Hyperpolarized NMR Metabolomics at Natural 13C Abundance

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Résumé

NMR metabolomics plays an important role to extract crucial information on biological systems owing to the high reproducibility and repeatability of NMR. For sensitivity reasons, this application relies mostly on 1D 1H NMR spectroscopy. However, 1D 1H NMR is limited by the strong peak overlap that is a feature of complex biological mixtures.

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Hyperpolarized 13C NMR, especially via dissolution Dynamic Nuclear Polarization (1) (d-DNP) offers an appealing solution for metabolomics studies as it improves the sensitivity of solution-state NMR by factors up to 10ˆ5 while retaining the intrinsic advantages of 13C, *ie.* broad spectral range and high resolution. In a preliminary d-DNP study, (2) we showed the unique ability to detect 13C signals on plant and cancer cell extracts in a single scan at natural abundance, results that are inaccessible by conventional state-of-the-art high field NMR. Later, we reported repeatability better than 4% for 13C signals on such extracts,(3) as suitable for analytical metabolomics.

Here, for the first time, we introduce d-DNP into a complete workflow for untargeted metabolomics. This consists of sequential steps starting from biological extract preparation, d - DNP hyperpolarization, solution-state NMR acquisition, spectra processing to statistical analysis for discriminating metabolic marker identification. We demonstrate the approach on two groups of samples, obtained from extracts of the same tomato variety at two ripening stages (4). A principal component analysis (PCA) on hyperpolarized 13C NMR spectral data results in very clear group separation and highlighted several biomarkers in full agreement with reported studies (5). We also optimize parameters of the semi-automated d-DNP system, where most steps can be performed by a single operator within a time compatible with high-throughput studies.

References

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