Visualization of Spin Dynamics in Parahydrogen-Based Spin-Lock Induced Crossing Experiments using Generalized Angular Momentum Probability Surface Approach

Jingyan Xu[1,2], Dmitry Budker[1,2,3], Danila A. Barskiy[1,2]

1. *Helmholtz-Institut Mainz, GSI Helmholtzzentrum für Schwerionenforschung, 55128 Mainz,*
2. *Institut für Physik, Johannes Gutenberg Universität-Mainz, 55128 Mainz, Germany*
3. *University of California at Berkeley, California 94720-7300, USA*

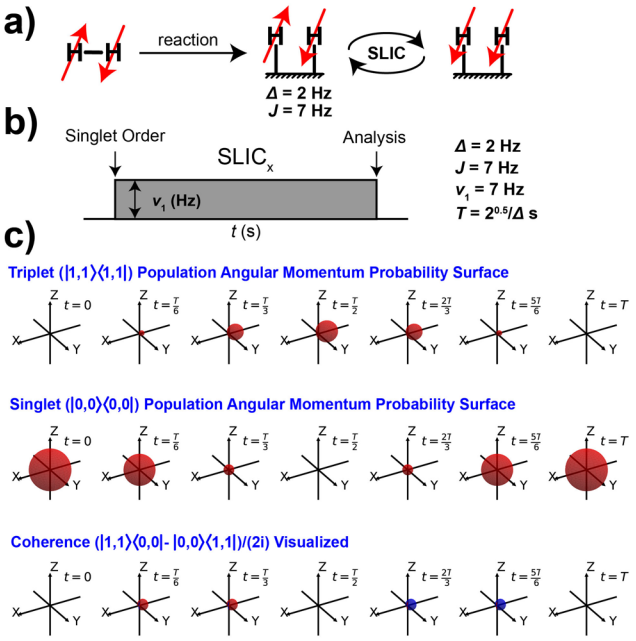

Figure 1. a) Hydrogenation with parahydrogen results in the formation of product with NMR parameters Δ (chemical shift difference) and *J* (spin-spin coupling) with subsequent application of the spin-lock induced crossing (SLIC) pulse. b) Parameters of the SLIC pulse used in the simulations. c) Generalized for multispin systems angular momentum probability surfaces in the rotating frame as a function of SLIC pulse duration for the states $|1,1\rangle\langle 1,1|$ (top), $|0,0\rangle\langle 0,0|$ (middle), and coherence $(|1,1\rangle\langle 0,0| - |0,0\rangle\langle 1,1|)/(2i)$, in the experiment defined in Figure 1b.

A pictorial description of nuclear spin dynamics is desirable for understanding parahydrogen-based hyperpolarization techniques as well as for the rational design of novel NMR pulse sequences [1]. Current descriptions are based either on energy level population diagrams or on product operators which are both visually incomplete. Here we seek to offer an alternative approach to visualizing spin dynamics in coupled multispin systems. Instead of using the shape of linearly combined spherical harmonics [2], we generalize the angular momentum probability surface method [3] and present its application for describing spin-lock induced crossing (SLIC) experiment [4] with initial parahydrogen-induced polarization (Figure 1). Mathematically, it can be proven that probability surface sets directly reflect the rotational symmetries and uniquely correspond to the specific states of the spin systems.

Generalized angular momentum probability surface plots in the rotating frame were calculated as a function of SLIC pulse duration (Figure 1c). They correspond to the probability of finding specific states with maximal projections, i.e., $|\mathbf{1},\mathbf{1}(\theta,\varphi)\rangle$ and $|\mathbf{0},\mathbf{0}(\theta,\varphi)\rangle$, along the measurement direction (θ,φ) for the populations as well as for the coherence (details will be given in the presentation). As expected, during application of the resonant SLIC pulse, magnetization along -*x* direction is formed at the expense of singlet population; maximum conversion occurs at half of the SLIC period, $T = \sqrt{2}/\Delta$, where Δ is the chemical shift difference in the parahydrogen-nascent pair. Generalized angular momentum probability surface method offers a convenient way to represent spin dynamics in parahydrogen-induced polarization experiments. We anticipate its further applications in describing SABRE and other experiments employing spin order transfer sequences.

REFERNCES: [1] Levitt M H. *Spin dynamics*. John Wiley & Sons, **2013**. [2] Garon A et al, *Phys. Rev. A*, **2015**, 91(4): 042122. [3] Auzinsh et al. *Optically polarized atoms.* Oxford University Press, **2010**. [4] DeVience et al, *Phys. Rev. L* 111.17 (2013): 173002.; Barskiy el al, *J. Magn. Reson.*, **2017**, 276: 78-85.; Barskiy et al, *J. Phys. Chem. C*, **2016**, 120(51): 29098-29106.

ACKNOWLEDGEMNT: We gratefully acknowledge the financial support from Alexander von Humboldt Foundation in the framework of the Sofja Kovalevskaja Award.

Multiparameter Optimization of the SABRE-relay-based Polarization of Methanol

Erik Van Dyke[1,2], James Eills[1,2], Dmitry Budker[1,2,3], Danila A. Barskiy[1,2]

1. *Helmholtz-Institut Mainz, GSI Helmholtzzentrum für Schwerionenforschung, 55128 Mainz*
2. *Institut für Physik, Johannes Gutenberg Universität-Mainz, 55128 Mainz, Germany*
3. *University of California at Berkeley, California 94720-7300, USA*

The advent of SABRE-relay has greatly expanded the range of molecules amenable to the non-hydrogenative PHIP methodology [1-2]. In this process, labile protons which are hyperpolarized though spin order transfer from parahydrogen, are exchanged to a secondary substrate (Figure 1a). This makes possible polarization of a wide range of substrates (e.g., alcohols) that cannot efficiently directly associate with the polarization transfer catalyst (Figure 1b).

In an effort to maximize the molar polarization of methanol in a SABRE relay system using the carrier amine benzylamine, we investigated molar polarization of system parameters as a function of catalyst and substrate concentrations (Figure 1c), and polarization transfer field magnitude (Figure 1d).

It is shown that molar ^{1}H polarizations of 0.2 mM in methanol is readily possible without using deuterated substrates and/or solvents (Figure 1c). It has been well documented that maximum spin order transfer from parahydrogen to substrate protons in a typical activated SABRE complex $[Ir(H)_2(IMes)(NR_2)_3]Cl$ occurs at a transfer field of ~6.5 mT [3]. However, it is observed that in our experiments another local maximum exists at higher field of ca. 19 mT (Figure 1d), hinting at a possible mechanism of polarization transfer [4] alternative to the one suggested for SABRE-relay.

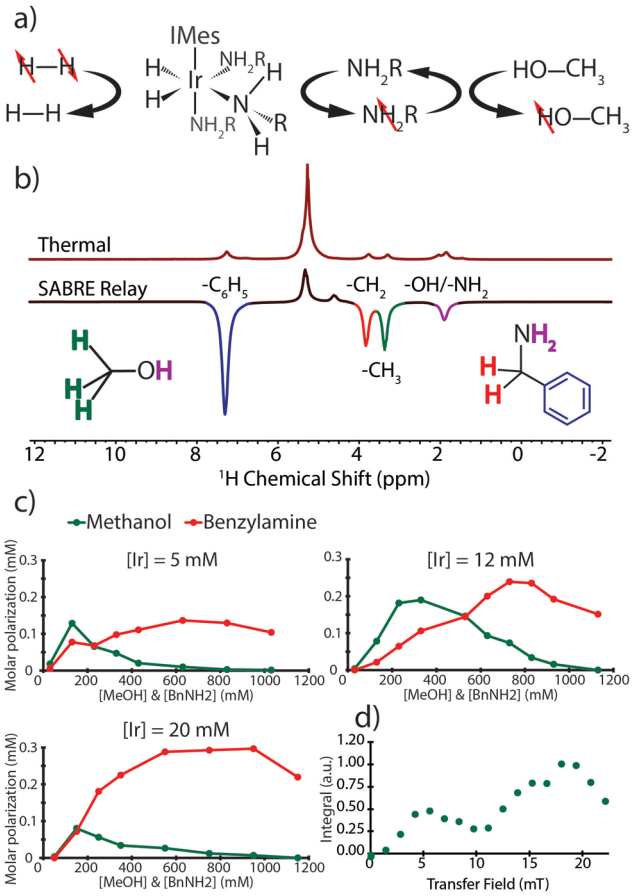

Figure 1. a) General SABRE relay schematic where polarization is first generated in a primary amine ligated to an active catalyst complex and then "relayed" to an alcohol. (b) Thermal ^{1}H NMR signal compared to SABRE-relay enhanced signal. Both spectra are of samples with 530 mM benzylamine and methanol and 12 mM Ir catalyst hyperpolarized by parahydrogen sparging at 6 mT and measured in a 1.4 T (Spinsolve Magritek) spectrometer. c) Plots showing the ^{1}H molar polarization of methanol CH_3 and benzylamine CH_2 as their concentrations are increased in tandem in the presence of three different catalyst concentrations. d) Transfer field dependence of SABRE-relay enhanced signal in ^{13}C methanol (polarization is transferred to ^{13}C using DEPT pulse sequence).

References: [1] Iali, W.; et al., *Chem. Sci*. **2018**, 9, 3677. [2] Iali, W.; et al., *Sci. Adv.* **2018**, 4, 6250. [3] Barskiy, D.A.; et al., *Prog. Nucl. Magn. Reson. Spectrosc.*, **2019**, 114-115, 33-70. [4] Emondts, M.; et al., *ChemPhysChem*, **2018**, 19 (20), 2614-2620.

Acknowledgements: We gratefully acknowledge the financial support from Alexander von Humboldt Foundation in the framework of the Sofja Kovalevskaja Award and the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No 766402.

Hyperpolarization of magnetic heteronuclei in amino acids and peptides by parahydrogen

Vitaly P. Kozinenko,[1,2] Alexey S. Kiryutin,[1,2] Alexandra V. Yurkovskaya,[1,2] Gerd Buntkowsky[3]

[1]International Tomography Center, Institutskaya str. 3a, 630090, Novosibirsk, Russia
[2]Novosibirsk State University, Pirogova str. 2, 630090, Novosibirsk, Russia
[3]Eduard-Zintl-Institut für Anorganische und Physikalische Chemie, Technische Universität Darmstadt
E-mail: vitaly.kozinenko@gmail.com

Over the last decade, parahydrogen-induced polarization (PHIP) has revealed itself as an exceptionally powerful method of NMR signal enhancement. One of the reasons for that stems from its ability to effectively hyperpolarize biologically relevant molecules by using low-cost experimental equipment.
Signal enhancement in PHIP method arises due to the non-equilibrium population of nuclear spin states in the para-hydrogen molecule and reaches a factor of 10^3 - 10^5. Moreover, PHIP build-up occurs on a timescale of several seconds, which makes a high throughput creation of hyperpolarized product possible. A particular interest is concentrated on the transfer of PHIP from protons to magnetic heteronuclei (^{13}C, ^{15}N, and others). Such heteronuclei are less susceptible to relaxation loss of polarization compared to protons and allow to record NMR spectra free of background signals.
We analyse the possibility of transferring PHIP to ^{13}C nuclei in specially designed compounds, comprising amino acid of interest and unsaturated alcohol moiety [1] (Fig. 1). This approach has already shown its efficiency for the hyperpolarization of metabolites (side arm hydrogenation PHIP). We test the efficiency of polarization transfer performed during hydrogenation at the ultralow magnetic field and compare it with the case of adiabatic inversion of magnetic field, often referred to as magnetic field cycling (MFC). Moreover, the feasibility of high field polarization transfer by using radiofrequency pulses is demonstrated. We also probe the long lived spin states in the product molecules suitable for polarization storage. We demonstrate the ^{13}C PHIP hyperpolarization for tyrosine, lysine and glycine esters, as well as for peptide.

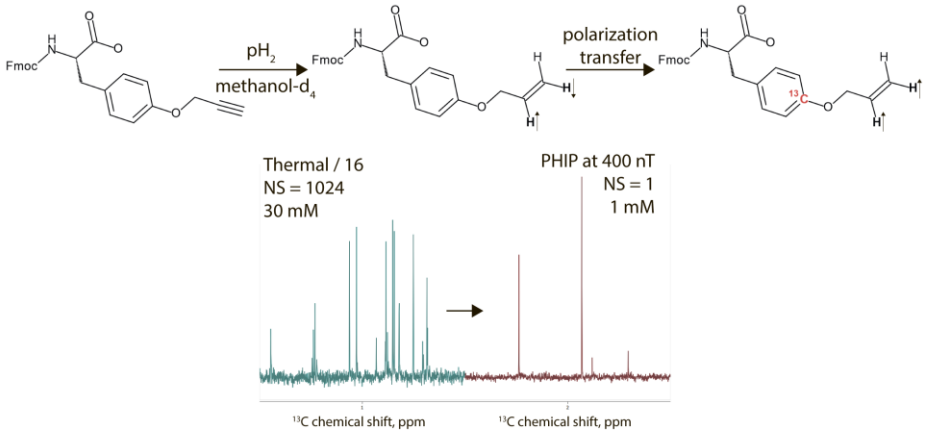

Fig. 1. A procedure for the creation of PHIP hyperpolarised Fmoc-L-tyrosine-(O-allyl)-OH with subsequent polarization transfer to ^{13}C in tyrosine fragment (top). Thermal and hyperpolarized ^{13}C spectra of the product molecule (bottom).

REFERENCES: (1) G. Sauer, D. Nasu, D. Tietze, T. Gutmann, S. Englert, O. Avrutina, H. Kolmar, G. Buntkowsky, *Angew. Chem., Int. Ed.* **2014**, *53*, 12941-12945.

ACKNOWLEDGEMENTS: This research has been supported by Russian Foundation for Basic Research (grant no. 19-29-10028). We acknowledge the Ministry of Science and Education of RF for providing access to NMR facilities at ITC.

Side-arm hydrogenation at fixed ultra-low field

Laurynas Dagys[1], Gamal A. I. Moustafa[1], Christian Bengs[1], Eleonora Cavallari[2], Francesca Reineri[2], and Malcolm H. Levitt[1]

[1]School of Chemistry, University of Southampton, SO17 1BJ, UK;
[2]Health Sciences, Centre of Molecular Imaging, University of Turin, 10126 Turin, Italy.

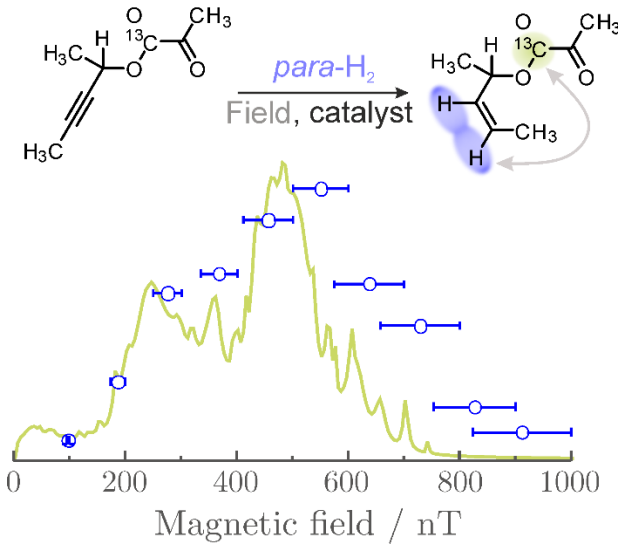

Figure 1. Hyperpolarised ^{13}C signal intensity of 3-penten-2-yl pyruvate as a function of magnetic field fixed during the hydrogenation reaction. Blue points indicate experimental values whereas green outline represents numerically simulated profile.

Hyperpolarisation using PHIP has led to promising progress towards production of highly polarised metabolites [1]. For example, in the context of pyruvate alone there are multiple methods that employ parahydrogen and transform its singlet spin-order into observable ^{13}C magnetisation, one of which – side-arm hydrogenation (SAH) is one of the most effective procedures [2,3]. This method involves a hydrogenation reaction and polarisation transfer that yields a precursor molecule and relays spin-order to ^{13}C site of the metabolite. The polarised metabolite is then detached from the side-arm and extracted from organic solvent. The polarisation transfer is often performed, in orderly fashion, either using pulsed NMR or magnetic field sweeps at ultra-low field [3,4,5]. This means that a chemical reaction is expected to take place *before* spin manipulations. In this study we explore the polarisation transfer by carrying out the reaction at fixed ultra-low magnetic field where the polarisation transfer occurs during the hydrogenation. Thus, the molecular system in the study is selected to have favourable spin evolution at ultra-low field that averages to high ^{13}C polarisation over the reaction time. In this work reaction of the 3-pentyn-2-yl pyruvate with parahydrogen was conducted under hydrogen pressure of 10 bar and at the boiling point of chloroform-d with $[Rh(dppb)(COD)]BF_4$ as the catalyst. The experimental observations are compared to the numerical simulations incorporating a simplified chemical reaction model. The results suggest that designing an optimal molecular system could be another simplifying step in ultra-low field SAH method for simpler and faster production of hyperpolarised metabolites.

REFERENCES: (1) Reineri F., et. al. MAGMA **2021**, 34, 24-47; (2) Iali W., et al. Angew. Chem. **2019**, 131, 30, 10377-10381; (3) Cavallari E., et. al. J. Magn. Reson. **2018**, 289, 12-17; (4) Korchak S., et. al. ChemistryOpen **2018**, 7, 344-348; (5) Dagys L., et. al. Analyst, **2021**, 146, 1772-1778.

Pilot Quality Assurance Study of Batch-Mode Clinical-Scale Automated Generation-3 Xenon-129 Hyperpolarizer

Md Raduanul H. Chowdhury,[1] Jonathan R. Birchall,[1] Peter Nikolaou,[2] Michael J. Barlow,[3] Anton Shcherbakov,[4,5] Boyd M. Goodson,[6] Eduard Y. Chekmenev[1,7]

[1]Department of Chemistry, Ibio, Karmanos Cancer Institute, Wayne State University, Detroit, MI 48202, USA
[2]XeUS Technologies LTD, Nicosia, Cyprus
[3]Sir Peter Mansfield Imaging Centre, University of Nottingham, Nottingham, NG7 2RD, United Kingdom
[4]Smart-A, Perm, Perm Region, 614000, Russia, [5]Custom Medical Systems (CMS) LTD, Nicosia, Cyprus
[6]Department of Chemistry and Biochemistry, Southern Illinois University, Carbondale, Illinois 62901, USA
[7]Russian Academy of Sciences, Moscow, 119991, Russia

Dynamic detection of lung functionality is challenging using conventional pulmonary MRI largely because of low proton density in the lung. Using hyperpolarized (HP) ^{129}Xe as a contrast agent in MRI for the detection of lung's ventilation, diffusion and gas exchange process can mitigate the challenges of lung's dynamic detection. The major complications associated with the use of HP Xe gas is the cost and complexity associated with the polarization process. NMR hyperpolarization increases the differences between two nuclear spin state far beyond thermal equilibrium level, and this is done by the process called Spin-Exchange Optical Pumping (SEOP). We use a clinical-scale batch-mode generation-3 polarizer device to perform the SEOP process to generate high degree of polarization with fast build-up rates, Figure 1a-c. As a part of our Quality Assurance (QA) study we performed several sweeping experiments of key operational parameters which will establish a robust operational range e.g., sweeping resonance frequency, electromagnet current, and RF pulse duration, temperature, and others. The consistency and reproducibility of the production of HP Xe gas using the device is one of its key features, as in this QA study it took ~700 SEOP cell refill for a significant drop in polarization. We observed no substantial deterioration of SEOP cell performance even with ~600 gas mixture refills of the SEOP cell (in first fill $\%P_{max}$ = 52.4±1.7%, T_b = 18.9±2.1 mins and after 600 refills $\%P_{max}$ = 40.5±1.3%, T_b = 18.7±1.9 mins), Figure 1d. Moreover, the quantitative trends of the SEOP cell's T_1 values ingrained the observations. This high level of polarization with fast buildup-rates accompanied with high degree of consistency will pave the way for the future in vivo imaging studies and further will make it feasible for clinical use.

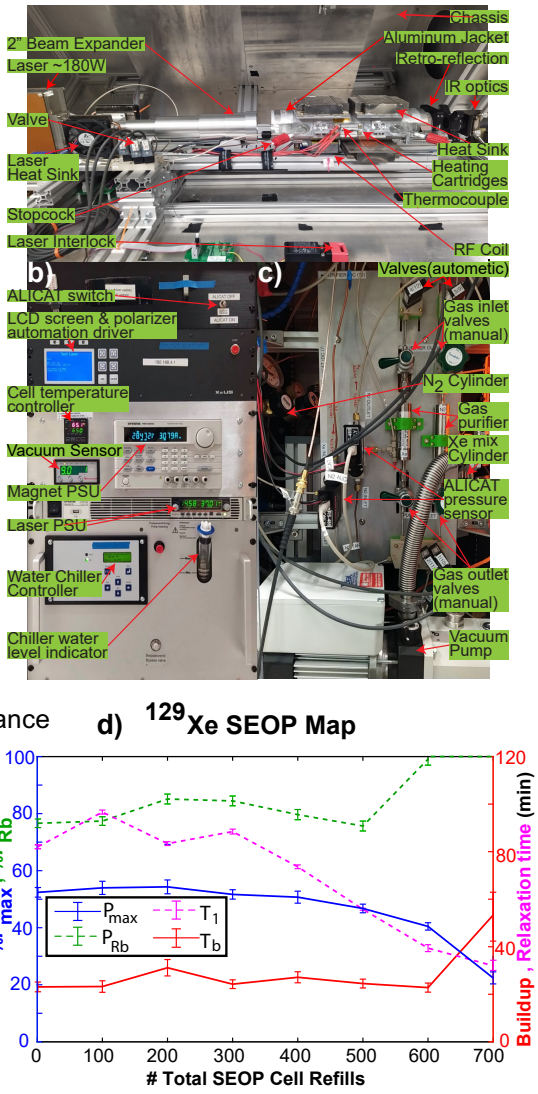

Figure 1. a) Annotated photo of open upper chassis of GEN-3 hyperpolarizer; b) Hyperpolarizer front panel; c) Internal hyperpolarizer gas-handling manifold; d) QA study data of ^{129}Xe polarization ($\%P_{max}$), Rb polarization (P_{Rb}), buildup time-constant (T_b) and relaxation time (T_1) as a function of the SEOP cell refill cycle count at 75 °C.

References: Birchall, J. R.; Nikolaou, P.; Coffey, A. M.; Kidd, B. E.; Irwin, R. K.; Murphy, M.; Molway, M.; Bales, L. B.; Goodson, B. M.; Barlow, M. J.; Chekmenev, E. Y., Batch-Mode Clinical-Scale Optical Hyperpolarization of Xenon-129 Using an Aluminum Jacket with Rapid Temperature Ramping. *Anal. Chem.* **2020,** *92* (6), 4309-4316.

Acknowledgements: DOD CDMRP W81XWH-15-1-0271, W81XWH-15-1-0271, W81XWH-20-1-0576 and W81XWH-20-1-0578.

Exploring SABRE Polarisation Transfer using *in-situ* Earth's field NMR

Matheus Rossetto[1], Fraser Hill-Casey[1] and Meghan Halse[1]
[1]Department of Chemistry, University of York, Heslington, York, YO10 5DD, UK

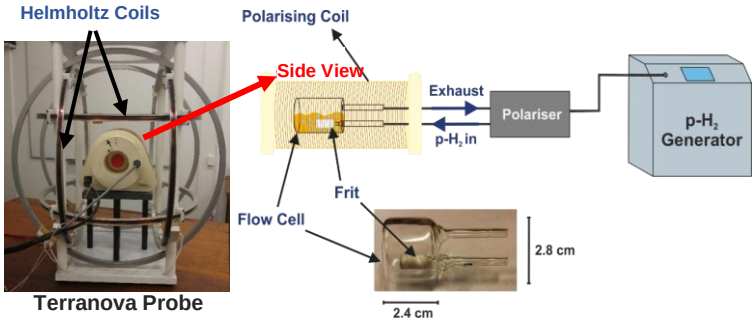

Figure 1. In-situ EFNMR SABRE setup consisting of a p-H_2 generator attached to a glass flow cell that sits within the EFNMR probe. The setup makes use of a built-in polarising coil and a set of triaxial Helmholtz coils.

The *para*-hydrogen (*p*-H_2) based hyperpolarisation technique, Signal Amplification by Reversible Exchange (SABRE) [1] is typically carried out with NMR detection in the high-field regime (> 1 T), while polarisation transfer occurs *ex-situ* in the ultra-low field regime (ca. 0 – 10 mT). This two-stage approach provides limited scope to explore the polarisation transfer step directly in the weak field regime.

In situ SABRE hyperpolarisation can be achieved using the Earth's Field NMR (EFNMR) setup shown in Figure 1, where electromagnets are used to generate the desired polarisation transfer field (PTF) and the highly homogeneous Earth's magnetic field (ca. 50 µT) is used for signal detection.[2] During bubbling of *p*-H_2 through the SABRE sample, PTF's in the mT range are achieved using the polarising coil on the outside of the EFNMR probe. PTFs in the nT - µT range are accessed using a set of 3-axis Helmholtz coils to actively cancel the Earth's magnetic field. In this way, the effect of the full range of PTF's, and hence both homo and heteronuclear polarisation transfer, can be probed directly using this apparatus.

In this work we focus on strongly coupled ^{1}H - ^{19}F systems. ^{19}F is our heteronucleus of choice due to its 100% natural abundance as well as the very small difference in Larmor frequency between ^{1}H and ^{19}F (~120 Hz) in the Earth's magnetic field, allowing for simultaneous observation of ^{1}H and ^{19}F in a single spectrum. Analysis of the form of the *J*-coupled EFNMR spectra for a range of SABRE-enhanced fluorinated N-heterocycles as a function of PTF provides insight into the magnetic states that are enhanced under different polarisation transfer conditions. Going forward, these insights can be exploited to optimize the SABRE polarisation transfer process, particularly for improved polarisation transfer from ^{1}H to heteronuclei.

References:

(1) Adams, R., *Science*, **2009**, *323*, 1708–1711.
(2) Casey, F.; et al *Molecules*, **2019**, *24*, 4126.

Acknowledgments: This work was supported by the EPSRC [grant number: EP/R028745/1]

Reaction monitoring on amide coupling of amino acid derivatives using parahydrogen based hyperpolarization technique

Keunhong Jeong[1*]

[1]Department of Chemistry, Korea Military Academy, Seoul, South Korea

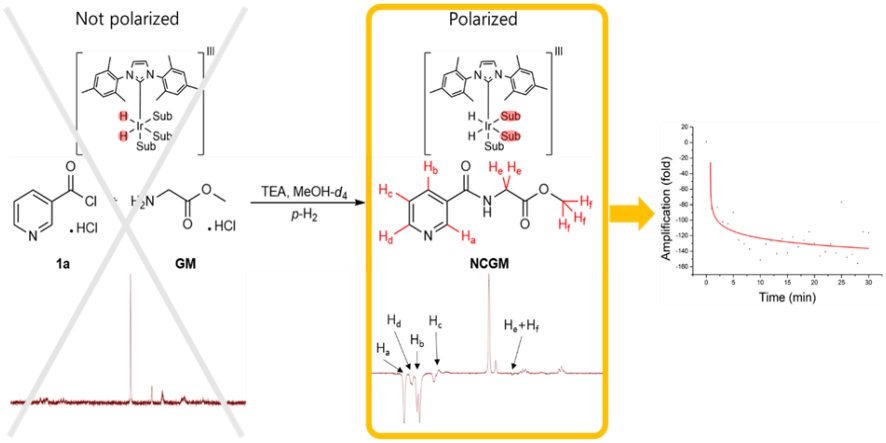

Figure 1. Esterified glycine with nicotinoyl chloride hydrochloride, were observed with using laboratory-built SABRE reaction monitoring system

NMR (Nuclear Magnetic Resonance) and MRI (Magnetic Resonance Imaging) are the key spectroscopic and medical imaging technology in both science and industry. However, a high cost and effort for installation and maintenance of superconducting magnets and cryogenic conditions are considered as the major obstacle in taking full advantage of NMR and MRI. One of the best ways to overcome the need for superconducting magnets is to exploit hyperpolarization, in which spins are polarized beyond the Boltzmann distribution. Of several potential hyperpolarization techniques, parahydrogen, one of the spin isomers of hydrogen, is in particular a promising tool for obtaining hyperpolarized materials and enhancing reaction monitoring sensitivities. Here, several recent data on hyperpolarized materials will be introduced[1,2] and reaction monitoring on amide coupling of amino acid derivatives using Signal Amplification by Reversible Exchange (SABRE) will be discussed with its meaning and its future applications[3].

REFERENCES [1] Signal amplification by reversible exchange for COVID-19 antiviral drug candidates Hye Jin Jeong, Sein Min, Heelim Chae, Sara Kim, Gunwoo Lee, Sung Keon Namgoong, Keunhong Jeong* *Scientific Reports*, 10(1), 1-13 (**2020**)

[2] Optimization of Signal Amplification by Reversible Exchange for polarization of Tridentate Chelating Bis [(2-pyridyl) alkyl] amine Sein Min, Heelim Chae, Hye Jin Jeong, Kiwoong Kim, Sung Keon Namgoong*, Keunhong Jeong * *Analyst*, 146(7), 2368-2373 (**2021**)

[3] Heelim Chae, Sein Min, Hyejin Jeong, Sung Keon Namgoong, Sangwon Oh, Kiwoong Kim, Keunhong Jeong* *Analytical Chemistry*, 92(16), 10902-10907 (**2020**)

Towards Photochemical Reaction Monitoring using Hyperpolarised Benchtop NMR Spectroscopy

Alastair Robinson[1], Meghan Halse[1], Simon Duckett[1]

[1]Deparment of Chemistry, University of York, York, UK, YO10 5DD

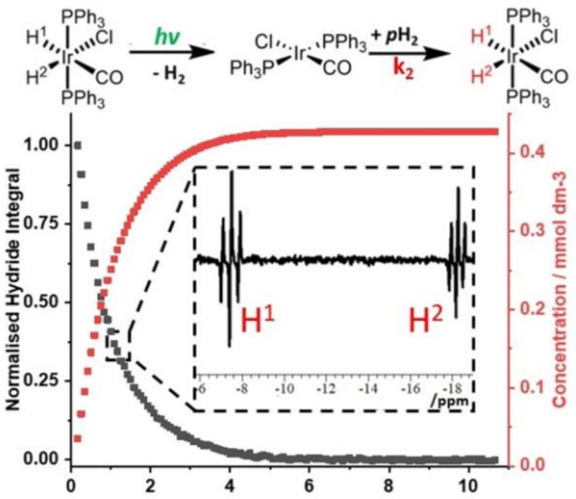

Figure 1. Reaction monitoring for the oxidative addition of pH_2 to $[IrCl(CO)(PPh_3)]_2$ after photoinitiation, highlighting the decay of hyperpolarised hydride signals (grey) and growth of the reaction product (red).

Benchtop NMR spectrometers offer unique capabilities for reaction monitoring compared to their high-field alternatives. The increased portability, *protio* solvent tolerance and higher accessibility of these spectrometers make them well suited for mixture analysis and allow for facile incorporation of additional features such as photochemical initiation or flow systems [1].

One drawback of the lower operational magnetic field strength of benchtop NMR (1 – 2 T) is a reduction in sensitivity. This is problematic for reaction monitoring where detecting low concentration, transient species is desirable for mechanistic insights. To overcome this limitation, hyperpolarisation techniques can be employed. One method, known as PHIP (*Para*Hydrogen Induced Polarisation), utilises *para*hydrogen (pH_2) to chemically modify an analyte. The hydrogenation process breaks the symmetry of pH_2, unlocking its latent polarisation, which enhances the signals observed for the product molecule [2]. This approach has been seen to be effective for thermal reaction monitoring at low-field [3] and experiments performed within this project have verified this method to be valid and robust.

The work presented focuses on the expansion of this technique to investigate photochemical reactions through the integration and optimisation of a low-cost, *in situ* photoinitiation step. This advancement dramatically increases the range of chemical reactions that can be explored (Figure 1) and opens a route to observe millisecond timescale processes. Within this regime, there is potential to detect the initial magnetic evolution of the chemical system post-irradiation, which encodes additional diagnostic information into the spectra recorded. This interesting spin physics phenomenon has been previously observed at high-field [4] and is now potentially viable at low-field for the first time using photochemical pump – NMR probe experiments.

REFERENCES:

[1] E. Danieli, J. Perlo, A. L. L. Duchateau, G. K. M. Verzijl, V. M. Litvinov, B. Blümich and F. Casanova, *ChemPhysChem,* **2014**, 15, 3060-3066.
[2] S. B. Duckett and R. E. Mewis, *Acc. Chem. Res.*, **2012**, 45, 1247-1257.
[3] K. Jeong, S. Min, H. Chae and S. K. Namgoong, *Magn. Reson. Chem*., **2019**, 57, 44-48.
[4] B. Procacci, P. M. Aguiar, M. E. Halse, R. N. Perutz and S. B. Duckett, *Chem. Sci*., **2016**, 7, 7087-7093.

Relaxation of Parahydrogen in Surfactant-Coated Glass NMR Tubes

James Sack[1*], Luciano Viola[1*], Dominic Caruso[1*], Jennifer Necsutu[2*], James Daley[1*], Robert Chimenti[1], and Nicholas Whiting[1,3]

[1]Dept. of Physics & Astronomy, Rowan University. Glassboro, NJ (USA)
[2]Dept. of Chemistry & Biochemistry, Rowan University. Glassboro, NJ (USA)
[3]Dept. of Molecular & Cellular Biosciences, Rowan University. Glassboro, NJ (USA)

*Undergraduate Researcher

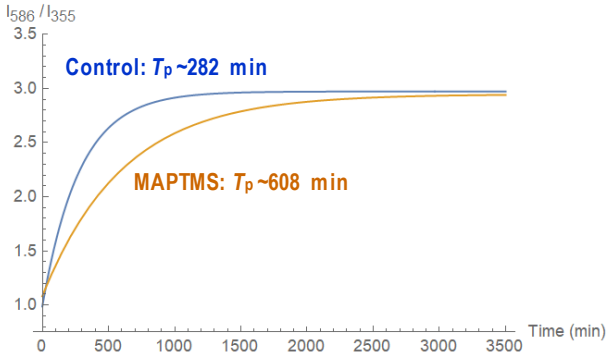

Fig. 1: Effect of surfactant on pH_2 relaxation (T_p). Longitudinal comparison of the ratio of the ground state ortho/para Raman peaks in valved NMR tubes: the control was bare glass (no surfactant) and the other was coated in MAPTMS. Both tubes were evacuated to ~90 mTorr prior to adding pH_2.

Following production, parahydrogen gas (pH_2) will relax to its normal isomeric abundance (25% at room temperature). This relaxation rate varies based on the surface chemistry of the container; for instance, while pH_2 retains its integrity for weeks while stored in an aluminum cylinder [1], it relaxes over the course of hours within a valved glass NMR tube [2]. This is due to paramagnetic impurities that are found within the glass itself, which accelerates the reconversion of pH_2 into normal hydrogen gas [3]. The work presented here investigates if the pH_2 relaxation time is effected by the addition of surfactant coatings on the inside surface of the valved NMR tubes, with the idea that the surfactant may act as a barrier between the pH_2 and paramagnetic impurities. Fig. 1 shows that the addition of a common silane-terminated surfactant (3-(Methacryloyloxy)propyltrimethoxysilane—'MAPTMS') increased the relaxation time by more than two-fold compared to bare glass. To date, we have investigated seven different surfactants of varying size and branching; these mostly increased the pH_2 relaxation time by 1.5x-2x. We also report the effects of oxygen exposure to pH_2 relaxation in an uncoated NMR tube; unsurprisingly, the oxygen significantly shortens the pH_2 relaxation rate [4]. Indeed, we expect that the addition of surfactants can provide even longer relaxation times than reported here, as tubes were only evacuated to ~90 mTorr. This work was carried out using longitudinal Raman spectroscopy directly on the NMR tube, comparing the ground state ortho peak at 586 cm^{-1} (J: $1\rightarrow3$) to the ground state para peak at 355 cm^{-1} (J: $0\rightarrow2$). The research presented here will be of interest to those pursuing longitudinal studies on a single aliquot of parahydrogen, as well as those who wish to shorten the time needed to calibrate their pH_2 percentage when optimizing their parahydrogen generator.

Acknowledgements: This research was supported by Rowan University Seed Funding.

References: [1] Feng, B., *et al. J. Magn. Reson*. 214 (2012); [2] Hovener, J.B., *et. al. NMR Biomed.* 26 (2013); [3] Parrott, A.J., *et. al. Appl. Spec*. 73 (2018); [4] Wagner, S. *Magn. Reson. Mat. In Phys., Bio., Med*. 27 (2014)