## Calcium Imaging and Optogenetics

Reading out and manipulating cellular level network activity patterns.

Peyman Golshani, MD/PhD Associate Professor

### How do we read out brain activity patterns?

- Temporal Resolution
- Spatial Resolution (Cellular Level?)
- Density of sampling.
- Cell-type specificity

#### Techniques in humans

# EEG. Advantage: non-invasive. Disadvantage: poor spatial resolution (cm). Disadvantage: not good for high frequency activity.



- MEG. Advantages:
- I. non-invasive.
- 2. high temporal resolution.
- 3. Good spatial resolution.
- MEG Disadvantages: Signal to noise small.



### Advantage: I.non-invasive. 2. Can give wholebrain signals

- Disadvantage: I. not direct measure of activity.
- 2. poor temporal/spatial resolution.



#### Techniques in humans

 Electrocorticography: Poor spatial resolution. Good temporal resolution. Disadvantage: Invasive.



### Depth Recordings

- Advantages: I. Excellent temporal resolution
- 2. Can be targeted to specific areas (though limited).
- Disadvantage: I.Very invasive. 2. Poor depth of sampling (a few cells). 3. Usually in people with epilepsy



### Techniques in animals

 I. EEG 2. fMRI 3. Electrocorticography. (same issues as humans)

### Tetrodes



Wednesday, February 17, 16

### Silicon Probes





whole-cell recordings Advantages: Subthreshold membrane potential Highest temporal resolution Disadvantages: One or Two cells at a time. Hard to perform





#### Needs:

Record the activity of all the cells a circuit (not sparsely)
Identify the cells we are recording (what cell type?)
Record at the speed of the brain
Record from the same cells over time (months)
Record during behavior (adjust for motion)
Ideally record from freely behaving animals.

#### What is 2-photon microscopy?









Wednesday, February 17, 16









#### Genetically encoded calcium indicators. Chen...Kim, Nature 2013



#### GCAMP6 can report action potential firing









### Bilateral, 6X8 mm



#### Chronic Optical Access





#### Harvey ... Tank, Nature 2012



Wednesday, February 17, 16

#### Harvey et al., Nature 2012



Wednesday, February 17, 16

### Optogenetics

- To link brain activity patterns to behavior we will need to control the activity patterns of specific cells in the brain.
- Electrical stimulation is non-specific.



#### Zhang ... Deisseroth, Nature Methods, 2006



#### Boyden, Zhang...Deisseroth, Nature Neuro 2006



### Arch (proton pump for neuronal silencing)





#### Step function opsins Berndt...Deisseroth, Nature Neuro 2008







### using holographic optogenetic stimulation to target specific cells

