IMAGING THROUGH A COVER SLIP UNDER AN ANGLE – THE CORE OPTICS OF AN INVERTED LATTICE LIGHT SHEET MICROSCOPE

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Light sheet microscopy has become an inevitable tool for low photodamage imaging in developmental biology. Dedicated beam shapes (lattice light sheets) [1] have extended this unrivalled sample preservation to live cell imaging with high spatio-temporal resolution. However, for the widespread use in cell biology an inverted lattice light sheet configuration is needed. In this paper we discuss various ideas of high-NA-imaging through a coverslip in light sheet-configuration (i.e. illumination and detection optical axis are oriented perpendicular to each other) [2,3]. We then present the core optics of the Zeiss Lattice Lightsheet 7, which utilizes free form optical elements to fully compensate the aberrations induced by oblique imaging through a cover glass. The compensation mechanism further allows for the adaptation to thickness variations common to commercial cover glasses, thereby enabling the use of any consumable type sample carrier for cell biological applications without compromising image quality.

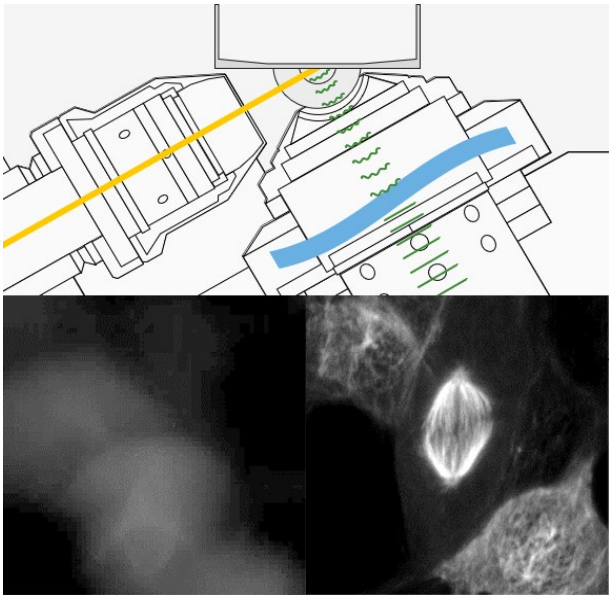

Figure 1: sketch of the core optics (top) and imaging without (bottom left) and with aberration correction (bottom right)

We characterize the optical performance of the system and show various applications ranging from single cells to multicellular organisms to demonstrate the potential of this approach for the easy and widespread use of an inverted lattice light sheet system.

[1] Chen, Bi-Chang, et al., "Lattice light-sheet microscopy: imaging molecules to embryos at high spatiotemporal resolution." *Science* **346,** 6208 (2014).
[2] McGorty, Ryan, Dan Xie, and Bo Huang, "High-NA open-top selective-plane illumination microscopy for biological imaging." *Optics express* **25.15,** 17798-17810 (2017).
[3] Barner, Lindsey A., et al. "Solid immersion meniscus lens (SIMlens) for open-top light-sheet microscopy." *Optics letters* **44.18,** 4451-4454 (2019).