microDoppler imaging of blood flow for ophthalmology

Internship proposal

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Mission : The students will contribute to the development of a cutting-edge retinal imaging device prototype. Their tasks will encompass optical interferometer design, wave-based coherent image formation, fluctuation analysis, statistical filtering, and digital correction of optical aberrations. Signal processing will be prototyped in Matlab, with high-performance implementation in C++/Cuda. All developed routines will be shared via GitHub for collaborative use and further enhancement.

Value proposition : Building on the success of Doppler holography for ophthalmology [Fischer 2024], now deployed in selected prestigious clinical research centers globally, this project aims to develop a real-time microDoppler holography technology for clinical use. It will enable blood flow imaging in capillary vessels in the anterior and posterior segments of the eye, enhancing the spatial resolution of Doppler holography. Unlike optical coherence tomographic angiography (OCT-A), which only allows for a quasi-static mapping of retinal capillaries, this technology will offer dynamic imaging in small retinal vessels and is designed for large-scale clinical use. It holds great promise for managing vision- and life-threatening conditions like glaucoma, diabetic retinopathy, ischemic optic neuropathies and papilledema related to intracranial tumors, and will make it possible to detect variations in blood flow during their first- and second-line treatments with precision. It will identify retinal hemodynamic biomarkers and support cardio-oculomic studies, with applications extending into cardiology, aiding in the assessment of conditions like atherosclerosis, heart failure and stroke.

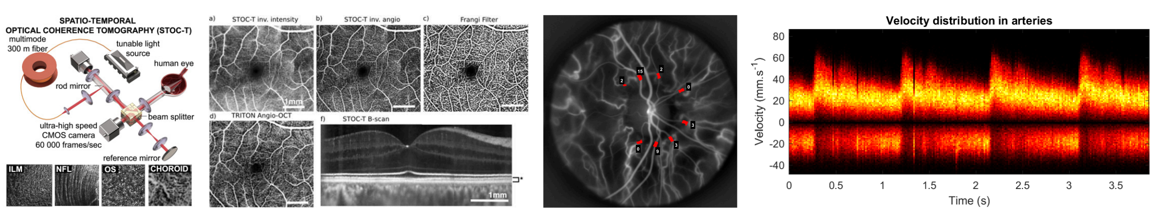

Fig. Swept-source OCT by beam shaping of coherent light via a multimode fiber (STOC-T) volumetric retinal imaging [Auksorius 2022] and angiography [Liżewski 2024] (left). Quantitative holographic Doppler imaging of retinal blood flow [Fischer 2024] (right).

Proposed device : This project introduces a highly innovative and much-anticipated approach for quantitative functional imaging of the retina, leveraging the fusion of two cutting-edge technologies: multimode optical wavefront shaping and detection

[Karamata 2005] and Doppler holography [Fischer 2024]. An imaging device for the human retina will be developed, combining a low temporal coherence laser light with holographic detection via a camera with a Michelson interferometer. Digital image reconstruction and filtering utilizing singular value decomposition will enhance the detection of on-axis interference signals, as in Doppler holography [Puyo 2020]. The laser beam, shaped through a multimode optical fiber to reduce its spatial coherence, will serve both as illumination reference wave, minimizing multiple scattered light interference by optical filtering [Karamata 2005], and ensuring ocular safety, akin to spatio-temporal optical coherence tomography (STOC-T) [Auksorius 2022].

Instrumental approach and technological development : The light source, operating in the near-infrared range, will be either a superluminescent or a laser diode, offering high spatial coherence and low temporal coherence (about few hundreds of micrometers). This light beam will be used for time-domain holographic OCT of the eye fundus [Sudkamp 2016], but via on-axis Michelson interferometry [Auksorius 2022]; Optical interference patterns will be captured by an ultra-fast streaming camera, up to 33,000 frames per second [Fischer 2024]. These interference patterns will arise from the interaction between the defocused image of the retina and the reference wave. Numerical reconstruction of the holographic image will be achieved at greater focus distances than with more spatially incoherent light [Trečiokaitė 2024], in order to leverage singular value decomposition to reveal the on-axis interference signal, and filter-out artifacts such as self-beating signals and overlapping ghost images [Puyo 2020]. Beam shaping using a multimode fiber [Auksorius 2022], will address coherent crosstalk and improve resolution by mitigating random optical paths in the retinal scattering layers [Karamata 2005]. Fourier temporal analysis [Puyo 2020] will uncover retinal dynamics in cross-sectional images with slice thickness matching the retina depth, allowing Doppler holography of blood flow in microvessels with acquisition speeds at least 100 times faster than current camera-based swept-source OCTA [Liżewski 2024].

Rationale : Retinal blood flow is crucial to most retinal pathologies and systemic diseases, making it a key diagnostic feature in the emerging field of oculomics. Clinical access to retinal circulation began with fluorescein angiography, which, though informative on flow dynamics, is invasive and non-quantitative. Other methods have included high-speed scanning laser ophthalmoscopy, Doppler ultrasound, laser Doppler velocimetry, laser speckle contrast imaging, and OCTA. Doppler holography, a newer technology, enables dynamic blood flow measurements with excellent temporal resolution, high repeatability, and the ability to assess total retinal blood volume rate in major vessels [Fischer 2024]. Already used in longitudinal studies, this clinical-grade technology will now be advanced to higher-resolution **microDoppler** angiography, focusing on capillary plexuses with multimode wavefront shaping and mode-matched detection, highly effective for high-resolution retinal imaging, filtering out multiple scattering [Karamata 2005]. This robust technology enhances image quality and reduces system complexity, offering key advantages for clinical applications :

- **Ocular safety compliance**: The multimode fiber generates around 250 transverse spatial modes, sequentially illuminating the sample with mode-hopping occurring every few nanoseconds. This broadens the focal point of illumination in front of the eyepiece, ensuring ocular safety compliance while preserving high imaging fidelity. [Auksorius 2022].

- **High-resolution imaging**: Coherent multimode wavefront shaping and camera detection will allow high-resolution holographic imaging, on par with confocal imaging, for detailed retinal angiographic studies through most anterior segment conditions.
- **Digital aberration correction**: This system will integrate digital aberration compensation for high-resolution imaging that is also already performed for Doppler holography [Bratasz 2024], eliminating the need for physical aberration compensation systems, which are ineffective for patients lacking suitable anterior segment conditions, and hence improving massively clinical relevance.

State-of-the-art STOC-T OCTA angiography analyzes fluctuations in successive swept-source OCT volumes, with a repetition rate of 113 Hz [Liżewski 2024], while cutting-edge methods like VISTA OCTA achieve 1000 Hz [Hwang 2023]. Clinical-grade **microDoppler** holography will reach up to 33,000 Hz in real-time by using a short-coherence laser. This will open the way to high temporal resolution imaging of the whole retina, crucial for capillary blood flow imaging. Some depth sectioning within the retina will be achieved through digital refocusing in post-processing, which will also crucially allow axial image registration. The retina contains up to four vascular networks: the superficial vascular plexus, two deeper capillary plexuses, and the radial peripapillary plexus [Campbell 2017], the deep ones being difficult to image with fluorescein angiography. The near-infrared transparency of the retina makes it ideal for digital holographic imaging. By trading volumetric depth sectioning for much higher temporal resolution, **microDoppler** will enable high-resolution imaging of blood flow in the capillary networks, offering better insight into conditions like glaucoma and diabetic retinopathy, which are linked to microvascular impairment. This device will provide :

- **Real-time blood flow monitoring**: The high temporal resolution, capturing tens of thousands of images per second, will enable detailed real-time analysis of blood flow dynamics in microcapillaries using Holovibes, the leading open-source software for high-throughput, low-latency digital hologram rendering and fluctuation analysis. It is already used for real-time Doppler holography clinical research worldwide.
- **True clinical utility**: This technology will deliver a clinical-grade imaging system for detailed hemodynamic analysis in retinal microvessels, offering unmatched speed, precision, and ease in practical settings. A laser with appropriate coherence length will enable full-depth retina imaging, while motion registration will be handled in post-processing for scalable clinical use.

References :

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