Brain-state and attention dependent membrane potential dynamics in visual cortex.

Peyman Golshani MD/PhD
Associate Professor
David Geffen School of Medicine
UCLA
Bridging the gap between synaptic physiology and behavior
Neurotransmitters
Receptors
Ion Channels

Dendritic integration

Local connectivity maps

Network Oscillations
Ensembles/ Synfire Chains

Behavior

plasticity or disease

Wednesday, February 17, 16
Bridging the gap: 
Appreciate the complexity of the circuit 

• There are 20 GABAergic interneuron types in cortex and hippocampus. 

• Excitatory neurons are NOT a homogenous group. Cells that appear identical even in the same layer can have distinct long-range projections and local connectivity.
There are more than 20 types of GABAergic neurons in the neocortex and hippocampus.
Bridging the gap:

Needs

• Record the activity of large populations of IDENTIFIED neurons in the behaving animal at the speed of the brain over long time periods (days to weeks.)

• Characterize the short and long range connectivity of each cell we record.

• Selectively manipulate the activity (and connectivity) of each cell type.

• Be able to follow how each cell type transforms synaptic input to spike output DURING BEHAVIOR.
• Part 1: Brain-state dependent changes in membrane potential dynamics in visual cortex.

• Part 2: Membrane potential and network dynamics during decision making.

• Part 3: New tool development
Neurons in visual cortex are modulated by attributes other than the pattern of light hitting the eye.

The role of attention, level of arousal, and non-visual attributes.
Attentional modulation of visual responses in V4

McAdams and Maunsell, 2002
Visual cortical neurons code for behavioral state rather than simple attributes of visual world

Reward Anticipation

Shuler and Bear, 1996
Changes in brain state modulate responsiveness of cortical neurons

Niell and Stryker, 2010
Questions

• What are the mechanisms underlying changes in the responsiveness of cortical neurons during changes in arousal state

• Which neuromodulatory systems mediate these changes?

• What are the contributions of identified interneurons to these alterations?
Stable whole cell recordings in running mice.
Depolarization and decreased variance of the membrane potential with running: L2/3 excitatory neurons.
Depolarization and decreased variance of the membrane potential with running: L2/3 excitatory neurons.
Unimodal membrane potential distributions in stationary and locomotive periods
Layer 2/3: No visual stimulus

No change in firing rate
Depolarization of Vm
Decrease in Vm SD
Depolarization starts before the start of locomotion.
L2/3 Drifting Grating Visual Stimuli
L4 behaves much like L2/3
PV+ interneurons depolarize with locomotion
Somatostatin cells depolarize with locomotion
Could neuromodulation play a role?
Cholinergic blockade does not prevent Vm changes with locomotion.
Cholinergic blockade does not prevent membrane potential changes associated with running.

Control

![Graph showing membrane potential changes in control condition]

Cholinergic Blockade

![Graph showing membrane potential changes after cholinergic blockade]

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Noradrenergic antagonists block Vm changes associated with locomotion

Prazosin, Yohimbine, Propranolol
Running induced depolarization persists after blockade of AMPA and NMDA receptors
4 Hz Oscillation
4 Hz Oscillation
4 Hz oscillation disrupts visually evoked spiking
Conclusions

• Long-lasting stable targeted whole-cell recordings in mice free to run on a treadmill are possible.

• Cells depolarize and their variance of the membrane potential decreases just prior to running.

• Noradrenergic input is essential for maintenance of the depolarized, low variance state.

• This depolarization increases firing rates to sensory stimuli.
Micheal Einstein

Pierre-Olivier Polack
visual attention
auditory attention
Membrane potential dynamics during a GO/NO-GO task
GCAMP6 Calcium Imaging: Visual Cortex Attention Task
Attention dependent effects on V1 activity
New Tools/ Future Directions

- Giant Cranial Window and Prism
- Development of New Miniaturized Microscopes.
Big Cranial Window and Prism

November 4, 2015
Bilateral, 6X8 mm

Chronic Optical Access
Coast-to-Coast imaging

Thy1-GCaMP6s transgenic mouse

Diverse neural dynamics across cortex

Mice described in Dana et al., PLOS ONE, 2014
Anterior (Motor)

Posterior

Bregma

Startle paradigm (sudden air puff to face)


Surface vasculature as landmarks

• imaged at 20x with 29 photon LSM,
• sequential imaging across the AP9 axis
• 500 um 2 FOV acquired every 300 um (resliced to form the cortex spanning image below)

Segmentation and Data Extraction using software from Pnevmatikakis et al.
Bilateral Access
East to West

Left PPC  RSC near midline  Right PPC
Left PPC
Left RSC
Open Source Miniaturized Microscope
miniscope.org
Figure 1: Drawings of our custom-designed miniaturized microscopes for calcium imaging in freely moving mice. The illumination is provided by an LED, focused through a GRIN lens, and imaged onto a miniaturized Aptiva sensor. Based on miniaturized microscopes developed by the Schnizter Lab.
CA1 hippocampal neurons during running
CA1 recordings by miniscope
Postdoctoral Fellows:

Pierre-Olivier Polack
Tristan Shuman
Jiannis Taxidis
Daniel Aharoni
Ben Huang

Graduate Students:

Michael Einstein
Maria Lazaro

Postgraduate Students:

Milad Javaherian
Christina Kaba
Jerry Lou

Undergraduate Students:

Pierre Bruneau
Aria Fariborzi
Ryan Manavi
Justin Daneshfar
Naina Rao
Michelle Azhdam
Kevin Chang
Pamela Guo
Mike Nedjat-Haiem
Danielle Dimacali
Duy Tran
Angela Avitua
Amelia Yates

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Tim Indersmitten
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David Chow
Ivan Soltesz
Csaba Varga
Matt Shtrahman
Stelios Smirnakis
Baljit Khakh
Jonathan Friedman
Sotiris Masmanidis
Andrey Mazarati
Carlos Portera-Cailliau
Carolyn Houser

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