Light-sheet fluorescence microscopy

Light-sheet fluorescence microscopy (LSFM) is a powerful technique for high-speed volumetric functional imaging. However, in typical light-sheet microscopes, the illumination and collection optics impose significant constraints upon the imaging of non-transparent brain tissues. Sacher et al. demonstrated that these constraints can be surmounted using a new class of implantable photonic neural probes. Aim: Mass manufacturable, silicon-based light-sheet photonic neural probes can generate planar patterned illumination at arbitrary depths in brain tissues without any additional micro-optic components. Approach: We develop implantable photonic neural probes that generate light sheets in tissue. The probes were fabricated in a photonics foundry on 200-mm-diameter silicon wafers. The light sheets were characterized in fluorescein and in free space. The probe-enabled imaging approach was tested in fixed, in vitro, and in vivo mouse brain tissues. Imaging tests were also performed using fluorescent beads suspended in agarose. Results: The probes had 5 to 10 addressable sheets and average sheet thicknesses < 16 μ m for propagation distances up to 300 μ m in free space. Imaging areas were as large as ≈ 240 μ m × 490 μ m in brain tissue. Image contrast was enhanced relative to epifluorescence microscopy.

The neural probes can lead to new variants of LSFM for deep brain imaging and experiments in freely moving animals [1)].

1)
Sacher WD, Chen FD, Moradi-Chameh H, Luo X, Fomenko A, Shah PT, Lordello T, Liu X, Almog IF, Straguzzi JN, Fowler TM, Jung Y, Hu T, Jeong J, Lozano AM, Lo PG, Valiante TA, Moreaux LC, Poon JKS, Roukes ML. Implantable photonic neural probes for light-sheet fluorescence brain imaging. Neurophotonics. 2021 Apr;8(2):025003. doi: 10.1117/1.NPh.8.2.025003. Epub 2021 Apr 19. PMID: 33898636; PMCID: PMC8059764.

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Last update: **2024/06/07 02:50**