Adding Solid-State ^{17}O NMR to the Toolbox for Studies of Organic and Biological Molecules

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Nuclear magnetic resonance (NMR) spectroscopy is a powerful technique for chemists to obtain detailed information about chemical bonding and molecular structure. However, most successful NMR applications for studying organic and biological molecules to date rely on the detection of "NMR friendly" spin-1/2 nuclei such as ^{1}H, ^{13}C, and ^{15}N. Another key element in organic and biological molecules, oxygen, has rarely been used in NMR studies, largely for two reasons. First, the only NMR-active oxygen isotope, ^{17}O, is exceedingly hard to find in nature (its natural abundance is a mere 0.037%). Second, *^{17}O has an unusual nuclear spin number (I = 5/2), and thus belongs to a special class of nuclei known as quadrupolar nuclei that yield more complex NMR spectra. As such, it is much harder to obtain high-quality, high-resolution NMR spectra for quadrupolar nuclei than for spin-1/2 nuclei*.

This research team has developed a synthetic strategy to introduce ^{17}O-labels onto all oxygen-containing functional groups in D-glucose, which increases the ^{17}O NMR signal intensity by a factor of 1000 over its natural abundance level. To further boost the sensitivity, the MagLab users employed two state-of-the-art NMR technologies. One was to perform the measurement on the most powerful NMR magnet in the world, the MagLab's 35.2T Series Connected Hybrid. The other was to use a new probe recently developed by Bruker that significantly reduces the noise levels of the detector and preamplifier by operating at very low temperatures. These two new technologies drastically enhance the ability to obtain high-quality ^{17}O NMR data for D-glucose (see **Figure**).

This work represents the first time that a complete set of ^{17}O solid-state NMR data was recorded for any carbohydrate molecule, which paves the way for researchers to consider ^{17}O NMR as a new spectroscopic tool in glucose-related research that can range from glucose-binding proteins to glucose metabolism in live cells.

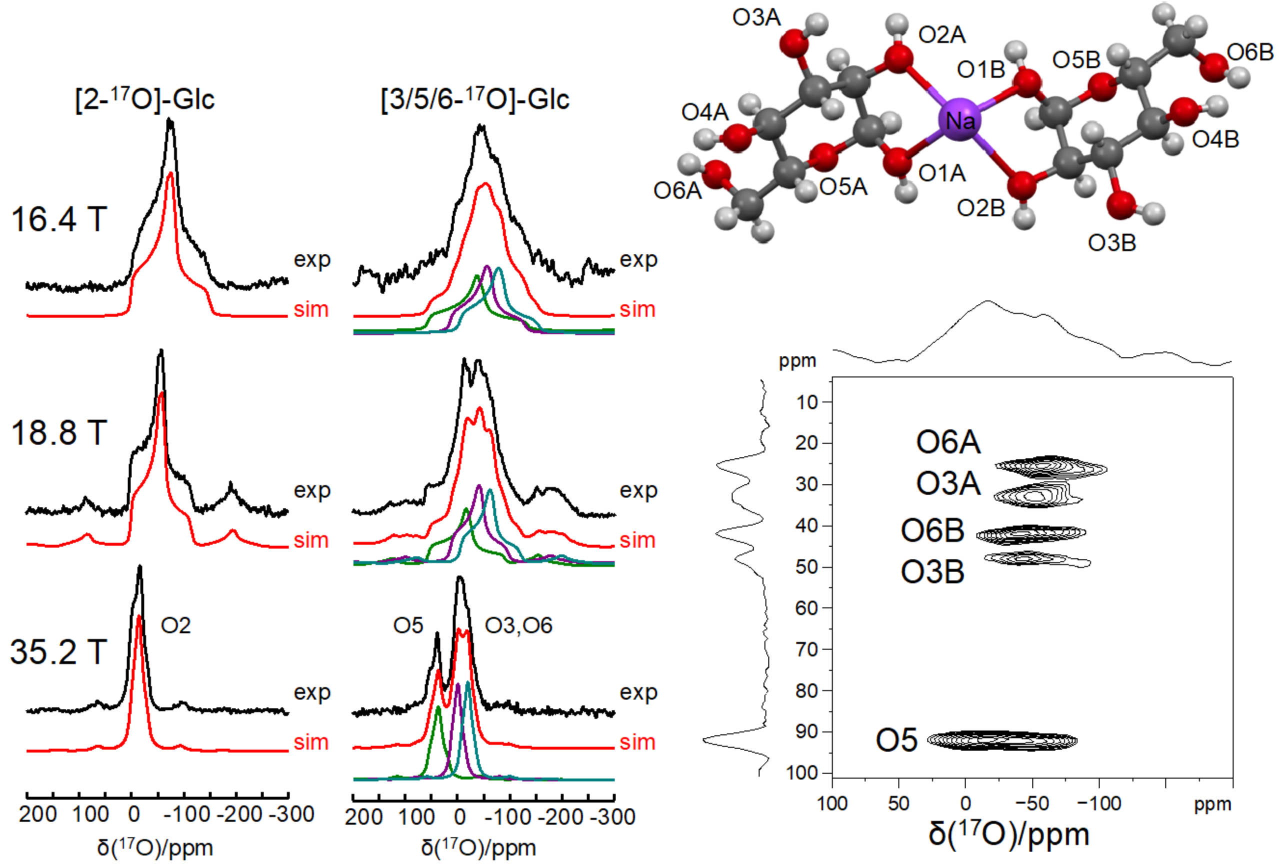

Figure: (top right) Dimer formation of α-D-glucose molecules in the crystal lattice of D-glucose/NaCl (1:1) co-crystal. **(left)** One- and two-dimensional (**bottom right**) ^{17}O NMR spectra of ^{17}O-labeled D-glucose/NaCl (1:1) cocrystal at different magnetic fields.

Facilities and instrumentation used: NMR/MRI Facility: MagLab's 18.8 T/800 MHz; DC Facility: MagLab's 36-T Series Connected Hybrid Magnet.

Citation: Shen, J.; Terskikh, V.; Struppe, J.; Hassan, A.; Monette, M.; Hung, I.; Gan, Z.; Brinkmann, A.; Wu, G., *Solid-state ^{17}O NMR study of alpha-D-glucose: exploring new frontiers in isotopic labeling, sensitivity enhancement, and NMR crystallography*, **Chemical Science, 13** (9), 2591--2603 (2022) **doi.org/10.1039/d1sc06060k**

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What is the finding? MagLab users have developed a synthetic strategy for introducing ^{17}O-labels into the D-glucose molecule in a site-specific fashion and then applied state-of-the-art nuclear magnetic resonance (NMR) techniques to obtain a complete set of ^{17}O NMR parameters. *This is the first time that a complete set of ^{17}O NMR parameters has been recorded for any carbohydrate compound*.

Why is this important? *The element oxygen is the only key constituent of organic and biological molecules that has remained largely "invisible" to the NMR spectroscopic techniques of chemists*. This work has started to venture into this "last piece of the puzzle" in biomolecular NMR spectroscopy (see **Figure**). One immediate question is whether and how ^{17}O-labeled glucose can be used as a new tracer for probing binding of glucose to other biological macromolecules - such as glucose transport proteins - or for monitoring glycolysis of live cancer cells. It may eventually be possible to extend the same methodology to introduce ^{17}O-labels into more complex carbohydrate molecules such as polysaccharides, or into the ribose/deoxyribose part of RNA/DNA molecules. *Broadly stated, this work adds ^{17}O NMR to the "NMR tool box" available to chemists for the study of the wide variety of oxygen-bearing materials of interest, including organic and biological molecules.*

Why did this research need the MagLab? *The measurement required the most powerful NMR magnet in the world, the MagLab's 35.2T Series Connected Hybrid magnet to overcome the intrinsically low NMR sensitivity of the ^{17}O nuclei*. The significantly-boosted sensitivity was critical to the successful detection of ^{17}O NMR signals from D-glucose. *The ultrahigh magnetic field also provides an unprecedented NMR resolving power that is uniquely suited to the study of carbohydrate compounds in which all oxygen-containing functional groups are chemically similar*.

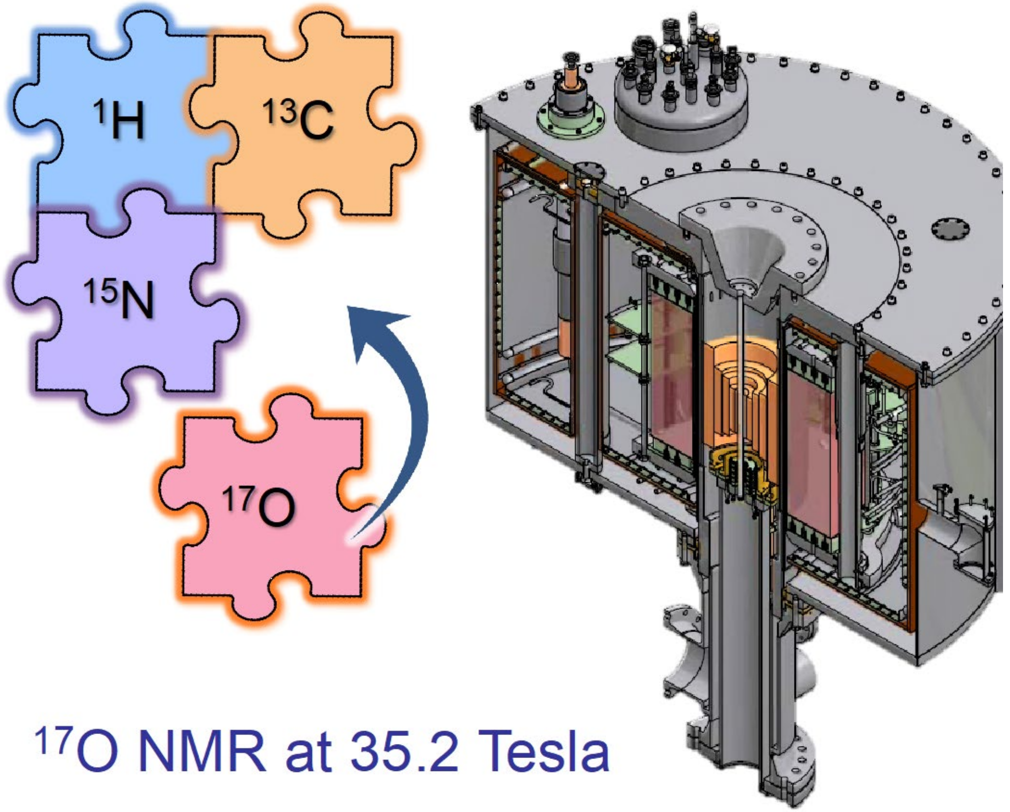

Figure: ^{17}O solid-state NMR is the final piece of the puzzle for characterizing organic and biological molecules. Experiments at 35.2 T on the MagLab's Series Connected Hybrid magnet are allowing for detailed investigations of oxygen atoms in glucose and carbohydrate molecules of increasing complexity.

Facilities and instrumentation used: NMR/MRI Facility: MagLab's 18.8 T/800 MHz; DC Facility: MagLab's 36-T Series Connected Hybrid Magnet.

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