Inferring dendritic and cortical neuronal assemblies during visual learning revealed with 3D random access microscopy

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Neural circuits in the visual cortex support rapid visual learning. However, due to technical roadblocks, it remains unknown how visual circuits represent multiple visual features of an environment during learning and how behaviorally relevant representations are selected for long-term memory. Here we developed Moculus, a head-mounted virtual reality platform for mice, which covers the entire visual field, allows binocular depth perception, and provides a fully immersive experience.

This highly naturalistic and controllable visual environment was combined with novel imaging and molecular biological technology. Namely fast acousto-optical imaging combined with genetically encoded calcium or voltage indicator, where especially for the latter one, the kHz imaging rate is essentially for reliable response detection. These methods afforded rapid visual learning uncovering novel circuit substrates of fast visual learning.

We find that sparse cortical representations encode visual cues initially. Then response amplitude and spatiotemporal extent of both the control and reinforcement-associated visual cue-coding neuronal assemblies increase. Finally, assembly activity representing the reinforced cue and the corresponding behavioral outcome selectively increases, indicating competition between different representations. During this competition, reinforced and control cues are represented by partially orthogonal and overlapping spatial clusters of neurons centered around hub cells, which have higher response amplitude, earlier response onset time, and locally increased functional connectivity. Thus, visual circuits can rapidly extend cortical representations during learning to maximize computational capability and allow competition between different assemblies to encode behaviorally relevant information.

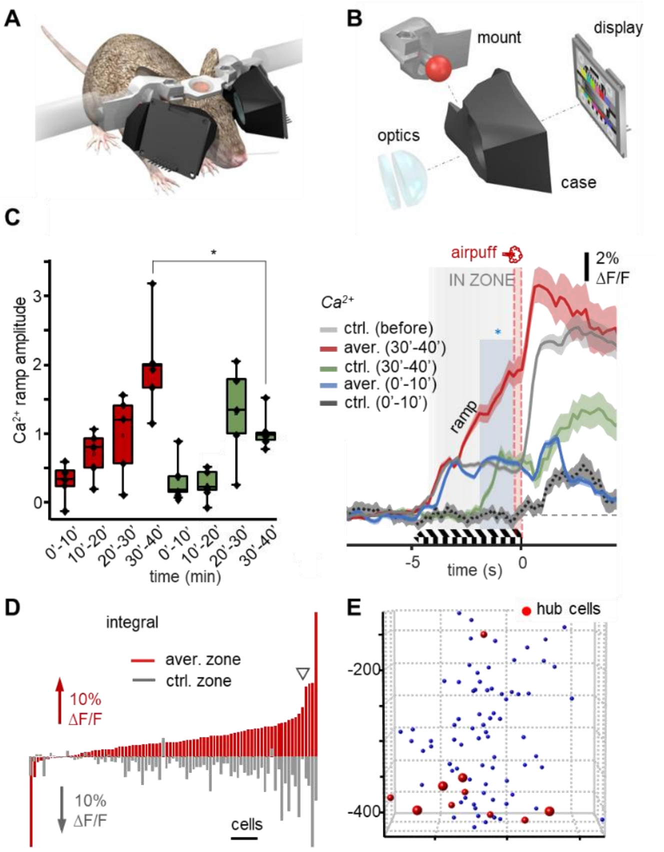

Figure legend (A) Schematic of Moculus with a head-fixed mouse. **(B)** 3D exploded view of the left side of the Moculus. **(C)** Ca^{2+} responses during aversive conditional training. Right: Average (mean±SEM) neuronal responses at the beginning (0-10min), and end (30-40min) of the fast visual learning in the aversive zone (‘aver’) and in one of the control zones (’ctrl’). The ramp-like population component was present after learning in both zones and was significantly larger in the aversive zone than in the control zone. Left: Ramp amplitudes integrated from -1 s to -0.4 s in the aversive (red) and control (green) zones as a function of time of learning. Asterix indicated a significant difference. **(D)** Integrals of the 3D Ca^{2+} responses for the individual cells at the end of the aversive and control zones. Neurons were sorted according to their response amplitude in the aversive zone. Triangle indicates a jump in the amplitude distribution. Note the weak correlation and amplitude fluctuation in neuronal responses between the aversive and the control zones. **(E)** Ten neurons from panel D with the largest response amplitude at the end of the aversive zone formed spatial clusters (hub cells, red spheres).

Balázs Rózsa was a student at two universities at the same time. In 2001 he graduated from the Faculty of Natural Sciences of Eötvös Loránd University with a degree in physics, mathematics and biophysics, and in 2007 he completed his PhD studies summa cum laude in Neurosciences at Semmelweis University.

Since 2002 he has been involved in research at the MTA KOKI. From 2005 to 2008 he was leader of the two-photon microscope development team, since 2008 he has been leader of the three-dimensional two-photon microscope development team. Since 2010, he is the Head of the Two-photon Imaging Laboratory at Pázmány Péter Catholic University and works at the KOKI Two-photon Imaging Centre. In the latter, he has been the head of the Neuronal Networks and Dendritic Activity Research Group since 2016.

His research covers a very broad range of expertise, ranges from IT, electronics, optics and mechanical engineering to a broad knowledge of laser physics, laser scanning, nonlinear optics and neural network imaging. His scientific interests include dendritic signal integration studies, fast 3D two-photon imaging and electrophysiological measurements in in vitro and in vivo experiments.

Since 2007, he has been the topic leader of numerous national and international scientific proposals. He has authored and co-authored dozens of national and international scientific publications and given nearly half a hundred international presentations.

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