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Development of commercially viable software for the automated whole-brain mapping of fluorescently labeled cells

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Background

The ability to perform rapid and reproducible brain-wide analysis has been the holy grail of neuroscience since the dawn of the era of modern microscopic techniques. Neuroscience labs the world over use fluorescent microscopy to quantify cellular changes in highly specific brain regions of interest. Such quantification is extremely time consuming and fraught with potential for bias and error. Moreover, most labs typically limit their analysis to only a few regions of interest, omitting brain-wide analysis that could move the brain sciences forward by leaps and bounds. Thus, a major unmet need in the field is the wide-spread capability to perform rapid, reliable and unbiased whole-brain mapping.

To investigate the function of brain circuits, it is essential to generate maps of neuronal connectivity on a wholescale. A major obstacle to this is the time it takes to collect and analyze the data in the entire brain. As computer and software technology progresses, the possibility to perform automated, computerized analysis has crept into the realm of reality. Public and private entities have dedicated extensive resources to achieving this vision. Imaging and computation methods currently allow large-scale mapping of rodent brain at cellular resolution, but such methods are not scalable to individual labs. Thus, a scalable technology that combines fluorescent imaging and computational methods to automatically acquire and analyze individual neurons in the whole brain remains elusive.

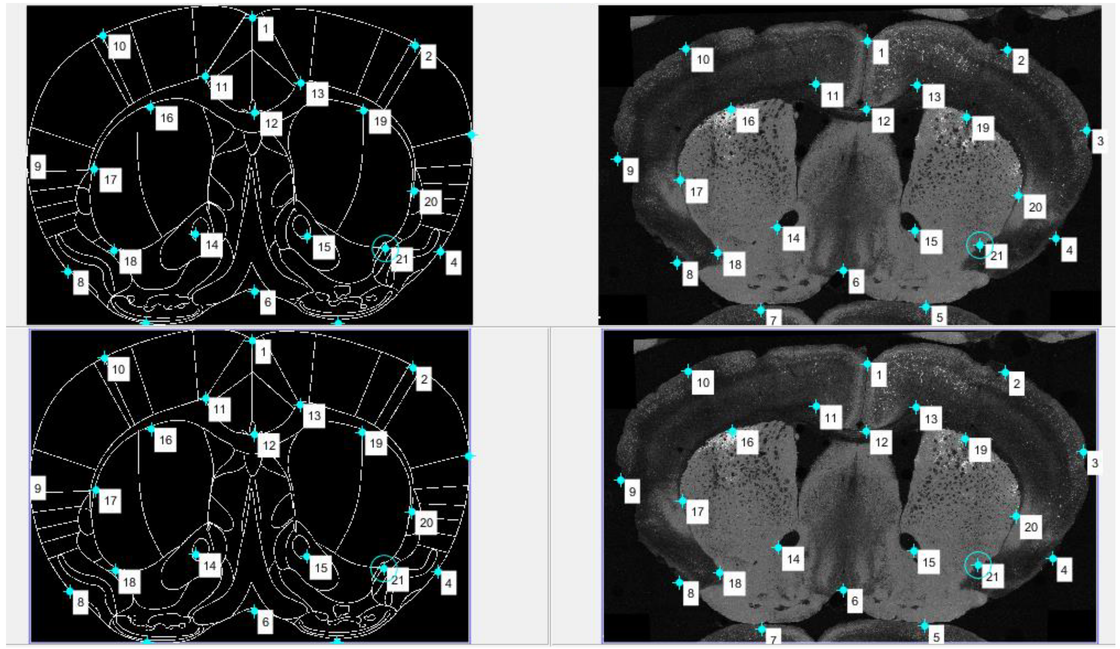
Approach

Through a multi-disciplinary collaboration, we have developed a working proprietary software prototype that enables us to automatically acquire, detect and analyze fluorescently-labeled brain cells throughout the entire brain of rodents (Fig. 1). Confocal microscopy is used to acquire fluorescent-labeled cells of the whole mouse brain at cellular levels. Our proprietary software automates the comparison of our captured images to existing neuroanatomical atlas databases. The software coordinates the matching of the distinct anterior, posterior, rostral and caudal planes of the captured images with those of the existing neuroanatomical maps. The software then performs image warping to accurately align the captured image with the existing neuroanatomical maps. This alignment allows the software to accurately define over 100 distinct neuroanatomical regions. Finally, the program quantifies the fluorescent neurons within each of the >100 distinct anatomical sub-regions in the reference atlas and exports the data into excel files. This software has enormous commercial potential, the ability for widespread use in individual labs and is scalable to the largest of labs, including a potential for the automated pathological analysis of human brains and organs, and brains and other widely used and defined experimental organisms.

We have initiated this project, in order to improve the error coefficient, and further develop a commercially viable product, we are looking for support and collaboration. Once this project is completed, we envision it will be in high demand by neuroscience labs the world over. We further envision interest from commercial entities, and we have received initial support from the TAMU office of Technology Commercialization. We strongly believe the approach will significantly facilitate neuroscience research and has a legitimate potential to generate funding and recognition to the \University and the Investigative team.

Technology

Current methods of brain mapping are either manual, or are incomplete, semi-automated processes. Existing methods are extremely time-consuming and inefficient, often taking months to collect data from only one or two out of over 144 distinct brain regions. There are over 144 different brain regions, and mapping the entire brain at a cellular level would require thousands of hours for a single brain. Our innovative software automates the process of segmenting and quantifying cells in an entire brain, in minutes, saving countless hours, and providing exponentially more data from each sample.
The software incorporates feature-based and data-driven methods. It combines feature engineering, image processing and unsupervised machine learning paradigms to overcome previous roadblocks to achieving fully-automated, brain-wide maps at the cellular level.



This image shows the registration process that is based on our custom algorithm that allows our captured image to be proportionately scaled and matched to the corresponding neuroanatomical atlas. Once registered, the software quantifies the numbers of cells in all brain regions and exports them to a spreadsheet.

Advantages

- **Cost Effective**: While competing software allows user-assisted analysis of specific regions, the competing software is cost-prohibitive, very time-consuming, and does not perform brain-wide analysis.
- **Time**: this software can complete analysis of an entire brain in minutes
- **Automatic**: this software requires minimal user input for the analysis

Applications

- Neuroscience (clinical, translational, basic, academic)
- Automate pathological/radiological data analysis and diagnosis (clinical, translational, basic, academic)

Stage of Development - Technology concept and/or application formulated; beta testing ongoing

Patent Status - U.S. patent application discussed; funding is needed to fully test and refine software