Light diversity microscopy. A journey to the center of living matter.

Alberto Diaspro[(a) (b)]
[(a)]*Department of Physics, University of Genoa, diaspro@fisica.unige.it*
[(b)]*Nanoscopy, Istituto Italiano di Tecnologia, alberto.diaspro@iit.it*

The possibility of integrating different light-matter interactions to form images and to correlate image data in optical microscopy is the starting point for the design and implementation of a brand new multi-messenger optical microscope. The multi-messenger microscope could represent a new paradigm in data collection and image formation with a potential high impact in biophysics exploiting the possibility to "tune" the microscope across a large, almost unlimited, range of spatial and temporal resolution. Fluorescence, including FLIM, FRET, FRAP, FCS and super resolved, and label free approaches, including multiphoton, SHG, Mueller matrix microscopy, fluorescence. Polarized light scanning microscopy has proven to be a label free approach to study the organization of macromolecules in biological systems. Polarization changes due to sample properties can be detected at different scattering angles. It was demonstrated in early works that differential scattering of circularly polarized light having opposite rotation, named as Circular Intensity Differential Scattering (CIDS), is sensitive to the properties of chiral conformation of biopolymers [1]. Differential images computed by using the Mueller Matrix formalism give access to information at the single molecular level using a high-numerical aperture objective in parallel with fluorescence imaging [2]. As a proof of principle of the technique, the CIDS configuration has been coupled with a modified confocal laser scanning microscope allowing a multimodal acquisition of the CIDS and the DNA fluorescence signals demonstrating the capability to distinguish heterochromatin and euchromatin regions. Such an approach is designed to be integrated in an image scanning microscope based on SPAD array detection [3].

[1] A. Diaspro, *et al. IEEE TBE*, **1991,** 38(7): 670.
[2] A. Le Gratiet *et al. OSA CONTINUUM*, **2018,** 1 (3): 1.
[3] M. Castello *et al. Nature Methods*, **2019**, 16(2):175-178