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Leonardo: a toolset to remove sample-induced aberrations in light sheet microscopy images

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Selective plane illumination microscopy (SPIM, also called light-sheet fluorescence mi-croscopy) is the method of choice for studying organ morphogenesis and function as it permits gentle and rapid volumetric imaging of biological specimens over days. In inho-mogeneous samples, however, sample-induced aberrations, including absorption, scat-tering, and refraction, degrade the image, particularly as the focal plane gets deeper into the sample. Here, we present Leonardo, the first toolbox that is able to resolve all sam-ple-induced aberrations by using two major modules: (1) DeStripe removes the stripe ar-tifacts in SPIM caused by light absorption; (2) FUSE reconstructs one single high-quality image from dual-sided illumination and/or dual-sided detection while eliminating optical distortions (ghosts) caused by light refraction. The efficacy of Leonardo is validated on a wide range of biological systems, from minimally invasive experiments on sensitive spec-imens, for example, zebrafish embryos and optically opaque larval zebrafish, to immuno-labeling of wild-type mouse bodies up to roughly 2 centimeters. We publish a napari-based graphical user interface (GUI) and model code so the SPIM community can apply and improve Leonardo to advance imaging of inhomogeneous and complex specimens.

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