Combining the atomic resolution of NMR with the cellular dimension

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Understanding functional biological processes requires their description both at system (e.g. a cell) and at molecular level, (e.g. atomic-resolution characterization of biomolecules). NMR is quite powerful towards this goal. Along a functional process, most interactions are transient in nature, suitably studied by NMR, which can also characterize processes in living cells with atomic resolution. The study of these aspects requires the development of suitable methodologies capable of addressing multiple, specific, and sometimes non conventional aspects and amenable to characterize functional processes in living cells, also integrating these data with those obtained in vitro.

Among processes involving transient interactions there are the metal transfer processes, in which metal is transferred, from metal transporters to the final recipient proteins, through a series of protein-protein interactions. This transfer is determined by metal affinity gradients among the various proteins, with kinetic factors contributing to the selectivity of the processes. They often also involve proteins whose folding and maturation are tightly linked to redox reactions. Furthermore, the presence of paramagnetic centers, such as iron-sulfur clusters, dramatically affects the NMR spectra, requiring tailored experiments also integrated with EPR spectra. In-cell NMR can provide the description of these processes within living cells. Furthermore, it can be integrated with other techniques, such as optical and XRF imaging, which allow us to span from the atomic resolution characterization to the cellular dimension. The power of NMR in describing cellular pathways at atomic resolution in a cellular environment will be presented for a few pathways responsible for copper trafficking in the cell and for the biogenesis of iron-sulfur proteins. New major advancements in in-cell NMR and in the characterization of highly paramagnetic systems will be also discussed within an integrated approach where, from single structures to protein complexes, the processes are described in their cellular context within a molecular perspective.