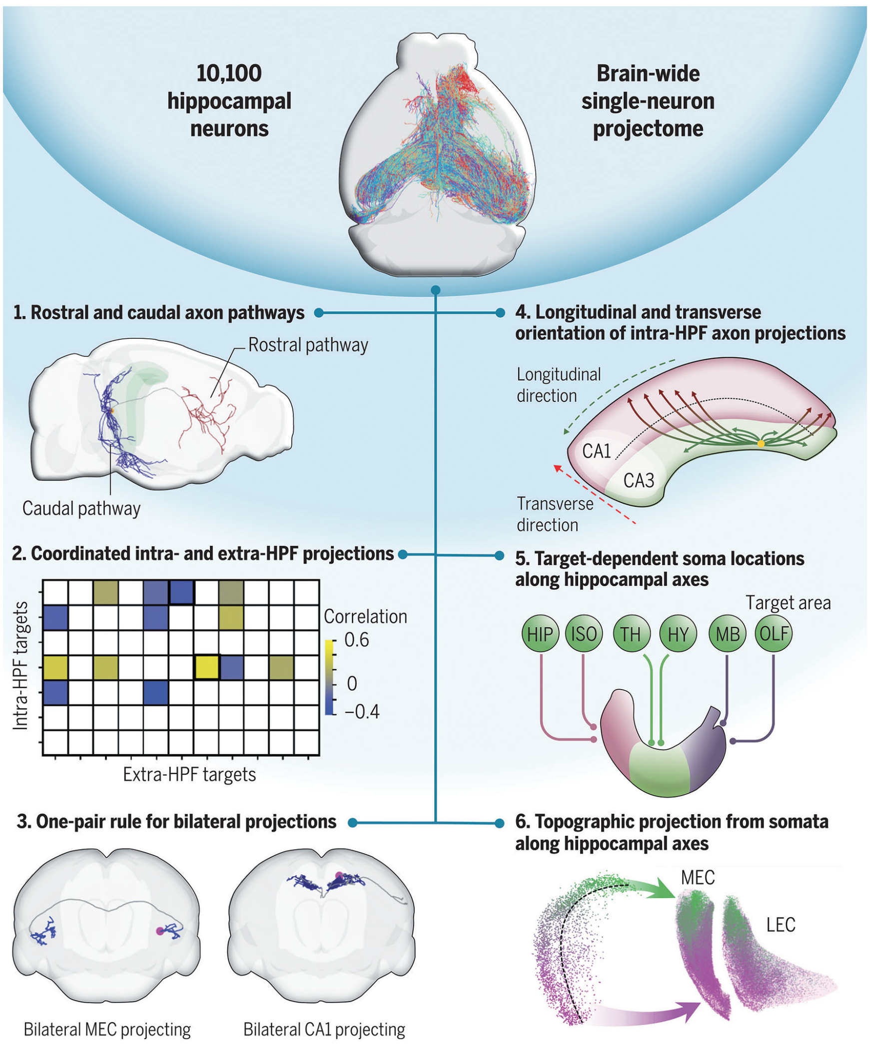
Unveiling the Whole-Brain Projection Patterns of Single Neurons in the Mouse Hippocampus

A study published in *Science* on February 2 revealed the spatial connectivity patterns of over 10,000 mouse hippocampal neurons at the mesoscopic level.

The study was conducted by teams from the Center for Excellence in Brain Science and Intelligence Technology (CEBSIT), the Institute of Neuroscience (ION) of the Chinese Academy of Sciences (CAS),



Schematic diagram depicting the spatial organization principle for hippocampal single-neuron projectomes. (Credit: CHEN Shishuo) the HUST-Suzhou Institute for Brainsmatics, Hainan University, the Kunming Institute of Zoology of CAS, Lingang Laboratory, and the Shanghai Center for Brain Science and Brain-Inspired Technology.

The hippocampus is an essential brain region for learning, memory, and various brain functions such as spatial cognition and emotional processing. It is one of the most extensively studied brain regions. Hippocampal neurons project widely to brain-wide targets; thus, it is critical to investigate the projection patterns of hippocampal neurons at the single-neuron level.

This study reconstructed the whole-brain axonal morphology of over 10,000 neurons in the mouse hippocampus at a single-cell resolution. The neuronal cell bodies covered all subregions and multiple locations along different hippocampal axes, making this the most extensive single-neuron projectome database in the world.

This study took an innovative approach to categorize axonal trajectories with machine learning algorithms. Thus, it allowed for a more efficient analysis of the morphological similarities among 341 projection patterns for mouse hippocampal neurons and ultimately identified 43 distinct projectome cell types. It also incorporated the spatial transcriptome of mouse CA1 areas.

Based on these analyses, the study was able to elucidate the axonal projection pathways of hippocampal neurons along the anterior-posterior axis and reveal new projection patterns of hippocampal neurons. It also outlined the correspondence between hippocampal neuron soma locations and projection targets and revealed basic organization principles of bilateral projections. Furthermore, correlation analysis of projectome cell types and spatial transcriptome data identified spatial correspondence between various genes and projectome subtypes, providing potential molecular and circuit targets for hippocampal functions.

This study provides a structural basis for future studies of hippocampal functions and deciphers the potential correspondences between their soma locations, gene expression, and circuitry functions.

The hippocampal single-neuron projectomes database, along with the database on the hippocampal longitudinal axis and spatial transcriptomes, is now freely accessible through the Digital Brain CEBSIT portal (https://mouse.digital-brain.cn/hipp). To facilitate broader usage of the databases, a team from the Computing and Data Center of CEBSIT has developed a website to integrate data visualization, user interface, online analysis, and data downloads.

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(Source: ION)