Contribution ID : **44** Type : **Poster**

Adaptive light-sheet microscopy for the systematic analysis of mitotic spindle scaling in vivo

Cells need to regulate the size and shape of their cellular structures for proper functioning. One classic example of such processes is the scaling of the mitotic spindle during early zebrafish embryogenesis. The mechanisms of how these spindles scale, however, are still unknown partly due to the lack of quantitative measurements of spindle dynamics. During early zebrafish development, the mitotic spindle only appears for three minutes out of the twenty minutes of cell cycle. Quantifying this short-lived event in an intact living embryo requires flexible and adaptive multi-resolution imaging, which is impossible with any state-of-the-art microscope. Here, we present a new type of light-sheet microscope, which autonomously adapts its detection scheme to the sample state. This microscope includes adaptable magnification to map the development of the millimeter-sized embryo and measure single-molecule dynamics of all individual spindles from the whole embryo in a single experiment. To automatically adapt the detection scheme, we have trained a Convolution Neural Network to detect the cell cycle state of individual cells from acquired fluorescence images. Using this new type of light-sheet microscope, we are studying the mitotic spindle scaling in freely developing zebrafish embryos. We will map the length, size, orientation, microtubule architecture and dynamics of all mitotic spindles in millimeter-sized zebrafish embryos with the necessary spatial and temporal resolution to solve the question of spindle scaling *in vivo*.

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Session Classification : Posters