Flexi-SPIM: A MODULAR MULTIMODAL PLATFORM FOR CLASSICAL AND HIGH-THROUGHPUT LIGHT-SHEET MICROSCOPY

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Light-sheet Fluorescence Microscopy (LSFM) has gained much interest recently due to the low induced photodamage, fast acquisition rates and the possibility to reconstruct high quality images of whole organisms. However, current LFSM microscopes, revealed to be unpractical for large-scale experimental application and high-throughput screens requiring special sample preparation. In the majority of the described systems, samples need to be one by one mounted, embedded in agar gel, limiting the number of samples analysed. In 2015 we created the first flow cytometry system based on LSFM able to handle 3D cell cultures and zebrafish, SPIM-Fluid [1, 2]. The fusion of LSFM and microfluidics, allowed massive 3D cell cultures studies and sophisticated cell-based assays in real-time.

Here we present a new modular system architecture, Flexi-SPIM, that overcome limitations of our previous designs at the same time that extend the microscope functionalities, making it ideal for imaging facilities that need to deal with different type of samples and multiple resolution scales. Three different fully automatized acquisition modes are combined on a single machine. Classical LSFM, with mechanical sample scanning and sample rotation; Flow-LSFM with fluidic control of the sample using specialized syringe pumps, which allows high-throughput screens (samples are image as they travels through the channel). In both cases double side illumination and detection using a single camera, allow to increase image quality with isometric resolution (NA=0.5). Finally, Hybrid LSFM combines fluidic loading of samples and classical scanning, providing high-resolution, multicolour, double side illuminated and single side detected images.

Using the Flexi-SPIM system, we are able to make HT quantitative analysis of the spatio-temporal organization of the different cell types in 3D cultures and zebrafish, as well as the response to different environmental conditions with high resolution, high speed and minimal photo-damage. We will show how the use of 3D-cell cultures and full imaging system automation contribute to measure with statistical relevance a large set of biological parameters on the central nervous system [3], cancer therapy [4] and cell differentiation.

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References

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