

Optical stimulation evokes sustained activity in the isolated medial septum

Karolína Korvasová^{1,2}, Felix Ludwig³, Sanja Bauer Mikulovic³, Liudmila Sosulina³,
Stefan Remy^{3,4}, Tom Tetzlaff¹

¹ Institute of Neuroscience and Medicine (INM-6), Institute for Advanced Simulation (IAS-6) and JARA BRAIN (INM-10), Jülich Research Centre and JARA, Jülich

² RWTH Aachen University, Aachen, Germany

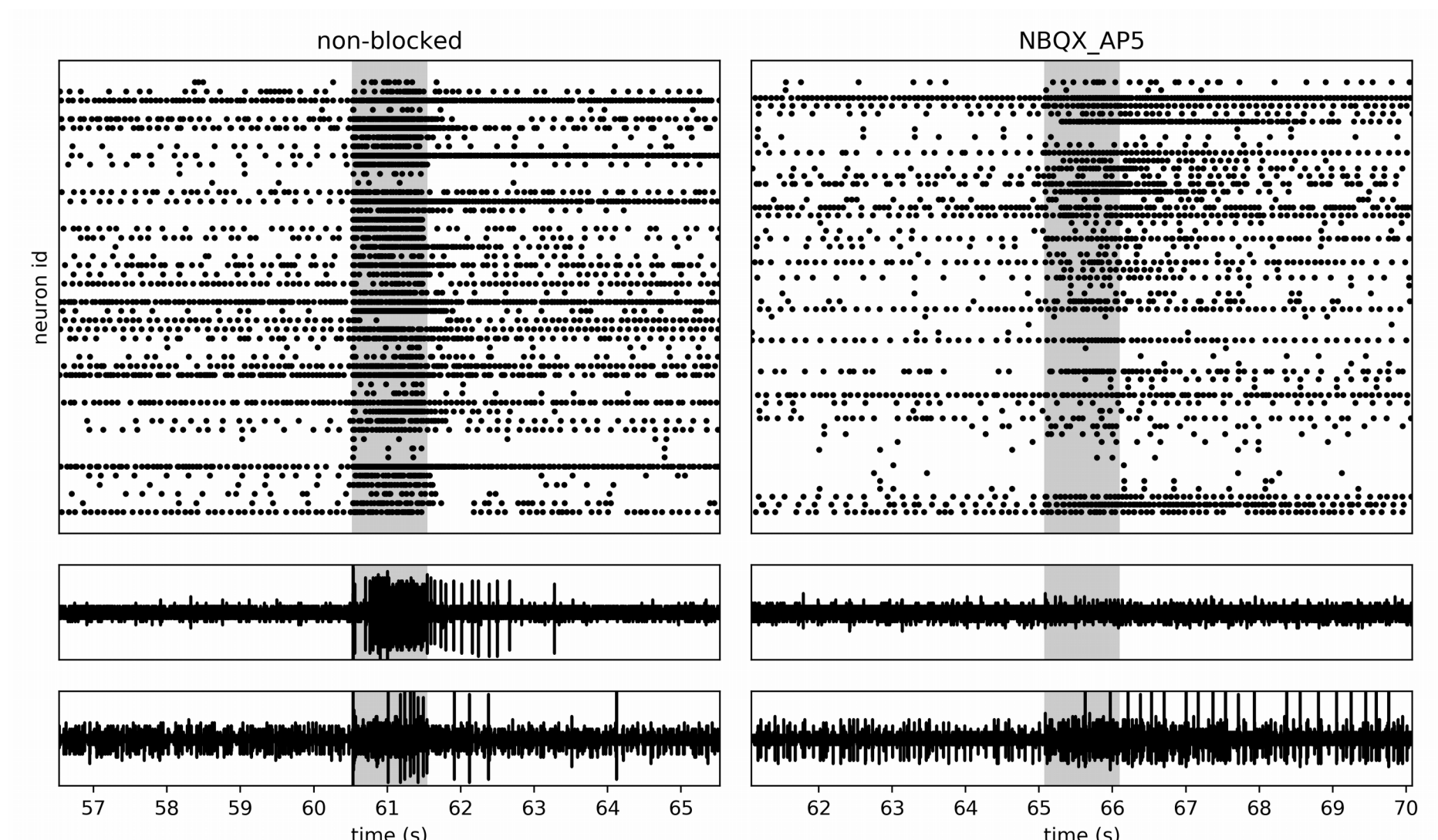
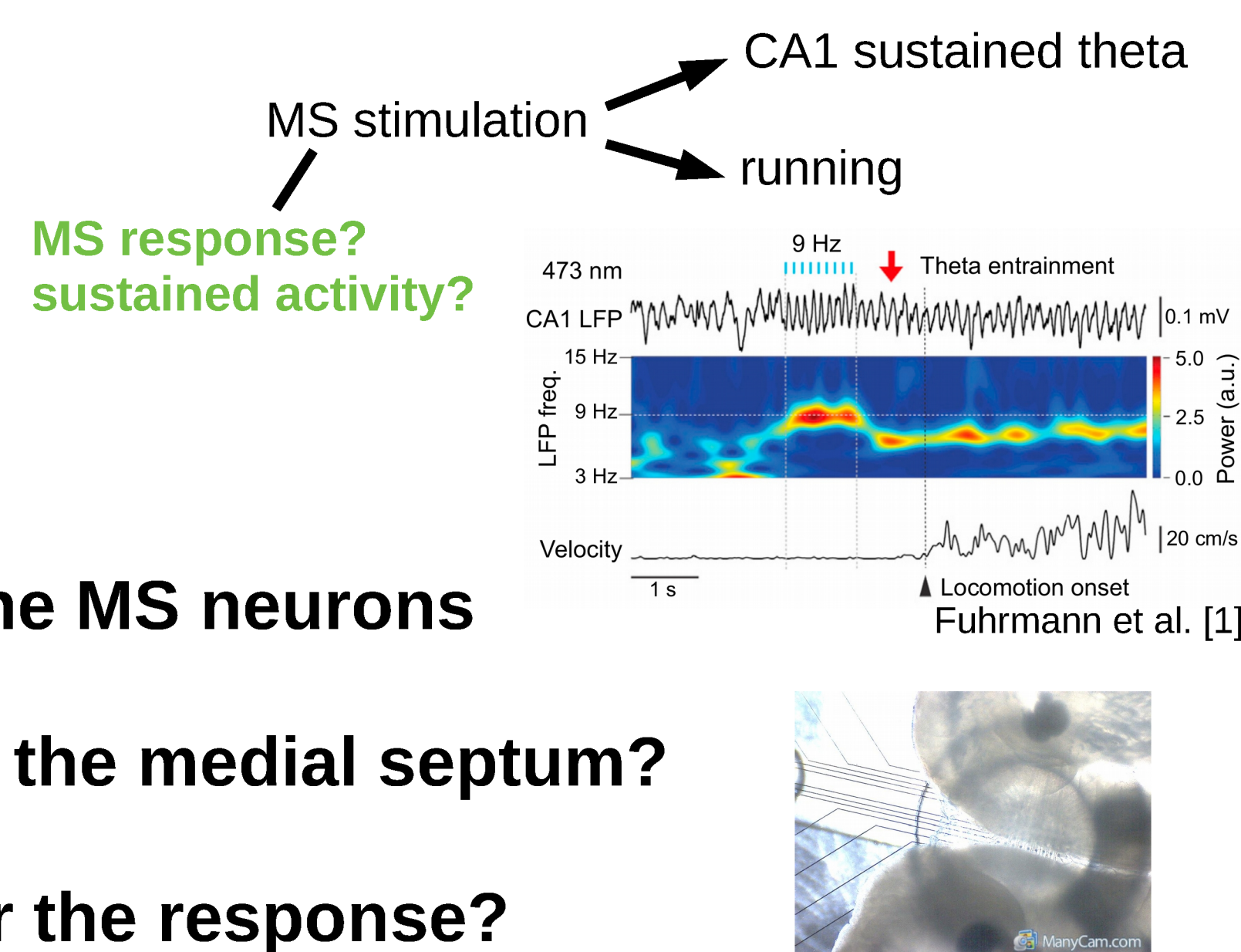
³ Neuronal Networks Group, German Center for Neurodegenerative Diseases, Bonn, Germany

⁴ Department of Epileptology, University of Bonn Medical Center, Bonn, Germany

Motivation

Optical stimulation of medial septal (MS) VGLUT2 neurons in vivo triggers sustained hippocampal theta oscillation and locomotion (Fuhrmann et al. [1]).

- What is the local response of the MS neurons to the stimulation?
- Do we see sustained activity in the medial septum?
- Do all of MS neurons respond?
- Is the MS network important for the response?

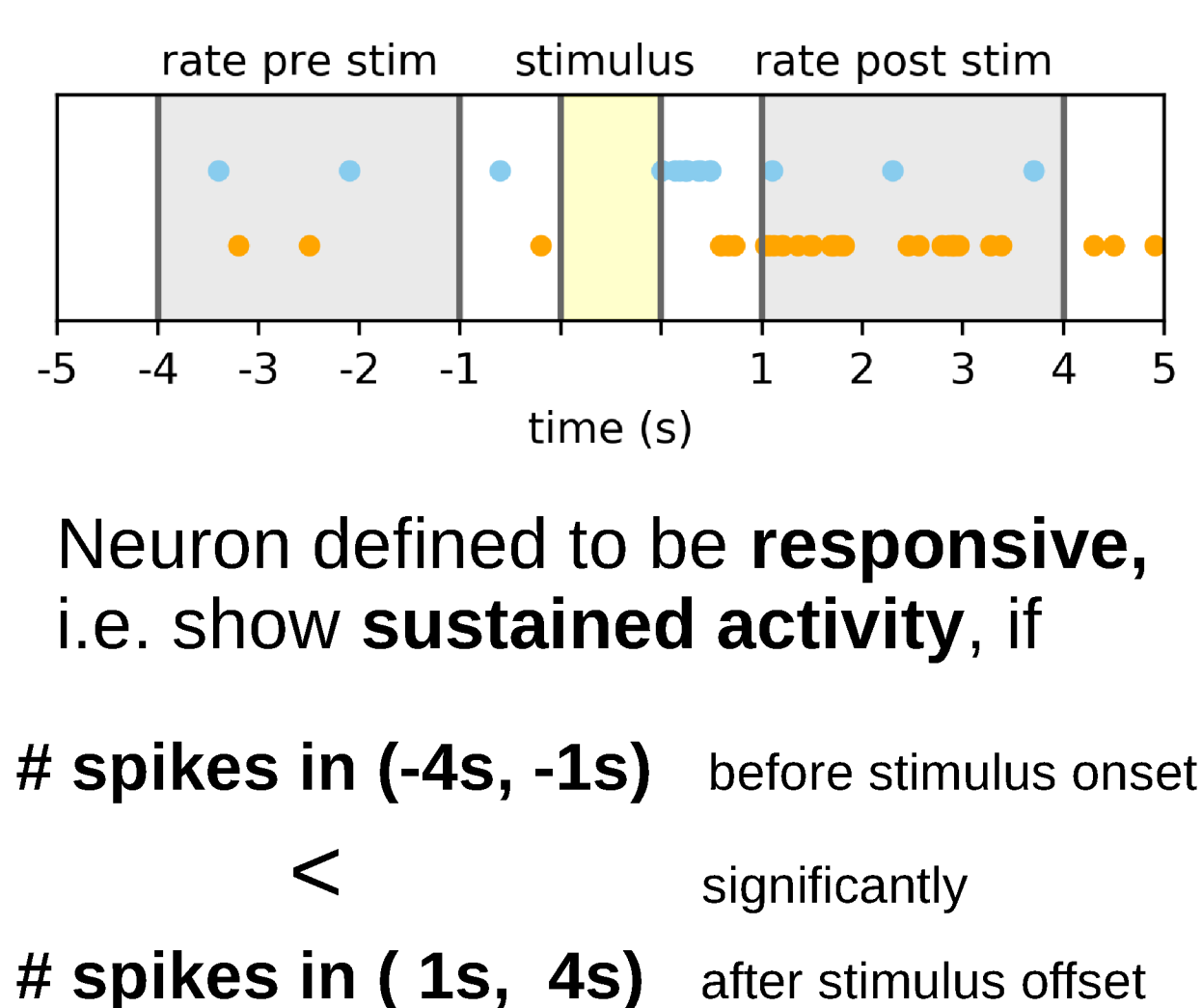


Activity of single units before, during and after 1s VGLUT2 continuous stimulation, and examples of potential traces high-pass filtered at 2000Hz.

Methods

- acute slices of mouse medial septum (MS): Channelrhodopsin (light-activated opsin) in VGLUT2-Cre and PV-Cre
400 μ m slice-preparation in sucrose
- MEA recordings:
6x10 electrodes with 100 μ m distance
- optical stimulation:
1 second (continuous, 9Hz, 6Hz, 3Hz)
0.9 Gain light intensity, 473 nm wavelength
- Conditions:
 - non-blocked
 - glutamatergic synapses blocked (NBQX, AP5)
 - GABAergic synapses blocked
- single units extracted using Mountainsort [2]

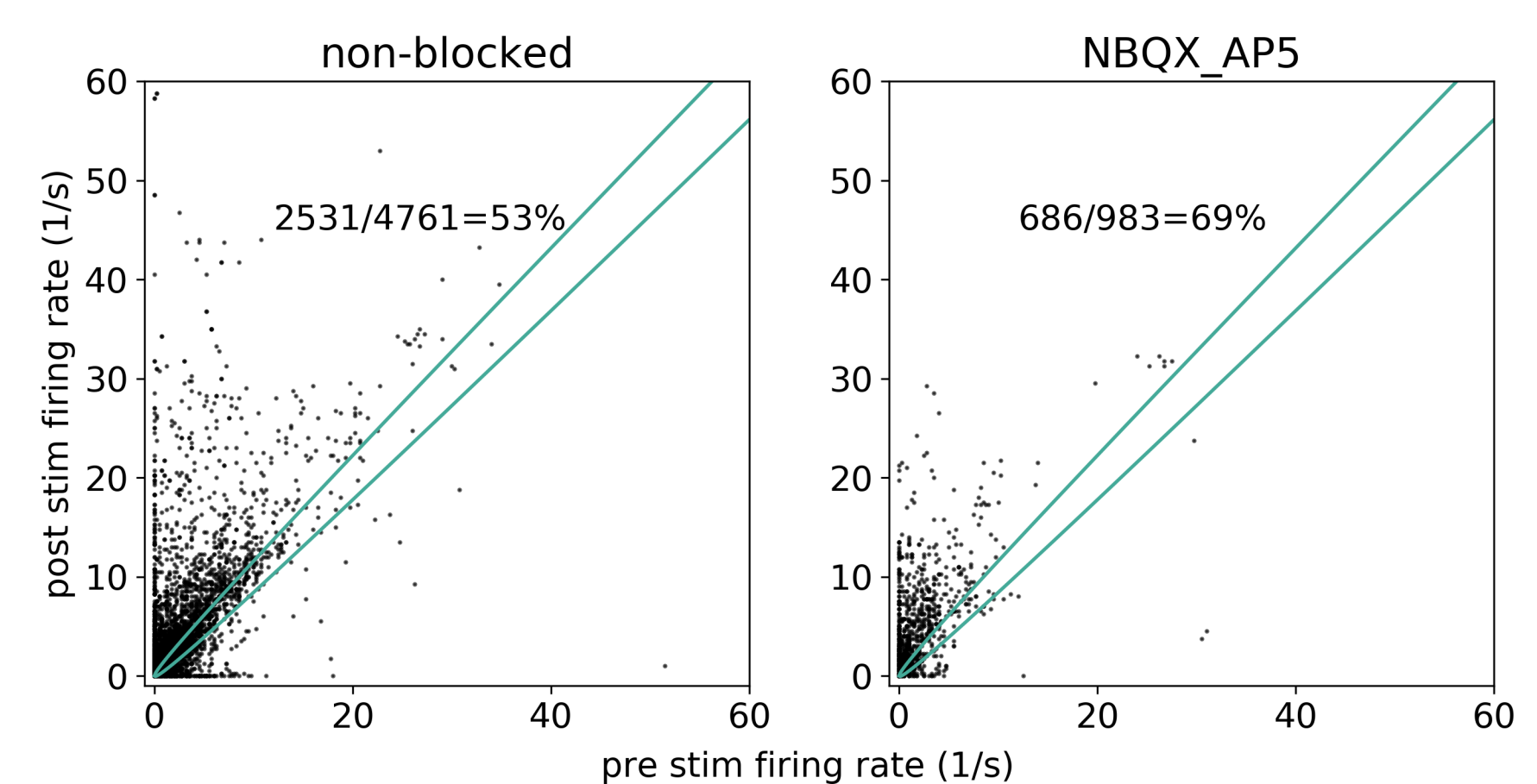
Sustained activity



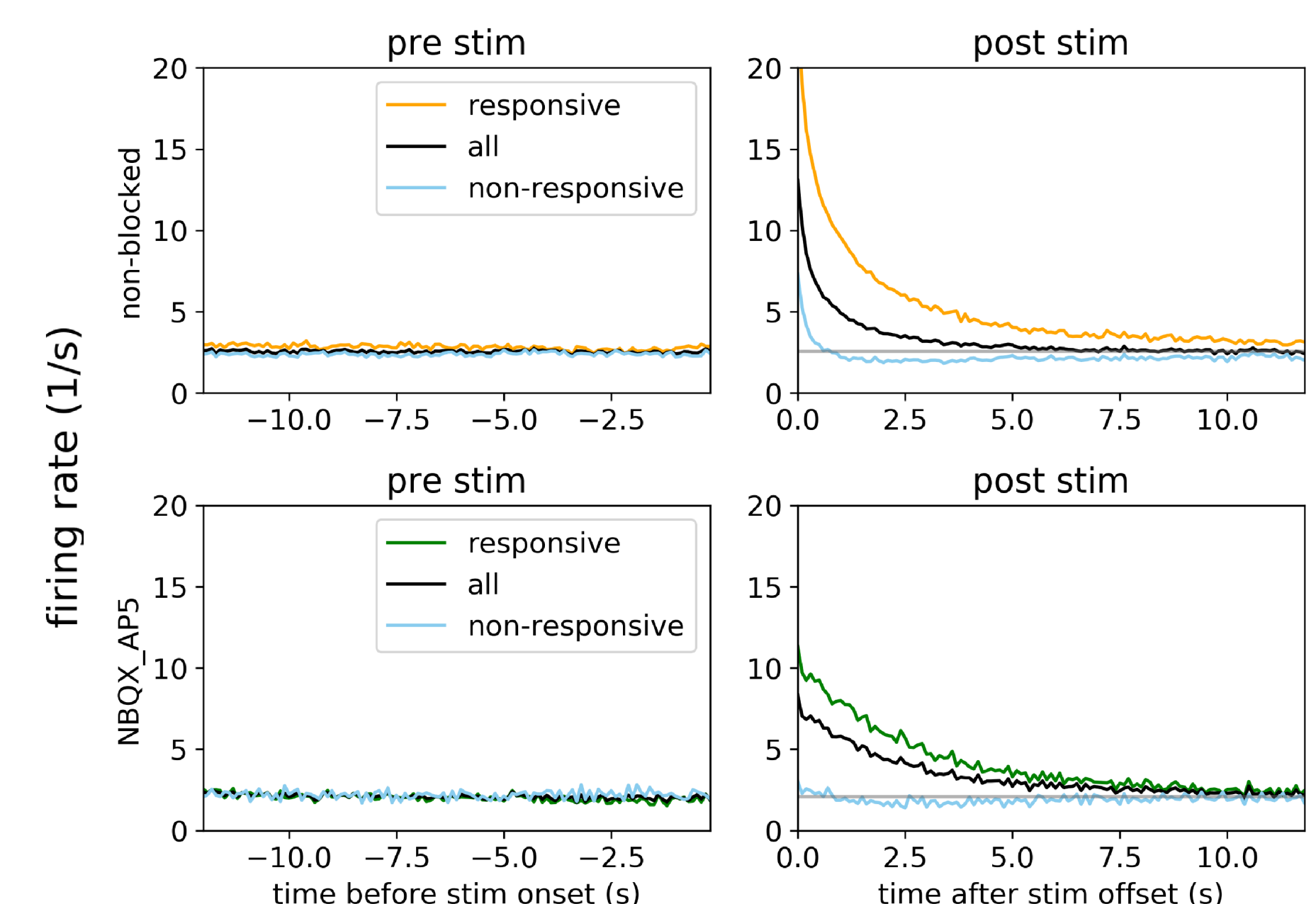
Neuron defined to be **responsive**, i.e. show **sustained activity**, if

$$\# \text{ spikes in } (-4s, -1s) < \# \text{ spikes in } (1s, 4s)$$

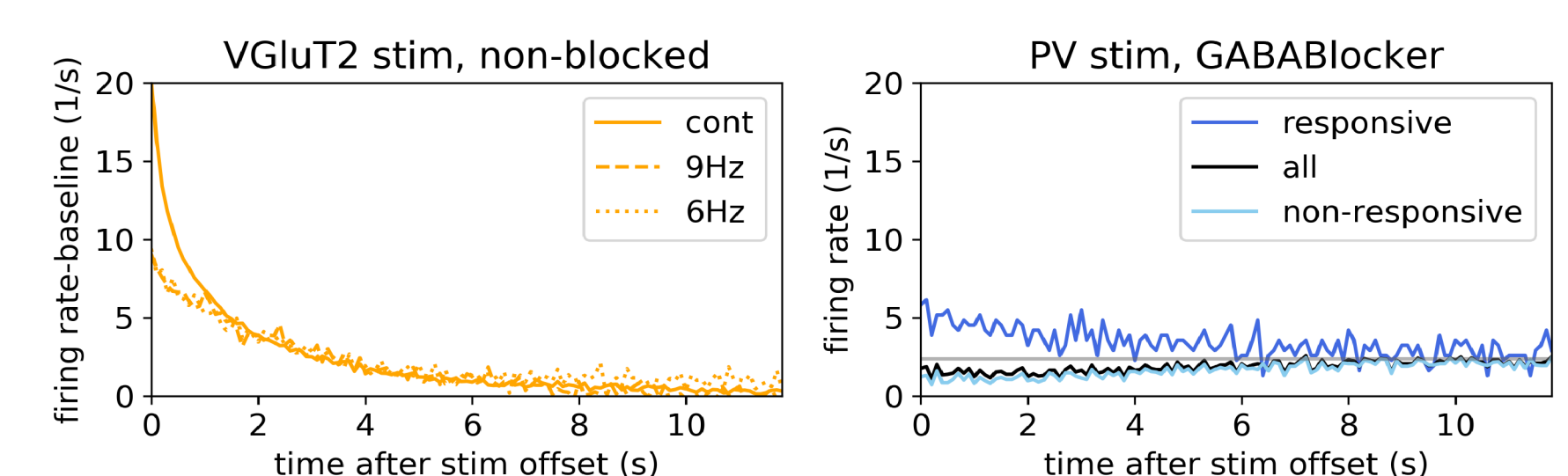
before stimulus onset
significantly
after stimulus offset



Firing rate before and after 1s VGLUT2 continuous stimulation. Blue lines mark regions with insignificant rate changes. Dots above this region correspond to responsive neurons.



Population-averaged activity before and after 1s continuous VGLUT2 stimulation.



Left panel: difference of population-averaged activity after stimulus from the baseline for different stimulation paradigms. VGLUT2 1s continuous stimulation, non-blocked network.

Right panel: population-averaged response to 1s continuous stimulation of PV neurons in a network with blocked GABAergic synapses.

Results

- Optical stimulation of VGLUT2 neurons triggers sustained activity (SA) in the isolated MS, even with blocked glutamatergic synapses.
- Not all MS neurons respond to stimulation.
- Sustained activity lasts for up to 10s (same timescale as sustained theta in the hippocampus).
- All types of stimuli evoke SA (6Hz, 9Hz pulses, continuous light).
- Stimulation of PV neurons does not evoke SA.

Conclusion

Isolated (coronal) MS slices can generate sustained activity, in the absence of input from other brain areas, and in the absence of glutamatergic connectivity within the MS.

References

- [1] Fuhrmann et al. (2015), Locomotion, Theta Oscillations, and the Speed-Related Firing of Hippocampal Neurons Are Controlled by a Medial Septal Glutamatergic Circuit, Neuron 86(5):1253-126
- [2] Barnett, Alex H., Jeremy F. Magland, and Leslie F. Greengard. "Validation of Neural Spike Sorting Algorithms without Ground-truth Information." Journal of Neuroscience Methods 264 (2016): 65-77