Label-free super-resolution and intelligent spectroscopy: nonlinear optics to uCAIR

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Abstract

In modern optical microscopy, fluorescence methods still set the standard for achieving molecular-scale detail in living cells. Techniques such as STED and single-molecule localization microscopy (SMLM) can push resolution to the nanometre range by carefully controlling fluorescent dyes. However, these approaches are not always ideal: they rely on adding external labels that can alter the chemistry or behaviour of the system being studied, which makes them unsuitable for biological or medical applications where maintaining natural conditions is crucial. This talk explores an alternative, label-free route to super-resolution, combining Image Scanning Microscopy (ISM) with Coherent Anti-Stokes Raman Scattering (CARS). ISM is an imaging technique where spatial information is collected across an array, instead of a point detector as in confocal microscopy. This enhances resolution through nearest neighbour reconstruction, due to the availability of additional information. When paired with CARS, which provides chemically specific contrast from intrinsic molecular vibrations, the system delivers both structural and chemical information without dyes, at the nm range. This is aided with the application of neural networks, trained to reconstruct super-resolved, chemically rich images. Demonstrations using polystyrene and PMMA nanoparticles as well as human glioblastoma cells show that this hybrid ISM–CARS framework can resolve sub-cellular details and particle distributions while maintaining the natural state of the sample. Overall, the work presents a new pathway toward quantitative, label-free optical super-resolution, with chemical specificity, spatial resolution, and live-cell compatibility convergence, which offers new opportunities for biological imaging and diagnostic applications.

About the lecturer

Dr. Charlie O'Mahony earned his BSc in Applied Physics, MSc in Advanced Materials Engineering, and PhD in Physics at the University of Limerick, where he works as a Postdoctoral Researcher in the Department of Physics. His research bridges experimental and computational physics, focusing on optical and thermal measurement, infrared and radiofrequency technologies, and modelling of electromagnetic and nanoscale systems. He has over eight years of experience in implementing research and R&D projects financed from national and EU funds, including SFI, Horizon 2020, Horizon Europe, etc. Since 2024, he has been a researcher in the European Commission's uCAIR project, which develops

AI-based nonlinear optical spectroscopy and hyperspectral imaging with near-infrared (NIR) picosecond excitation using real-time CARS microscopy for advanced biomedical diagnostics, such as in vivo optical tissue biopsy with subcellular resolution, intelligent endomicroscopy for clinical purposes, microfluidics-based screening etc. Dr O'Mahony's work integrates materials science, photonics, and instrumentation, reflecting a broad interest in both theoretical modelling and experimental innovation.