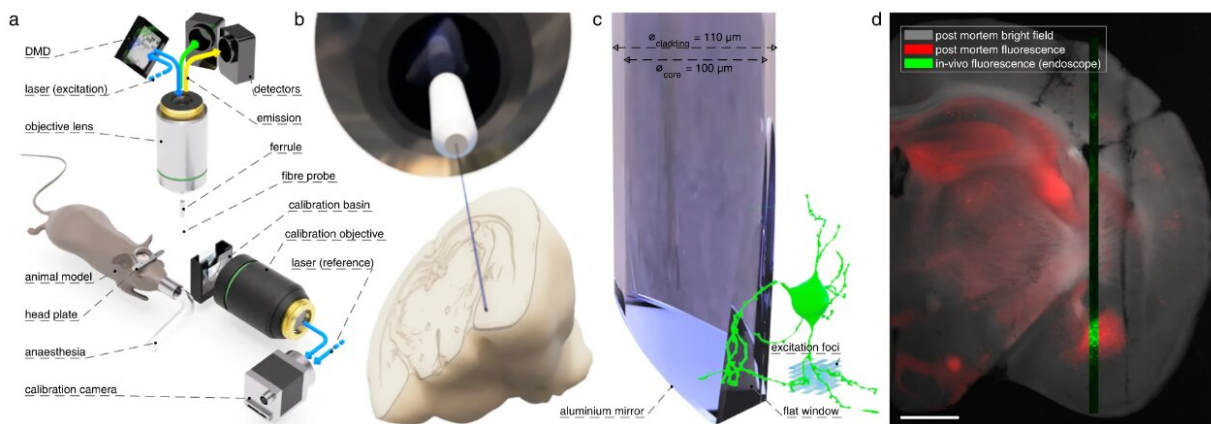


Neuroscientists investigate neuronal communication with ultra-thin fiber-based endo-microscope

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Deep-brain in vivo structure imaging using 110 μm thick MMF endo-microscope. a Experimental geometry for TM acquisition and imaging (see "Methods" for details). b To-scale fiber probe and mouse brain. The brain model has been compiled using Allen Reference Atlas—Adult Mouse, available from atlas.brain-map.org. c Detail of the side-view fiber probe and 3D grid of foci scanning the scene. d Overlay in vivo MMF endo-microscope record with post-mortem bright-field and confocal fluorescence microscopy. Another parallel endoscope insertion trace is visible on the right. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-36889-z

In order to investigate the activity of neuronal structures as well as the interaction of nerve cells, minimally invasive technologies providing

images from delicate deep-brain tissues are required. A new hair-thin endo-microscope, developed by an international team with the participation of Leibniz IPHT, promises extremely gentle in-depth observations and offers the potential to investigate areas of the brain in great detail and to study the onset and progression of severe neuronal diseases.

The instrument is expected to help neuroscientists in defining new strategies to combat these debilitating conditions. The researchers published their results in the journal *Nature Communications*.

Neuronal diseases such as autism, epilepsy, Alzheimer's, or Parkinson's disease are still poorly understood. Therefore, preventing, treating, or alleviating these illnesses remains a major challenge. In order to better understand the causes and the origins of these diseases, and to develop and monitor tailored therapies, it is important to decipher and study how the affected nerve cells, which are frequently located in very deep structures of the brain, behave within the natural complexity of the whole organism.

Neuroscientists investigate these conditions in small animal models and exploit minimally invasive endoscopy techniques to study deep-brain structures. To this end, scientists at Leibniz Institute of Photonic Technology (Leibniz IPHT) in Jena, Germany, are working together with the team of Complex Photonics from the Institute of Scientific Instruments of the Czech Academy of Sciences in Brno, Czech Republic, on a novel fiber-based approach.

Hair-thin and miniaturized endoscope

With a diameter of only 110 micrometers, the endoscope is about as thin as a [human hair](#) enabling the acquisition of images at an unprecedented tissue depth and at the subcellular level. This not only allows research

into deep-residing brain structures, which were previously difficult to access, but also to precisely study the neuronal connectivity and signaling activity of individual neurons in the brain.

"At the heart of the endoscopic system is an ultra-thin optical glass fiber that serves as a probe. Using digital holography, we can use it to image and visualize [individual cells](#) and [blood vessels](#) with high-resolution, distortion-free and with high-contrast. The hair-thin endoscopy design enables extremely atraumatic in-vivo examination without damaging surrounding tissues," explains Prof. Dr. Tomáš Čižmár, head of the Fiber Research and Technology Research Department at Leibniz IPHT, who has led the development of the instrument.

Conventional endoscopic solutions used in in-vivo neuroscience research usually use specialized rod lenses (GRIN), which convey images from one of its ends to the other. Due to their footprint, they may pose a great risk of tissue damage and severely affect the validity of neuroscience studies. The newly developed holographic endoscope overcomes this disadvantage by using a single multimode optical fiber as the imaging probe, making it the least invasive method for visualizing sensitive brain areas.

The researchers have also exploited a new type of fiber probe, a so-called side-view probe, which allows observation of the tissue perpendicular to the fiber axis. In this way, the tissue being imaged is much less stressed and damaged by the insertion of the endoscope into the tissue than by using conventional bare-terminated probes. As the probe offers the potential to penetrate deeper into the tissue, the side-view probe also offers the possibility to stitch together individual frames taken along the way into a panorama-like image, allowing a continuous view of the entire depth of the brain.

In addition to the direct observation of structural connectivity between

neurons, particularly the [dendritic spines](#) (microscopic structures emerging from dendrites), intracellular processes can also be observed with the developed endoscopic solutions. Dynamics of subcellular structures, changes in intra-cellular calcium concentration (closely linked to the signaling activity of the nerve cells), and the speed of the blood flow in individual vessels could be studied. All these properties could provide neuroscientists with indications to pathological changes in the brain.

"In neuronal diseases, the cognitive and motor performance of the affected organism may be irreversibly limited by changes or loss of nerve cells. We are developing technologies to monitor signs of a disease, for example, through altered neuronal communication, at an early stage. With these new and powerful light-based instruments, we can help to provide unprecedented insights into the [control center](#) of vital functions with high image quality and thus expand the understanding of neuronal diseases," says Prof. Dr. Tomáš Čižmár.

More information: Miroslav Stibůrek et al, 110 μm thin endo-microscope for deep-brain in vivo observations of neuronal connectivity, activity and blood flow dynamics, *Nature Communications* (2023). [DOI: 10.1038/s41467-023-36889-z](https://doi.org/10.1038/s41467-023-36889-z)

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