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Editorial: Specialty grand challenge: Structure, spectroscopy, and imaging

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Introduction

Aims and protagonists in the field

In the interdisciplinary field of chemical biology, different scientists, generally chemists and biologists, undertake their best efforts to develop advanced methodologies and innovative approaches to address important scientific goals and societal demands. Furthermore, confronting the complexity of problems to be solved and sophisticated systems to be discerned, the partnership of diverse other specialists is demanded, including physicists, spectroscopists, pharmacologists, and physicians. Collectively, their complemented work brings together several areas of research, experimental as well as theoretical, to accomplish higher levels of knowledge about the structural and functional characterization of biological systems. A profound understanding of life and its wide-ranging processes are their final aims.

Recently, AlphaFold, a revolutionary artificial intelligence (AI) network, predicted the structures of more than 200 million proteins in a universe of 1 million species, reaching to determine the protein structures of nearly every organism with known protein sequence data. It made it possible to understand the relationships between protein functions and its 3D structures, and the results are now available to scientists in a database (Callaway, 2022). These data can certainly encourage numerous types of studies in the future.

A significant example of the structural feature's importance in basic and applied investigations is the development of messenger RNA (mRNA)-based therapeutics (Dammes and Peer, 2020). Since its discovery in the 1960s, improvements in its engineering to express therapeutic proteins or manipulate specific genes' expression have enabled a broad range of applications in intractable diseases, such as severe infections, varied forms of cancer, and genetic diseases, besides new vaccines, and accelerate its clinical translation (Kim, 2022; Qin, Tang, Chen et al., 2022). Because of the unfavorable characteristics of mRNA's, such as large size, instability, immunogenicity, sensitivity to enzymatic degradation by RNases, and limited cellular uptake, many pivotal issues had to be solved during the development of mRNA-based therapeutics. Additionally, a variety of delivery strategies, including nanolipids, exosomes, or polymeric micelles as carriers, was crucial for their wide applicability (Uchida et al., 2020).

Moreover, investigations in this chemico–biological field frequently lead to the conception, design, and provision of new molecules capable of interacting efficiently with selected biomolecules, and consequently causing remarkable modifications in their functional behavior. Results can establish new parameters and lead to new drugs that are more efficient, safe, and selective in facing illnesses and syndromes. Significant examples are found in the literature, illustrating important and innovative chemical–biological studies. They include small peptides and large protein effects in Alzheimer's disease (Picone et al., 2022), emergence of bimolecular condensates as attractive targets for drug discovery (Mitrea et al., 2022), and designed aptamers that bind small-molecule targets with high affinity and specificity, developed to diverse applications, from therapeutics to biosensing (Auwardt et al., 2018; Ruscito and DeRosa, 2016).

Interrelation between structure and spectroscopy

Both in chemistry and biology, correlations verified between structure and reactivity are crucial to clarify concepts and go forward in the development of both fields and in enlarging their applications. Detection, description, and classification of bonding, interaction, folding, compartmentation, and communication among atoms, ions, molecules, clusters, membranes, and organelles are needed to achieve such goals.

Mainly in the field of chemical biology, structural features of vital biomolecules and their correlation to their activity in fundamental processes for life are of capital importance. In addition to the comprehension of properties of biological compounds, the knowledge of their distribution, localization, insertion in cells, molecular recognition among surrounding biomolecules, and modes of action toward organelles or membranes allows a more global and complete idea of the context where such processes occur.

Astonishing progress in the description of biomolecules verified in the last decades was made possible due to the simultaneous and enormous development of varied spectroscopic methods. Some of them are listed here. Detailed characterization of many crucial proteins assumed importance, unveiling their 3D structures, only after the advent of X-ray crystallography, which was applied to biological macromolecules, although the first crystals of hemoglobin were observed two centuries ago. Mimetic compounds were largely used in the meantime to clarify macromolecule structures and activities. Nevertheless, many spectroscopic approaches allowed remarkable enlightening advancements in the field. More recently, advanced X-ray luminescence methodologies for applications in imaging, biosensing, and theranostics, by using inorganic perovskite nanocrystal scintillators, provided high-resolution X-ray imaging of the internal structure of biological samples (Hong et al., 2023).

In a frontier investigation, Raman and IR spectroscopic methods were simultaneously used to study pathogenic bacteria isolated from humans suffering from sepsis, a severe dysfunction caused by dysregulated response to infection, which is reported as a leading cause of death worldwide (Lima et al., 2022). This emerging technology combining both spectroscopic methods is a pledge in the study of microorganisms to avoid time-consuming current protocols used for bacterial recognition, that usually cause detrimental delays in treatments.

Magnetic spectroscopic methods such as nuclear magnetic resonance (NMR) and electron paramagnetic resonance (EPR) also play essential roles in the elucidation of biomolecules and fundamental processes, wherein they are protagonists. NMR spectroscopy provides an essential and dynamic view of structural biology by capturing biomolecular motions at atomic resolution, over a range of time-scales, complementing other methodologies that offer a mostly static description of molecules (Alderson and Kay, 2021). On the other hand, continuous wave and pulsed EPR methods are powerful biophysical tools to detect long-range distance constraints on the nanometer scale by measuring the magnetic dipole coupling between two unpaired electrons in biomolecules, both in aqueous buffer solutions or in membranes, where the spin centers can be metal ions, radicals, or spin labels (Schiemann, and Prisner, 2007). Furthermore, this technique can verify minor conformational changes in any biomolecule or macromolecular complex, induced by metal ion binding, with high resolution and sensitivity, monitoring their environment during a chemical or biological reaction (Hofmann and Ruthstein, 2022).

Imaging as a consequent progress in the field

More than inferring the properties of single molecules or biomolecules using all techniques available, it was necessary to 'see' their performance inside cells. So, as an expected trend in the field, imaging tools became valuable and now comprise a very dynamic research area.

Fluorescence has been used for many decades to detect organelles or specific molecules intracellularly. A wide range of label compounds were designed and prepared, according to different requirements by biologists and biophysicists (Klymchenko, 2023). Such studies included redox-active transition metal-based probes, containing essential metal ions such as iron, manganese, and copper, some of them approved as optical and magnetic resonance imaging agents [Xue et al., 2022].

Additionally, non-invasive methodologies merging spectroscopic and microscopic approaches have been developed to search intracellular processes in living cells. Aiming to monitor the distribution of multiple cellular components, the dynamics of intracellular reactions, and/or modifications caused by exogenous compounds with pharmacological or medicinal uses, these methodologies exhibited significant progress in the last decade (Silge et al., 2022). Among them, vibrational spectroscopy and imaging, both at infrared (IR) and Raman scope, showed significant advances when applied to biomedical purposes. Raman spectroscopy, mostly surface-enhanced Raman scattering (SERS), attracted remarkable interest about 20 years ago, providing detailed information at the molecular level and enabling the tracking of specific intracellular species (Spedalieri and Kniepp, 2022; Willets, 2014). Recently, by using stimulated Raman scattering (SRC) microscopy combined with multivariate analysis, it was possible to visualize the size and distribution of lipid droplets in prostate cell models with high spatial resolution and chemical specificity (Hislop et al., 2022). Therefore, based on the number and importance of investigations already reported, continuous progress in those techniques is expected in the next years.

Perspectives

Different approaches are being developed to encompass new trends into the frontiers of chemistry and other sciences for biological and biomedical applications. The Structure, Spectroscopy, and Imaging section in the journal *Frontiers in Chemical Biology* intends to be an open optional publishing platform, integrating new ideas and a series of advancements in the interface of chemistry and biology, focusing on structural and spectroscopic studies correlated to biological processes.

As a recent impacting example, a creative team of scientists working on chemical and biological problems put together a multidrug delivery *via* a wearable bioreactor to achieve long-term limb regeneration and functional recovery in a vertebrate model (*Xenopus laevis*). This work initiated a long-standing goal targeting developmental and regenerative biology by using chemical tools (Murugan et al., 2022). It can be an early attempt to respond to the needs of a massive number of patients around the world and a promising accomplishment of scientific progress.

In brief, by combining accurate spectroscopic methods and paired imaging tools to describe and follow natural and synthesized molecules, endogenous or exogenous, capable of outstanding performance in biological systems, influencing physiological as well as pathological processes, a continuous flourishing of the scientific community is expected, pursuing to solve more complex emergent challenges.

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