Microfluidic system for on-demand imaging of neural dynamics in organotypic brain slices

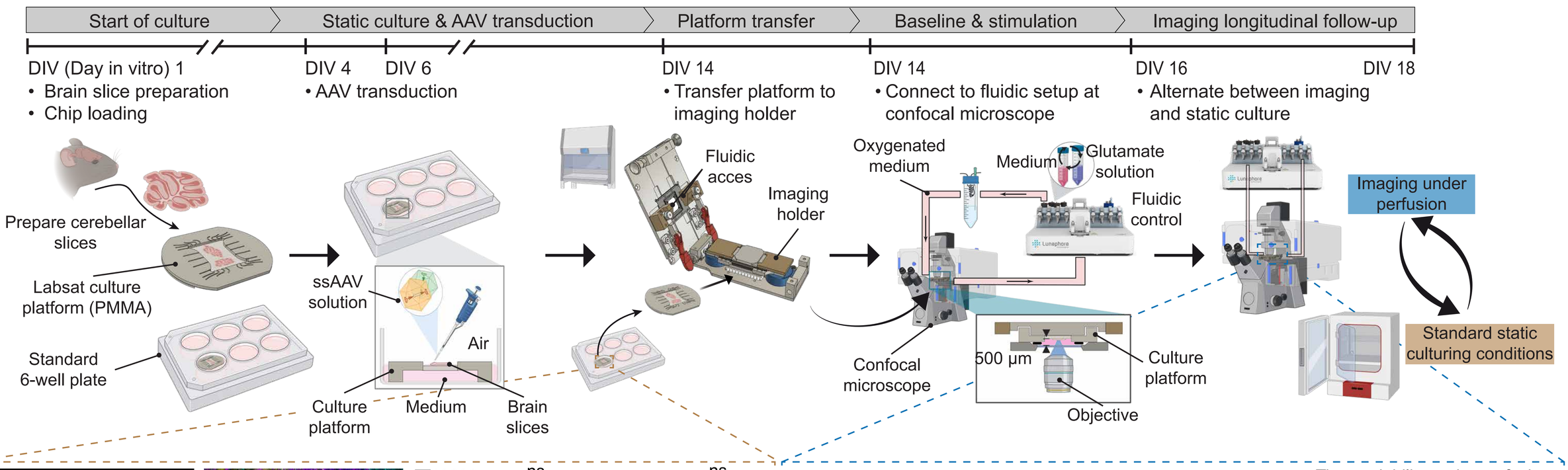
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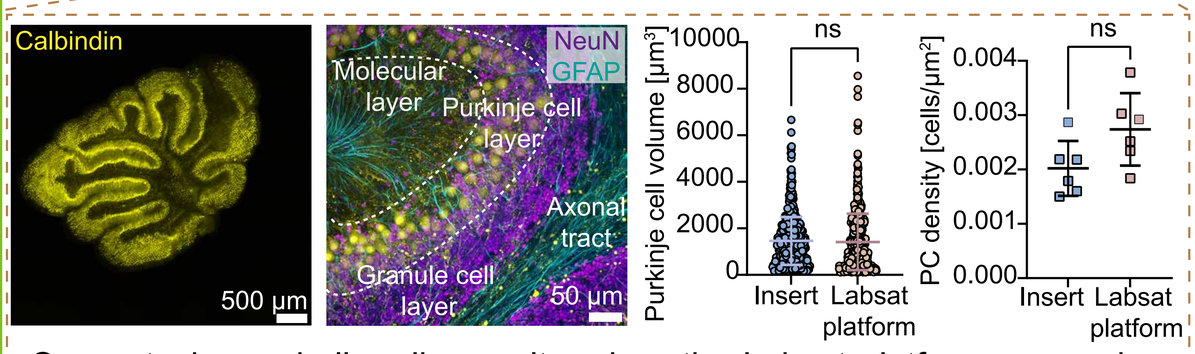
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Abstract

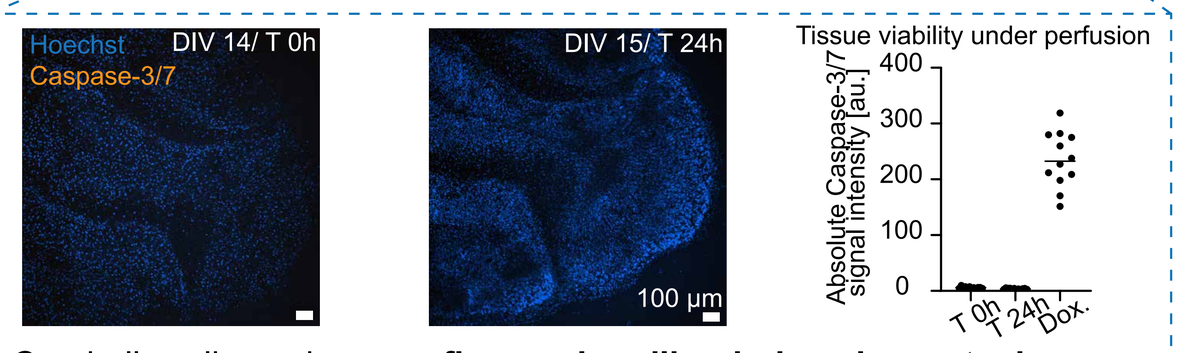
Organotypic brain slice cultures (OSCs) provide a physiologically relevant model to recapitulate the complex brain cytoarchitecture in vitro, as they preserve native cell heterogeneity, cytoarchitecture, and intrinsic chemical signalling. Brain-tissue slices require culturing at the air-liquid interface (ALI), typically achieved with membrane-based tissue inserts. However, these inserts restrict high-resolution optical access, thereby severely limiting the study of dynamic processes. To overcome these limitations, we have developed a culture platform that is compatible with standard culturing conditions in 6-well plates. For live-cell imaging, the platform was integrated into a modified version of Lunaphore's Labsat instrument, enabling improved user friendliness of flow protocols, including compound exposure. In proof-of-concept experiments, we exposed cerebellar slices to various glutamate concentrations and investigated Purkinje cell and astrocyte morphology, as well as calcium dynamics at baseline, during acute exposure, 48 h and 96 h after stimulation.

Platform design for ex vivo brain-slice culturing and live-cell imaging





Organotypic cerebellar slices cultured on the Labsat platform reorganize into an **intact cerebellar environment**, maintaining the spatial organization of **neuronal and glial cells.**



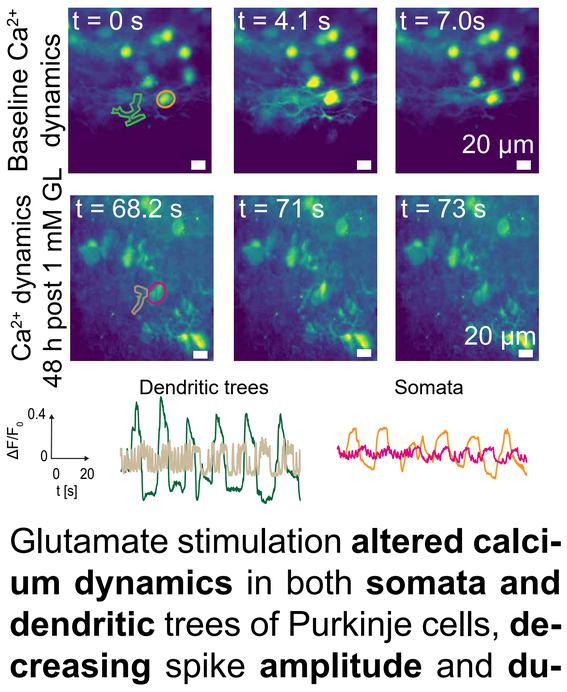
Cerebellar slices show **no flow or handling-induced apoptosis,** even when exposed to continuous flow for 24 h.

Platform key features

- No post-placement handling
- Flexible experimental workflow
- Automated compound exposure
- Full environmental control

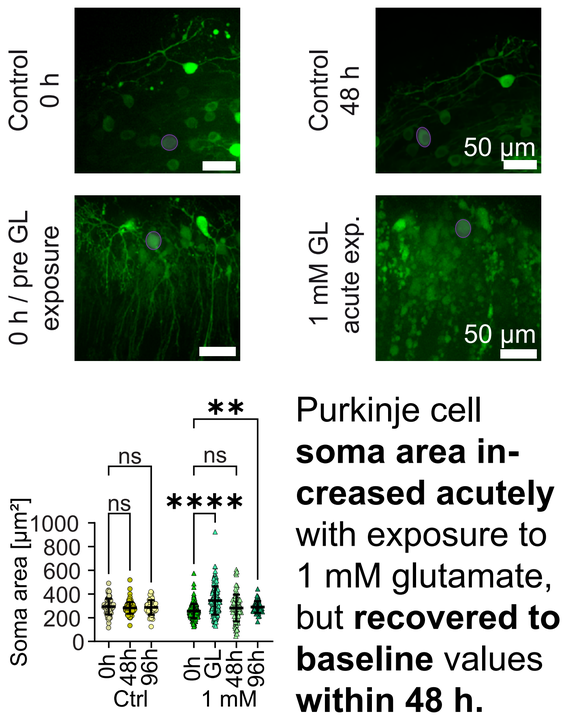
Long-term effects of glutamate stimulation in Purkinje cells and cerebellar astrocytes

Purkinje cell activity



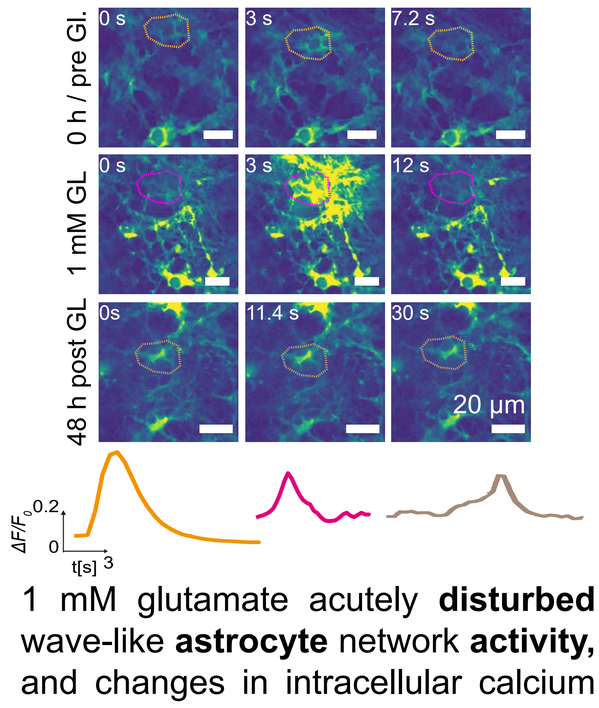
Glutamate stimulation **altered calcium dynamics** in both **somata and dendritic** trees of Purkinje cells, **decreasing** spike **amplitude** and **duration**.

Purkinje cell morphology



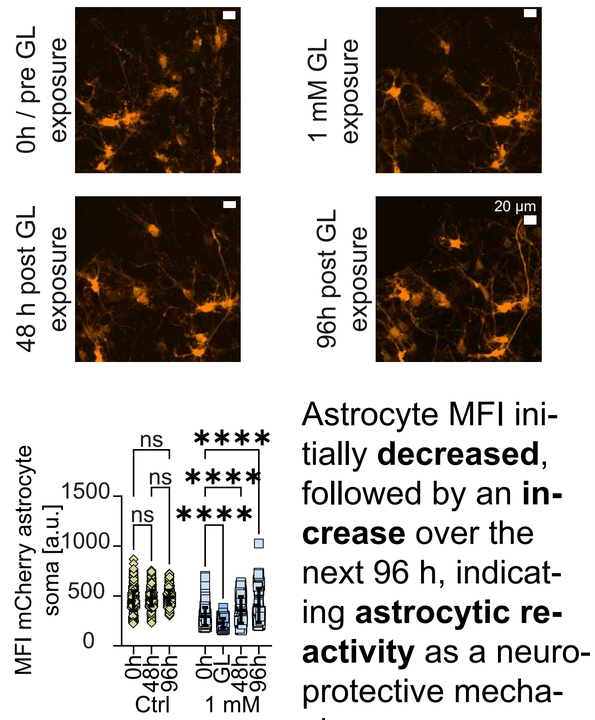
Purkinje cell **soma area increased acutely** with exposure to 1 mM glutamate, but **recovered to baseline** values **within 48 h.**

Astrocyte activity



1 mM glutamate acutely **disturbed** wave-like **astrocyte** network **activity,** and changes in intracellular calcium dynamics were not recovered in 96 h.

Astrocyte morphology



Astrocyte MFI initially **decreased**, followed by an **increase** over the next 96 h, indicating **astrocytic reactivity** as a neuroprotective mechanism.

Conclusion and outlook

We validated the suitability of the developed platform for automated compound exposure, combined with longitudinal follow-up of morphological and functional effects, by exposing cerebellar slices to different glutamate concentrations. Our system enables mechanistic studies in a physiologically relevant context.

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