Unveiling Research Frontiers: Coherent Anti-Stokes Raman Spectroscopy Insights

ShT-01.9-2

P. G. Argudo[I], M. Brzezinski[I,II], W. Chen[III], B. Dúzs[III], W. Liu[III], A. Samanta[III], A. Walther[III], S. H. Parekh[I,II]

[I]Max Planck Institute for Polymer Research, Mainz, Germany, [II]The University of Texas at Austin, Austin, TX, United States of America, [III]University of Mainz, Mainz, Germany

The study of proteins, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) and their interactions is a cornerstone of modern biochemistry and molecular biology. They drive biological phase separation processes leading to the formation of membraneless organelles (MLOs) within cells with distinct material properties and which structure will be directly linked to their final behavior.[1] Thus, understanding and controlling them is key in any biological process, as demonstrated in degenerative diseases such as amyotrophic lateral sclerosis (ALS) or frontotemporal dementia (FTD).[2] However, although their competing molecular interactions are known to play a key role in regulating condensate composition and structure, they remain poorly understood.

Here, we propose the use of Coherent Anti-Stokes Raman spectroscopy (CARS) as a suitable technique to unravel what changes are taking place over time in any biological system, free from dyes, markers or nanoparticles, as in surface-enhanced Raman spectroscopy, that could induce secondary interactions. Focusing on nucleic acids, their fingerprint region will allow us to determine the internal and external interactions taking place. Using DNA biomolecular condensate model systems, ssDNA to dsDNA hybridization or salt effects in the final assembled conformation can be followed. For proteins, their secondary structure can be also elucidated, from an ordered α-helix or β-sheet, to a disordered random coil. Furthermore, we employ this technique as a reliable source for the characterization of protein-RNA interactions. While adding another layer of complexity, the ramanshifts observed in specific regions of the formed condensate can give an indication of its characteristics, such as its structure or viscoelastic state. Furthermore, they can be related to its ultimate behavior, as observed in living systems.

[1]Garcia-Jove Navarro, *et al*. Nat Commun 10, 3230 (2019)
[2]Arseni, D., *et al*. Nature 601, 139–143 (2022)