METABOLIC NMR WITHOUT THE MAGNET

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Zero- to ultralow-field (ZULF) NMR is a modality of NMR experiment performed in the absence of a strong magnetic field. In this regime, Larmor precession is suppressed, and other interactions such as J-couplings dominate. This grants three important advantages: the low frequency signals readily penetrate metals and conductive materials, magnetic susceptibility-induced line broadening from sample inhomogeneity is suppressed, and no bulky superconducting magnet is needed. In this work we form the biomolecules [1-^{13}C]fumarate and [1-^{13}C]pyruvate in aqueous solution via parahydrogen-induced polarization. We acquire the low-frequency ZULF signals using optical magnetometers, with Helmholtz coils surrounding the sample to apply magnetic field pulses. This is all contained within a mu-metal shield to attenuate Earth's field. With this apparatus we are able to acquire zero-, ultralow-, and low-field spectra. The conversion of fumarate into malate, and pyruvate into lactate, are metabolic processes observed *in vivo* in hyperpolarization-enhanced magnetic resonance imaging experiments.[1,2] We show that ZULF NMR can be used to study metabolism by observing these two biochemical reactions. This work paves the way to a heretofore unexplored class of biomedical imaging applications.

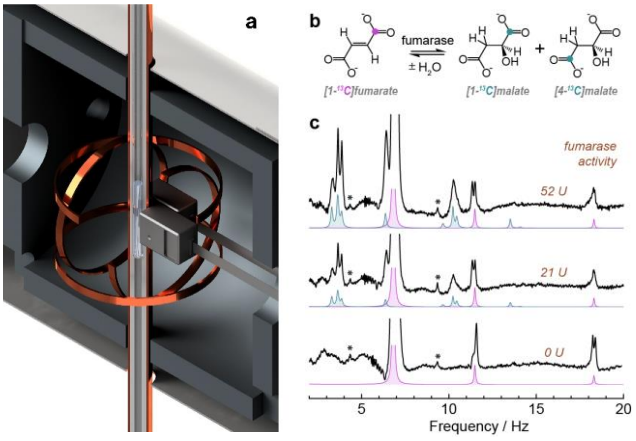

Figure 1. (a) The ZULF setup used in this work. (b) The transformation of fumarate into malate. (c) Zero-field spectra of hyperpolarized [1-^{13}C]fumarate after addition of the enzyme fumarase (given in enzyme units U), with simulated fumarate and malate spectra beneath.

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REFERENCES

[1] S. J. Nelson et al., *Sci. Transl. Med.* **2013**, *5*(*198*), 198ra108.
[2] M. R. Clatworthy, M. I. Kettunen, D.-E. Hu, R. J. Mathews, T. H. Witney, B. W. C. Kennedy, S. E. Bohndiek, F. A. Gallagher, L. B. Jarvis, K. G. C. Smith, K. M. Brindle, *Proc. Natl. Acad. Sci.*, **2012**, *109*(*33*), 13374–13379.