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0 Neurophotonics for recording and activation of neurons

0.1 Genetically expressed optical-based indicators of intracellular Ca^{2+}

These molecules are expressed in vivo in specific cell types and initiate an increase in fluorescence in response to the Ca^{2+} influx that follows an action potential.

Figure 1: The cyclically permutable GFP turned into a detector of intracellular Ca^{2+} . From Chen, Wardill, Sun, Pulver, Renninger, Baohan, Schreiter, Kerr, Orger, Jayaraman, Looger, Svoboda and Kim, 2013.



0.2 In vivo recording of neuronal structure and function with two-photon laser scanning microscopy

Two-photon laser scanning microscopy, properly done, allows changes in intracellular Ca^{2+} to be measured in neuronal soma down to spines.

0.3 In vivo recording of calcium signaling with two-photon laser scanning microscopy

In vivo Ca^{2+} signals may be recorded after a single spikes, but still the interpretation in terms of numbers of spikes in imperfect and can be unreliable. Figure 3: Essential components of a state-of-the-art two photon microscope. From. Liu, Li, Marvin and Kleinfeld 2019. Cy5.5-dextran labeled vasculature imaged at 1.25 µm



Figure 4: The distortion of cell images by the point spread function is most severe along the optical axis. From Tsai, Mateo, Field, Schaffer, Anderson and Kleinfeld, 2015.



0.4 In vivo recording of activity in the locomoting animal

The use of virtual reality in combination with two-photon microscopy permits behavior and circuit dynamics to be concurrently measured.

0.5 Genetically expressed optical-based drivers of spiking

Optical activation of channelrhodopsin expressed in the membrane of neurons can be used to photo-excite, or photo-inhibit, neurons.

0.6 All optical schemes for feedback control of spiking

The use of two-photon microscopy and concurrent photoactivation permits behavior and circuit dynamics to be concurrently measured and perturbed.

Figure 5: Intracellular responses in superficial V1 of mouse visual cortex using GCaMP6. From Chen, Wardill, Sun, Pulver, Renninger, Baohan, Schreiter, Kerr, Orger, Jayaraman, Looger, Svoboda and Kim, 2019.



Figure 6: Intracellular responses in hippocampal brain slice with cell culture using Oregon Green BABTA. From Sasaki, Takahashi, Matsuki and Ikegaya, 2008.



Figure 7: Intracellular responses in L5 of mouse somatosensory cortex. From Liu, Li, Marvin and Kleinfeld, 2019.



Figure 8: Intracellular Ca^{2+} is an unreliable measure of spike count and may fail to detect single spikes in vivo. From Theis, Berens, Froudarakis, Reimer, Roson, Baden, Euler, Tolias and Bethge 2016.



Figure 9: Intracellular Ca^{2+} in distal dendrites of L5b neurons can dissociate from somatic electrical activity. From Helmchen and Waters 2002.



 $Figure \ 10: \ {\tt In vivo hippocampus preparation.} \ {\tt From Dombeck, Harvey, Tian, Looger and Tank \ 2010.}$



Figure 11: In vivo recording in hippocampus. From Dombeck, Harvey, Tian, Looger and Tank 2010.



Figure 12: Natural transmembrane proteins that use light to pump ion of open ion selective pores.



Figure 13: One photon absorption and dynamics of channelrhodopsin. From Klapoetke, Murata, Kim, Pulver, Birdsey-Benson, Cho, Morimoto, Chuong, Carpenter, Tian, Wang, Xie, Yan, Zhang, Chow, Surek, Melkonian, Jayaraman, Constantine-Paton, Wong and Boyden, 2014



Figure 14: Schematic for feedback induced long-term synaptic potentiation. From Zhang, Russell, Packer, Gauld and Hausser 2018.



Figure 15: Test of feedback induced long-term synaptic potentiation. From Zhang, Russell, Packer, Gauld and Hausser 2018.

