Illuminating Biomolecular Complexity: X-ray Free Electron Lasers and Vibrational Spectroscopies for Protein, Aggregates, and Cellular Architectures



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Vibrational Spectroscopy to Tackle Cancer

Sunday, June 29, 2025 11:25 AM (35 minutes)

Normal-to-cancer transition (NTC) is still an ill-understood process, closely associated to cellular biomechanical properties. These are strongly dependent on intracellular water's structural and dynamical profiles, which play a fundamental role in cellular function. Improved chemotherapeutic strategies are an urgent clinical need, since cancer is still the second leading cause of death worldwide, with an expected rising incidence. Metal-based drugs developed upon the discovery of cisplatin (cis-(NH3)2PtCl2) have aimed at coupling an enhanced efficacy to decreased acquired resistance and harmful side effects. These metallodrugs encompass Pt- and Pd-complexes with more than one metal centre [1], extensively studied by the authors in the last decade [2-9], which trigger a selective DNA damage –through metal coordination to the purine bases or via electrostatic interaction with the phosphate groups.

Inelastic and quasi-elastic neutron scattering techniques (INS and QENS), combined with Raman and Fourier Transform Infrared (FTIR, including with synchrotron radiation) spectroscopies, are currently reported to deliver a comprehensive set of data, at the conformational and dynamic levels, on: (i) NTC transformation [6]; (ii) activity of newly developed Pt/Pd-anticancer agents (on DNA, glutathione, proteins, cellular metabolism and intracellular water) [7-9]. Variations in the dynamical profile of intracellular water were unveiled for malignant cells/tissues as compared to healthy ones. In addition, clearly distinct effects were revealed for Ptvs Pd-agents regarding their impact on either the cellular cytoplasm or hydration water in cancer cells, as well as concerning their specific interactions with biomolecules. This is a pioneer study on the impact of cisplatinlike hemotherapeutic agents on vital cellular components, which is key for a thorough understanding of their molecular basis of cytotoxicity.

These results are expected to foster the development of improved anticancer drugs -displaying high specificity and optimised efficacy. Ideally, these are aimed to act simultaneously on more than one site (multitarget approach), intracellular water being suggested as a potential pharmacological target. Advanced chemotherapeutic strategies such as these will contribute to a better prognosis and quality of life of cancer patients.

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Scholarship elegibility

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