OPTICAL CHARTING OF BRAIN-WIDE ACTIVATION MAPS
NEURON BY NEURON

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The ability to map neuronal activity patterns in the brain with single-cell resolution is a crucial technological step to afford a clearer view of brain activity and of its relation with long-range connectivity architecture. Despite a number of technological efforts, quantitative cellular-resolution activation maps of the whole brain have not yet been obtained. In fact, many state-of-the-art techniques are limited by coarse resolution or by a narrow field of view. High-throughput imaging methods, such as light sheet microscopy [1], can be used to image large specimens with high resolution and in reasonable times. However, the bottleneck is then moved from image acquisition to image analysis, since many TeraBytes of data have to be processed to extract meaningful information.

Here, we present a full experimental pipeline to quantify neuronal activity in the entire mouse brain with cellular resolution, based on a combination of genetics, optics and computer science. We used a transgenic mouse strain (Arc-dVenus mouse) in which neurons which have been active in the last hours before brain fixation are fluorescently labelled. Samples were cleared with CLARITY and imaged with a custom-made confocal light sheet microscope [1]. To perform an automatic localization of fluorescent cells on the large images produced, we used a novel computational approach called semantic deconvolution [2].

The combined approach presented here allows quantifying the amount of Arc-expressing neurons throughout the whole mouse brain. When applied to cohorts of mice subject to different stimuli and/or environmental conditions, this method help finding correlations in activity between different neuronal populations, opening the possibility to infer a sort of brain-wide ‘functional connectivity’ with cellular resolution.