

REFRACTIVE INDEX MATCHING FOR *IN VIVO* LIGHT-SHEET MICROSCOPY

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The emergence of Selective Plane Illumination Microscopy (SPIM) 15 years ago enabled scientists to study the development of whole embryos (e.g. fruit fly, zebrafish, mouse) with unmatched spatiotemporal resolution and low phototoxicity [1]. Yet, true *in toto* recordings of only few model organisms have been realized thus far. As any light microscopy technique, SPIM suffers from optical aberrations, light absorption and scattering – especially when imaging large samples, e.g. embryos. Our goal is to push further the current depth limitations in light-sheet microscopy and enable the study of *in toto* organogenesis and development in frequently used model organisms. To achieve this, it is crucial to minimize aberrations induced by the optical setup, the interface between sample and the mounting medium, and the sample itself.

Recently OptiPrep™ has been shown to be a linear refractive index tuning medium that can be used for live imaging of different samples [2]. Here, we present our results of refractive index matching in light-sheet microscopy to minimize aberrations arising from the refractive index mismatch between sample and mounting medium. We show that by adjusting the refractive index in light-sheet microscopy one can reduce aberrations and restore image quality in deep tissue layers of mouse and Medaka embryos, as well as in the root tip of Arabidopsis. Further, we discuss our results of matching the refractive index to specimens with different optical properties as the fruit fly embryo.

- [1] Jan Huisken, Jim Swoger, Filippo Del Bene, Joachim Wittbrodt, Ernst H. K. Stelzer, "*Optical Sectioning Deep Inside Live Embryos by Selective Plane Illumination Microscopy*", Science, Vol. 305, Issue 5686, pp. 1007-1009, August 2004.
- [2] Tobias Boothe, Lennart Hilbert, Michael Heide, Lea Berninger, Wieland B Huttner, Vasily Ziburdaev, Nadine L Vastenhouw, Eugene W Myers, David N Drechsel, Jochen C Rink, "*A tunable refractive index matching medium for live imaging cells, tissues and model organisms*", eLife, Tools and Resources, July 2017