Dissolution Dynamic Nuclear Polarization for *in vivo* Application

Downes, D. (UF, Biochemistry and Molecular Biology); Lama, B. (UF, Biochemistry and Molecular Biology); Collins, J. (UF, Biochemistry and Molecular Biology); Long, J. (UF, Biochemistry and Molecular Biology).

Introduction

Nuclear magnetic resonance (NMR) is an invaluable tool for determining chemical structure and carbon metabolite flux *in vitro*, *in vivo*, and *ex vivo*. Although NMR is very useful, it is an inherently insensitive technique, especially to the carbon nucleus, due to the low gyromagnetic ratio of carbon and the 1.1 % natural abundance of magnetically active ^{13}carbon[1]. Additionally, *in vivo* spectroscopy suffers from notoriously poor signal-to-noise ratio (SNR) and difficulties in resolving signals spatially and spectrally due to significantly broader line widths. The development of dissolution dynamic nuclear polarization (dDNP) enables carbon signal enhancement of 10,000 fold or more *in vivo*[1,2,3]. This technique has great potential to improve the measurement of metabolic flux in real time while drastically increasing SNR.

Experimental

In vitro

With the intent of optimizing experimental and polarization conditions for use in an *in vivo* model we have performed solid state polarization of isotopically labeled [1-^{13}C] sodium pyruvate, sodium acetate and sodium butyrate. Once polarized, these labeled metabolites were rapidly heated and injected into an empty phantom or a vessel containing live *Escherichia coli* cells in a 4.7 T or an 11.1 T imaging magnet. We then observed carbon signal with a custom ^{13}C RF coil for a period of 10 minutes (Fig 1).

In vivo

Several injections into healthy adult mouse and rats have been performed (data not show) and further optimization is needed to accurately detect *in vivo* metabolism in a living animal. Hyperpolarized [1-^{13}C] sodium pyruvate and sodium acetate have been injected into live animals in either the 4.7 T or 11.1 T imaging magnet with the intent of monitoring mitochondrial metabolic processes in real time.

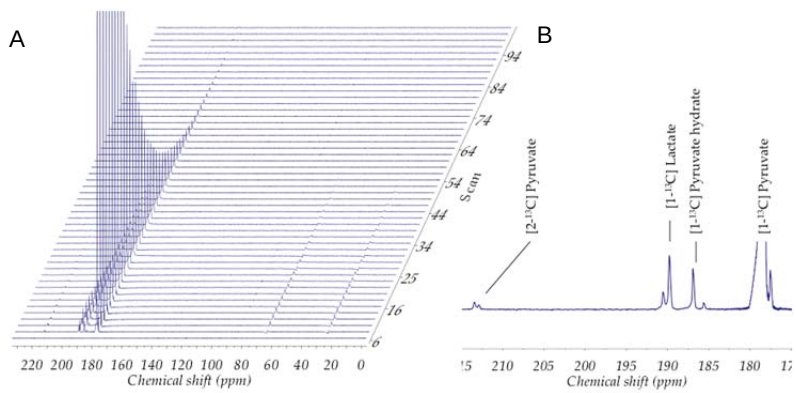

Figure 1: (A) Time course array of solution state polarization of [1-^{13}C] pyruvate after injection into *Escherichia coli* culture into an 11.1 T imaging magnet. Each spectral line represents a 3 second arrayed scan. (B) Polarized [1-^{13}C] pyruvate (and natural abundance [2-^{13}C] pyruvate) shown with major metabolic products.

Conclusions

Through use of bacterial cultures as a proof of concept of real time metabolic observation, we now are transitioning into applying the technique of dissolution DNP to an animal model. Further testing and technique development is needed to obtain the SNR necessary to detect *in vivo* metabolism.

Acknowledgements

A portion of this work was performed at the National High Magnetic Field Laboratory, which is supported by National Science Foundation Cooperative Agreement No. DMR-1157490, the State of Florida, and the U.S. Department of Energy.

References

[1] Comment. Concepts in Magnetic Resonance Part B (Magnetic Resonance Engineering), 255–69 (2007).
[2] Nelson SJ, *et al*., Appl Magn Reson, **34**(3-4), 533-44 (2008).
[3] Yen YF, *et al*., Magn Reson Med Sci.**10**(4), 211-7 (2011).