

NEUROSCIENCE

Automated brain mapping

A computational framework enables automated annotation, analysis, and sharing of mouse brain data at single-cell resolution.

Advances in imaging have made it possible to produce cell-type-specific connectivity maps at the whole-brain scale. However, methods for registering labeled neurons and fiber tracts to standard atlases have remained rudimentary—currently this mainly relies on manual inspection, which is time consuming and error prone. To overcome this bottleneck, a research group led by Konstantinos Meletis at Karolinska Institute developed a computational framework that automatically registers and analyzes labeled cells at the whole-brain scale (<http://wholebrain-software.org>). In addition, the researchers developed tools for visualization and sharing of data (<http://openbrainmap.org>).

Central to this computational framework is an interactive reference atlas of the adult mouse brain. The researchers extracted ana-

tomical definitions from the Allen Mouse Brain Atlas, and they generated a reference atlas in which brain regions are represented as smooth curves and surfaces instead of as pixels. This new atlas can be applied to images of any pixel resolution. Furthermore, atlas intersections are versatile and not limited to coronal or sagittal planes.

The computational framework can automatically map any light-microscopy-derived images onto this reference atlas and detect features such as fluorescently labeled cell bodies and fiber tracts with minimal human input. It also supports further data analysis, such as automated cell counting, and quantification of gene expression at the single-cell level. As an example, the researchers used this approach to analyze brain sections in which different types of interneurons were fluorescently labeled, and they showed that the system can reliably differentiate various cell types based on marker expression, pinpoint

the position of each labeled cell, and quantify the distribution of neuron types across different brain regions.

The researchers applied this approach to analyze large data sets from rabies virus tracing experiments, and they mapped the anatomical localization of neurons presynaptic to five major neuron types in the corticostriatal circuit. Furthermore, they mapped whole-brain *c-fos* expression following acute cocaine administration and identified the orbital cortex as a major corticostriatal hub that underlies cocaine-induced increase in locomotion.

The framework is available as an open-source R package, and it could be a useful tool for analyzing whole-brain data on neuronal identity, circuit, and function.

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RESEARCH ARTICLES

Fürth, D. *et al.* An interactive framework for whole-brain maps at cellular resolution. *Nat. Neurosci.* **21**, 139–149 (2018).