Challenges of imaging human brain sections with Light Sheet Microscopy

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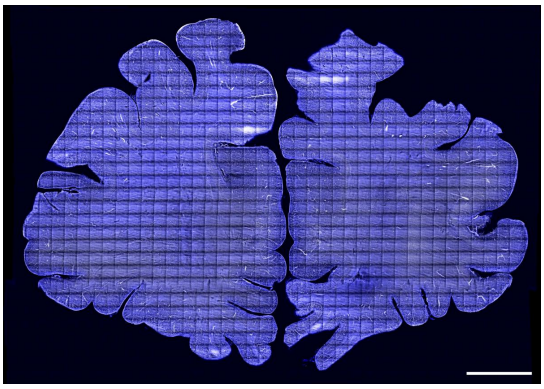
Abstract

Light Sheet microscopy allows us to image fluorescent probes in whole cleared organs. ALICe (Advanced Light-sheet Imaging Center) at the Wyss Center in Geneva has developed expertise in imaging the whole mouse brain with mesoSPIM and COLM light-sheet systems. Those imaging devices using orthogonal illumination are however no suitable to image large human brain sections. We therefore had to adapt new imaging strategies to cater for this type of need.

The challenge was to image from 1 cm thick human brain sections to investigate pathological biomarkers distribution. The Lamylab at University of Geneva developed a custom tissue clearing and labelling protocol adapted to pathological human brains preserved for decades in fixative at the Geneva Brain Bank. To image those large sections without constraints on the lateral dimensions of the sample, we opted for a theta lightsheet microscope design (ClearScope®, MicroBrightfield). After ensuring the proper calibration of the instrument, we ran tests on smaller human brain samples. This led us to multiple round of optimization of the software and hardware to produce accurate imaging. To scale up to full brain section, we designed a custom brain section holder that can keep the sample steady for multi-day acquisition times. To facilitate the transfer, storage and post-processing of the multi-terabytes imaging datasets generated by the microscope, we adapted a size-reduction software tool, based on Adaptive Particle Representation, which we run on-the-fly during the data collection.

This paper will outline the challenges and opportunities of imaging large human archival tissue samples. We will also discuss the ways to optimize those emerging methods.



Max intensity projection of APR transformed 50 planes of 2 merged acquisitions of the Alzheimer's disease frontal cortex 1cm thick section cleared and labelled with lectin (blue) and amyloid β-plaques (white) Scale bar: 1cm.

References

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