CNR-INO

LENS European Laboratory for Non-Linear Spectroscopy

AUTOMATED LIGHT-SHEET MICROSCOPY

EUROPEAN LABORATORY FOR NON-LINEAR SPECTROSCOPY

A NEW MICROSCOPY PARADIGM FOR QUANTITATIVE ANALYSIS OF 3D SAMPLES

TECHNOLOGY DESCRIPTION

We have devised a complete pipeline of light-sheet microscopy, encompassing sample clearing and staining, fully automated high-resolution high-speed imaging, and teravoxel image processing. The microscopy pipeline makes it possible to analyse macroscopic tissue samples at sub-cellular resolution. Our system has two fundamental advantages: first, imaging quality is always kept high thanks to automated feedback systems for light-sheet stabilization and autofocusing. Second, a dedicated set of software tools enables management and effective access to teravoxel-sized images, allowing subsequent data analysis.
Competitors do not provide any active stabilization of the light sheet, requiring continuous adjustment of imaging parameters by the user. On the other hand, they also do not provide links between imaging system and image analysis tools.

TIGHT INTERCONNECTION BETWEEN IMAGING SYSTEM AND IMAGE ANALYSIS TOOLS ENABLES EFFECTIVE MANAGEMENT OF TERAVOXEL-SIZED IMAGING DATASETS

FULLY AUTOMATED MICROSCOPY ENABLES SCALABLE 3D ANALYSIS OF BIOLOGICAL TISSUES FOR RESEARCH AND CLINICAL PURPOSES

AREAS

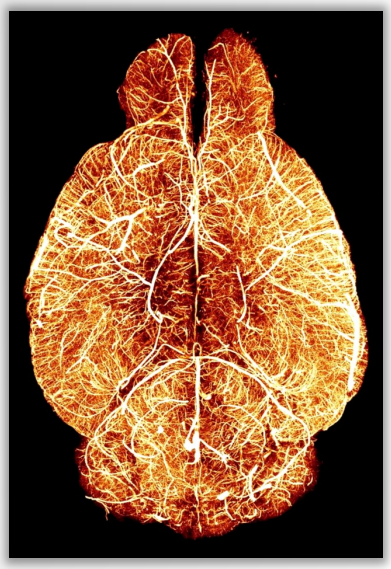
Neuronal imaging | High-throughput microscopy 3D histology | Digital pathology
Automated microscopy | Autofocus systems

Human Brain Project
EBRAINS
Co-funded by the European Union

COMPETITIVE ADVANTAGES

- High-resolution, fast, fully automated 3D imaging of tissue samples. Few hours needed to process 1 cm^3 with 1 μm^3 resolution
- Patented feedback solutions for real-time stabilization of the light sheet and autofocusing
- User is not left alone with a huge quantity of raw data, as with current commercial solutions
- Allows scalable volumetric analysis of multiple tissue samples.

NEW LIGHT-SHEET MICROSCOPY ENABLES SCALABLE ANALYSIS OF LARGE SAMPLES AT SUBCELLULAR RESOLUTION



vasculature network in the whole mouse brain

APPLICATION & MARKET POTENTIAL

Preclinical research: quantitative and reliable quantification of drug effects at whole-organ scale

Histopathological analysis of human tissue for augmented diagnostic & prognostic power

Personalised medicine: Improved assessment of drug efficacy on patient-derived organoids

Worldwide optical microscopy market in 2018 is about 2 billions $ and histopathology market about 3.5-4 billions $ (source: marketsandmarkets.com)

REFERENCES

- High-throughput automated light-sheet microscope used within Human Brain Project and the NIH BRAIN Initiative
- Top-tier published papers (Silvestri et al., Nature Methods 2021)
- Collaboration with University of Florence and National Research Council for technology R&D
- Patent WO2018122093A1

The LENS facility hub offers access to two microscopy setups capable of high-speed and high-resolution imaging with simultaneous two-colour acquisition. More info here

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WITH THE RAPID TECHNOLOGY

We devised a new method for focus stabilization in optical microscopy. Standard methods rely either on contrast optimization (thus working offline) or on triangulation (requiring a reflective surface).

RAPID (Rapid Autofocus via Pupil-split Image phase Detection) extends to the entire field of view of the instrument the phase-detection principle, which is limited to selected points of interest in professional photography.

This method allows direct evaluation of the defocusing state of the system simply using the detected image. Therefore, RAPID is completely agnostic with respect to sample or microscope, and can be applied to all systems, in all settings.

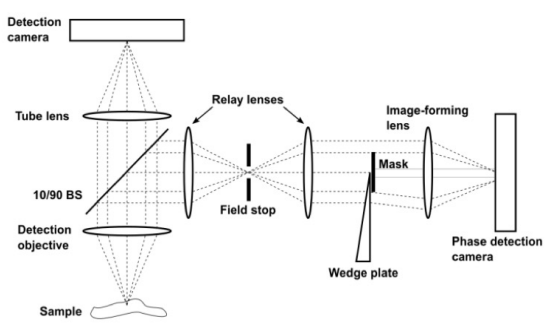
RAPID OVERCOMES LIMITATIONS OF CURRENT AUTOFOCUS SYSTEMS FOR MICROSCOPY

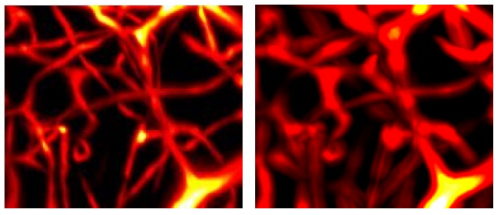
RAPID PROVIDES REAL-TIME OPERATION WITHOUT ANY REFERENCE REFLECTION

A SINGLE SOLUTION CAN BE USED FOR ALL WIDE-FIELD MICROSCOPES

A UNIVERSAL SOLUTION FOR REAL-TIME, IMAGE-BASED AUTOFOCUS IN MICROSCOPY

- RAPID IS APPLICABLE TO ANY KIND OF WIDE- FIELD MICROSCOPY: BRIGHT-FIELD, DARK-FIELD, EPIFLUORESCENCE, LIGHT-SHEET MICROSCOPY.
- RAPID IS SUITABLE FOR HIGH-CONTENT SCREENING, OF FIXED AS WELL OF LIVING SAMPLES.
- RAPID CAN AUTOMATE MICROSCOPY OF COMPLEX SAMPLES.





REFERENCES

- https://www.biorxiv.org/content/10.1101/170555v1
- Collaboration with University of Florence and National Research Council for technology R&D

TECHNOLOGY READINESS LEVEL

1 2 3 **4** 5 6 7 8 9

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