Wide-Field Optical Imaging of Brain Activity

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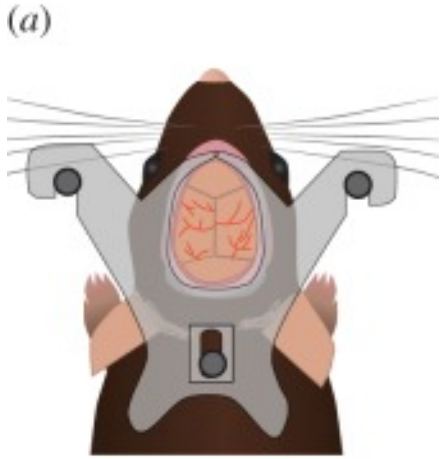
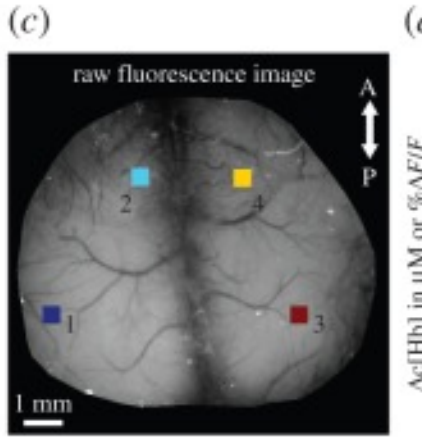
What is Wide-Field Optical Imaging?

- Fast imaging of neural activity through wide optical window (> 2 mm diameter)
  - Usually using fluorescent indicators
- Dorsal surface of cortex
- Mostly done with 1 photon illumination from laser or LED
- Various indicators
  - Calcium indicators track spiking
  - Voltage indicators track membrane voltage
  - Glutamate indicators show synaptic activity

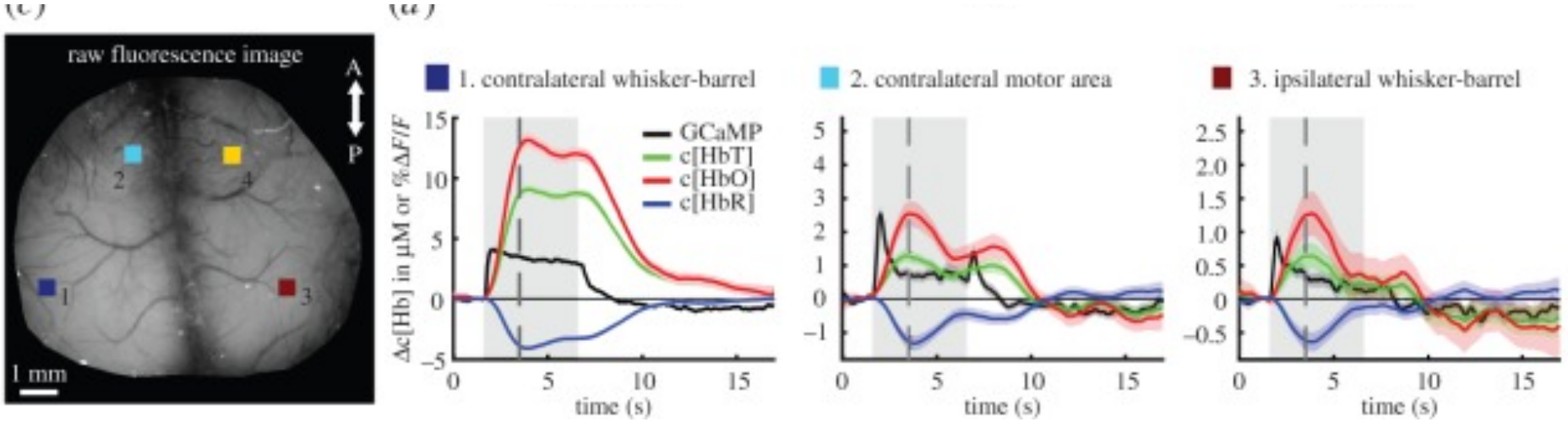




Ma et al PRS 2016

Uses of Wide Field Imaging

- To monitor coordinated activity in different cortical regions
- Especially useful with rapid indicators (voltage and glutamate)
- Infer rapid network communication



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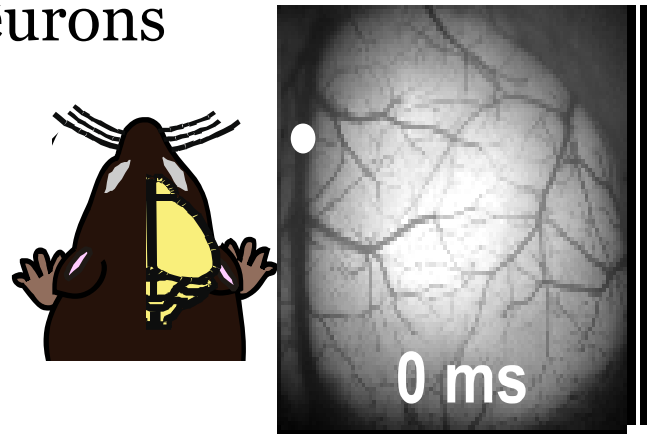
Limitations of Wide Field Imaging

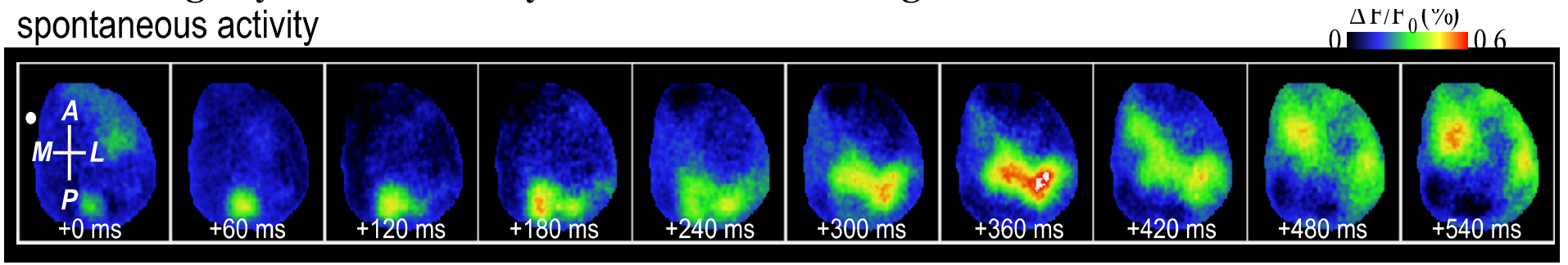
- Limited to fluorescence from upper 300 μ of cortical surface
- Most GECIs and GEVIs diffuse into neurites (Only ~10% of neuron volume in soma and ~5% of membrane area around soma)
- Very difficult to resolve individual cells

Wide-Field Imaging with Voltage Indicator

- Neurons signal through voltage changes on time
- Voltage-sensitive dye added to surface of cortex
  - Cortical surface is illuminated
  - Luminescence changes with extra-cellular voltage
- Tracks bulk activity of hundreds of neurons
- Can detect rises of < 1/50 second



Voltage dyes track activity levels in different regions of brain as mouse 'dreams'

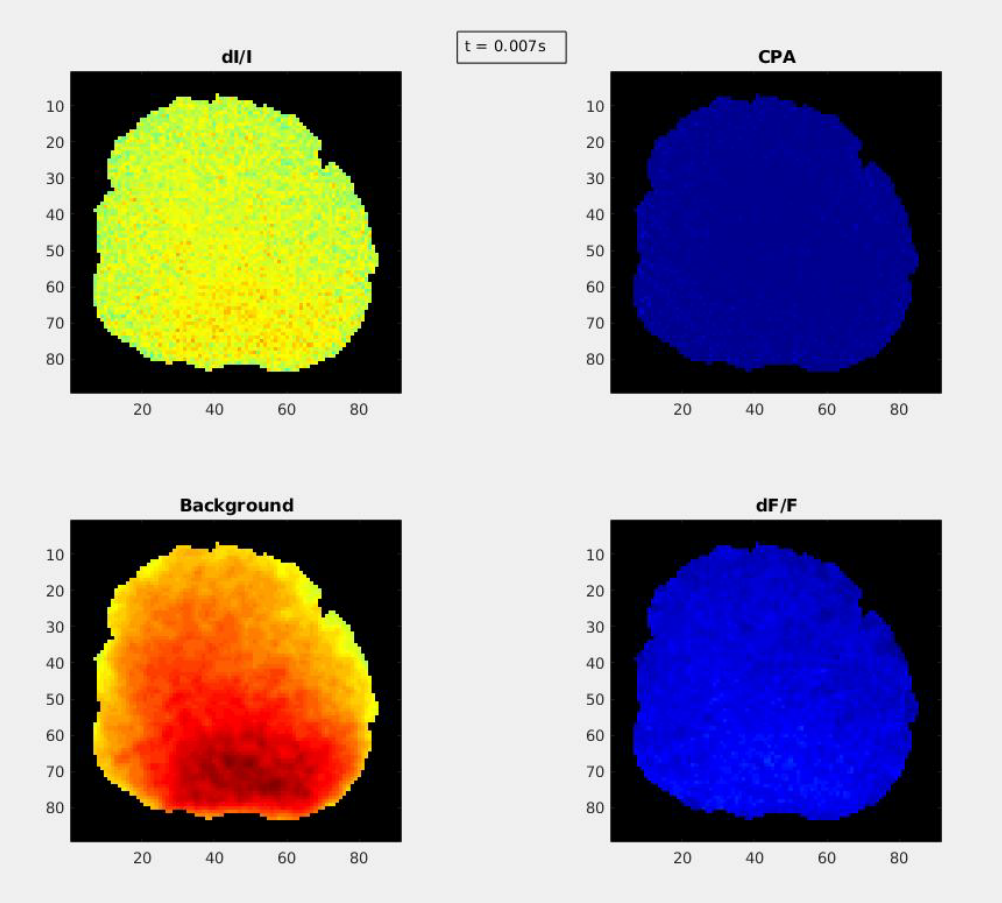


Pre-processing Is Essential

Wide-field dynamics visible at rapid time scales

Splitting Noisy Voltage Signal Into Three Parts

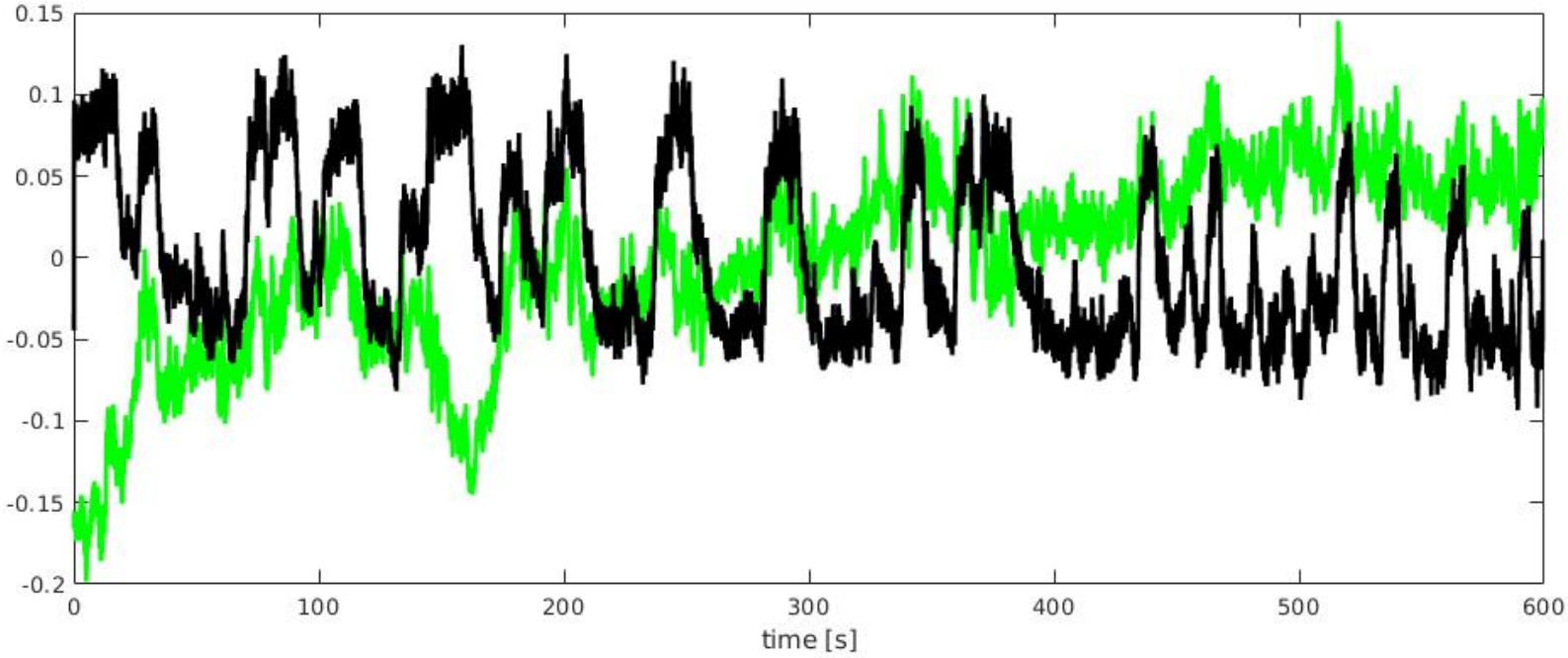
Using TV and other approaches we can separate the raw signal (top left) into breathing (top R), slow background (including neurovascular) (bottom L) and high-resolution neural signal (bottom R)



Pre-processing to Remove Hemodynamics from WF Calcium Imaging Data

- Also methods to remove largest hemodynamic artifacts; substantially changes activity profile
- About half of variation due to hemodynamics

GCaMP signal (green) and demixed signal (black)



What Good Pre-processing Can Reveal

Wide-field dynamics visible at rapid time scales

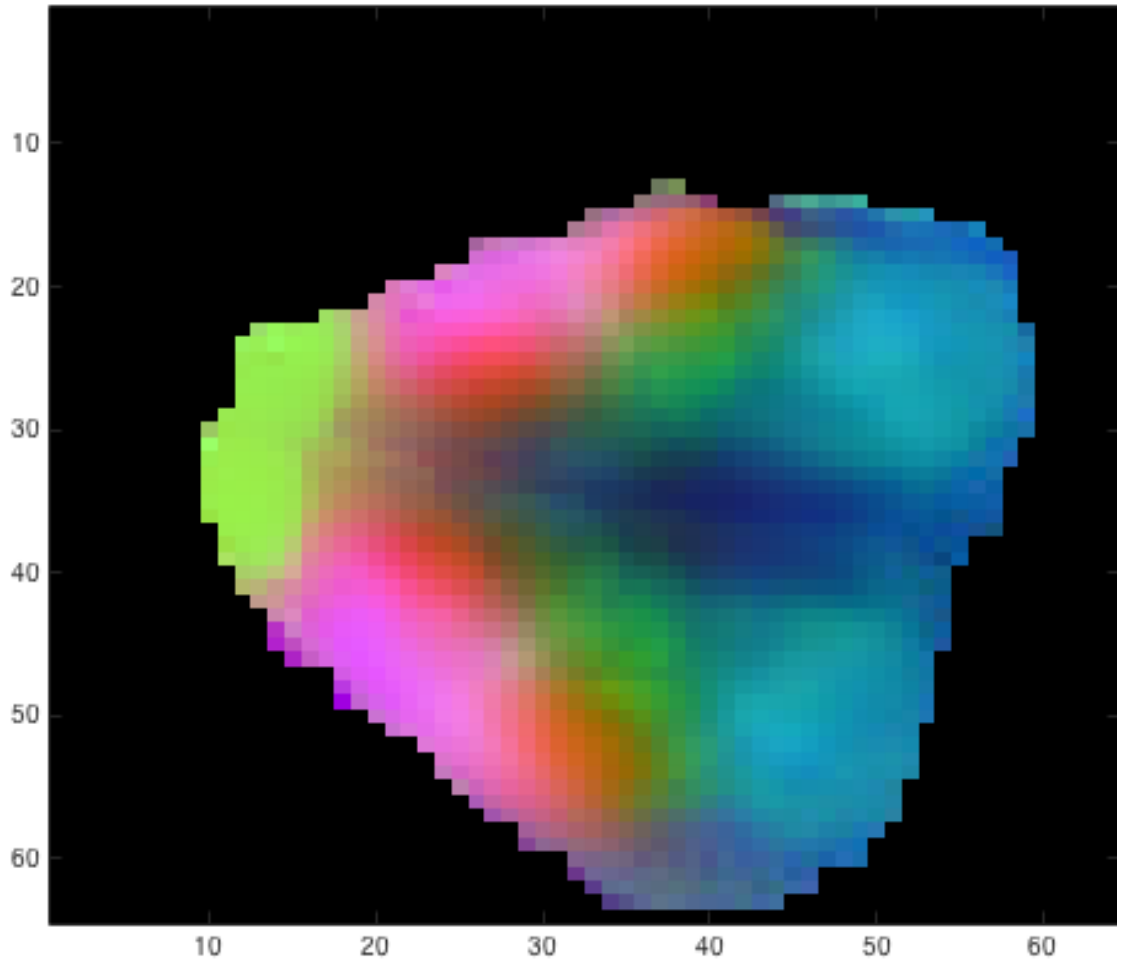
Correlation Map of Mouse Cortex in Resting State Activity

Data of Matt Valley, Waters lab with GCaMP6f

Pixels colored to reflect correlations with others

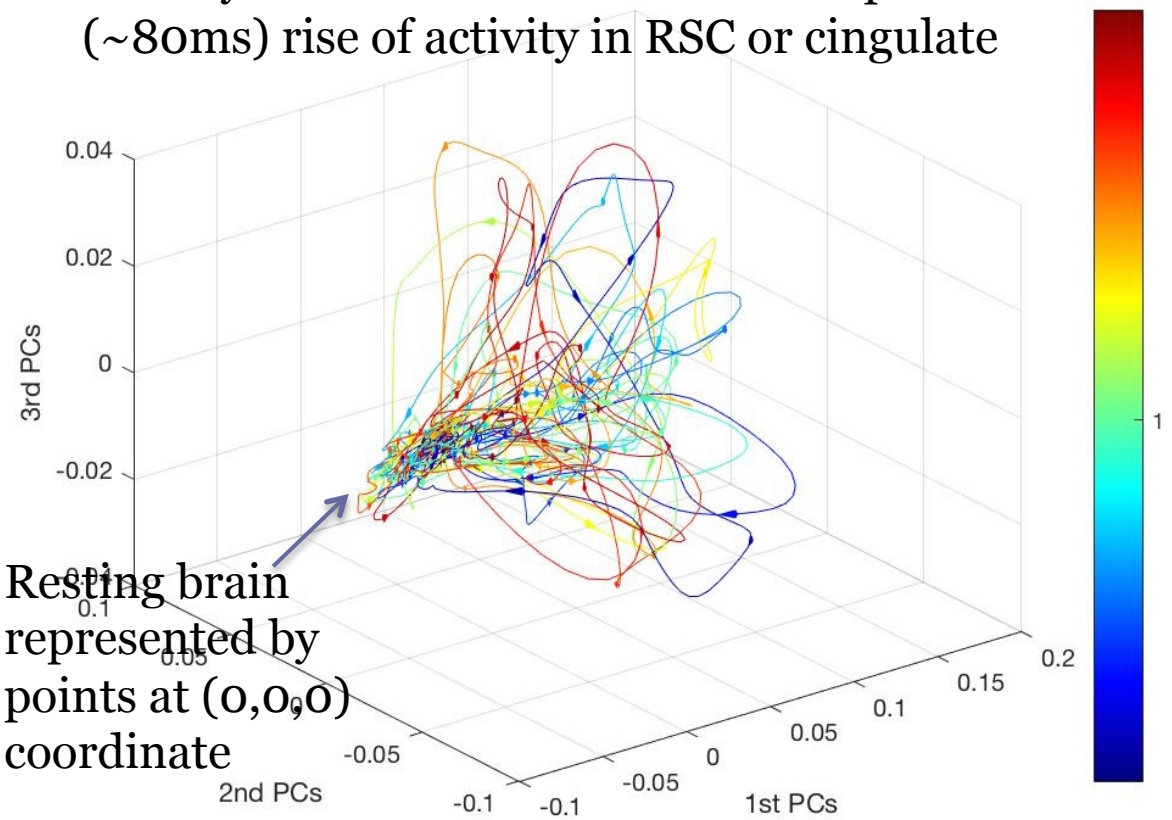
Correlation bands don't correspond to annotated anatomical regions

Sensorimotor integration visible



Rapid Cortical Dynamics by Voltage

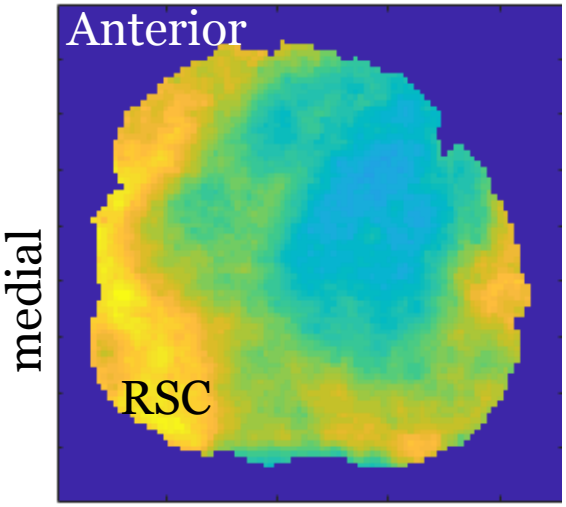
Representing 25 s of cortical activity patterns by scores of first 3 PCS
Color represents elapsed time blue -> red
Activity often starts from rest with rapid (~80ms) rise of activity in RSC or cingulate



Resting brain represented by points at (0,0,0) coordinate

Data of Majid Mohajerani, Murphy lab, UBC

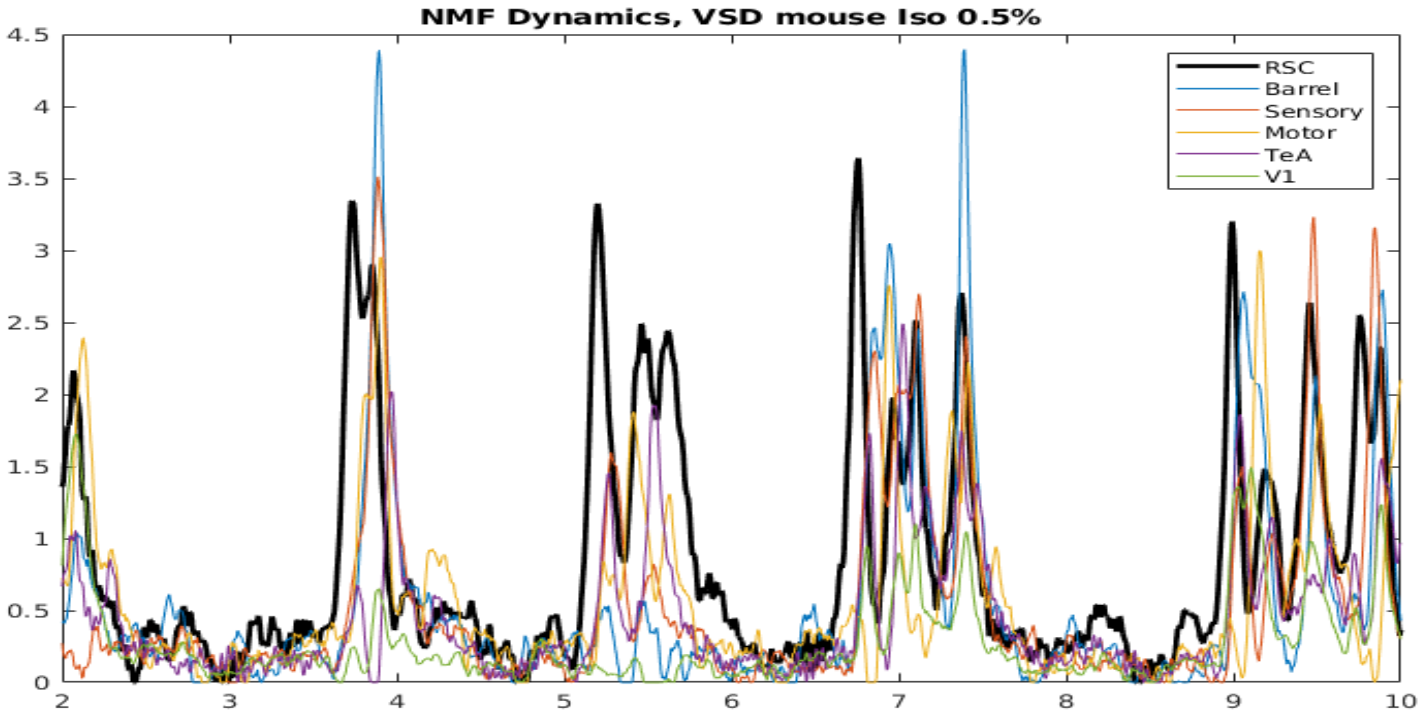
Loadings of PC1 mostly on RSC



Human EEG and MEG studies find a time scale of about 100 ms for state transitions.
Comparable to time scale for stable directions in mouse PC space

NMF Analysis of Cortical Dynamics

- Butterfly indicator in resting awake mouse
- Most commonly RSC activation leads off activity burst from quiet state; sometimes auditory cortex



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