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Dear editor,

We wish to submit a new manuscript entitled “*Comprehensive optical and data management infrastructure for high-throughput light-sheet microscopy of whole mouse brains*” for consideration for publication in the Journal of Neurophotonics for its special issue on “Light Microscopy of Connectivity” in Oct.-Dec. 2015.

In this paper, we report on a comprehensive and streamlined framework for fast, high-throughput acquisition of whole-brain data sets with light-sheet microscopy. This is significant because the mapping and quantification of neuronal projections in structurally intact mouse brain requires novel methodology and tight integration of all links in the imaging chain. The paper should be of interest to readers in the areas of neuroanatomy, light microscopy development and computational methods for the management of optical measurements yielding very large data sets.

Here we present a complete and detailed framework for whole mouse brain imaging. Starting with a full description of our double-sided light-sheet microscope and its constituent components we further give details of the custom-written control software which coordinates the microscope's reliably synchronised operation. The data produced in our experiments easily amounts several TB per data set and needs to be compressed, stored, transferred, retrieved and processed necessitating the concurrent development of novel computational interface and analysis methods. Here we present a comprehensive, robust and fully automated pipeline of data management starting from the streaming of raw images up to the stitching of 3D data sets. The meso-scale neuroanatomy imaged at micron-scale resolution in those data sets allows characterization and quantification of neuronal projections in unsectioned mouse brains.

We believe this paper is of Neurophotonics standard, fits the scope of light microscopy for the elucidation of connectivity and brings novel methodology in an area of broad interest. I confirm that this work is original and has not been published elsewhere nor is it currently under consideration for publication elsewhere.

Please address all correspondence concerning this manuscript to me at: francesco.pavone@unifi.it.

Thank you for your consideration of this manuscript.

Yours faithfully,

Francesco Saverio Pavone