L4H SEMINAR: Two-photon optogenetics, shaping light in space and time for the precise study of neuronal circuits

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12:00 to 13:00
Auditorium & Online (Zoom)

Neuronal circuits are composed of hundreds of interconnected neurons that activate across the brain in complex spatial and temporal patterns. Understanding how neuronal circuits encode and process information to give rise to perception and guide animal behaviour is one of the greatest challenges in modern neuroscience, which requires novel methods specifically designed to address their enormous complexity.
In recent years the use of light has established itself as one of the most promising tools to study the brain, thanks to two main advances. First, genetically encoded calcium and voltage indicators enable to optically image neurons firing [1]. Second, optogenetics has provided

the key to activate or inhibit neurons with light [2]. To understand how neuronal circuits influence brain computations, we now need to develop specific optical methods capable of precisely targeting hundreds of neurons at will with high spatial and temporal precision, which is the objective of two-photon (2P) optogenetics [3].

In this presentation I will show that the spatial and temporal shaping of ultrafast laser beams, using spatial light modulators and computer-generated holography, is a powerful technique to selectively target tens of individual neurons within a dense ensemble through scattering tissues [4]. Next, I will demonstrate that micro-optical components, such as gradient index (GRIN) lenses [5], are ideal to extend 2P optogenetics to deep brain structures that cannot be accessed by standard microscopy because of scattering. Finally, I will summarize our recent efforts towards the development of a flexible micro-endoscope for the study of neuronal circuits in freely behaving animals [6]. By using bundles of optical fibers, carefully compensating for their dispersion, and exploiting intrinsic temporal decomposition effects, I will show that it is possible to perform sensitive and high-speed 2P imaging of neuronal activity and 2P optogenetic activation of tens of individual neurons at the tip of the fiber.

References

1. Knopfel (2012), Nat. Rev. Neurosci., 13, 1, DOI: 10.1038/nrn3293
2. Deisseroth (2011), Nat. Methods, 8, 26, DOI: 10.1038/nmeth.f.324
3. Emiliani et al. (2015), J. Neurosci., 35, 13917, DOI: 10.1523/JNEUROSCI.2916-15.2015
4. Accanto et al. (2018), Optica, 5, 1478, DOI: 10.1364/OPTICA.5.001478
5. Accanto et al. (2019), Sci. Rep., 9, 7603, DOI: 10.1038/s41598-019-43933-w
6. Accanto et al. (2022), Submitted.

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