



**Carlo Manzo** is currently Research Fellow in the Single Molecule Biophysics group at ICFO-The Institute of Photonic Sciences in Castelldefels (Barcelona). He obtained the PhD in Physics at the University of Naples (Italy) in 2005 and worked as postdoctoral fellow at the Emory University (Atlanta, GA, USA) and at the IBEC of Barcelona on the development of single molecule techniques and optical tools for the investigation of fundamental processes in cell biology.

His research interests focus on the study of molecular mechanisms in cellular biophysics to determine how cell function is controlled by the dynamic interplay of molecular components. His investigation combines the development and the use of fluorescence nanoscopy, advanced methods in data science and stochastic modeling to provide a quantitative view on biological processes.

He authored over 30 papers in high-impact peer-reviewed journals (Cell, PNAS, Phys. Rev. Lett. And Phys. Rev. X), 5 book chapters and a patent.

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**Título: The role of spatiotemporal heterogeneity in the regulation of cellular function**

Molecular organization and diffusion regulate numerous processes underlying biological functions in living cells. In the last decade, advances in single-molecule fluorescence and super-resolution nanoscopy have allowed the visualization of cellular components at unprecedented spatial and temporal resolution, providing novel insights on a variety of cellular processes. These experiments have revealed that the complexity of the cellular environment often produces large heterogeneity both at the structural and dynamical level, whose implications for the cellular function are not fully understood.

Based on recent experimental results [1-3], I will present two examples of function regulation in living cells influenced by spatial and/or temporal heterogeneity. The first involves the structure of chromatin inside the cell nucleus, controlling the regulation of gene expression and the access of transcriptional factors to genes. By means of stochastic optical reconstruction microscopy (STORM), we have visualized the organization of histone proteins in the nucleus of mammalian cells and found that the nucleosomes are arranged in heterogeneous groups, displaying a broad distribution of composing units, sizes and densities [1]. Importantly, the comparison

of this organization in stem and somatic cells shows that these properties are correlated with the degree of pluripotency, i.e. the cell propensity to differentiate. Second, I will discuss the organization and dynamics of DC-SIGN, a transmembrane pathogen-recognition receptor involved in the capture of viruses, bacteria and parasites. By combining stimulated emission depletion (STED) microscopy and single particle tracking, we have found that DC-SIGN displays a multiscale organization in the cell membrane [2]. In addition, its motion deviates from a purely Brownian behavior, exhibiting anomalous diffusion with signatures of weak-ergodicity breaking and aging [3, 4]. The comparative investigation of receptor mutants allowed us to correlate the receptor's motion with molecular structure and function, thus establishing a link between nonergodicity and DC-SIGN capability in pathogen capture and internalization.

#### References:

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