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The artificial optical microscope. A bridge between label-free and fluorescence microscopy at the nanoscale.

Abstract: Modern optical microscopes are analytical instruments able to produce images that are rich sources of quantitative information towards an unprecedented insight into the molecular mechanisms that govern and determine the fate of living cells. Their developments are positioned at the interface between biology and physics. Multimodal optical microscopy is a growing attitude boosted by artificial intelligence that makes intelligent the microscope. Definitely, fluorescence plays a key role coupling microscopy and spectroscopy by adding to image formation photochemical parameters, from brightness to lifetime, and non-linear approaches, like those associated with multi-photon excitation able to exploit intrinsic fluorescence and SHG/THG. In this framework, polarization methods like Mueller matrix microscopy expand those contrast mechanisms available for imaging towards labe-free. Such an “optical and probe” based state of the art is boosted by the growing use of artificial intelligence and the increasing availability of single photon detectors. The ambitious target is to create an artificial optical microscope “to see "what we could not perceive before” by transforming labs-free into molecular fluorescence-like content without the need of labelling. An interesting case study is related to understanding the visualization of chromatin organization.

Alberto Diaspro is a biophysicist, Full Professor of Physics at the University of Genoa and Director of Research in Nanoscopy at IIT. He has published over 500 scientific articles. He mainly works in optical nanoscopy and nanoscale biophysics. He received the Emily M. Gray Award from the Biophysical Society and the award for scientific communication from the Italian Physical Society. In 2022, he received the international Gregorio Weber Award for excellence in studies concerning fluorescence. In 2024, he was awarded the honour of Knight of the Order "of Merit of the Italian Republic" and the Enrico Fermi Prize for Physics from the SIF "for original contributions to the development and application of optical microscopy and the crucial impact on cellular and molecular biophysics". He also received the Sant'Eligio Special Prize from Federpreziosi and the "Beppe Pericu" Prize from the Società di Letture e Conversazioni Scientifiche of Genoa for scientific activity and dissemination in 2024, and the Eugenio Montale “In limine” award in 2025.

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