional states. The requirement for sample rotation and maintenance of a relative position with respect to the THz polarization, however, has limited ATM's applications in studies of biomolecule dynamics. Niessen et al. developed polarization-varying ATM (PV-ATM), which removes the sample-rotation requirement, thus allowing for the rapid resolution of closely spaced resonances. Using the PV-ATM system, they demonstrated the benefits of their method by examining lysozyme-inhibitor binding and by measuring the dynamical fingerprints of benchmarking proteins and RNA G-quadruplex. *LT*

https://doi.org/10.1038/s41592-019-0419-6

NEUROSCIENCE

Sensing norepinephrine

Feng, J. et al. *Neuron* https://doi.org/10.1016/j.neuron.2019.02.037 (2019).

Genetically encoded fluorescent sensors for several neurotransmitters have recently been reported. Feng et al. have added to this toolbox by developing norepinephrine sensors with high and medium sensitivity. Norepinephrine has crucial roles in vertebrates, allowing organisms to cope with the environment and internal states. Malfunction of the noradrenergic system has been implicated in stress, anxiety, depression, and attention deficit hyperactivity disorder. The norepinephrine sensors are based on the α2-adrenergic receptor and include a circularly permuted EGFP that fluoresces when the receptor undergoes a conformational change after norepinephrine binding. The sensor variants are specific to norepinephrine (and epinephrine) and do not detect other neurotransmitters at relevant concentrations. The researchers imaged norepinephrine signaling in zebrafish that were exposed to looming stimuli. Furthermore, the researchers monitored norepinephrine in behaving mice via fiber photometry. *NV*

https://doi.org/10.1038/s41592-019-0418-7

GENOMICS

Optically mapping methylation

Sharim, H. et al. *Genome Res.* **29**, 646–656 (2019).

Methylation of cytosine adjacent to a guanine is a hallmark of many functional elements in the human genome. CpG methylation patterns are most often studied at the population level by means of bisulfite conversion followed by high-throughput sequencing. To investigate methylation at the level of individual DNA molecules, Sharim et al. developed reduced-representation optical methylation mapping (ROM). They use a bacterial methyltransferase that is engineered to incorporate a fluorophore at a TCGA motif only if the C is not methylated. When combined with traditional optical mapping, which labels a region of interest and visualizes the labels on the DNA stretched out in a nanochannel, ROM provides information on the methylation state of 10-kb windows along the human genome. The researchers quantified the methylation state and copy number of DNA tandem repeats, regions that are challenging to resolve by sequencing. They demonstrated that ROM can be used to diagnose a form of muscular dystrophy related to a reduction in the number of tandem repeats on chromosome 4. *NR*

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