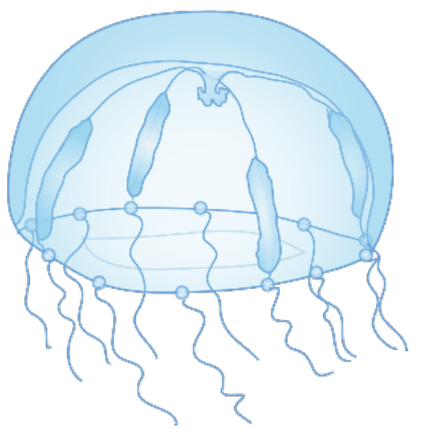
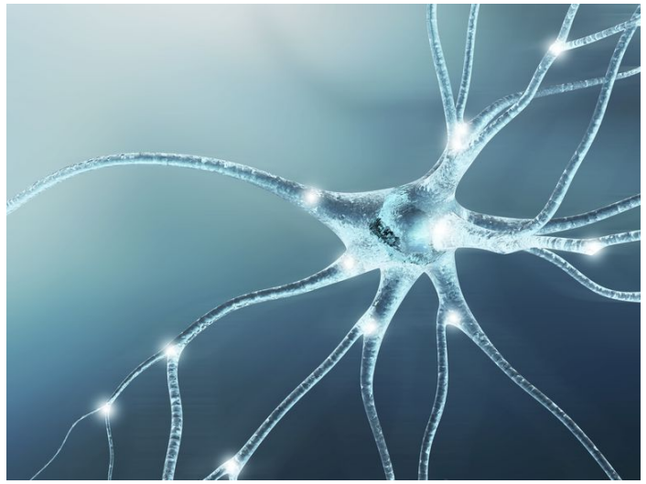
Registration and inverse problems in in vivo neural imaging

Laboratory of David J. Anderson

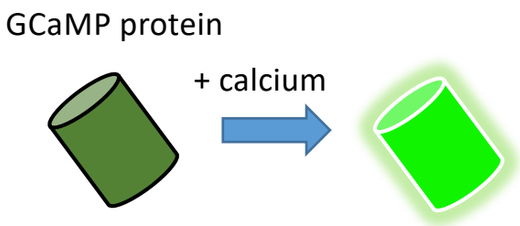
Ann Kennedy, Amit Vinograd, Brady Weissbourd

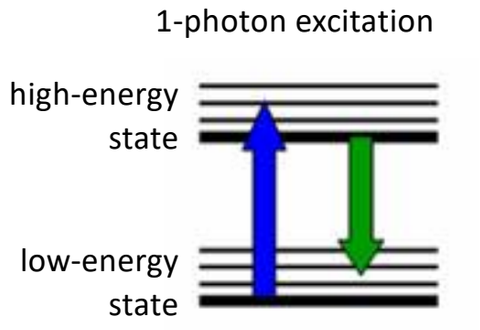


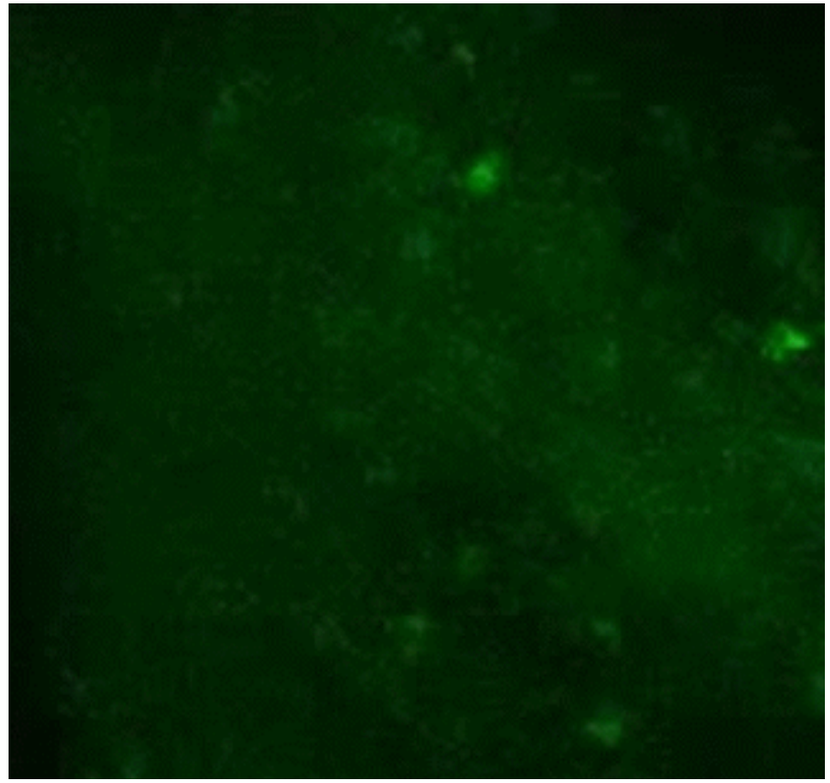
We can observe the spiking activity of neurons using calcium imaging



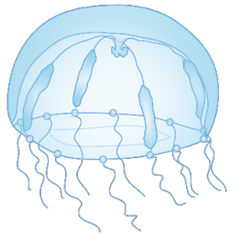
The concentration of calcium in neurons transiently increases when they spike (fire action potentials).

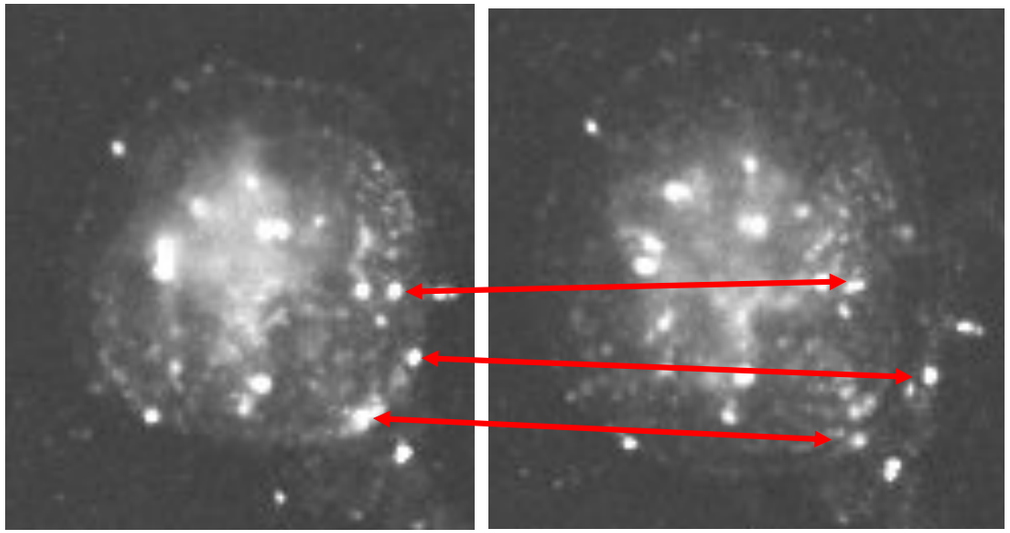






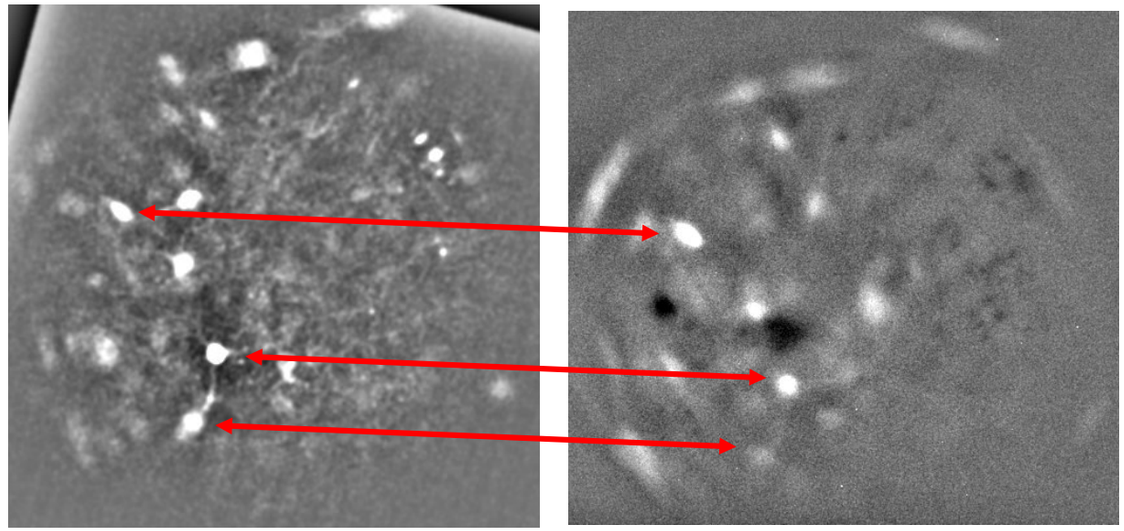
Solving two related technical challenges in calcium imaging





(neurons in the jellyfish mouth)

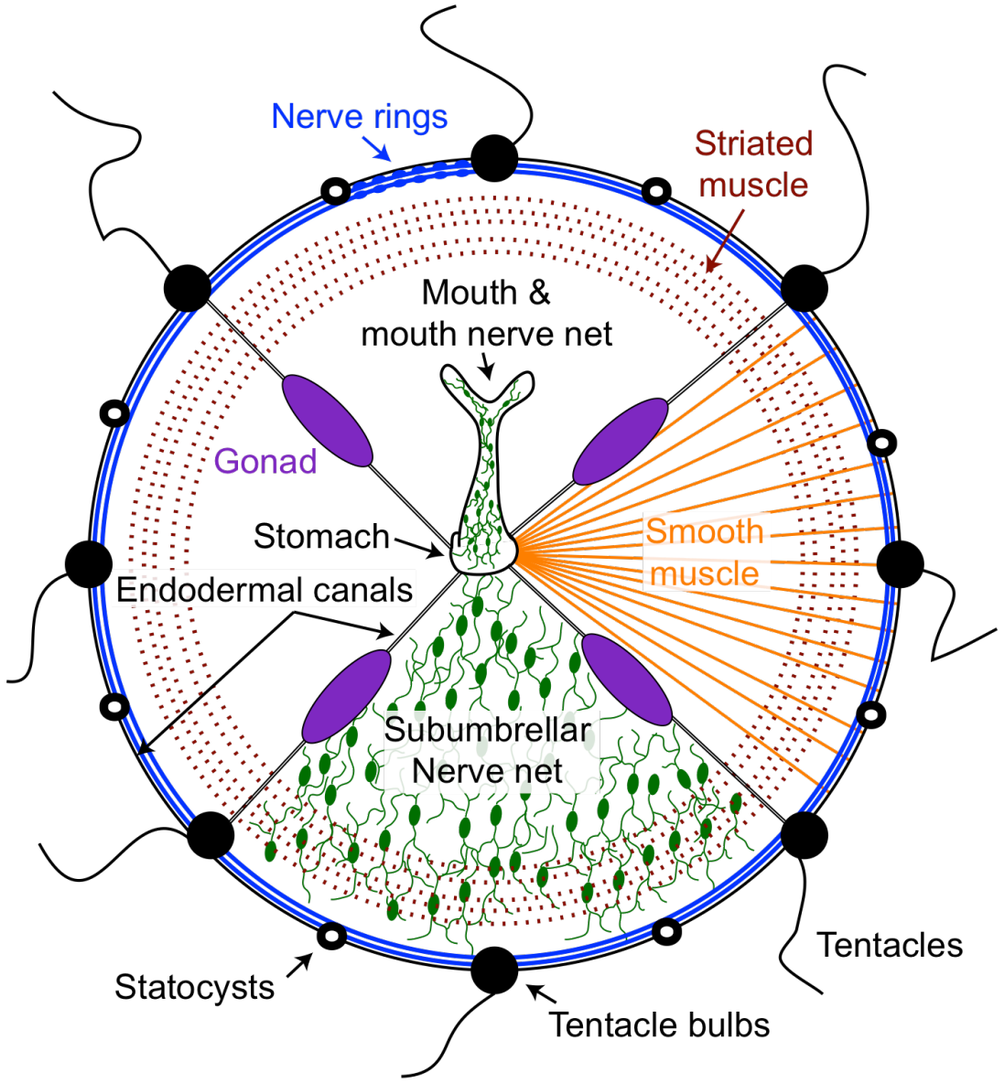
Jellyfish: identifying the same neurons over time during non-rigid movement



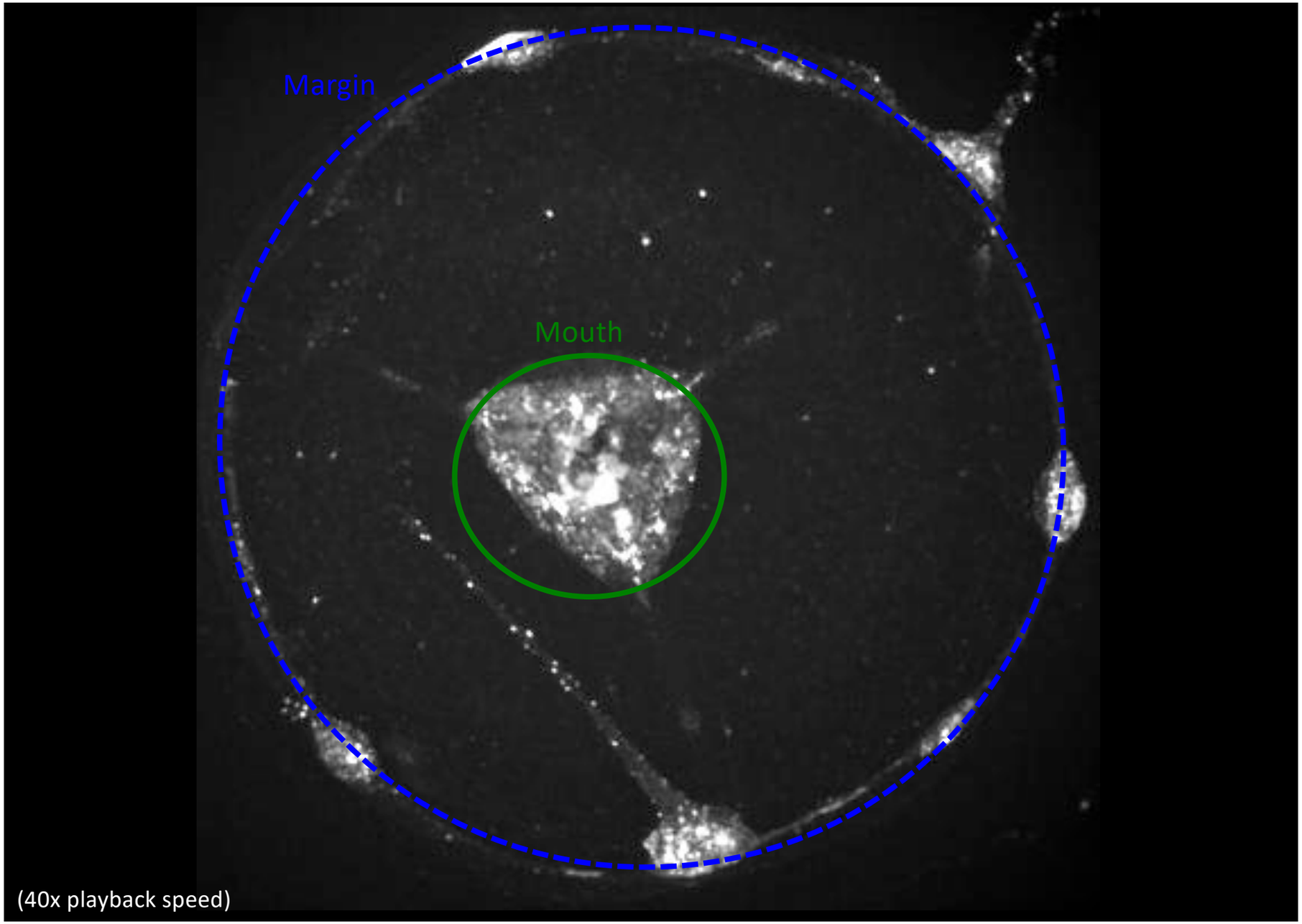
(neurons in mouse hippocampus)

Mice: identifying the same neurons under different imaging conditions

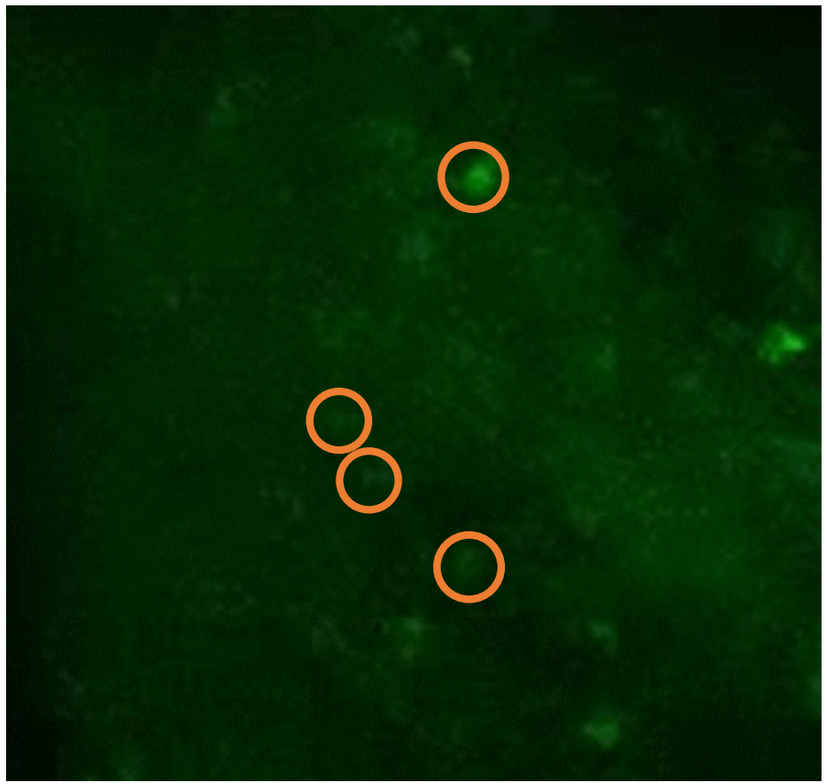
Overview of anatomy

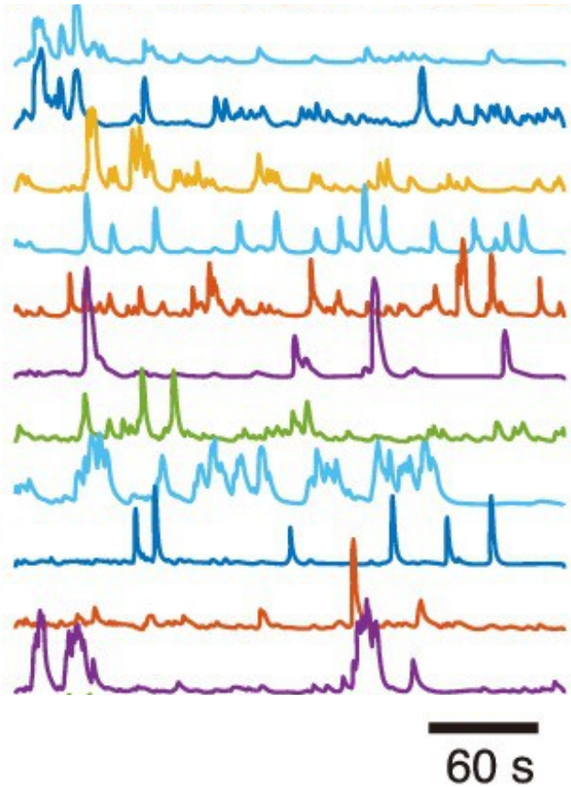


Calcium imaging of RFamide neurons using transgenic jellyfish: **the flashing is neural activity!**



There are algorithms for extracting neuron activity from calcium movies, but they fail when cells are moving

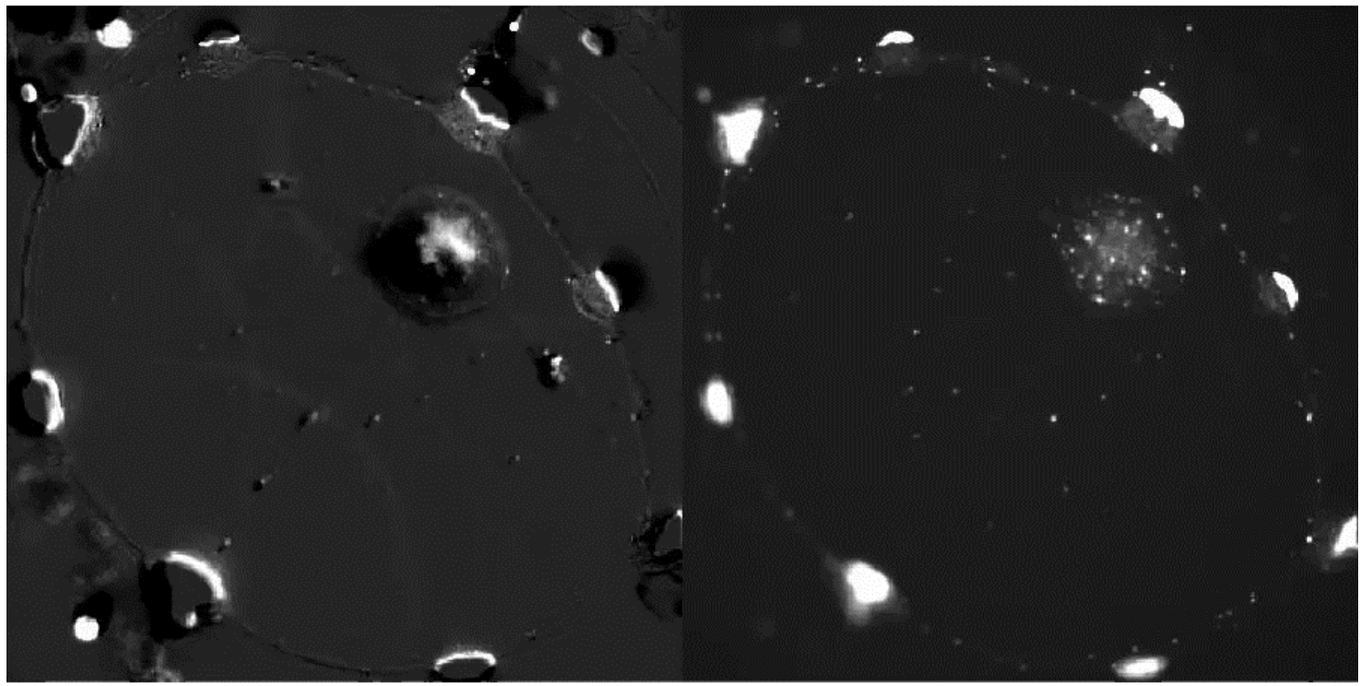




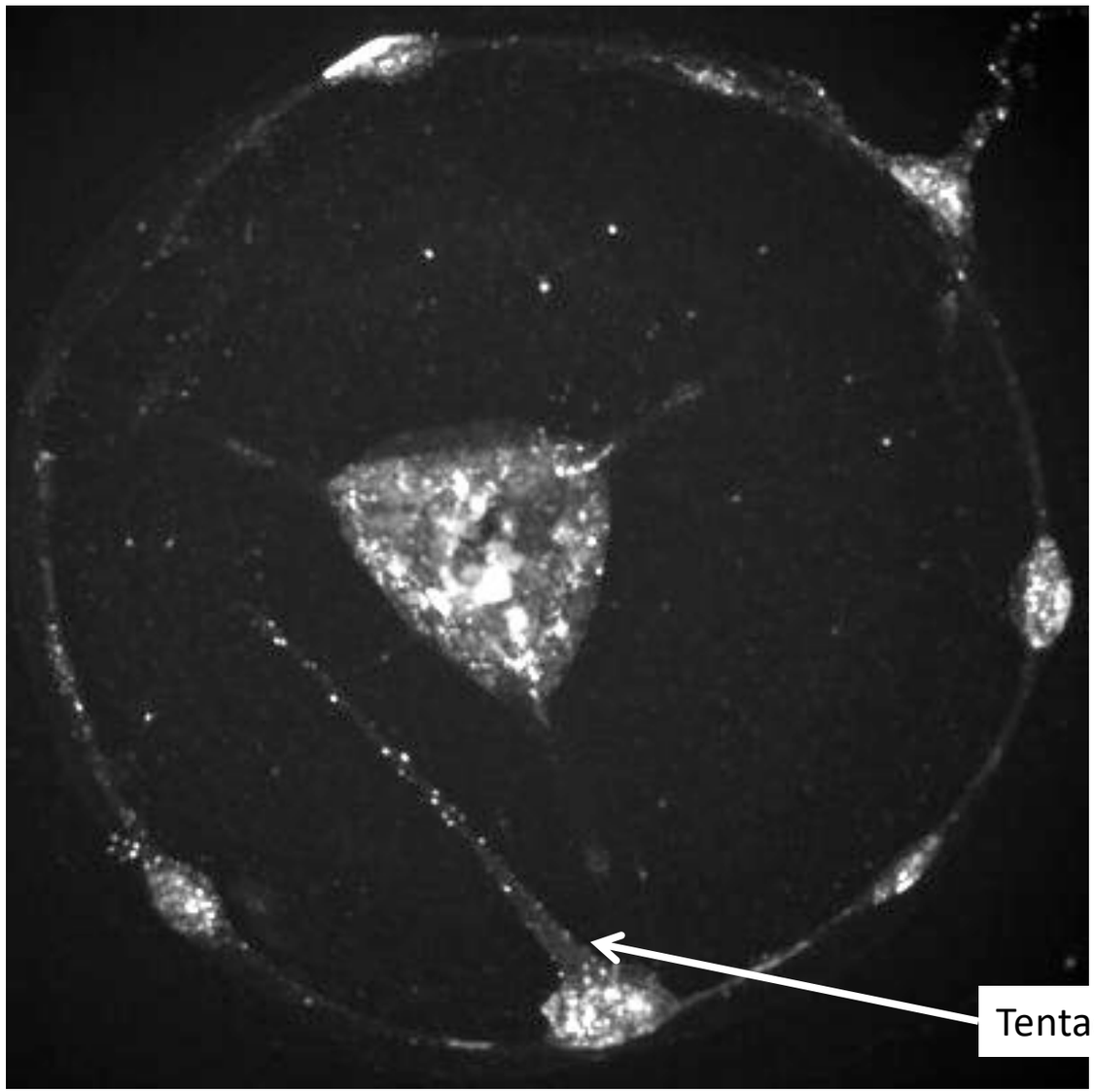
The challenge: non-rigid motion correction (or tracking) of neurons in jellyfish

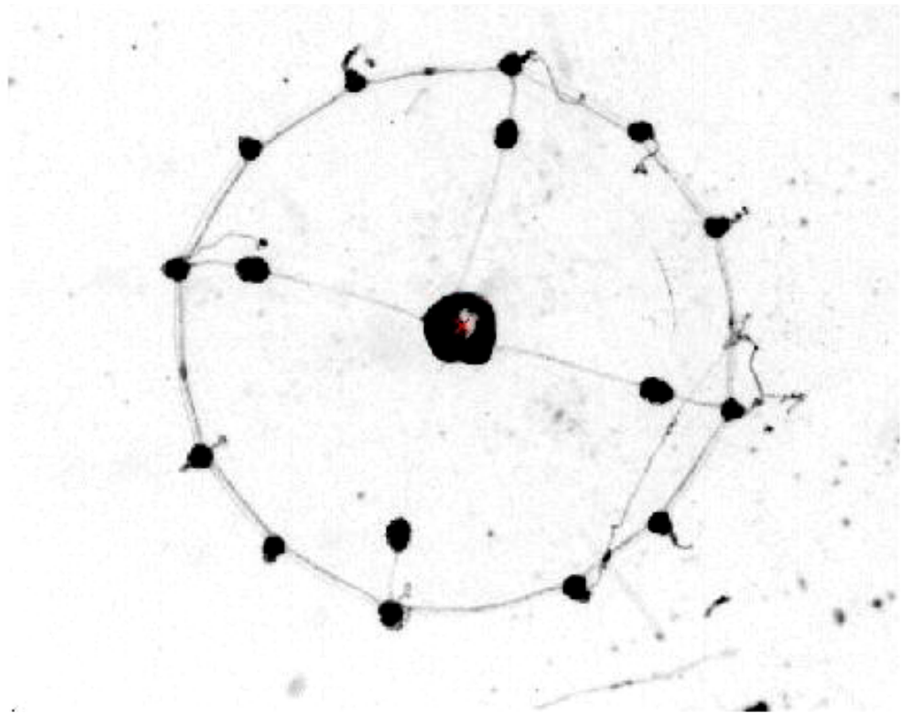
Activity-dependent
GCaMP fluorescence

Constant
red-channel fluorescence



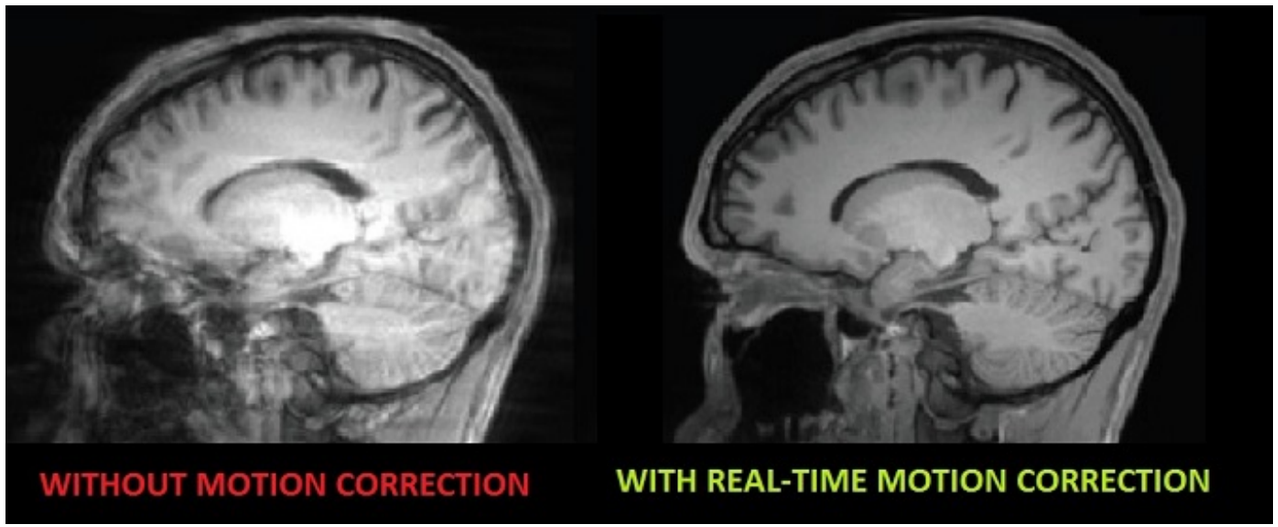
The challenge: non-rigid motion correction (or tracking) of neurons in jellyfish



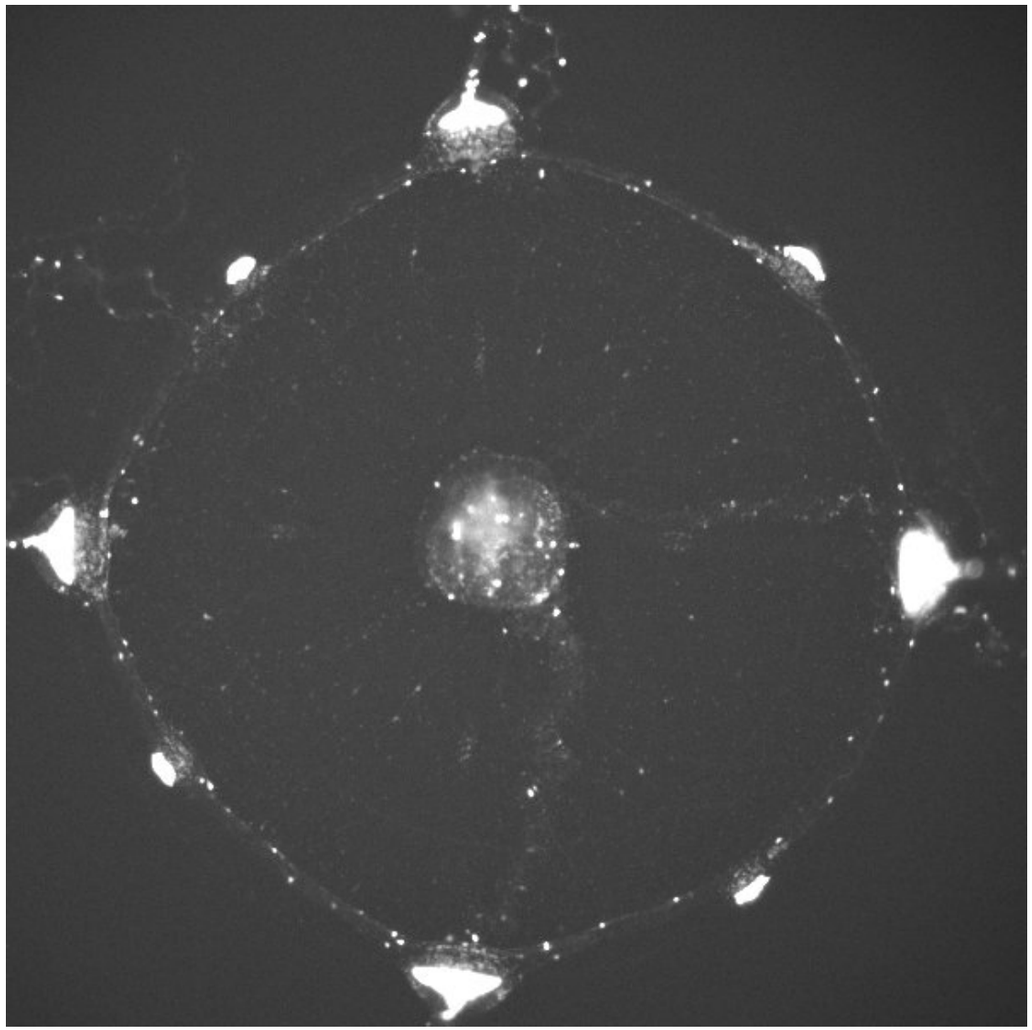


Extreme occlusion in less constrained animals

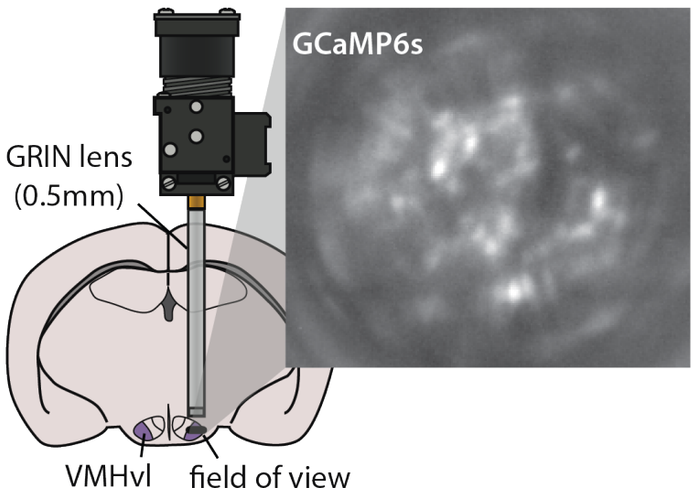
Can we design a biologically informed motion correction method that works when imaging data is sparse?

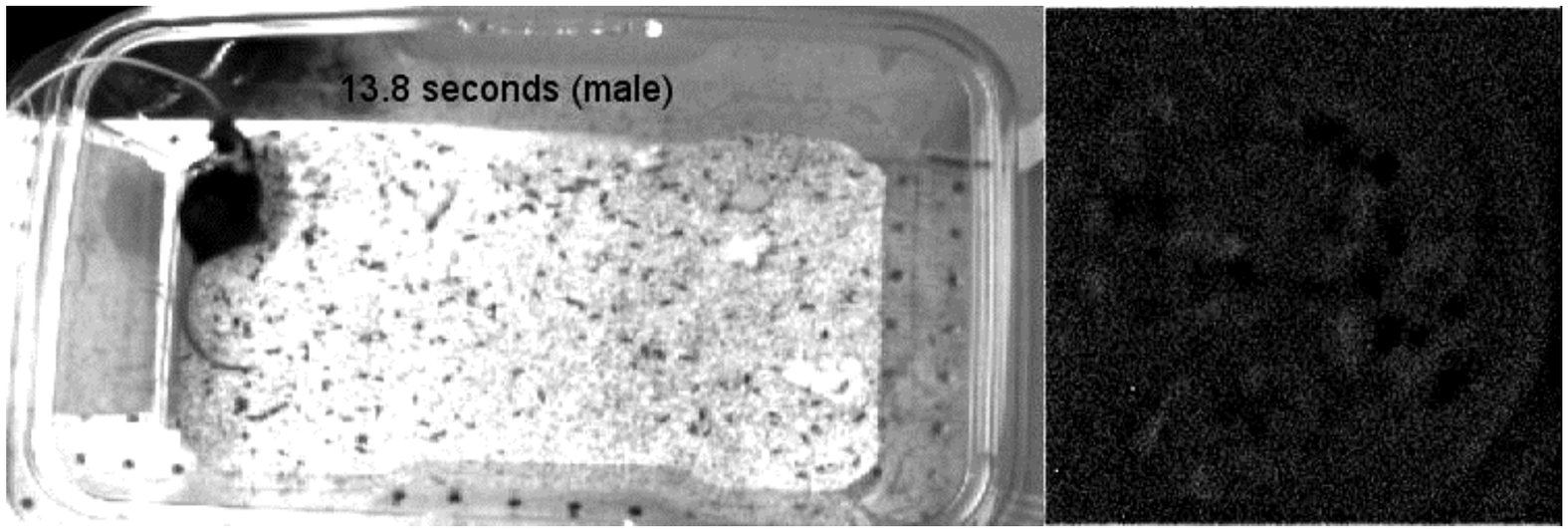


Motion correction in medical imaging



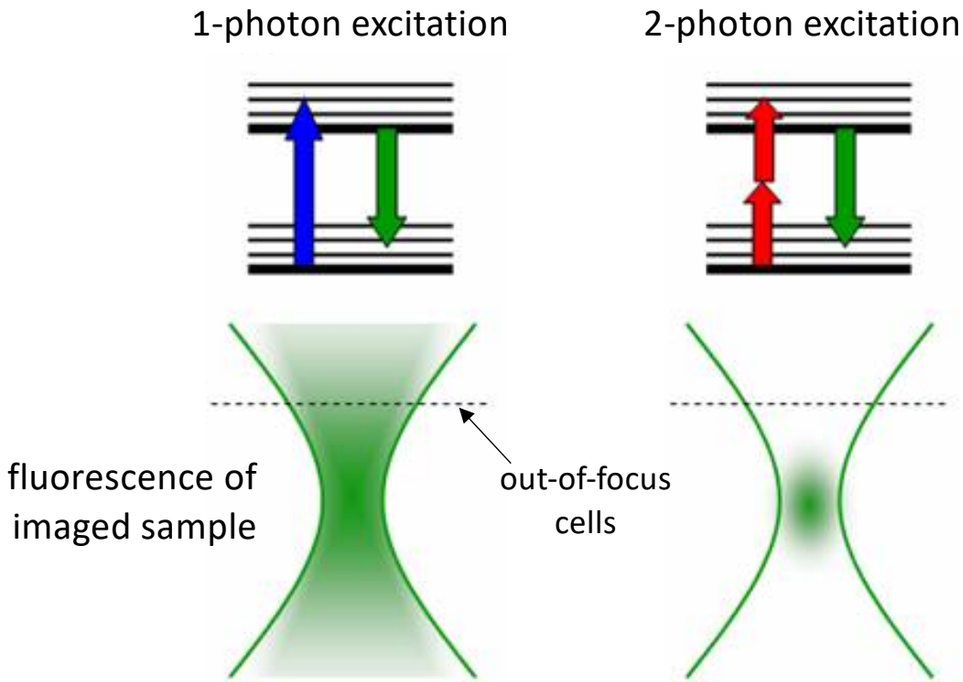
Microendoscopic imaging let us measure GCaMP fluorescence in a freely behaving mouse

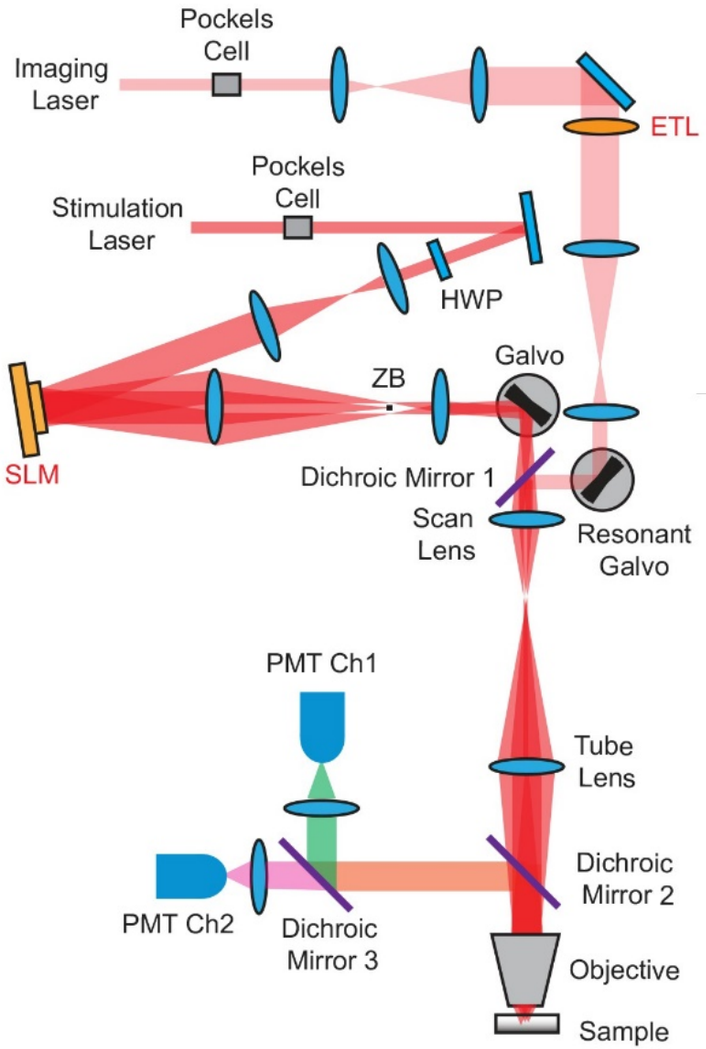




But we don’t use microendoscopes for everything: 2-photon (2P) excitation of GCAMP gives better signal, and enables many interesting experiments

- Image cell morphology more clearly
- Image in multiple colors
- Precisely stimulate individual neurons while imaging





The challenge: can we get the best of both worlds in the same mouse + in the same neurons?

Image with microendoscope to understand neural activity during behavior

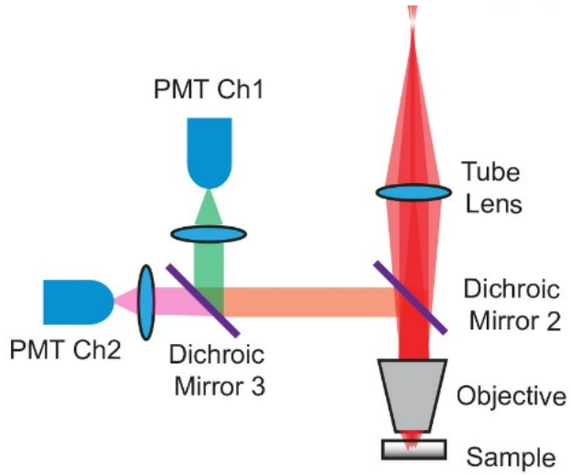
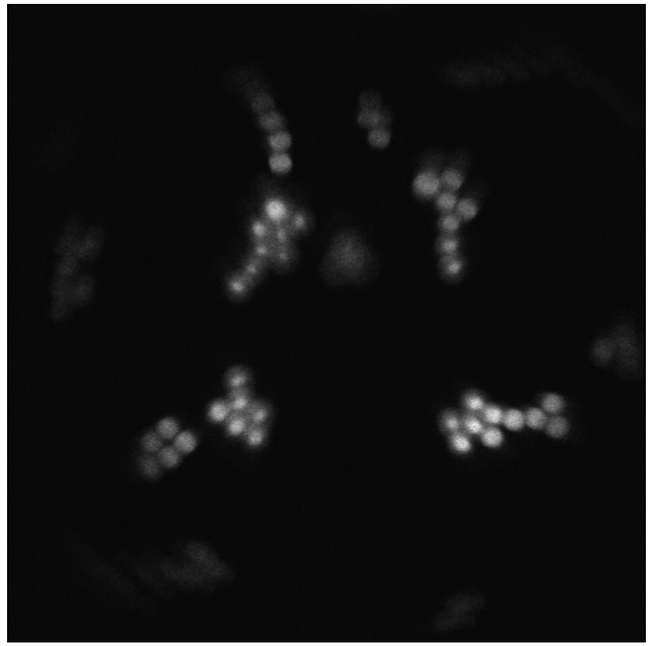


Image same cells with 2-photon microscopy to understand neural circuit architecture

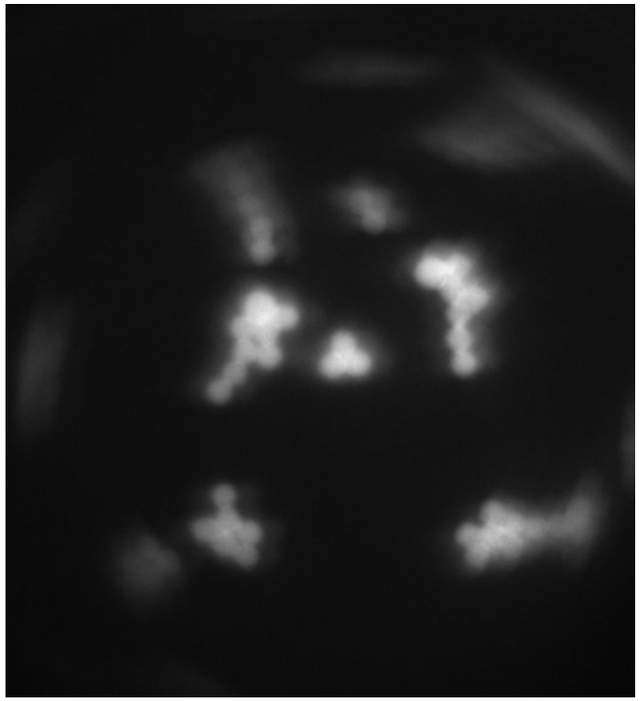
Imaging with microendoscope vs 2-photon microscope

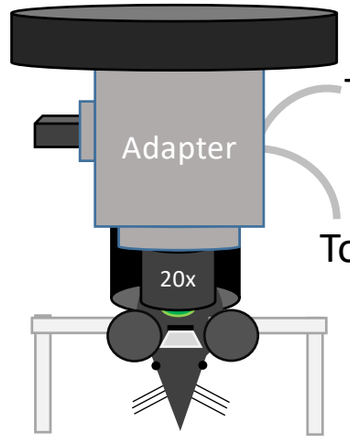
Calibration with fluorescent beads



2P field of view

Microendoscope field of view





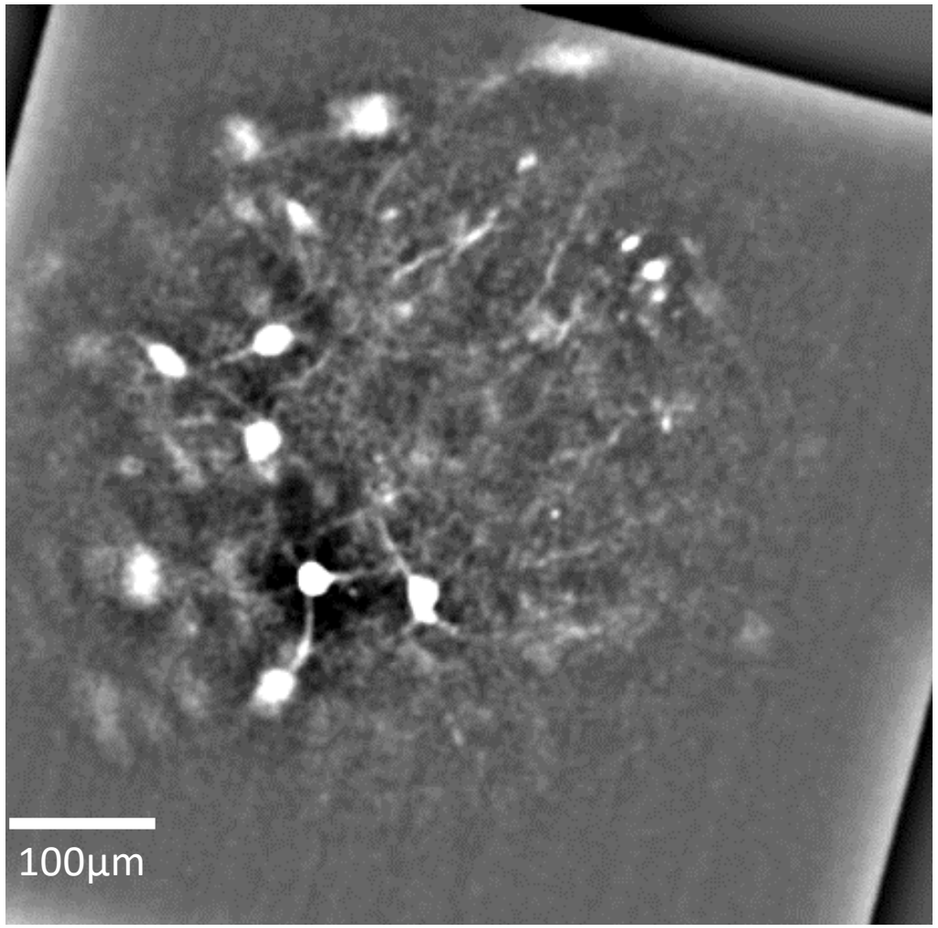
To microendoscope

To 2-photon

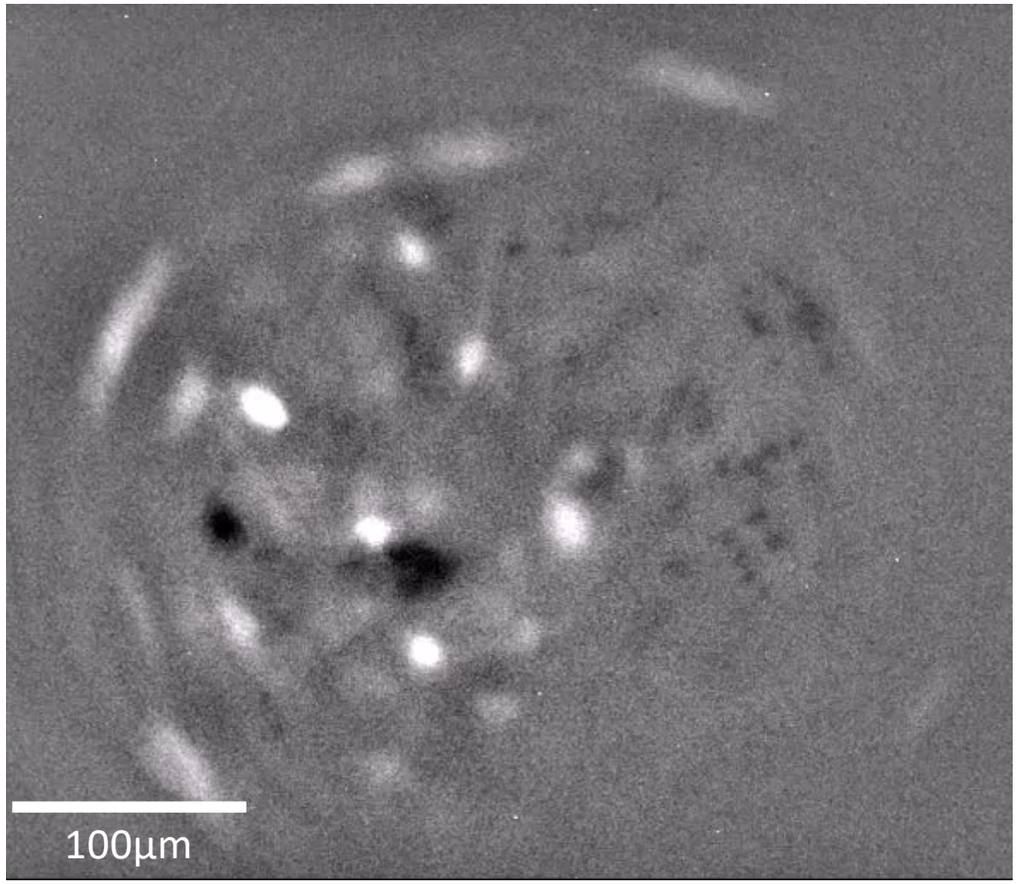
w/ Inscopix

How do we register neurons between these two types of data?

2-Photon

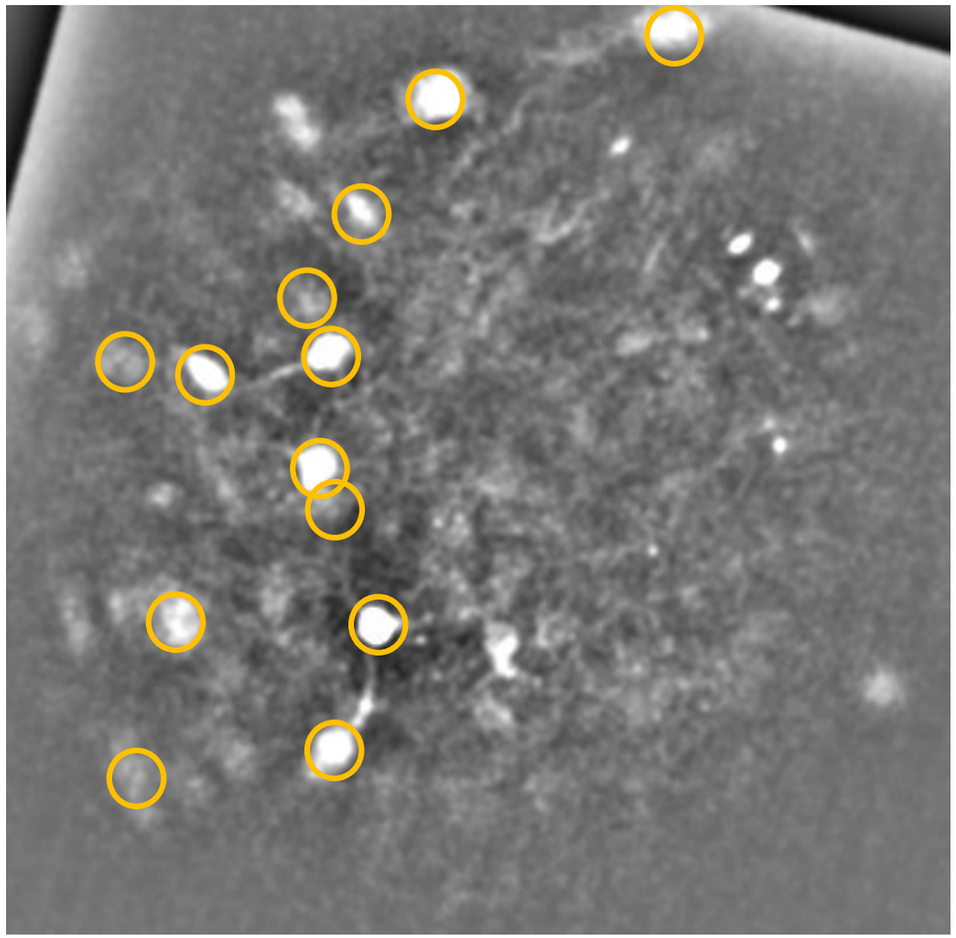


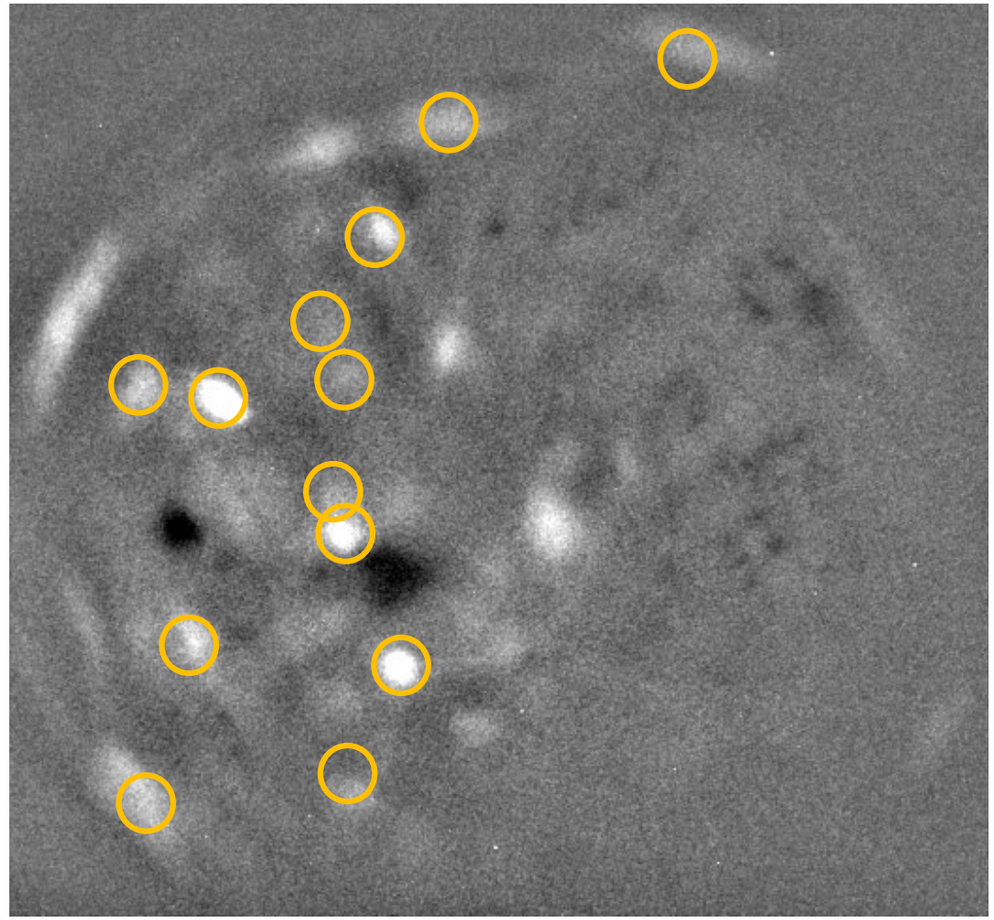
1-Photon (microendoscope)



Neurons in mouse hypothalamus imaged at 20 fps while gradually changing focal plane

How do we register neurons between these two types of data?





How do we register neurons between these two types of data?