Automated Spatio-temporal Adaptive Alignment in Multi-View Light-Sheet Microscopy

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Long-term imaging of biological processes with light-sheet microscopy demands accurate and robust instrument alignment. State-of-the-art microscopes often employ multiple illumination arms, detections arms and color channels, which introduce numerous opto-mechanical degrees of freedom [1, 2, 3]. These degrees of freedom directly affect image quality and mechanical, electrical and thermal drifts need to be constantly compensated. Even more importantly, biological specimens themselves exhibit heterogeneous optical properties that change during development and demand a spatio-temporal alignment adaptation. An automated framework is indispensable to accomplish these tasks and ensure high image quality without compromising imaging speed. We developed such a framework, which comprises (1) a light-sheet microscope design with digitally adjustable opto-mechanical degrees of freedom and (2) an automated control software that constantly monitors and systematically optimizes image quality in space and time. We demonstrate that our framework is robust with respect to the choice of different biological model systems, fluorescent marker strategies and spatio-temporal patterns of marker expression. We performed time-lapse imaging of cellular dynamics during zebrafish and fruit fly development and show that our framework maintains optimal image quality over long periods of time, enables on-demand system alignment on dynamic cell-type specific labels, and readily adapts to large-scale cell movements in early development. The optimization theory and algorithmic implementation of our framework are general and applicable to other light-sheet microscope designs.

References: