Optical technologies for high-speed, single cell specific functional imaging and control of large neuronal population

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Questions and research areas of interest

How are **complex objects encoded and classified** by neuronal populations?

What are the underlying **computational principles for information processing** and generating behavior?

What is the **relationship between the structural and functional map** of neuronal circuits?

Structural connectivity puts only a constraint on dynamics of network → **Not sufficient to predict** behavior (see *C. Elegans*)

- Density of interconnections in the brain → **Information distributed** across the entire network → recordings from few neuron carry little information abut the states of network

Tools for dynamical interrogation of neuronal populations required:

a) Stimulation of defined spatio-temporal patterns of activity

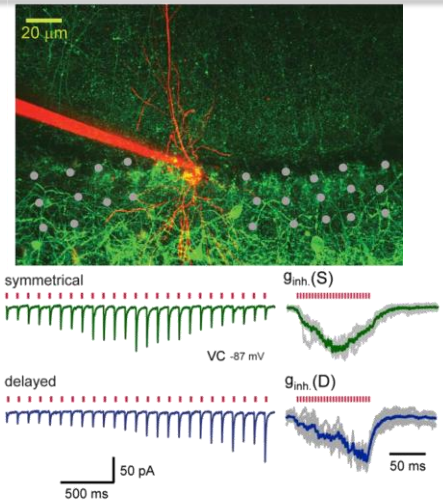
b) Parallel and unbiased recording from large populations

Fast: Physiologically relevant time scale: ~30Hz

Large: Size of cortical columns: ~100k neurons

Development of tools for dynamic interrogation of neuronal circuits

High speed optogenetic control of defined spatiotemporal patterns at single neuron resolution



- Based on temporal focusing (2-photon technique)
- Confinement along Δz ~ 2µm lateral ~ 5-10 µm
- ~1-2 ms dwell time / neuron to trigger AP

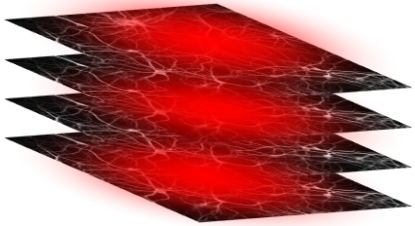
Mimicing spatiotemporal excitation patterns that neurons receive from their environment

B. Andrasfalvy et al. PNAS, 107(26):11981-6 (2010)

A. Losonczy et al. Nature Neuroscience, 13(8):967-72 (2010)

Brain-wide high-speed functional imaging of neuronal population activity

High speed volumetric Ca^+-imaging with WF-TEFO

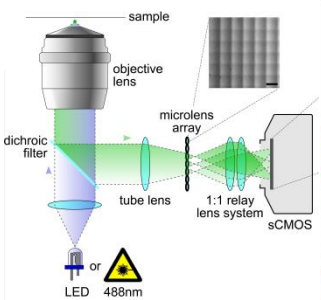


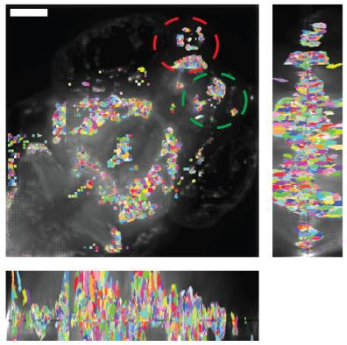
- 2-photon confinement along z via temporal focusing
- wide-field in x-y
- FOV up to ~Ø 120 µm
- Δz ~ 2um
- ~200 fps – 22MVox/sec → video rate volume imaging

T. Schroedel et al. Nature Methods, 10.10: 1013-1020 (2013)

Ca imaging of entire *C. elegans* brain (~120 neurons) @ single neuron resolution and 5Hz volume rate

Simultaneous whole brain Ca imaging using light-field deconvolution microscopy





- Single snapshot captures entire 3D information
- Deconvolution → Δx,y ≤ 1.4µm Δz ≤ 2.6 µm
- ICA to identify and track over 5000 regions (mostly single neurons) in zebrafish brain

Simultaneous whole brain Ca imaging: zebrafish larvae 700×700×200µm @20 Hz volume rate; *C. elegans* imaging 350 × 350 × 60µm @50Hz volume rate

R. Prevedel, et al. Nature Methods, 11, 727–730 (2014)

Expertise required / want to join

- Need **advanced statistics and machine learning** tools for segmentation, classification and signal extraction
- Making **sense of the data**: **Mathematical modeling** to guide and interpret our experimental results
- Join groups that work on **hierarchical temporal modeling**, **predictive coding** and **Bayesian networks**

Contact Information

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