New microscopy method reveals detailed images of complex biological tissues

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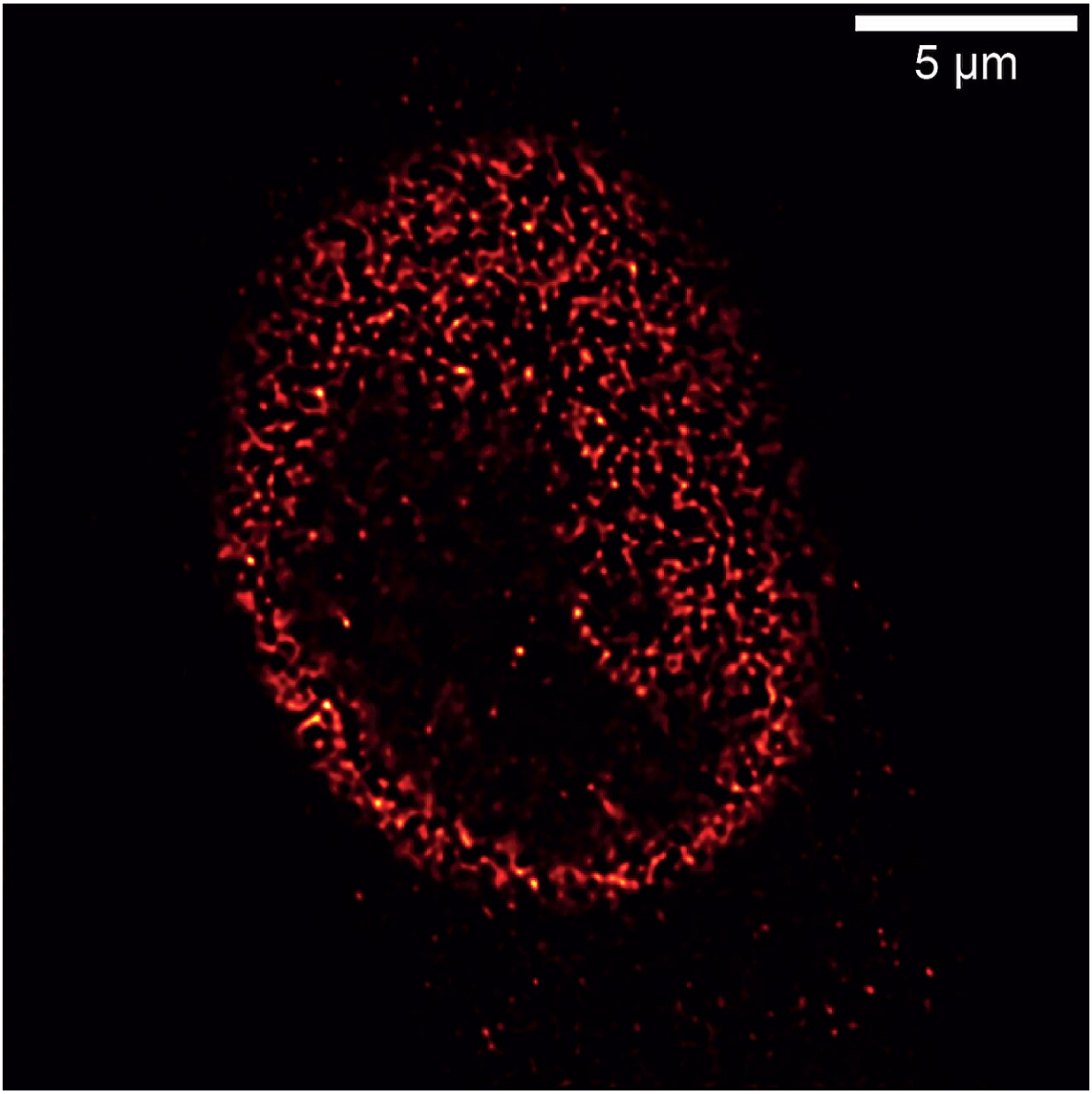


Researchers at IIT identified a new optical microscopy method capable of addressing a very specific issue in the field: obtaining extremely sharp and detailed images of thick and complex biological samples, such as HeLa cancer cells (in the picture). Credit: IIT-Istituto Italiano di Tecnologia

Until today, skin, brain, and all tissues of the human body were difficult to observe in detail with an optical microscope, since the contrast in the image was hindered by the high density of their structures. The research group of the Molecular Microscopy and Spectroscopy Lab at the Istituto Italiano di Tecnologia (IIT-Italian Institute of Technology) in Genoa has devised a new method that allows scientists to see and photograph biological samples in all their complexity, obtaining clear and detailed images. The new technique has been made available to the scientific community in "open science" mode, representing an advantage in the biomedical field, since it allows us to observe active cells, even in the presence of diseases, as well as to understand how drugs interact with living tissues.

The work was published recently in the journal *Nature Photonics* and is part of the research conducted by the group of Giuseppe Vicidomini, Principal Investigator of the Molecular Microscopy and Spectroscopy Lab, within the Brighteyes project.

The objective of the project was the use of new single-photon sensors to develop new optical microscopy techniques capable of observing biomolecular processes inside a living cellular system, such as organoids, in order to study their behavior and understand the causes of certain pathologies and the process of human aging. The project also led to several innovations that have already reached the market, thanks to international industrial collaborations and the creation of the start-up Genoa Instruments.

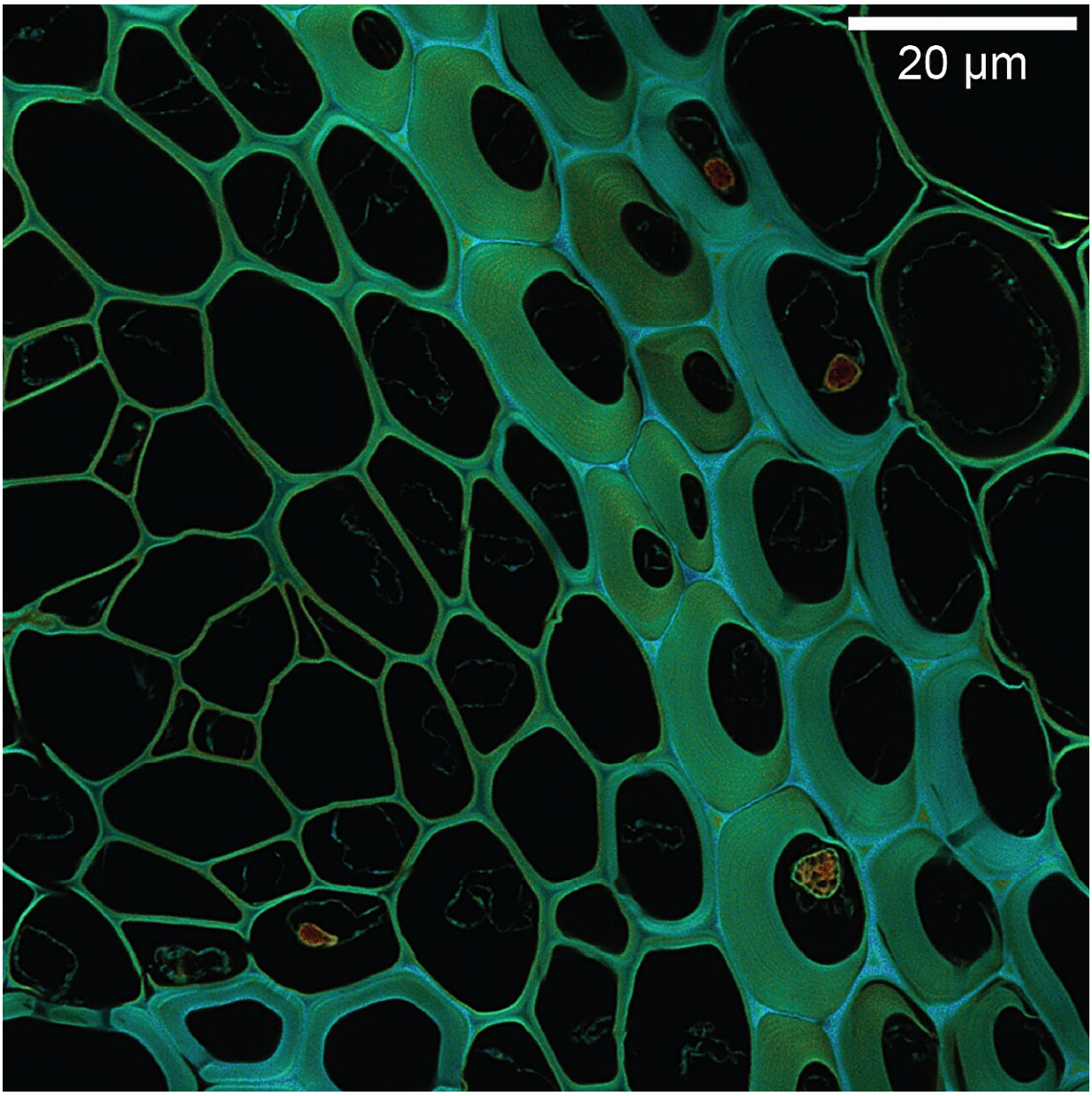
This latest study introduced a new optical microscopy method capable of addressing a very specific issue in the field: obtaining extremely sharp and detailed images of thick and complex biological samples.

"What we did was rethink the way microscopes measure the light that hits the samples under observation, improving both the spatial resolution and the contrast when studying thick tissues, where background light would normally overpower their structure, creating noise in the images," explains Vicidomini, coordinator of the study.

The research group created an instrument that acts like a light scalpel, penetrating deeply and observing the sample without damaging it. A small array of sensors captures both the light at the point where it hits and the variations with which the light spreads in the sample. Once this information is recorded, a reconstruction algorithm processes it, identifying the path of the light through the sample and producing sharper and better-sectioned images, without losing signal quality.

"The optical microscope used is equipped with an array of SPAD detectors (single-photon avalanche diode), capable of detecting the arrival of individual photons with very high spatial and temporal precision," explains Alessandro Zunino, first author of the study and post-doc researcher at the Molecular Microscopy and Spectroscopy Lab at IIT in Genoa.

"This characteristic not only improves the resolution and optical sectioning, but also enables advanced techniques such as fluorescence lifetime, which are fundamental to explore molecular dynamics in living tissues and to provide functional as well as structural information."



Researchers at IIT identified a new optical microscopy method capable of addressing a very specific issue in the field: obtaining extremely sharp and detailed images of thick and complex biological samples, such as Rhizome of Convallaria Majalis (in the picture). Credit: IIT-Istituto Italiano di Tecnologia

Given its relevance in the field of optical microscopy and in life sciences

, the obtained result has been made accessible to the entire international community following the principles of open science. The new method is open-source and open-access.

Any laboratory can adopt, modify, and apply it to their work at no cost and without the need for complex equipment. The authors have freely released the software and data, paving the way for rapid dissemination and further innovation within the scientific community.

Potential applications are numerous: from studying brain tissue, tumors, organoids, and other complex biological systems, to direct observation of cellular life to understand disease progression. In the pharmaceutical field, the technique could be used to visualize in real time how drugs interact with living biological tissues, speeding up and enhancing the accuracy of the discovery of new treatments and therapies.

More information: Alessandro Zunino et al, Structured detection for simultaneous super-resolution and optical sectioning in laser scanning microscopy, *Nature Photonics* (2025). DOI: 10.1038/s41566-025-01695-0

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