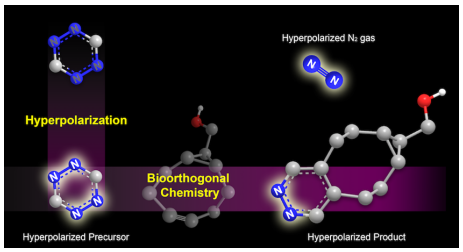
The production of hyperpolarized 15N2 gas and molecular probes for use in magnetic resonance imaging

Unmet Need

Magnetic resonance (MR) is a valuable tool for studying the structure, function, and dynamics of molecular species both *in vitro* and *in vivo*. However, conventional MR suffers from poor sensitivity at thermal equilibrium. To overcome the low sensitivity of conventional MR, hyperpolarized-MR (HP-MR) was developed allowing for the detection of target nuclei with greater sensitivity. In particular, hyperpolarization of ^{13}C and ^{15}N can provide more comprehensive structural information than conventional ^{1}H nuclear MR (NMR). However, current applications of HP-MR mostly rely on hyperpolarization of target compounds in dedicated hyperpolarizers as biomolecules can typically not be hyperpolarized directly *in vivo*. The *ex vivo* hyperpolarized molecules often enter multiple metabolic pathways in living systems and cannot be localized and targeted to specific locations. Therefore, the development of new chemicals tools for the accurate and sensitive imaging of biomolecules, metabolites and small molecules is needed.

Technology

Scientists at Duke have developed a novel hyperpolarization strategy that utilizes biorthogonal chemistry to hyperpolarize molecular targets for use in biomedical and clinical imaging research. The invention allows for the examination of molecular targets with high sensitivity and may be useful for the study of small molecules, metabolites, and other biomolecules *in vivo* and *in vitro*. The strategy involves hyperpolarization of ^{15}N-labeled tetrazines by SABRE-SHEATH (Signal Amplification by Reversible Exchange in Shield Enables Alignment Transfer to Heteronuclei),



Duke File (IDF) Number

IDF #:T-006230

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Chemistry

Publication(s)

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External Link(s)

• From the lab of Dr. Qiu Wang

followed by cycloaddition of the hyperpolarized tetrazine with an azadienophile to produce $^{15}N_2$-labeled products and hyperpolarized $^{15}N_2$ gas. In addition to offering a useful molecular tag in HP-NMR and HP-MRI, this is also the first reported production of para-$^{15}N_2$ gas. The tag has been demonstrated with a range of biologically important molecules, including amino acids, sugars, and drug compounds.

Advantages

- Generally applicable and chemically specific tags for monitoring molecules using HP-NMR and HP-MRI
- Does not require *ex vivo* hyperpolarization
- Offers a method for producing hyperpolarized $^{15}N_2$ gas, a biologically innocuous gas that may be useful for *in vivo* applications, including pulmonary imaging