

### First Conference on Zero and Ultra-Low Field NMR

A virtual school and conference



The 20 posters below have been posted on Twitter by the poster presenters from Friday August 28<sup>th</sup> to Tuesday September 1<sup>st</sup> 2020. Virtual rooms will be set during two sessions so that participants can talk with the poster presenters, one room per poster. Poster 1-10 will have a dedicated virtual room during Session I (4:00-5:30 pm UTC, Wednesday September 2<sup>nd</sup> 2020) while posters 11-20 will have a dedicated virtual room during Session II (4:00-5:30 pm UTC, Thursday September 3<sup>rd</sup> 2020)

#### Poster session I – 4:00-5:30 pm UTC, Wednesday September 2<sup>nd</sup> 2020

##### **Poster 1:** Optical detection of zero to earth's field nuclear magnetic relaxation dispersion (NMRD)

***Sven Bodenstedt<sup>1</sup>, Morgan Mitchell<sup>1</sup>, Michael Tayler<sup>1</sup>***

<sup>1</sup> ICFO, The Institute of Photonic Sciences, 08860 Castelldefels (Barcelona), Spain

Nuclear magnetic relaxation dispersion can be used to study nanoscale dynamic processes that occur on milli- to microsecond timescales. For relaxation mechanisms with correlation times above  $\tau_c > 10 \mu\text{s}$  accurate fitting to a model requires spin relaxation data below or close to the earth's magnetic field. Here, we demonstrate a detection method based on an optically pumped magnetometer that is capable of efficiently measuring  $^1\text{H}$   $T_1$ ,  $T_2$  and  $T_2^*$  relaxation between zero and 2.5 times the earth's field.

##### **Poster 2:** Effect of solvents on J-spectrum of Urea

***S. Alciček<sup>1</sup>, P. Put<sup>1</sup>, V. Kontul<sup>1</sup>, S. Pustelny<sup>1</sup>***

<sup>1</sup> Institute of Physics Faculty of Physics, Astronomy and Applied Computer Science, Jagiellonian University, Krakow, Poland

Urea is the major end-product of protein catabolism and an amide with two  $-\text{NH}_2$  groups joined by a carbonyl functional group. Protein exchange kinetic of amides, peptides, and proteins can provide information about the structure of the molecules in solution. We are investigating the behaviour of urea under different solutions and conditions using zero-field NMR. In our poster, we present the effect of proton exchange between urea amide protons and/or solvent on the J-spectra of urea.

##### **Poster 3:** Homemade high-resolution NMR spectrometer

***Pavel Kupriyanov<sup>1</sup>***

<sup>1</sup> Russia, St.-Petersburg state University

Despite the seeming simplicity, many complex problems were solved when creating the laboratory device. Laboratorian room have a many inconveniences. Far from industrial sites and cities, it is easy to use NMR in the Earth's field if solar activity is low.

## Poster 4: Photo-chemically induced dynamic nuclear polarization of heteronuclear singlet order

*Kirill Sheberstov<sup>1,2</sup>, **Liubov Chuchkova**<sup>3</sup>, John W. Blanchard<sup>1,2</sup>, Dmitry Budker<sup>1,2,4</sup>, Konstantin L. Ivanov<sup>5,6</sup>, Alexey S. Kiryutin<sup>5,6</sup>, Ivan V. Zhukov<sup>5,6</sup>, Alexandra V. Yurkovskaya<sup>5,6</sup>*

<sup>1</sup> Institut für Physik, Johannes Gutenberg Universität Mainz, 55128 Mainz, Germany

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<sup>3</sup> University in Bourgogne, 21000 Dijon, France

<sup>4</sup> University of California at Berkeley, California 94720-7300, USA

<sup>5</sup> International Tomography Center SB RAS, Novosibirsk, 630090, Russia

<sup>6</sup> Novosibirsk State University, Novosibirsk, 630090, Russia

Nuclear spins are usually polarized by a strong magnetic field, still resulting in just a small level of about 10<sup>-5</sup> of the total possible polarization. One way to boost the NMR signals is to perform chemically induced dynamic nuclear polarization (CIDNP), allowing in some cases to enhance signals up to thousands of times. The range of magnetic fields below ~10 mT is not usually considered to be interesting for CIDNP, as the achievable hyperpolarized magnetization goes down to zero, whereas the polarization character stays the same. In this work we report the case for which polarization character essentially changes when the magnetic field is lowered below ~1  $\mu$ T. This range is called zero-to ultra-low fields (ZULF) and it is special because in these fields nuclear spins of different types, e.g. <sup>1</sup>H and <sup>13</sup>C, may become strongly coupled. Here we show that photo-CIDNP hyperpolarizes heteronuclear singlet order of directly bonded <sup>1</sup>H-<sup>13</sup>C spin pair in para-benzoquinone molecule.

## Poster 5: Proton-relayed side-arm hydrogenation in high- and low-field

***Laurynas Dagys**<sup>1</sup>, Anil Jagtap<sup>2</sup>, Sergey Korchak<sup>1</sup>, Salvatore Mamone<sup>1</sup>, Philip Saul<sup>1</sup>, Malcolm H. Levitt<sup>1</sup>, Stefan Glöggler<sup>2</sup>*

<sup>1</sup> University of Southampton

<sup>2</sup> Max Planck Institute for Biophysical Chemistry

In this work we compare two different methods to polarize pyruvate with para-hydrogen via a side-arm hydrogenation routine that uses one additional proton to relay the polarization to a heteronucleus. One method is a pulsed transfer at high field and the second being a field cycling approach in nanotesla fields. The polarization transfer efficiency was experimentally tested at high-field and is compared to the numerically simulated efficiency for a magnetic field cycling experiment which has not yet been performed. The results suggest that both methods should be potentially applicable in a system where polarization is relayed to heteronuclei via a single proton.

## Poster 6: Rapid generation and purification of parahydrogen-polarized fumarate

*Stephan Knecht<sup>1</sup>, John W. Blanchard<sup>2</sup>, Danila Barskiy<sup>3</sup>, Eleonora Cavallar<sup>4</sup>, Laurynas Dagys<sup>5</sup>, Erik Van Dyke<sup>3</sup>, Maksim Tsukanovo<sup>3</sup>, Bea Bliemel<sup>3</sup>, Kerstin Münnemann<sup>6</sup>, Silvio Aime<sup>4</sup>, Francesca Reineri<sup>4</sup>, Malcolm H. Levitt<sup>5</sup>, Gerd Buntkowsky<sup>1</sup>, Alexander Pines<sup>3</sup>, Peter Blümle<sup>7</sup>, Dmitry Budker<sup>2,7</sup>, **James Ells**<sup>2,7</sup>*

<sup>1</sup> Eduard-Zintl-Institute for Inorganic Chemistry and Physical Chemistry, Technical University Darmstadt, 64287 Darmstadt, Germany

<sup>2</sup> Germany Helmholtz-Institut Mainz, GSI Helmholtzzentrum für Schwerionenforschung GmbH, 55128 Mainz, Germany

<sup>3</sup> Department of Chemistry, University of California, Berkeley, U.S.A.

<sup>4</sup> USA Dept. of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy

<sup>5</sup> University of Southampton, Southampton, United Kingdom

<sup>6</sup> Technical University of Kaiserslautern, Kaiserslautern, Germany

<sup>7</sup> Johannes Gutenberg University, D-55090 Mainz, Germany

Hyperpolarized fumarate is a novel biosensor for magnetic resonance imaging. It can be hyperpolarized cheaply and conveniently using parahydrogen-induced polarization. However, this process requires a chemical reaction, and the resulting hyperpolarized fumarate solutions are contaminated with the catalyst, unreacted precursor, and reaction side product molecules, and are hence unsuitable for use in vivo. We show hyperpolarized fumarate can be purified by acid precipitation as a pure solid, and later redissolved at a chosen concentration in a clean aqueous solvent. We form hyperpolarized fumarate in ~150 mM concentrations, at  $^{13}\text{C}$  polarization levels of 20-45%.

## Poster 7: $^{15}\text{N}$ SABRE Hyperpolarization of Radio sensitizing Antibiotic Nimorazole in Micro-tesla Magnetic Fields

**Oleg G. Salnikov**<sup>1,2,3</sup>, Nikita V. Chukanov<sup>1,2</sup>, Alexandra Svyatova<sup>1,2</sup>, Ivan A. Trofimov<sup>1,2</sup>, Mohammad S. H. Kabir<sup>4</sup>, Kirill V. Kovtunov<sup>1,2</sup>, Eduard Y. Chekmenev<sup>4</sup> and Igor V. Koptiyug<sup>1,2</sup>

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<sup>3</sup> Boreskov Institute of Catalysis SB RAS, Novosibirsk, Russia

<sup>4</sup> Wayne State University, Detroit, Michigan, United States

Nimorazole is a 5-nitroimidazole-based antibiotic which is now in Phase 3 clinical trial in Europe for potential use as a hypoxia radiosensitizer for treatment of head and neck cancers. Here we report hyperpolarization of three  $^{15}\text{N}$  nuclei of isotopically labeled [ $^{15}\text{N}_3$ ]nimorazole using SABRE in microtesla magnetic fields. Polarization ( $P_{15\text{N}}$ ) of the  $^{15}\text{NO}_2$  group reaches 3.2% and has a long-lasting lifetime of 5.9 min at the clinically relevant 1.4 T magnetic field. Dependences of  $P_{15\text{N}}$  on polarization transfer field and temperature showed the maxima at ~0.4  $\mu\text{T}$  and 54  $^\circ\text{C}$ , respectively. The feasibility of  $^{15}\text{N}$  MRI visualization of hyperpolarized [ $^{15}\text{N}_3$ ]nimorazole was demonstrated with high spatial and temporal resolution.

## Poster 8: Probing SABRE Polarisation Transfer to Heteronuclei with Earth's Field NMR

**Matheus Rossetto**<sup>1</sup>, Fraser-Hill Casey<sup>1</sup>, Meghan Halse<sup>1</sup>

<sup>1</sup> Department of Chemistry, University of York, Heslington, York, YO10 5DD, UK

Earth's field NMR (EFNMR) detection enables hyperpolarisation of target substrates *in-situ* of the detection field through the use of an additional switchable electromagnetic coil to meet conditions necessary for SABRE polarisation transfer during para-Hydrogen ( $p\text{-H}_2$ ) bubbling. SABRE-polarised  $^1\text{H}$  and  $^{19}\text{F}$  signals of 3,5-bis(trifluoromethyl)pyridine (3,5-bis TFMP) under different Polarisation Transfer Fields (PTF) of 6 mT and 48  $\mu\text{T}$  show the influence the polarisation transfer condition has on the substrate spin-state that is hyperpolarised, using EFNMR simulations to predict those hyperpolarised states. By integrating SABRE-polarisation *with in-situ EFNMR* detection we hope to better understand the processes involved in SABRE.

## Poster 9: Nuclear Magnetic Resonance Gyroscopes for Precise Positioning

**Riccardo Cipolletti**<sup>1,2</sup>, Janine Riedrich-Möller<sup>1</sup>, Robert Rölver<sup>1</sup>, Tino Fuchs<sup>1</sup>, Arne Wickenbrock<sup>2</sup> and Dmitry Budker<sup>2</sup>

<sup>1</sup> Robert Bosch GmbH, Corporate Sector Research and Advance Engineering, Advanced Technologies and Micro Systems

<sup>2</sup> Helmholtz-Insitut Mainz, Johannes Gutenberg-Universität Mainz

Precise positioning of vehicles is essential for modern mobility solutions. In the case when GPS signals and other systems are temporarily unavailable, high performance inertial sensors become a key component of navigation systems that widely use dead reckoning i.e. localization based on a previously determined position and precise directional sensor signals, including rotation and acceleration. Nuclear Magnetic Resonance (NMR) based gyroscopes enable high precision measurement of rotation rates – with a high potential of miniaturization. We present modelling of a Xenon and Rubidium based NMR gyroscope for parameter studies.

## Poster 10: Might a magnet be a spinning top?

***Pavel Fadeev<sup>1</sup>***, *Tao Wang<sup>2</sup>*, *Y. B. Band<sup>3</sup>*, *Dmitry Budker<sup>1,4</sup>*, *Peter W. Graham<sup>5</sup>*, *Alexander O. Sushkov<sup>6</sup>* and *Derek F. Jackson Kimball<sup>7</sup>*

<sup>1</sup> Helmholtz Institute Mainz, Johannes Gutenberg University, 55099 Mainz, Germany

<sup>2</sup> Department of Physics, Princeton University, Princeton, New Jersey 08544, USA

<sup>3</sup> Department of Chemistry, Department of Physics, Department of Electro-Optics, and the Ilse Katz Center for Nano-Science, Ben-Gurion University, Beer-Sheva 84105, Israel

<sup>4</sup> Department of Physics, University of California at Berkeley, Berkeley, California 94720-7300, USA

<sup>5</sup> Department of Physics, Stanford Institute for Theoretical Physics, Stanford University, California 94305, USA

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<sup>7</sup> Department of Physics, California State University - East Bay, Hayward, California 94542-3084, USA

Might a magnet be a spinning top?

Instead of pointing to once north,

wobble around it and nod  
by intrinsic spins cohort.

Aye, at small enough magnetic field  
a spectrum splitting is revealed.

We propose a strategy to construct a solid-state magnetometer operating in ultra-low fields, which we call a ferromagnetic gyroscope (FG). In it, intrinsic spins in a ferromagnet precess coherently around the direction of the magnetic field due to its intrinsic spins. In low enough magnetic fields, a splitting is predicted to occur in the resonance of the device, which will serve as a telltale sign of the precessing behaviour. Once realized, it can be used to test the reaction of intrinsic spin to general relativistic precession.



## Poster 11: Instrumentation for Probing and Optimizing SABRE Processes at Ultra-low Fields

**Fraser-Hill Casey**<sup>1</sup>, *Matheus Rossetto*<sup>1</sup>, *Aminata Sakho*<sup>1,2</sup> and *Meghan Halse*<sup>1</sup>

<sup>1</sup> Department of Chemistry, University of York, York, UK

<sup>2</sup> Centre for Hyperpolarisation in Magnetic Resonance, University of York, York, UK

Efficient Signal Amplification By Reversible Exchange (SABRE) hyperpolarisation for a given analyte requires the optimisation of a wide range of experimental conditions. In the standard approach, SABRE experiments are achieved using a two-stage method, where hyperpolarisation and detection are separated in time and space. Integration of a liquid nitrogen-based para-hydrogen generator with Earth's Field NMR (EFNMR) detection enables SABRE experiments to be performed in situ and allows for processes to be decoupled. Combined with an active field correction device, complex time-resolved and multi-step experiments, such as monitoring the formation of the SABRE-active catalyst, can be performed in a simple and reproducible manner.

## Poster 12: Towards ZULF detection of parahydrogen polarized metabolite

**Oksana Bondar**<sup>1</sup>, *James Eills*<sup>2</sup>, *John W. Blanchard*<sup>2</sup>, *Eleonora Cavallari*<sup>1</sup>, *Carla Carrera*<sup>1</sup>, *Kirill Sheberstov*<sup>2</sup>, *Silvio Aime*<sup>1</sup> and *Francesca Reineri*<sup>1</sup>

<sup>1</sup> Dept. of Molecular Biotechnology and Health Science, University of Torino

<sup>2</sup> Johannes Gutenberg-Universität Mainz

[1-<sup>13</sup>C]-pyruvate into lactate, is widely used to study different types of cancer. To obtain polarized metabolites, our laboratory uses the PHIP-SAH method, that greatly expands the number of molecules that can be polarized using para-hydrogen. In this work we explore the possibility to observe metabolites derivatives, hyperpolarized by means of PHIP-SAH, at Zero Magnetic Field.

## Poster 13: Relaxation measurements from zero to Earth's magnetic field

**Piotr Put**<sup>1</sup>, *Danila Barskiy*<sup>2</sup> and *Szymon Pustelny*<sup>1</sup>

<sup>1</sup> M. Smoluchowski Institute of Physics, Jagiellonian University, Łojasiewicza 11, 30-348 Kraków, Poland

<sup>2</sup> Department of Chemistry, University of California Berkeley, Berkeley, CA, 94720-3220, USA

NMR relaxometry is an important tool for characterization of heterogeneous materials, porous media, and chemical mixtures. Its combination with portability and operation at ultra-low magnetic fields makes such incarnation of NMR an attractive tool for chemical characterization.

We present a novel ultra-low-field NMR setup enabling relaxometry in a magnetic field range from Earth's magnetic field all the way to zero field. We demonstrate initial results on aqueous solution of glucose and propose research program aiming at low-field relaxation studies of blood and long-lived pyridine derivatives used as contrast agents.

## Poster 14: NV center based super resolution Nano-NMR

**VS Anjusha**<sup>1</sup>, *D Cohen*<sup>2</sup>, *A Marshall*<sup>3</sup>, *C Findler*<sup>1</sup>, *J Lang*<sup>1</sup>, *J Scheuer*<sup>3</sup>, *P Neumann*<sup>3</sup>, *A Retzker*<sup>2</sup>, *GT Genov*<sup>1</sup> and *F Jelezko*<sup>1</sup>

<sup>1</sup> Institute for Quantum Optics, Ulm University, Albert-Einstein-Allee 11, D-89081, Ulm, Germany

<sup>2</sup> Racah Institute of Physics, The Hebrew University of Jerusalem, 91904 Jerusalem, Givat Ram, Israel

<sup>3</sup> NVision Imaging Technologies GmbH, Albert-Einstein-Allee 11, D-89081, Ulm, Germany

NV center based room-temperature spectrometer is a promising tool for performing NMR in nanoscale volume at low field. However, poor spectral resolution is one of the major challenges in NV Nano-NMR. In this work, we try to investigate the correlation function of the temporal magnetic field noise induced by the diffusing spins at the NV centre and thereby understanding the line shape of the NMR spectrum. We show that the magnetic noise power spectrum can be deviated from the Lorentzian noise spectrum due to diffusion and this can lead to an improved resolution.

## Poster 15: Dissolution dynamic nuclear polarization-enhanced ZULF NMR (*d*DNP-ZULF NMR)

**R. Picazo-Frutos**<sup>1</sup>, **Q. Chappuis**<sup>2</sup>, *J. Eills*<sup>1</sup>, *S. F. Cousin*<sup>2</sup>, *Morgan Ceillier*<sup>2</sup>, *S. J. Elliott*<sup>2</sup>, *O. Cala*<sup>2</sup>, *John Blanchard*<sup>1</sup>, *D. Budker*<sup>1</sup> and *S. Jannin*<sup>2</sup>

<sup>1</sup> Helmholtz Institute Mainz, GSI Helmholtzzentrum für Schwerionenforschung, Mainz 55090, Germany

<sup>2</sup> Centre de Résonance Magnétique Nucléaire à Très Hauts Champs, 5 Rue de la Doua, 69100 Villeurbanne, France

Zero- and ultra-low field NMR is a modality of NMR experiment that do not require strong magnets with applications ranging from molecular spectroscopy and chemical-reaction monitoring to dark-matter searches and study of physics outside of the standard model. However, as any NMR experiment, it suffers from low sensitivity. In this work we combine a hyperpolarization technique called dissolution Dynamic Nuclear Polarization to enhance our signal and thus extend the reach of future applications.

## Poster 16: Zero-field NMR J-Spectroscopy of Organophosphorus Compounds

**S. Alcicek**<sup>1</sup>, *P. Put*<sup>1</sup>, *V. Kontul*<sup>1</sup>, *S. Pustelny*<sup>1</sup>

<sup>1</sup> Institute of Physics Faculty of Physics, Astronomy and Applied Computer Science, Jagiellonian University, Krakow, Poland

Organophosphorus compounds are a wide and diverse class of chemicals often investigated in NMR. The interest is driven by their role in biology and medicine as phosphorus-31 (<sup>31</sup>P) is key element of such important molecules as nucleic acids, ATP, etc. Here we present our investigation of organophosphorus compounds using zero-field NMR. We report the results of theoretical and experimental studies on phosphorus-based organic compounds by analysing their J-spectra. We demonstrate a good agreement between measurements and simulations.

## Poster 17: Real-time Nano diamond thermometry probing in-vivo thermogenic responses

Masazumi Fujiwara, Simo Sun, Alexander Dohms, Yushi Nishimura, Ken Suto, Yuka Takezawa, Keisuke Oshimi, Li Zhao, Nikola Sadzak, Yumi Umehara, Yoshio Teki, Naoki Komatsu, Oliver Benson, **Yutaka Shikano**<sup>1,2</sup>, and Eriko Kage-Nakadai

<sup>1</sup> Quantum Computing Center, Keio University

<sup>2</sup> Institute for Quantum Studies, Chapman University

Real-time temperature monitoring inside living organisms provides a direct measure of their biological activities, such as homeostatic thermoregulation and energy metabolism. Here, using quantum nanothermometers based on optically accessible electron spins of nitrogen vacancy centers in nanodiamonds, we demonstrate in-vivo real-time temperature monitoring inside nematode worms. We developed a thermometry system that can measure the temperatures of mobile nanodiamonds inside the worms. Using this system, we determined the increase in temperature based on the thermogenic responses of the worms during the chemical stimuli of mitochondrial uncouplers.

## Poster 18: Optimising SABRE of amines via *in-situ* Earth's Field NMR

**Aminata Sakho**<sup>1</sup>, Fraser-Hill Casey<sup>2</sup>, Meghan Halse<sup>2</sup> and Simon B. Duckett<sup>1</sup>

<sup>1</sup> Centre for Hyperpolarisation in Magnetic Resonance, University of York, York, UK

<sup>2</sup> Department of Chemistry, University of York, York, UK

Amines have previously been successfully hyperpolarised by SABRE and detected using high-field (HF) instruments. In this study, we report the detection of amine hyperpolarisation using an Earth's field NMR (EFNMR) instrument, where the catalytic activation process of SABRE has been followed in situ. The hyperpolarization level of these amines is increased by adding a co-ligand, dimethyl sulfoxide (DMSO). The effect of the addition of co-ligand on polarisation efficiency is studied herein. In parallel, the chemical exchange rate of the ligands (both amines and hydrides) and the corresponding thermodynamic parameters for these complexes have been explored at 11.7 T (500 MHz) to produce further insight into these processes.

## Poster 19: Applications of the NV centers in diamonds

**D. Olivares-Postigo**<sup>1,2</sup>, F. Gorrini<sup>1,2</sup> and A. Bifone<sup>1,2</sup>

<sup>1</sup> Center for Neuroscience and Cognitive Systems, Istituto Italiano di Tecnologia, Corso Bettini 31, 38068 Rovereto, Trento, Italy

<sup>2</sup> Department of Molecular Biotechnology and Health Sciences, University of Torino, Italy

Diamonds with nitrogen-vacancy (NV) centers provide intrinsic biocompatibility, robust chemistry within and on the surface of the diamond, combination of very high photostability, significant coupled magneto-optic properties, etc. that exceed the characteristics of other classes of fluorophores. This exceptional combination of properties makes NV centers unique fluorophores with emerging applications in a variety of fields such as ultra-sensitive nanoscale metrology as temperature / electric field sensors or measuring the magnetic field of biological molecules, as a magnetic resonance contrast agents or in the field of bioimaging among many other more applications.

## Poster 20: Chemical reaction monitoring at zero magnetic field

***Dudari B. Burueva***<sup>1,2</sup>, *James Eills*<sup>3,4</sup>, *John W. Blanchard*<sup>3</sup>, *Antoine Garcon*<sup>3,4</sup>, *Román Picazo Frutos*<sup>3,4</sup>, *Kirill V. Kovtunov*<sup>1,2</sup>, *Igor V. Koptug*<sup>1,2</sup>, *Dmitry Budker*<sup>3,4,5</sup>

<sup>1</sup> International Tomography Center, Novosibirsk, Russia

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<sup>3</sup> Helmholtz Institute Mainz, GSI Helmholtzzentrum für Schwerionenforschung, Mainz, Germany

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<sup>5</sup> University of California Berkeley, Berkeley, U.S.A.

Herein, the kinetics of the two-step hydrogenation of dimethyl acetylenedicarboxylate with parahydrogen was studied by zero-field nuclear magnetic resonance spectroscopy. It was shown that heterogeneous/biphasic chemical reactions can be monitored with high spectroscopic resolution using ZULF NMR. Importantly, the reaction can be monitored even when it is carried out in a metal container.

# Optical detection of zero to earth's field nuclear magnetic relaxation dispersion (NMRD)

Sven Bodenstedt<sup>1</sup>, Morgan Mitchell<sup>1</sup>, Michael Tayler<sup>1</sup>

<sup>1</sup> ICFO, The Institute of Photonic Sciences, 08860 Castelldefels (Barcelona), Spain

**Abbreviated abstract:** Nuclear magnetic relaxation dispersion can be used to study nanoscale dynamic processes that occur on milli- to microsecond timescales. For relaxation mechanisms with correlation times above  $\tau_c > 10 \mu\text{s}$  accurate fitting to a model requires spin relaxation data below or close to the earth's magnetic field. Here, we demonstrate a detection method based on an optically pumped magnetometer that is capable of efficiently measuring  $^1\text{H}$   $T_1$ ,  $T_2$  and  $T_2^*$  relaxation between zero and 2.5 times the earth's field.

## Related publications:

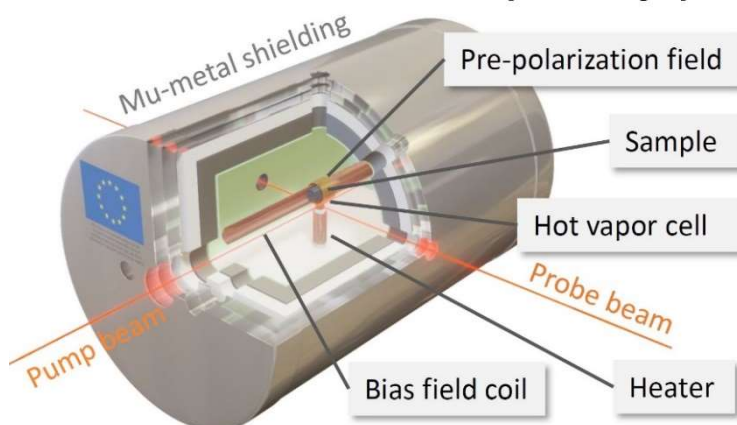
- Michael Tayler *et al*, JMR 297, 1-8 (2019); doi.org/10.1016/j.jmr.2018.09.014
- Michael Tayler *et al*, RSI 88, 091101 (2017); doi.org/10.1063/1.5003347



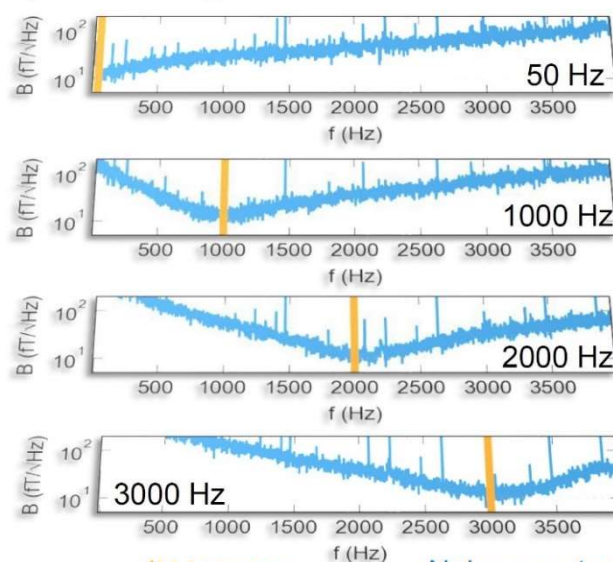
S. Bodenstedt - 1



## Methods: tunable optically pumped magnetometer



- Hartmann-Hahn matching of nuclear and atomic Larmor frequencies
- $\sim 10 \text{ fT}/\sqrt{\text{Hz}}$  sensitivity over a wide range of frequencies (0 Hz – 5500 Hz)



—  $^1\text{H}$  Larmor

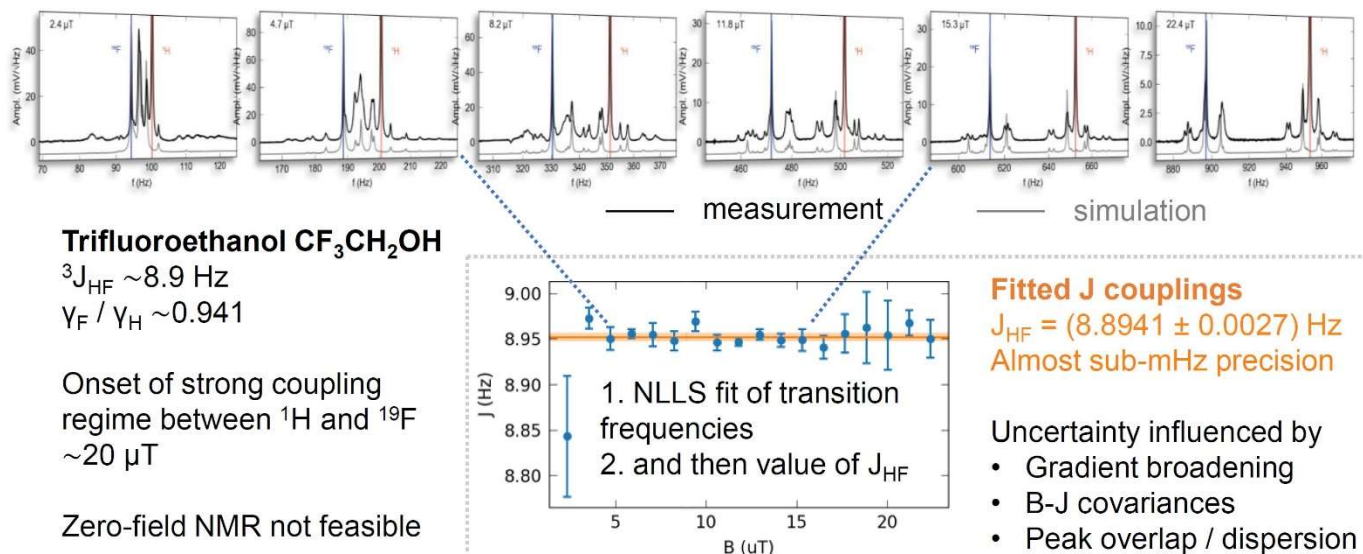
— Noise spectrum



S. Bodenstedt - 2



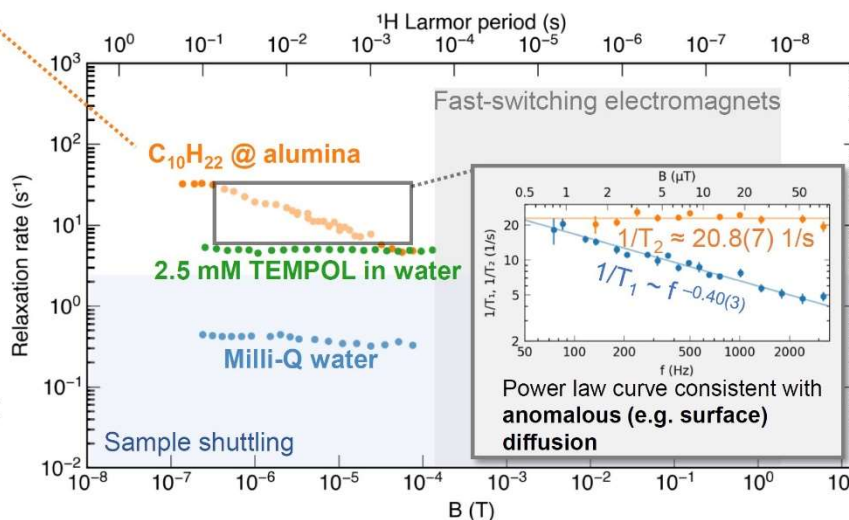
## Previous work: high resolution J-spectroscopy



## Results: NMRD over a wide field range



- Pre-polarization field  $> 20 \text{ mT}$
- No sample shuttling requirement
- 100% current duty cycle, due to active cooling
- Sample temperature  $\sim 30^\circ\text{C}$  (atomic vapor cell  $150^\circ\text{C}$ )





## Effect of solvents on J-spectrum of Urea

*S. Alcicek, P. Put, V. Kontul, S. Pustelny*

*Institute of Physics Faculty of Physics, Astronomy and Applied Computer Science, Jagiellonian University, Krakow, Poland*

**Abstract:** Urea is the major end-product of protein catabolism and an amide with two  $\text{-NH}_2$  groups joined by a carbonyl functional group. Protein exchange kinetic of amides, peptides, and proteins can provide information about the structure of the molecules in solution. We are investigating the behaviour of urea under different solutions and conditions using zero-field NMR. In our poster, we present the effect of proton exchange between urea amide protons and/or solvent on the J-spectra of urea.

### Related publications:

1. Yavari, I. et al. Org. Magn. Reson. 13, 68–71 (1980).
2. Barskiy, D. A. et al. Nat. Commun. 10, 1–9 (2019).



*S. Alcicek - 1*

**ZULF NMR**

### Why we do this?

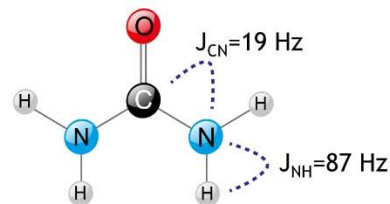
**NH hydrogen exchange (HX)** rate depends on:

- solvent
- pH
- concentration
- temperature

All these parameters influence  $^{15}\text{N}$ - $^1\text{H}$  **J coupling** interactions.

**Quadrupolar coupling** of urea with deuterium in  $\text{D}_2\text{O}$  solvent strongly modifies the molecular exchange leading faster relaxation.

**Zero-field NMR** enables investigations of chemical exchange processes.



### How we do this?

We use zero-field NMR to investigate **chemical exchange** processes in urea.

We measure fully labelled urea and  $^{15}\text{N}$  labelled urea in DMSO as an aprotic solvent,  $\text{H}_2\text{O}$  as an protic solvent, and  $\text{D}_2\text{O}$ .

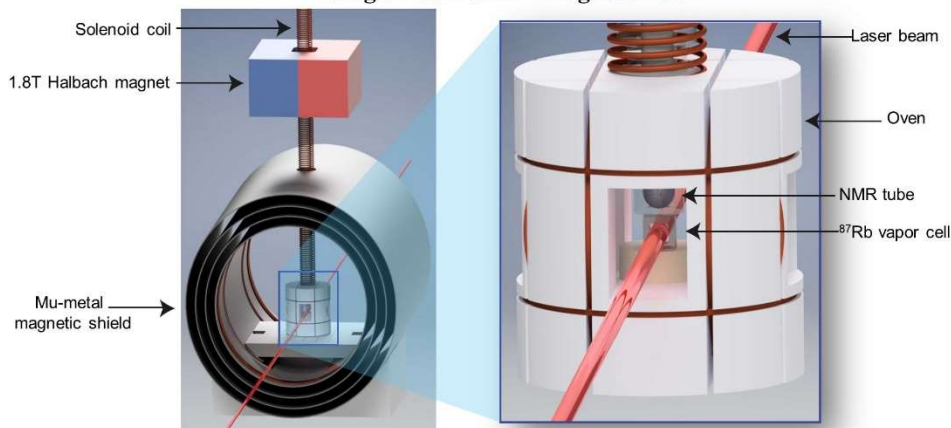


*S. Alcicek - 2*

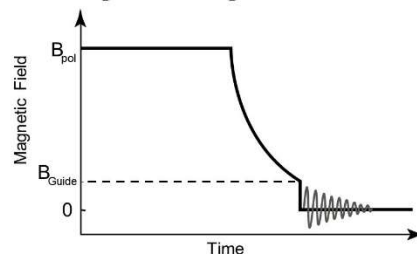
**ZULF NMR**

# Techniques and Methods

## Single Beam SERF Magnetometer



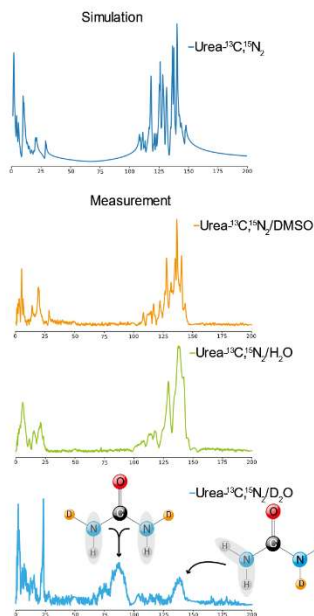
## Experimental procedure



Key elements of experimental setup.

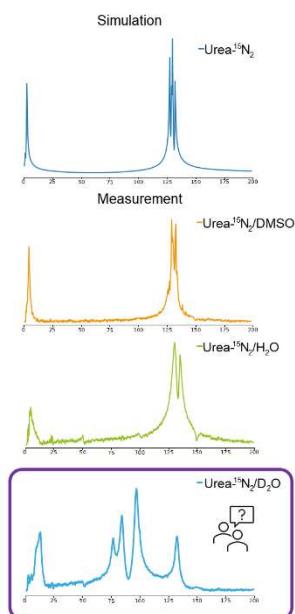
- Liquid sample is polarized in strong permanent magnet.
- Sample is transported to zero field region (magnetic shield).
- Laser light traversing vapor cell measures magnetic field -NMR signal detection-

## Results and Conclusion



- ❑ **Narrow lines** in DMSO despite HX between amide protons
- ❑ HX with water protons resulting in **line broadening**
- ❑ The additional broad peak due to -NHD group in D $_2$ O
- ❑ The narrower and stronger peak at ~23 Hz caused by  $J_{\text{CN}}$  in D $_2$ O

Let's discuss! ➡



WORK IN PROGRESS!



## Poster 3



St.-Petersburg state University

ZULF2020

# Homemade high-resolution NMR spectrometer

Pavel Kupriyanov, Russia, St.-Petersburg state University [p.kupriyanov@spbu.ru](mailto:p.kupriyanov@spbu.ru)

Despite the seeming simplicity, many complex problems were solved when creating the laboratory device. Laboratorian room have a many inconveniences

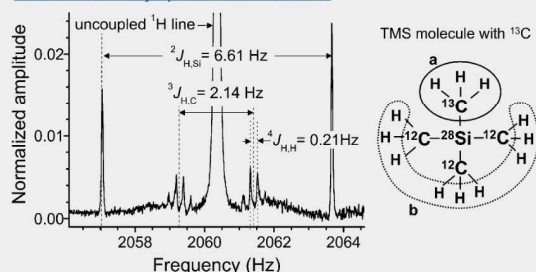
Far from industrial sites and cities, it is easy to use NMR in the Earth's field if solar activity is low.

### Main problems:

1. Electromagnetic interference
2. Local field inhomogeneity
3. Fluctuations of the Earth's magnetic field

**FUSERMORE:** The device must be portable. This is one of the main advantages over high-field NMR spectrometers. The second advantage is already included in the idea, this is the price.

What inspired the search for solutions to problems: Appelt S., Häsing F. W., Kühn H. et. All  
[DOI: 10.1016/j.cplett.2007.03.096](https://doi.org/10.1016/j.cplett.2007.03.096)



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# SENSOR

Electromagnetic interference is not just an electromagnetic shield problem.

### Initial sensor version



### Sensor today

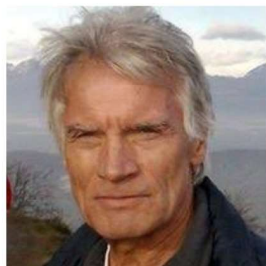
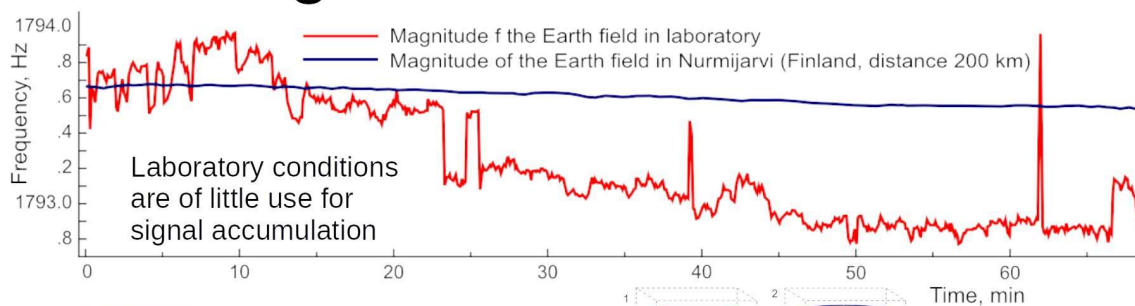


the same battery

The special geometry of the coil made it possible to reduce the thickness of the electromagnetic shield



# Signal accumulation

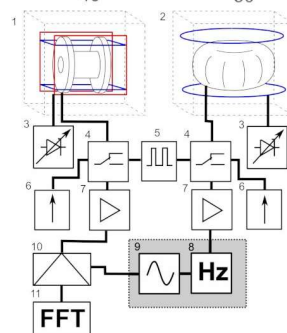


Jaynes Stepišnik used a second NMR sensor and used the signal to quadrature detect the signal from the first sensor

[DOI 10.1081/CI-200037034](https://doi.org/10.1081/CI-200037034)

This method is suitable for short signals in MRI, we have improved it for spectroscopy.

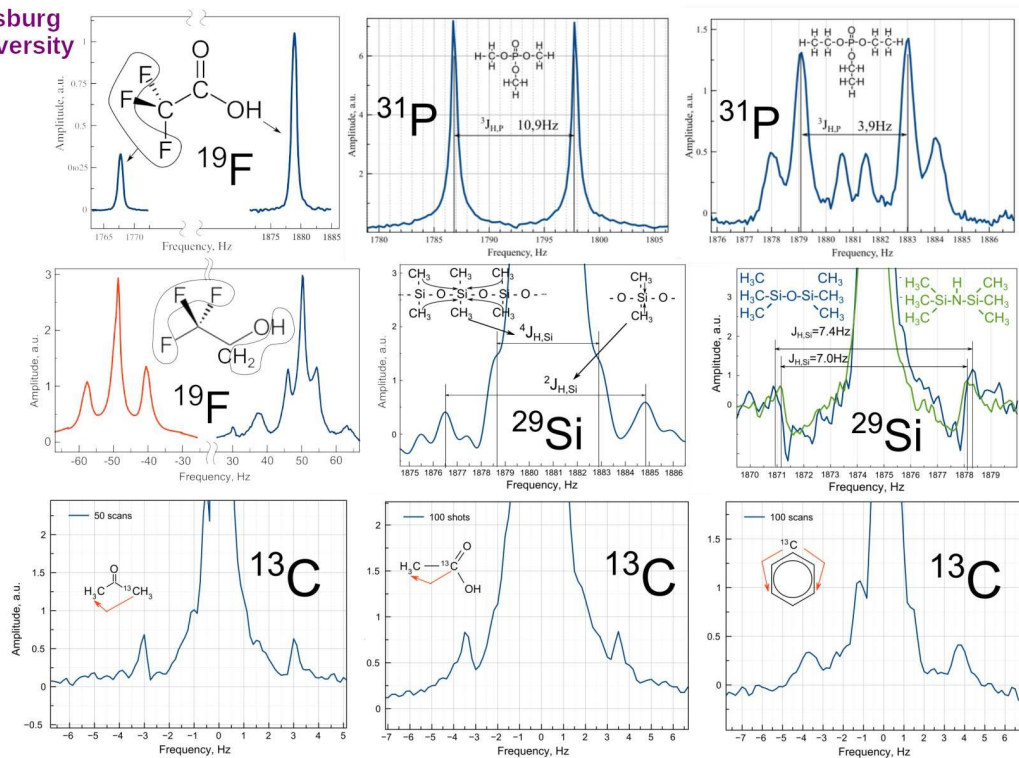
[Eurasian Patent № 034623](#)



1. Sensor for the sample
2. Additional sensor
3. Current stabiliser for shimming
4. Switching device
5. Microcontroller
6. Current source
7. Preamplifier with narrowband filter
8. Frequency meter
9. Sine Generator
10. Quadrature demodulator



## Spectra



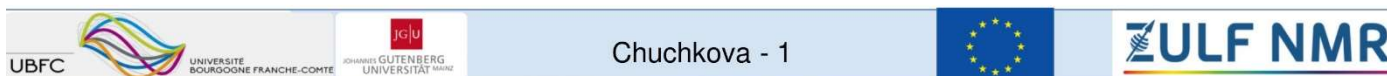


# Photo-chemically induced dynamic nuclear polarization of heteronuclear singlet order

Kirill Sheberstov<sup>1,2</sup>, Liubov Chuchkova<sup>3</sup>, John W. Blanchard<sup>1,2</sup>, Dmitry Budker<sup>1,2,4</sup>, Konstantin L. Ivanov<sup>5,6</sup>, Alexey S. Kiryutin<sup>5,6</sup>, Ivan V. Zhukov<sup>5,6</sup>, Alexandra V. Yurkovskaya<sup>5,6</sup>

1. Institut für Physik, Johannes Gutenberg Universität-Mainz, 55128 Mainz, Germany
2. Helmholtz-Institut, GSI Helmholtzzentrum für Schwerionenforschung, 55128 Mainz, Germany
3. University in Bourgogne, 21000 Dijon, France
4. University of California at Berkeley, California 94720-7300, USA
5. International Tomography Center SB RAS, Novosibirsk, 630090, Russia
6. Novosibirsk State University, Novosibirsk, 630090, Russia

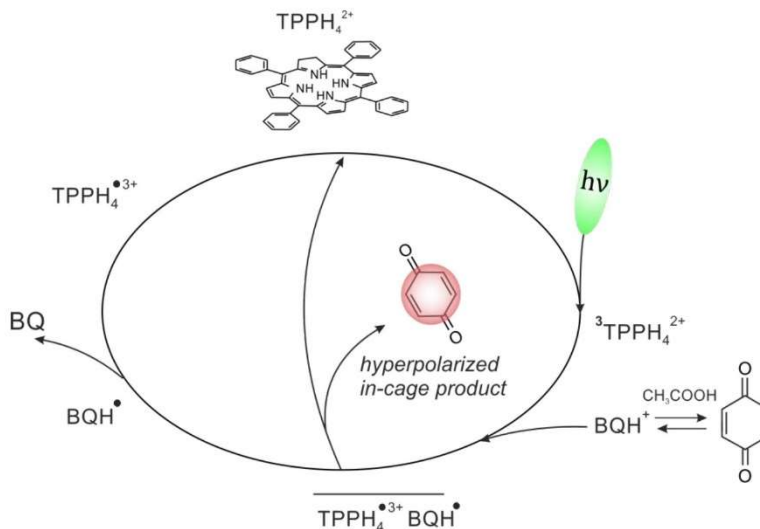
**Abstract:** Nuclear spins are usually polarized by a strong magnetic field, still resulting in just a small level of about  $10^{-5}$  of the total possible polarization. One way to boost the NMR signals is to perform chemically induced dynamic nuclear polarization (CIDNP), allowing in some cases to enhance signals up to thousands of times. The range of magnetic fields below  $\approx 10$  mT is not usually considered to be interesting for CIDNP, as the achievable hyperpolarized magnetization goes down to zero, whereas the polarization character stays the same. In this work we report the case for which polarization character essentially changes when the magnetic field is lowered below  $\approx 1$  uT. This range is called zero- to ultra-low fields (ZULF) and it is special because in these fields nuclear spins of different types, e.g.  $^1\text{H}$  and  $^{13}\text{C}$ , may become strongly coupled. Here we show that photo-CIDNP hyperpolarizes heteronuclear singlet order of directly bonded  $^1\text{H}$ - $^{13}\text{C}$  spin pair in para-benzoquinone molecule.



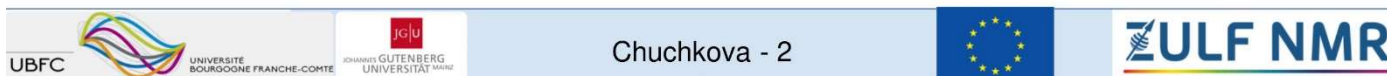
## Photo-CIDNP of tetraphenylporphyrin (TPP) with para-benzoquinone (BQ)

CIDNP originates due to spin selective reactions. Here are the important stages:

- (i) Photoexcitation of the TPP.
- (ii) Formation of a radical pair between the excited TPP and BQ.
- (iii) Intersystem crossing. Due to the inequivalence of the electron spins, the initial triplet state of the electrons evolves into the singlet state. This evolution depends on the nuclear spin states.
- (iv) Spin sorting. Triplet radical pairs have higher probability to form escape products; singlet radical pairs have higher probability to recombine in-cage. Difference of relaxation rates of the nuclear spins in escape products and in-cage product allows observation of the hyperpolarization.



Reaction according to D. Gust et. al., J. Phys. Chem. 95, 4442 (1991)



# Simulation of photo-CIDNP in zero field

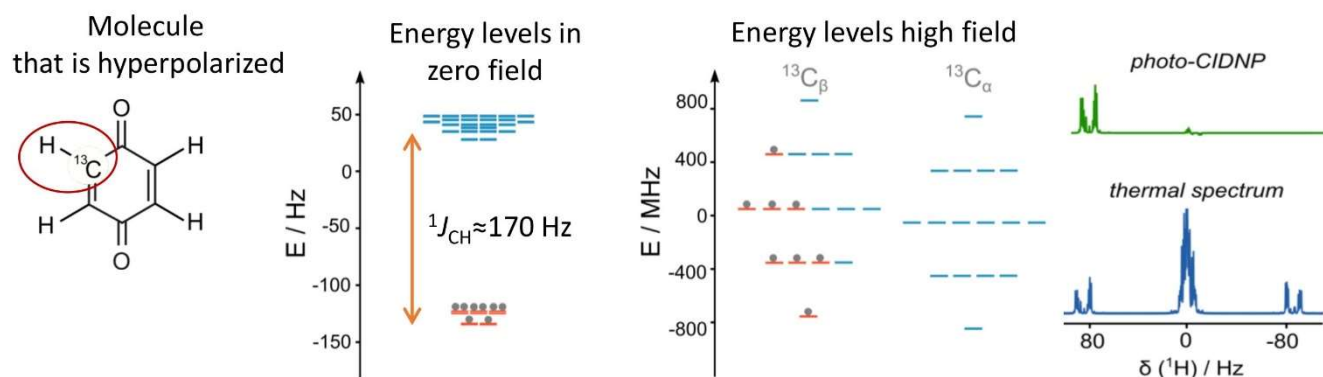
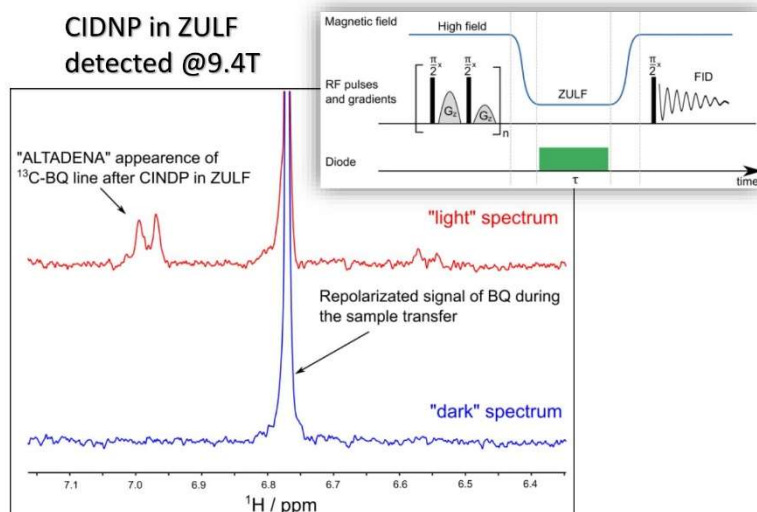
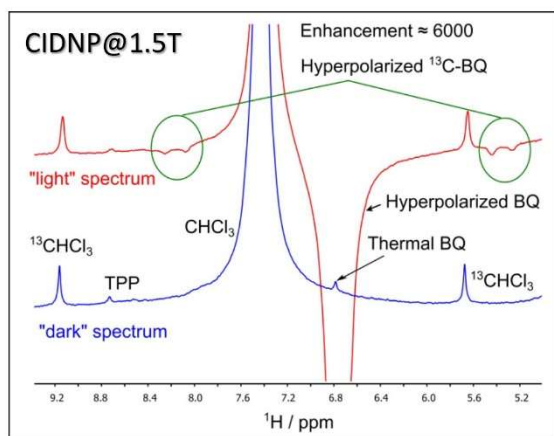


Photo-CIDNP in zero-field polarizes singlet order of the directly bonded  $^{13}\text{C}$ - $^1\text{H}$  spin pair. Upon adiabatic transfer the overpopulated states can be brought to the high-field and detected by conventional NMR.

## Results



Here we show that photo-CIDNP can efficiently hyperpolarize signals of BQ and  $^{13}\text{C}$ -BQ. In ZULF only  $^{13}\text{C}$ -BQ molecules are polarized and the polarization character is different from high field case. Analysis of the observed spectra testifies that the singlet order of  $^{13}\text{C}$ - $^1\text{H}$  spin pair is hyperpolarized.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 766402.

# Proton-relayed side-arm hydrogenation in high- and low-field

Laurynas Dagys<sup>1</sup>, Anil Jagtap<sup>2</sup>, Sergey Korchak<sup>2</sup>, Salvatore Mamone<sup>2</sup>, Philip Saul<sup>2</sup>, Malcolm H. Levitt<sup>1</sup>, Stefan Glöggler<sup>2</sup>

<sup>1</sup> University of Southampton

<sup>2</sup> Max Planck Institute for Biophysical Chemistry

**Abbreviated abstract:** In this work we compare two different methods to polarize pyruvate with para-hydrogen via a side-arm hydrogenation routine that uses one additional proton to relay the polarization to a heteronucleus. One method is a pulsed transfer at high field and the second being a field cycling approach in nanotesla fields. The polarization transfer efficiency was experimentally tested at high-field and is compared to the numerically simulated efficiency for a magnetic field cycling experiment which has not yet been performed. The results suggest that both methods should be potentially applicable in a system where polarization is relayed to heteronuclei via a single proton.

## Related publications:

- S. Korchak *et al*, Chemistry Open 7, 344–348 (2018)
- F. Reineri *et al*, Nature Communications 6, 5858 (2015)

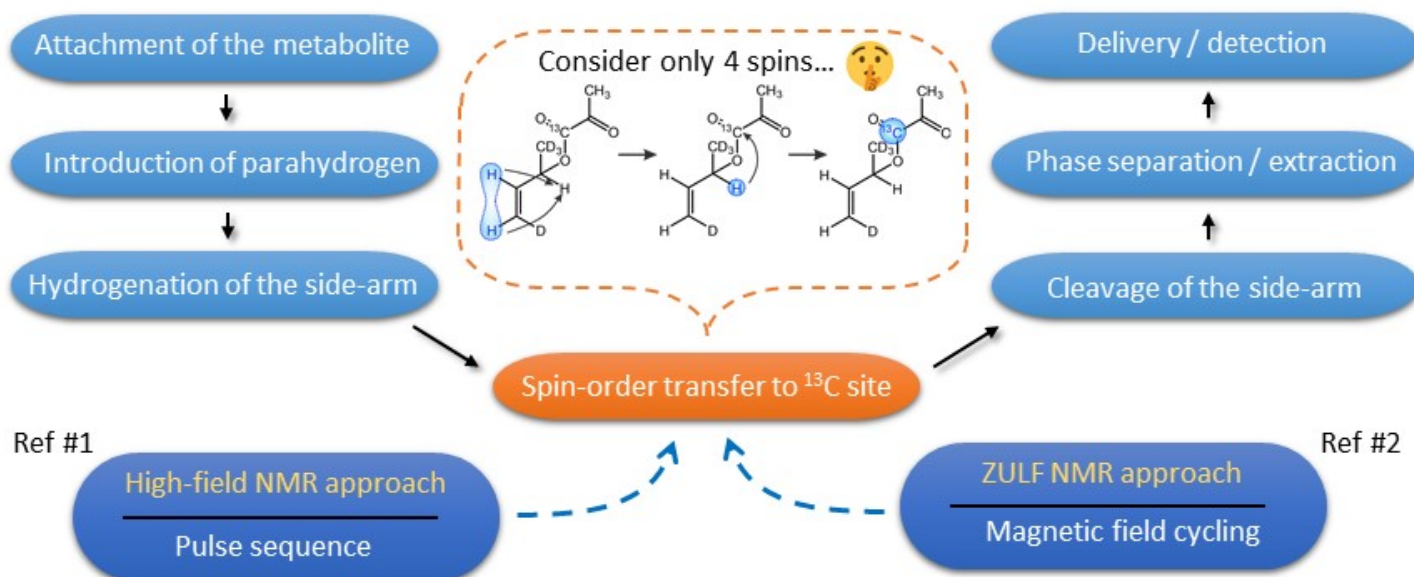


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ZULF NMR

## Side-arm hydrogenation (SAH). The molecular system



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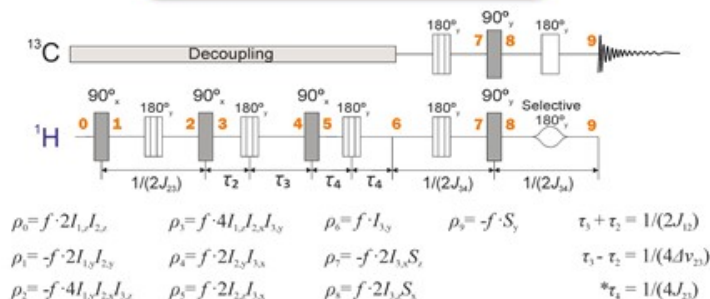
L. Dagys - 2

ZULF NMR



# Polarization transfer methods

## High-field NMR approach

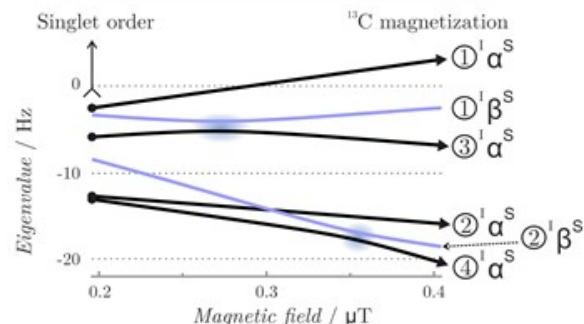


Resonant pulses manipulate spin states of proton and carbon spin ensembles using several spin echoes.

Total duration of the sequence is around 1 second.

Proof of concept – experiment (at 7.05 T field)

## ZULF NMR approach



Avoided level crossings allow some populated states to adapt to slowly changing eigenstates. For example, singlet order of two protons can become  $^{13}\text{C}$  magnetization after magnetic field cycling.

Proof on concept – simulation (SpinDynamica)



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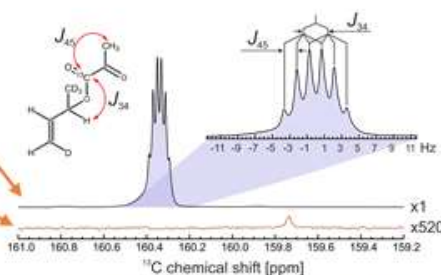
L. Dagys - 3

ZULF NMR

## Results and conclusions

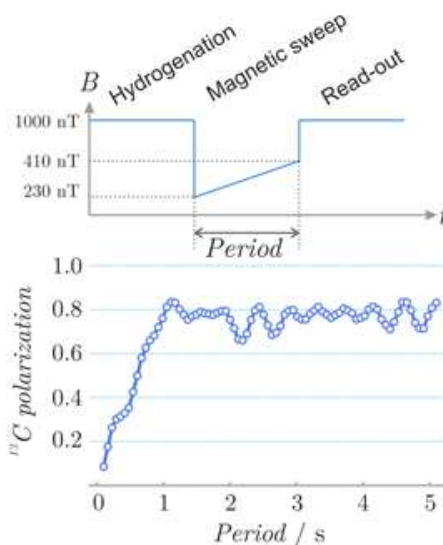
After polarization transfer using the pulse sequence

Before SAH



$^{13}\text{C}$  polarization level = 7.1% (starting with 15.5%)

- ✓ The selected molecular system is applicable to both high-field and low-field SAH routines;
- ✓ Both methods promise an efficient polarization transfer neglecting such effects as relaxation and dephasing;
- ✓ Experimentally, polarization transfer was tested utilizing the pulse sequence. Comparison to magnetic field cycling is envisioned.



Simulation suggests good polarization yield utilizing the low-field approach. The timescale is comparable to the pulse sequence duration.

Experimental  $^{13}\text{C}$  polarization level = ??? ☹



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L. Dagys - 4

ZULF NMR

## Rapid generation and purification of parahydrogen-polarized fumarate

Stephan Knecht<sup>a</sup>, John W. Blanchard<sup>b</sup>, Danila Barskiy<sup>c</sup>, Eleonora Cavallari<sup>d</sup>, Laurynas Dagys<sup>e</sup>, Erik Van Dyke<sup>c</sup>, Maksim Tsukanov<sup>c</sup>, Bea Blieme<sup>c</sup>, Kerstin Münnemann<sup>f</sup>, Silvio Aime<sup>d</sup>, Francesca Reineri<sup>d</sup>, Malcolm H. Levitt<sup>e</sup>, Gerd Buntkowsky<sup>a</sup>, Alexander Pines<sup>c</sup>, Peter Blümle<sup>g</sup>, Dmitry Budker<sup>b,g</sup>, James Eills<sup>b,g,\*</sup>

a) Eduard-Zintl-Institute for Inorganic Chemistry and Physical Chemistry, Technical University Darmstadt, 64287 Darmstadt, Germany

b) Helmholtz-Institut Mainz, GSI Helmholtzzentrum für Schwerionenforschung GmbH, 55128 Mainz, Germany

c) Department of Chemistry, University of California, Berkeley, U.S.A.

d) Dept. of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy

e) University of Southampton, Southampton, United Kingdom

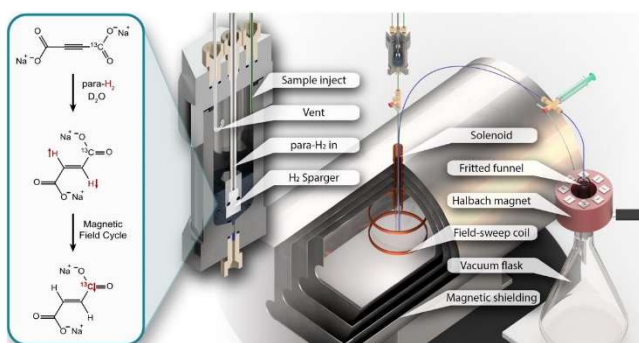
f) Technical University of Kaiserslautern, Kaiserslautern, Germany

g) Johannes Gutenberg University, D-55090 Mainz, Germany

**Abbreviated abstract:** Hyperpolarized fumarate is a novel biosensor for magnetic resonance imaging. It can be hyperpolarized cheaply and conveniently using parahydrogen-induced polarization. However, this process requires a chemical reaction, and the resulting hyperpolarized fumarate solutions are contaminated with the catalyst, unreacted precursor, and reaction side product molecules, and are hence unsuitable for use *in vivo*. We show hyperpolarized fumarate can be purified by acid precipitation as a pure solid, and later redissolved at a chosen concentration in a clean aqueous solvent. We form hyperpolarized fumarate in ~150 mM concentrations, at <sup>13</sup>C polarization levels of 20-45%.

### Related publications:

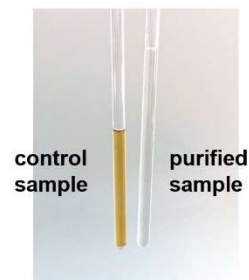
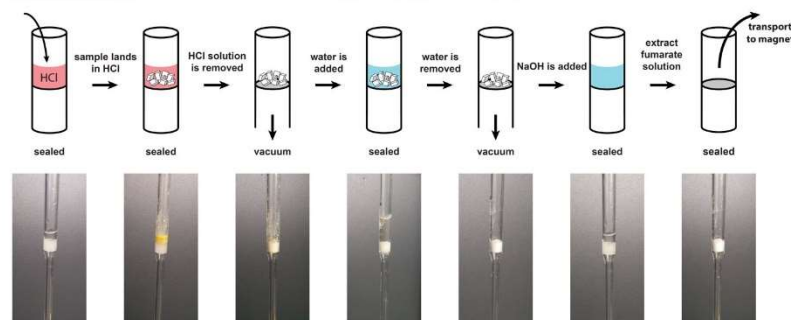
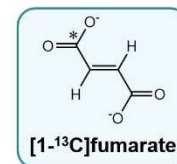
Eills, J.; Cavallari, E.; Carrera, C.; Budker, D.; Aime, S.; Reineri, F. Real-Time Nuclear Magnetic Resonance Detection of Fumarase Activity Using Parahydrogen-Hyperpolarized [1-<sup>13</sup>C]Fumarate. *J. Am. Chem. Soc.* **2019**, *141* (51), 20209–20214



### Our Approach

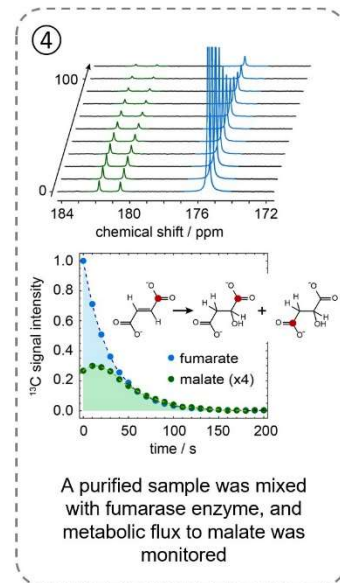
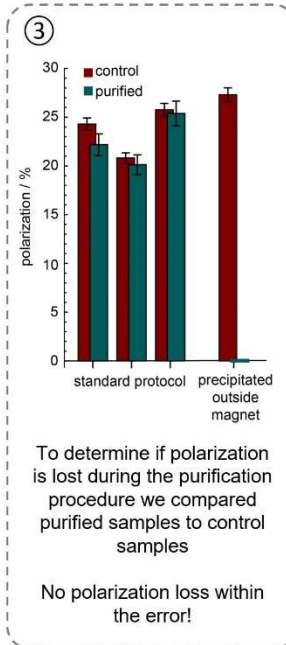
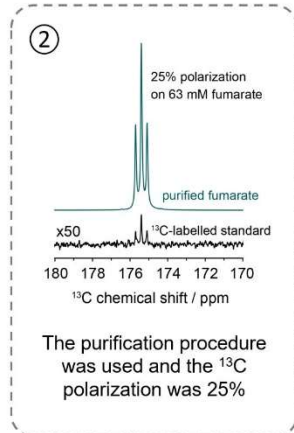
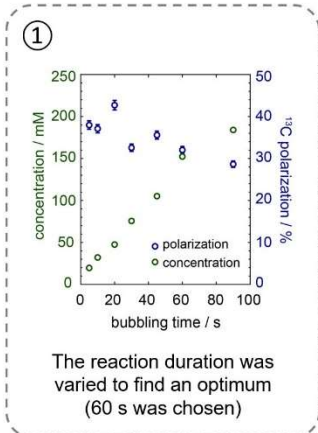
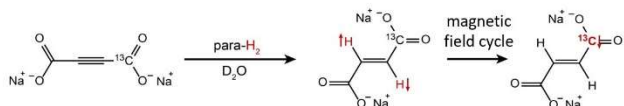
#### Procedure

1. The chemical reaction is carried out in a steel reactor
2. A ZULF magnetic field cycle is used to polarize the <sup>13</sup>C nucleus
3. The sample is purified by acid/base extraction
4. The hyperpolarized solutions are measured in a benchtop NMR magnet



residual catalyst concentration: <20 µM

## Results





# $^{15}\text{N}$ SABRE Hyperpolarization of Radiosensitizing Antibiotic Nimorazole in Microtesla Magnetic Fields

Oleg G. Salnikov<sup>1,2,3</sup>, Nikita V. Chukanov<sup>1,2</sup>, Alexandra Svyatova<sup>1,2</sup>, Ivan A. Trofimov<sup>1,2</sup>, Mohammad S. H. Kabir<sup>4</sup>, Kirill V. Kovtunov<sup>1,2</sup>, Eduard Y. Chekmenev<sup>4</sup>, Igor V. Koptug<sup>1,2</sup>

<sup>1</sup> International Tomography Center SB RAS, Novosibirsk, Russia

<sup>2</sup> Novosibirsk State University, Novosibirsk, Russia

<sup>3</sup> Boreskov Institute of Catalysis SB RAS, Novosibirsk, Russia

<sup>4</sup> Wayne State University, Detroit, Michigan, United States

**Abbreviated abstract:** Nimorazole is a 5-nitroimidazole-based antibiotic which is now in Phase 3 clinical trial in Europe for potential use as a hypoxia radiosensitizer for treatment of head and neck cancers. Here we report hyperpolarization of three  $^{15}\text{N}$  nuclei of isotopically labeled [ $^{15}\text{N}_3$ ]nimorazole using SABRE in microtesla magnetic fields. Polarization ( $P_{^{15}\text{N}}$ ) of the  $^{15}\text{NO}_2$  group reaches 3.2% and has a long-lasting lifetime of 5.9 min at the clinically relevant 1.4 T magnetic field. Dependences of  $P_{^{15}\text{N}}$  on polarization transfer field and temperature showed the maxima at  $\sim 0.4 \mu\text{T}$  and  $54^\circ\text{C}$ , respectively. The feasibility of  $^{15}\text{N}$  MRI visualization of hyperpolarized [ $^{15}\text{N}_3$ ]nimorazole was demonstrated with high spatial and temporal resolution.

## Related publications:

– O. G. Salnikov et al., Angew. Chem. Int. Ed., under review (2020)

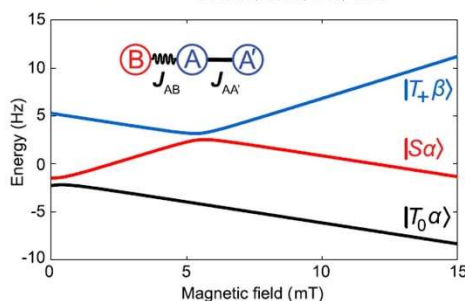
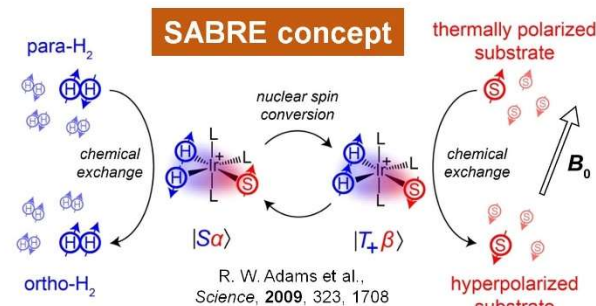


O. G. Salnikov - 1

ZULF NMR

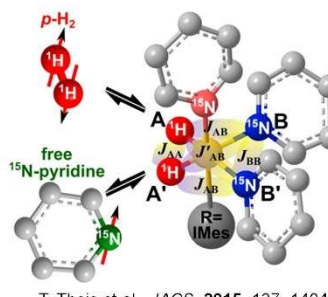
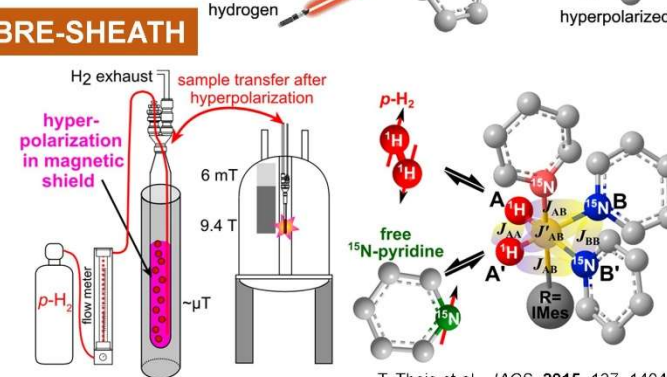
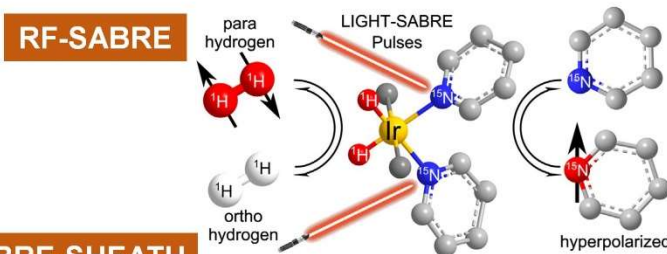
## SABRE hyperpolarization of heteronuclei

SABRE = Signal Amplification by Reversible Exchange



### Heteronuclei:

- ✓ Longer hyperpolarization lifetime
- ✓ No background NMR signal *in vivo*



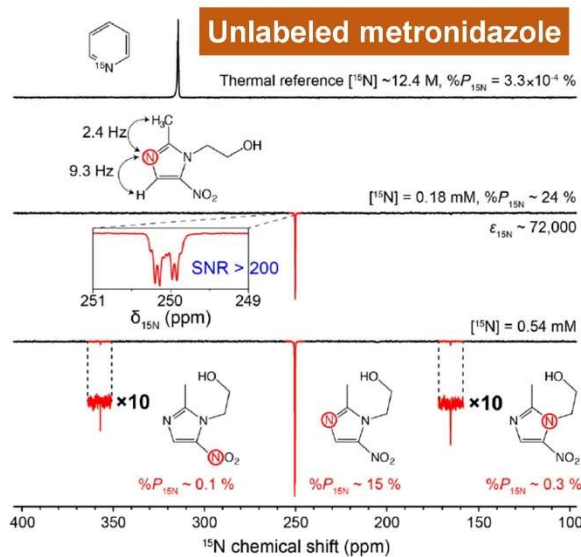
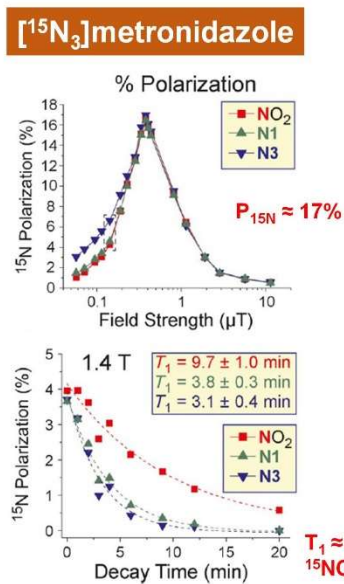
T. Theis et al., *JACS*, 2015, 137, 1404



O. G. Salnikov - 2

ZULF NMR

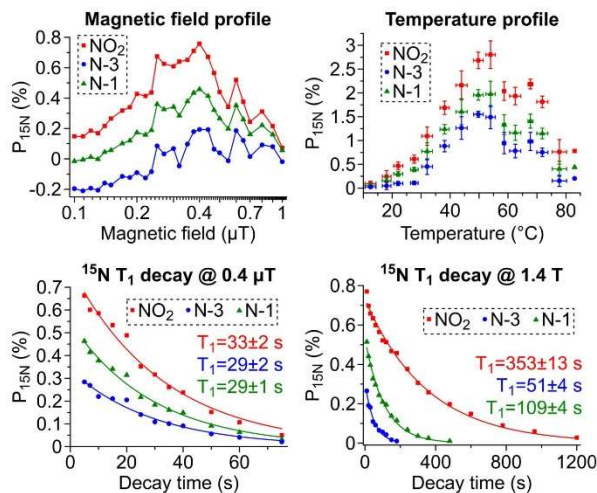
Previous work:  $^{15}\text{N}$  SABRE-SHEATH of metronidazole

D. A. Barskiy et al., *JACS*, **2016**, 138, 8080R. V. Shchepin et al., *Chem. Eur. J.*, **2019**, *25*, 8829

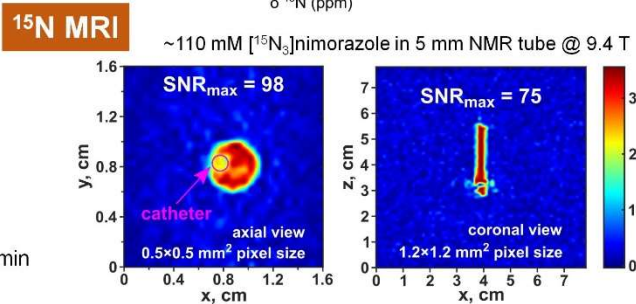
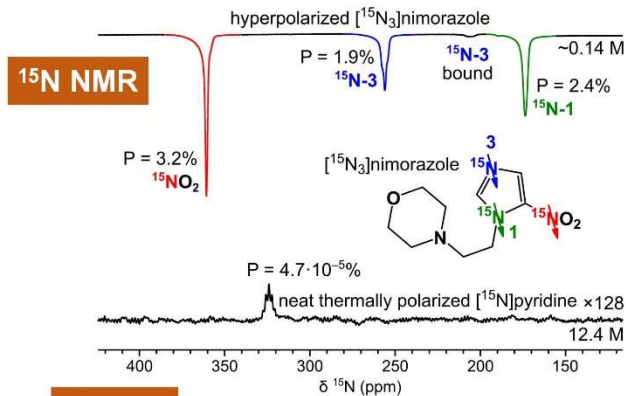
### Hypoxic radiosensitizer

Under Phase 3 clinical study for the treatment of head and neck cancer

## Results and Conclusions



- ✓  $^{15}\text{N}$  SABRE-SHEATH hyperpolarization of potential theragnostic hypoxia contrast agent nimorazole with up to 3.2%  $^{15}\text{N}$  polarization
- ✓ Polarization lifetime for  $^{15}\text{NO}_2$  group in  $^{15}\text{N}_3$  nimorazole reaches ~6 min
- ✓ High-resolution  $^{15}\text{N}$  MRI of hyperpolarized  $^{15}\text{N}_3$  nimorazole





# Probing SABRE Polarisation Transfer to Heteronuclei with Earth's Field NMR

Matheus Rossetto<sup>1</sup>, Fraser-Hill Casey<sup>1</sup>, Meghan Halse<sup>1</sup>

<sup>1</sup> Department of Chemistry, University of York, Heslington, York, YO10 5DD, UK

**Abbreviated abstract:** Earth's field NMR (EFNMR) detection enables hyperpolarisation of target substrates *in-situ* of the detection field through the use of an additional switchable electromagnetic coil to meet conditions necessary for SABRE polarisation transfer during para-Hydrogen ( $p\text{-H}_2$ ) bubbling. SABRE-polarised  $^1\text{H}$  and  $^{19}\text{F}$  signals of 3,5-bis(trifluoromethyl)pyridine (3,5-bisTFMP) under different Polarisation Transfer Fields (PTF) of 6 mT and 48  $\mu\text{T}$  show the influence the polarisation transfer condition has on the substrate spin-state that is hyperpolarised, using EFNMR simulations to predict those hyperpolarised states. By integrating SABRE-polarisation with *in-situ* EFNMR detection we hope to better understand the processes involved in SABRE.

## Related publications:

– Hill-Casey F *et al*, *Molecules* (24), 4126 (2019)

R. W. Adams *et al*, *Science*, 2009, 323, 1708–1711

A. M. Olaru, *ChemistryOpen*, 2018, 7, 97–105

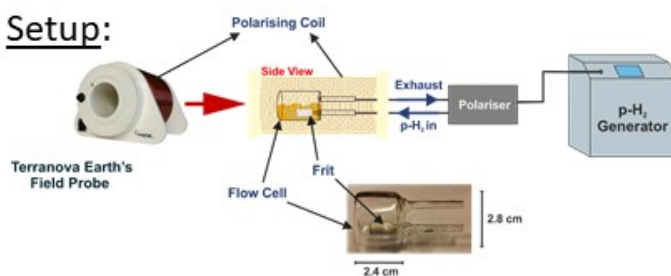


Matheus Rossetto - 1



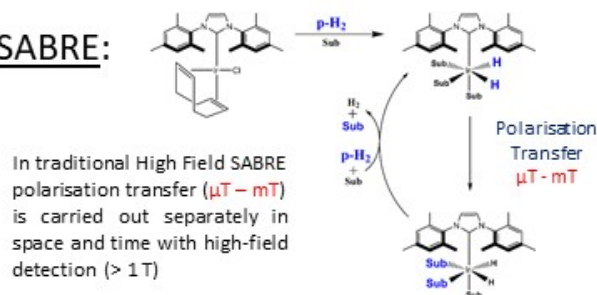
## *In-situ* SABRE with EFNMR Detection

### Setup:



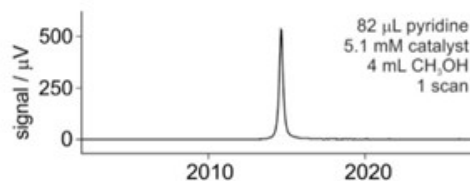
- The EFNMR instrumentation and setup enables *in-situ*  $p\text{-H}_2$  bubbling of the SABRE pre-catalyst in the presence of the PTF and the detection field. This provides a route towards decoupling the SABRE processes (e.g. polarisation transfer, catalyst activation, etc.)
  - Transfer from PTF to detection field not required
  - Minimising the delay between  $p\text{-H}_2$  addition and NMR detection

### SABRE:



### Benefits of Earth's Field Detection:

- Naturally available field ( $\sim 50 \mu\text{T}$ )
- Very homogeneous ( $< 1 \text{ Hz}$  linewidths)



Matheus Rossetto - 2



# Polarisation Transfer Field Control

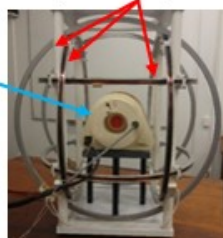
## Polarisation Transfer Coil (>50 $\mu\text{T}$ )



EFNMR Probe

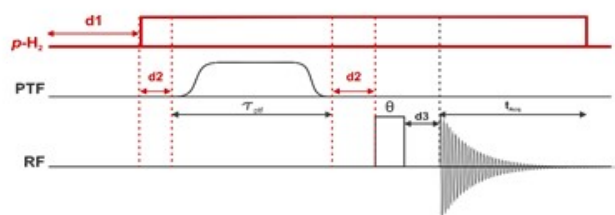
The polarisation transfer coil is used to access polarisation transfer fields above the Earth's magnetic field to achieve homonuclear polarisation transfer.

## 3-Axis Helmholtz Coils (<50 $\mu\text{T}$ )



Additional Helmholtz coils are employed to perform active field correction and access polarisation transfer fields below the Earth's magnetic field to achieve heteronuclear polarisation transfer.

## EFNMR SABRE Pulse Sequence:



In-situ SABRE polarisation pulse sequence demonstrating the use of the switchable PTF coils to induce polarisation transfer before detection in the Earth's magnetic field.

PTFs are estimated using LAC theory:

$$J_{xy} \equiv \Delta\nu_{H_{para}} Z_{nuc} = \frac{B_0 \gamma_H (\delta_z - \delta_{para})}{2\pi} \text{ or } \frac{B_0 (\gamma_H - \gamma_F)}{2\pi}$$

Homonuclear PTF  $\approx 6 \text{ mT}$

Heteronuclear ( $^{19}\text{F}$ ) PTF  $\approx < 10 \mu\text{T}$

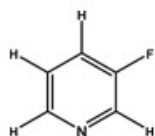
M. L. Truong et al, J Phys Chem C Nanomater Interfaces, 2015, 119(16), 8786-8797  
A. M. Olaru et al, ChemistryOpen, 2017, 7(1), 97-105



Matheus Rossetto - 3

ZULF NMR

# SABRE Hyperpolarised Fluorinated N-heterocycles



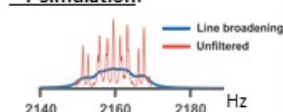
## 3-fluoropyridine:

3-fluoropyridine (82  $\mu\text{L}$ , 250 mM) + [Ir(IMes)(COD)Cl] (50 mM) + solvent (4 mL)

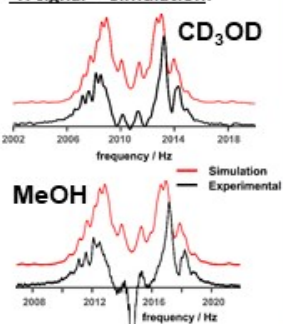
$^{19}\text{F}$  hyperpolarisation not observed due to multiple strong  $J_{H-F}$  interactions and only one  $^{19}\text{F}$  nucleus present. Signal is very broad and is most likely hidden in the noise.

EFNMR simulations show presence of negative  $^1\text{H}$  signal that does not correspond to a substrate nucleus and is concluded to be hyperpolarised solvent (MeOH) undergoing competitive binding to the SABRE-catalyst.

## $^{19}\text{F}$ Simulation:

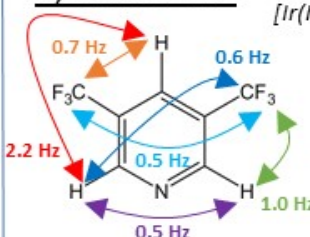


## $^1\text{H}$ signal + Simulation:

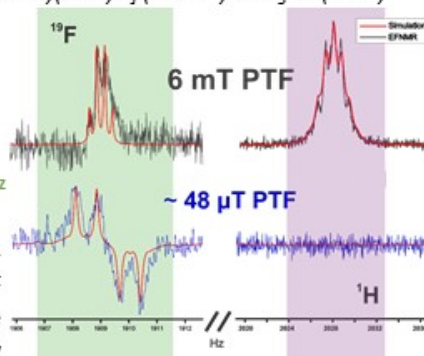


## 3,5-bisTFMP:

3,5-bisTFMP (240 mg, 250 mM) + [Ir(IMes)(COD)Cl] (50 mM) +  $\text{CD}_3\text{OD}$  (4 mL)



The form of the SABRE-enhanced  $^1\text{H}$  and  $^{19}\text{F}$  EFNMR spectra are diagnostic of the identity of specific magnetic states that have been hyperpolarised and so can be used to explore the SABRE-polarisation transfer process.



Spectra suggest directing of polarisation transfer towards  $^{19}\text{F}$  at  $\mu\text{T}$  PTFs.

Wider range of PTFs (PTF sweep) to be implemented in the future

H.J. Hogben et al, Journal of Magnetic Resonance, 208 (2011) 179-194



Matheus Rossetto - 4

ZULF NMR



# Nuclear Magnetic Resonance Gyroscopes for Precise Positioning



Riccardo Cipolletti<sup>1,2</sup>; Janine Riedrich-Möller<sup>1</sup>; Robert Rölver<sup>1</sup>; Tino Fuchs<sup>1</sup> Arne Wickenbrock<sup>2</sup> and Dmitry Budker<sup>2</sup>

<sup>1</sup>Robert Bosch GmbH, Corporate Sector Research and Advance Engineering, Advanced Technologies and Micro Systems

<sup>2</sup>Helmholtz-Insitut Mainz, Johannes Gutenberg-Universität Mainz

## Abstract:

Precise positioning of vehicles is essential for modern mobility solutions. In the case when GPS signals and other systems are temporarily unavailable, high performance inertial sensors become a key component of navigation systems that widely use dead reckoning i.e. localization based on a previously determined position and precise directional sensor signals, including rotation and acceleration.

Nuclear Magnetic Resonance (NMR) based gyroscopes enable high precision measurement of rotation rates – with a high potential of miniaturization. We present modelling of a Xenon and Rubidium based NMR gyroscope for parameter studies.



Riccardo Cipolletti | riccardo.cipolletti@de.bosch.com  
Robert Bosch GmbH, Corporate Sector Research and Advance Engineering,  
Advanced Technologies and Micro Systems



## NMR Gyroscopes: Working Principle



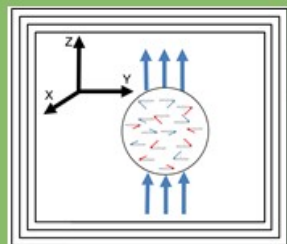
### Working Principle Scheme:

Rubidium (●) and Xenon (▲) magnetic moments.  
Static (→) and oscillating (↔) magnetic fields.  
Lasers (→) with positive propagation direction.  
Linear and circular polarization (↔).  
Global magnetization of the cell is illustrated in the coordinate representation.

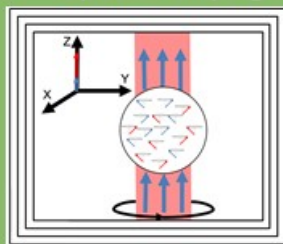
Previous work [1] measuring a shift in the measured frequency of Xenon Larmor-precession due to rotation, with an in-situ Rubidium magnetometer has shown an angular random walk of  $0.005^\circ/\sqrt{h}$  and a bias drift of  $0.02^\circ/h$ .



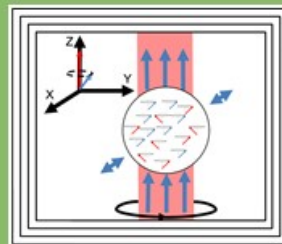
### Larmor-Precession



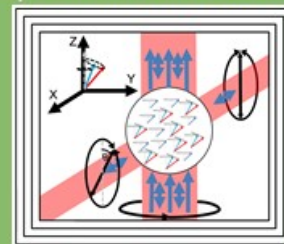
### Spin Exchange Optical Pumping



### Resonant Driving



### Parametric Modulation and Optical Rotation Detection



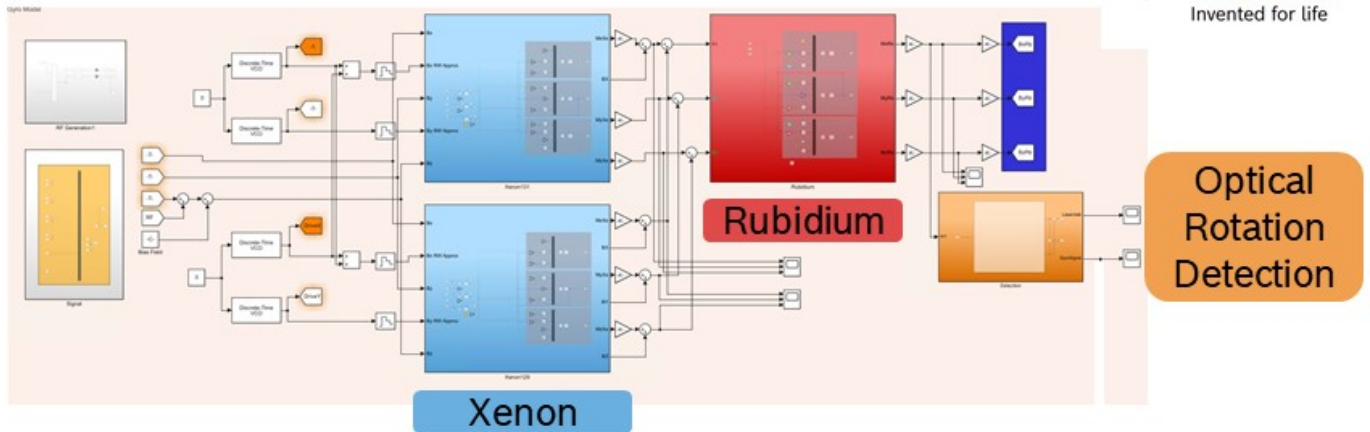
[1] T.G. Walker and M.S. Larsen: Spin-Exchange Pumped NMR Gyros, Adv. Atom. Mol. Opt. Phys. 65, 373-401 (2016)



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Advanced Technologies and Micro Systems



# Modelling with MATLAB and Simulink



- Numerical solution of the Optical Bloch equations for arbitrary fields
- No steady state approximation
- Feedback of the alkali field.
- Simulation for arbitrary system parameters

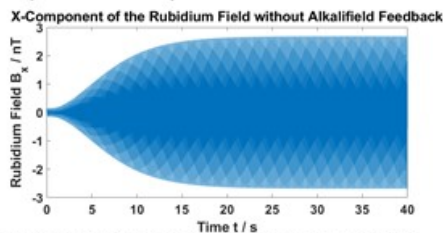


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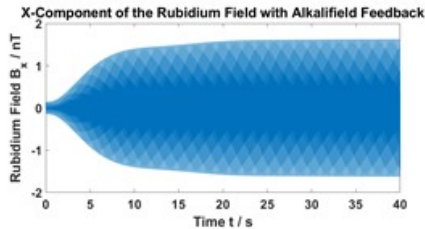


## Results and Conclusions

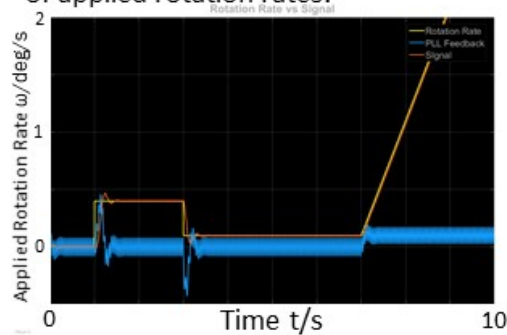
Precession signals that agree with the analytical steady state solution:



Adding interaction terms e.g. due to the alkali field:



Functional reconstruction of applied rotation rates:



The Gyroscope Signal (Red) reconstructs an applied Rotation Rate (yellow). Blue shows the non-integrated feedback of a Phase Locked Loop.

Outlook:

- Parameter studies
- Optimized control and read-out



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## Poster 10

Might a magnet be a spinning top?

Instead of pointing to once north,

wobble around it and nod

by intrinsic spins cohort.

Aye, at small enough magnetic field  
a spectrum splitting is revealed.

We propose a strategy to construct a solid-state magnetometer operating in ultra-low fields, which we call a ferromagnetic gyroscope (FG). In it, intrinsic spins in a ferromagnet precess coherently around the direction of the magnetic field due to its intrinsic spins. In low enough magnetic fields, a splitting is predicted to occur in the resonance of the device, which will serve as a telltale sign of the precessing behaviour. Once realized, it can be used to test the reaction of intrinsic spin to general relativistic precession.

Pavel Fadeev, Tao Wang, Yehuda B. Band, Dmitry Budker, Peter W. Graham, Alexander O. Sushkov, Derek F. Jackson Kimball, arXiv:2006.09334 (2020).

The authors above with Chris Timberlake, Andrea Vinante, and Hendrik Ulbricht, invited letter to *Quantum Science and Technology* (2020).

Why does a compass orient along the magnetic field, while atomic and nuclear spins precess about the field?

Because a compass is in the regime  $L \gg S$ ,  
while nuclear spins are in  $S \gg L$ .

For a compass,  $S \gg L$  translates  
to external magnetic field  $B$   
being smaller than...

$B \ll$

$$B_i + \frac{\omega_I}{\gamma}$$

$$\frac{\omega_I}{\gamma}$$

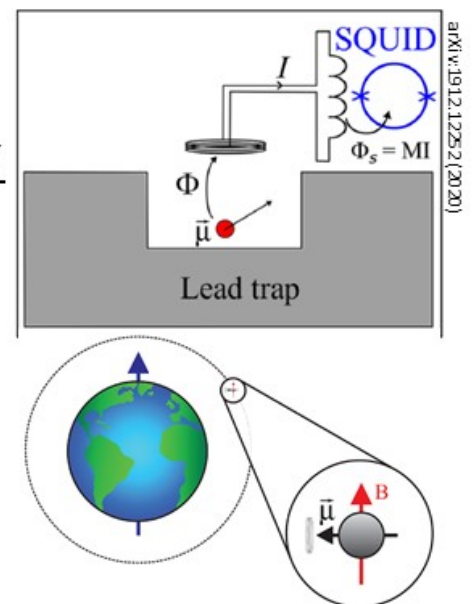
Sensitivity might be below the quantum limit.

$L$  rotational angular momentum;  $S$  total intrinsic spin

$B_i$  magnetic field from the superconductor

$\omega_I$  Einstein-de Haas frequency

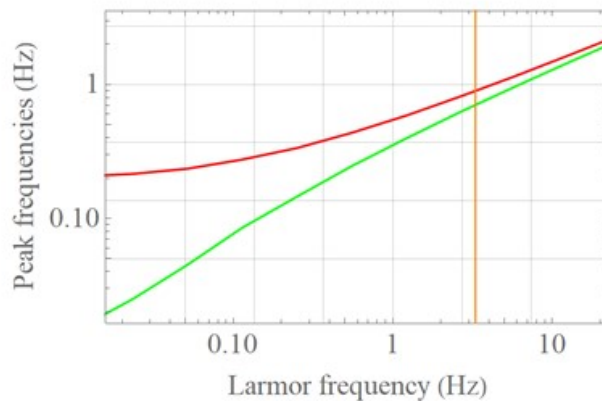
$\gamma$  gyromagnetic ratio



## Strategy:

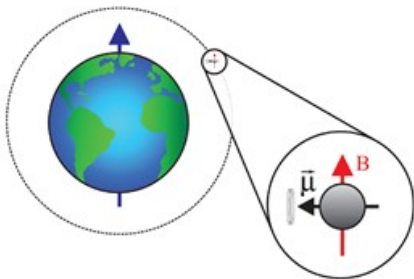
Start with a magnetic field above the threshold (vertical orange line) and detect librational mode resonance – has been observed.

Then, lower the magnetic field until a fractional splitting in the resonance is detected – pending.



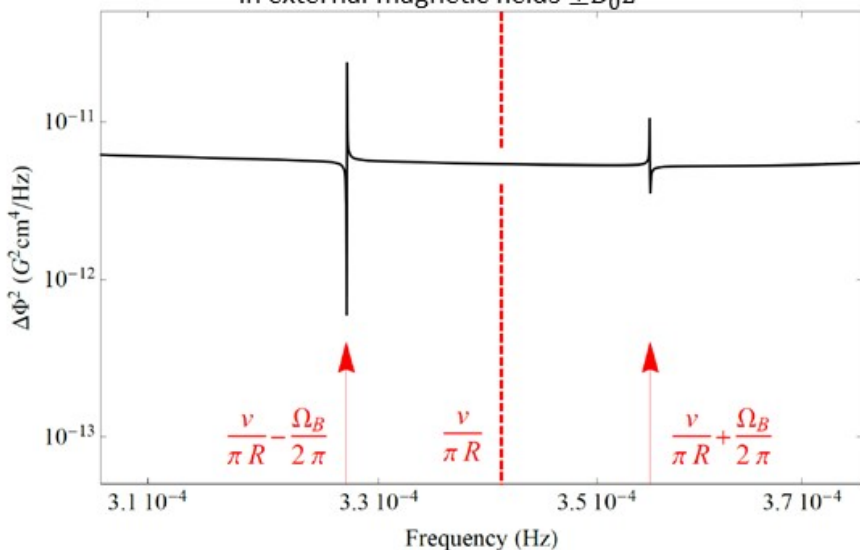
The librational resonance in the spectrum of the ferromagnet will be effectively split below the threshold field, allowing for a telltale sign of the gyroscopic behaviour.

## What is it good for? Example: general-relativistic precession



Modelling:  
Possible modulation of FG precession at twice the orbital frequency due to Lense-Thirring precession

Power spectral density of the difference in flux signal between two FGs in external magnetic fields  $\pm B_0 \hat{z}$





# Instrumentation for Probing and Optimizing SABRE Processes at Ultra-low Fields

Fraser Hill-Casey<sup>1</sup>, Matheus Rossetto<sup>1</sup>, Aminata Sakho<sup>1,2</sup>, Meghan E. Halse<sup>1</sup>

<sup>1</sup>Department of Chemistry, University of York, York, UK

<sup>2</sup>Centre for Hyperpolarisation in Magnetic Resonance, University of York, York, UK

**Abbreviated abstract:** Efficient Signal Amplification By Reversible Exchange (SABRE) hyperpolarisation for a given analyte requires the optimisation of a wide range of experimental conditions. In the standard approach, SABRE experiments are achieved using a two-stage method, where hyperpolarisation and detection are separated in time and space. Integration of a liquid nitrogen-based *para*-hydrogen generator with Earth's Field NMR (EFNMR) detection enables SABRE experiments to be performed *in situ* and allows for processes to be decoupled. Combined with an active field correction device, complex time-resolved and multi-step experiments, such as monitoring the formation of the SABRE-active catalyst, can be performed in a simple and reproducible manner.

## Related publications

– Hill-Casey F *et al.*, *Molecules* 24 (2019) 4162.

Adams *et al.*, *Science*, (2009), 323, 1708–1711

Adams *et al.*, *JCP* 131 (2009) 194505.

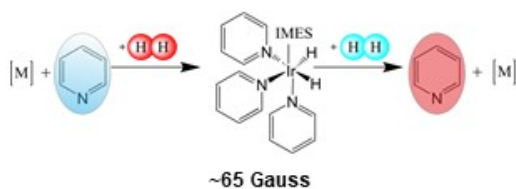
Semenova *et al.*, *Anal. Chem* 91 (2019) 6695 – 6701.



Hill-Casey F. - 1

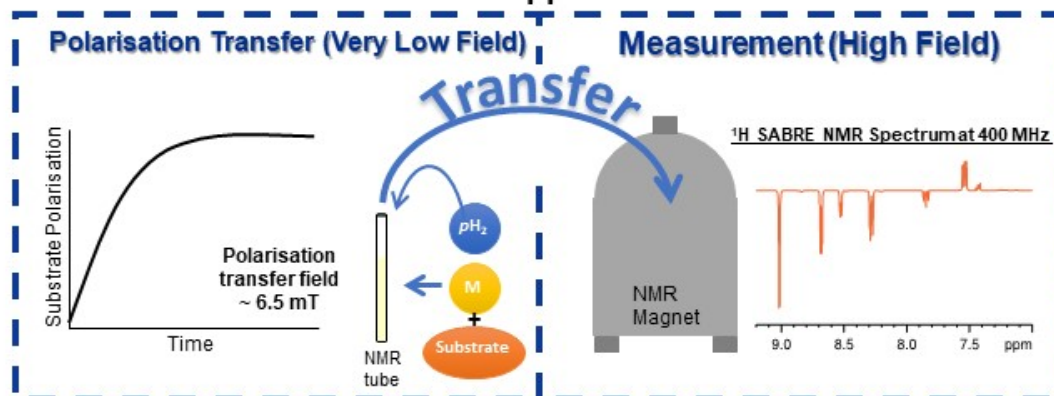


## SABRE Hyperpolarisation at High Field



SABRE is a catalytic process which occurs in solution and allows for polarization of a wide range of analytes at **low-field** before performing measurement at **high-field**.

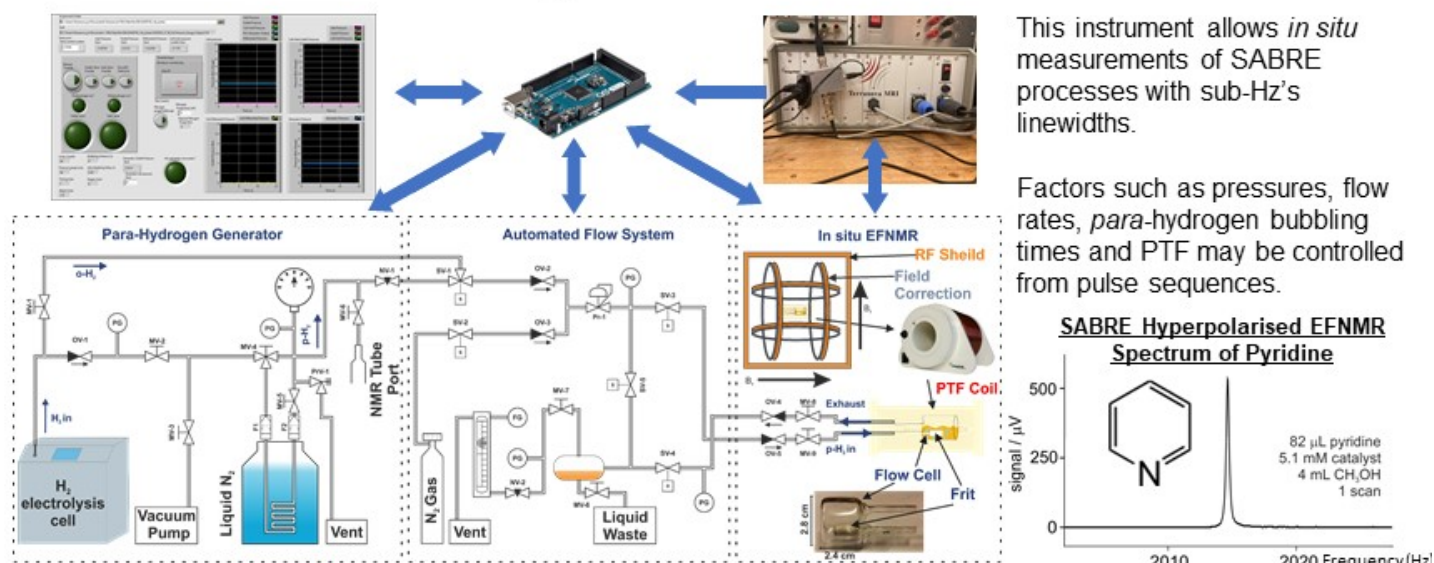
This leads to a **discontinuity** in polarization transfer locations/field and measurement which can be rectified via an *in situ* approach.



Hill-Casey F. - 2



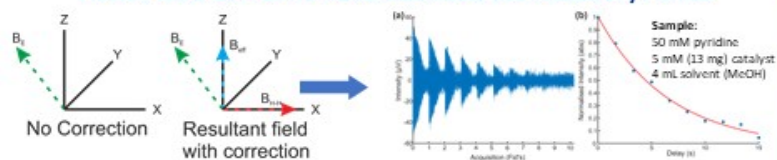
# Platform to Investigate SABRE in the Earth's Field



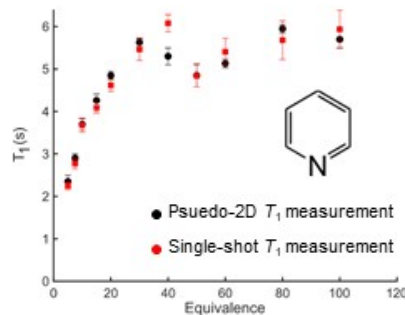
**Figure 1:** Simplified manifold diagram and schematic of the *in situ* SABRE system with EFNMR detection. The modular system is controlled by an Arduino MEGA via LabVIEW.  $H_2$  is produced via an electrolysis cell and enriched by a liquid  $N_2$  generator to produce ~52 %  $pH_2$ . This is bubbled through the solution inside the probe. The NMR detector includes a flow cell, RF shield and field correction/sweep coils. The EFNMR electromagnet generates the required PTF=65 G before NMR is performed in the Earth's field ~0.5G.

## Reaction Monitoring SABRE Processes

### Active field Correction Enables Accurate Nutation/Pulses



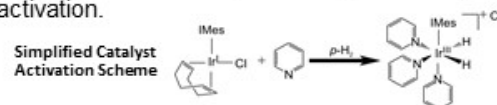
**Figure 2:** Cartoon of field correction showing the bulk Earth's field ( $B_0$ ), the Helmholtz pair field correction ( $B_{corr}$ ) and the resultant field ( $B_{res}$ ). (a) Example FID train produced during a single shot, variable flip angle experiment. (b) Example  $T_1$  decay curve.



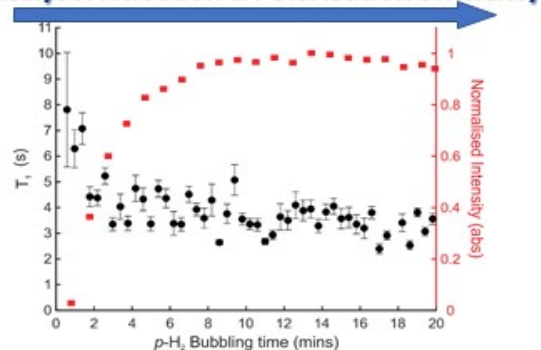
The field correction enables accurate nutation and hence allows complex experiments. One such experiment is the **Single-shot Variable Flip Angle hyperpolarisation lifetime ( $T_1$ )** measurement.

**Figure 3:** Comparison between single-shot (red) and multi-step (black)  $T_1$  experiments for a range of SABRE catalyst (5 mM) to pyridine substrate ratios in MeOH (4 mL).

*In situ* SABRE with EFNMR detection enables direct investigation into SABRE processes, including catalyst activation.



### Catalyst Activation & Polarisation efficiency



**Figure 4:** Activation curve for 50 mM of pyridine with 5 mM SABRE pre-catalyst in 4 mL of  $CH_3OH$ , monitored by single shot  $T_1$  measurements (black), and SABRE signal intensity (red).



# TOWARDS ZULF DETECTION OF PARA-HYDROGEN POLARIZED METABOLITES

Oksana Bondar<sup>a</sup>, James Eills<sup>b</sup>, John W. Blanchard<sup>b</sup>, Eleonora Cavallari<sup>a</sup>, Carla Carrera<sup>a</sup>, Kirill Sheberstov<sup>b</sup>, Silvio Aime<sup>a</sup>, Francesca Reineri<sup>a</sup>

<sup>a</sup> Dept. of Molecular Biotechnology and Health Science, University of Torino

<sup>b</sup> Johannes Gutenberg-Universität Mainz

E-mail: oksana.bondar@unito.it

**Abbreviated abstract:** Hyperpolarized metabolites such as acetate, pyruvate and lactate are widely used by the biomedical MRI community as a markers of metabolic changes associated with a number of diseases and response to treatment. Enzymatic conversion of [1-<sup>13</sup>C]-pyruvate into lactate, is widely used to study different types of cancer<sup>[1]</sup>. To obtain polarized metabolites, our laboratory uses the PHIP-SAH method<sup>[2]</sup>, that greatly expands the number of molecules that can be polarized using para-hydrogen. In this work we explore the possibility to observe metabolites derivatives, hyperpolarized by means of PHIP-SAH, at Zero Magnetic Field.

## Related publications:

[1] K. M. Brindle, *J. Am. Chem. Soc.* **2015**, *137*, 6418–6427

[2] F. Reineri, T. Boi, S. Aime, *Nat. Commun.* **2015**, *6*, 5858.

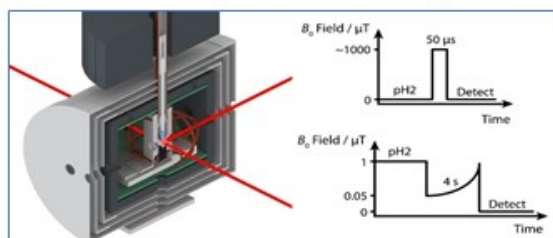


O. Bondar - 1

ZULF NMR

## Techniques and Methods:

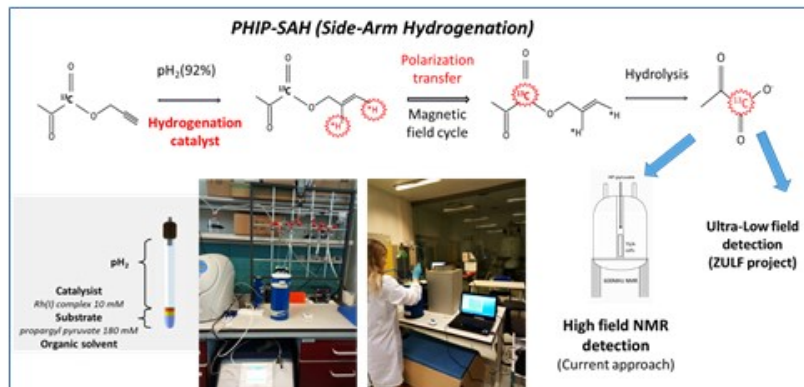
#ZULFNMR of allyl esters at ZULF apparatus\*



**Left:** schematic of the ZULF apparatus. The sample is held in a Twin leaf MC-IF shield, with Helmholtz coils for the pulsing, and a Rb magnetometer for signal acquisition. Pump and probe lasers are shown in red. **Right:** Magnetic field applied in two types of experiments performed: "pulse-acquire" (top) and "field cycle" (bottom).

Experiments in ZULF were performed by bubbling 5 bar Para-hydrogen into a sample at 60°C for 5 s in the ZULF apparatus. Unless otherwise stated, the samples were 250 mM starting material and 13.8 mM Rh<sup>+</sup> catalyst in chloroform. Two types of magnetic field manipulations were used to generate spectra: A) parahydrogenation at zero field and pulse/acq; B) parahydrogenation at ~1 μT, magnetic field cycle and acquisition at ZF

\*@Helmholtz Institute Mainz



Parahydrogen hyperpolarization requires:

- A hydrogenation catalyst (i.e. a metal complex);
- An unsaturated precursor of the desired, hyperpolarized product while for in-vivo studies we need;
- an aqueous solution;
- no toxic impurities (metal, solvents...);
- biological molecules (metabolites are preferable);

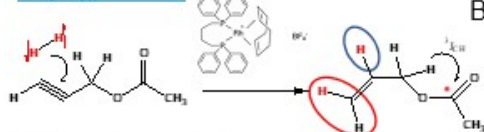
All these requirements are met in #PHIP-Side Arm Hydrogenation. This strategy allows to hyperpolarize molecules, such as acetate and pyruvate or lactate, on which the H<sub>2</sub> molecule cannot be incorporated directly. At the same time, the hydrogenation complex and solvents are removed and an aqueous solution of the hyperpolarized product is obtained.



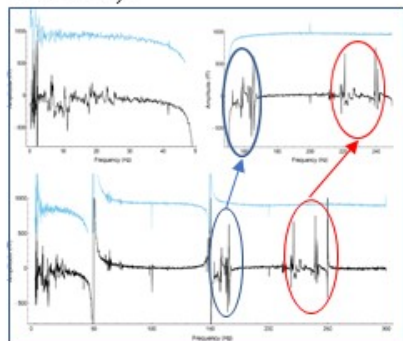
O. Bondar - 2

ZULF NMR

### Propargyl-acetate:

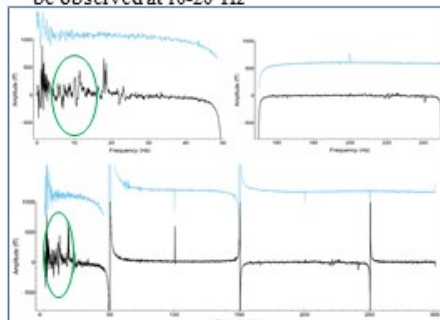


A) When the parahydrogenation of propargyl-acetate is carried out at zero field, the ZULF spectrum acquired in-situ shows hyperpolarized peaks at ~230 Hz (circled red at the figure) that can be related to the protons circled red at the scheme and at ~160 Hz (region and proton circled blue).

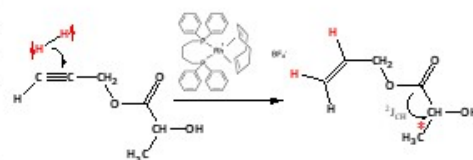


## Results and discussion:

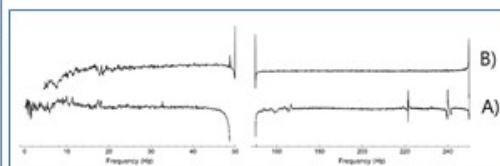
B) When the parahydrogenation is carried out at 1  $\mu$ T field and MFC is applied, the high frequency, related to the allyl protons disappear – we might observe hyperpolarized signals in the low-frequency region (~6 Hz and 12 Hz) given by the (naturally abundance)  $^{13}\text{C}$  of the carboxylate group which is J-coupled with the methyl-protons and with methylene-protons ( $^3J_{\text{CH}} \sim 3.2 \text{ Hz}$ ). Unfortunately, the low frequency region is too noisy and we cannot observe any hyperpolarized signal at ~6 Hz-12 Hz (circled green at the figure), while enhanced signals can be observed at 10-20 Hz



### Propargyl-lactate:



In the experiment with propargyl-lactate- $^{13}\text{C}$ , we would expect to see a peak at ~3.8 Hz due to the  $^2J_{\text{CH}}$  coupling to the single proton near the  $^{13}\text{C}$  spin. This isn't obvious in the "pulse-acquire" spectrum, and in the "field-cycle" spectrum this region was too noisy to observe anything.



## Results and Conclusions:

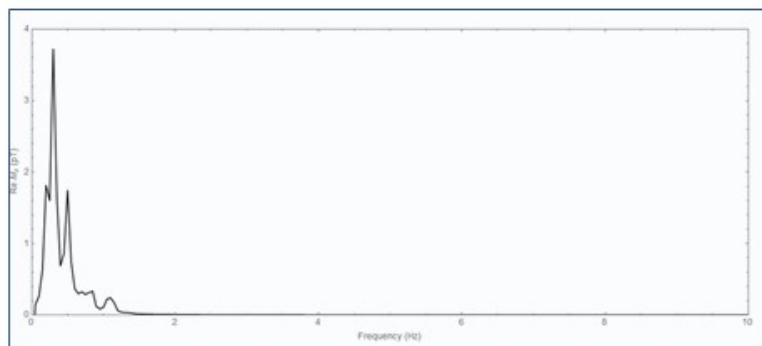


Figure1. Simulated ZULF-spectra of  $^{13}\text{C}$ -Vinyl-acetate

- The observable peaks, in the Zero Field spectra, are given by the parahydrogenated allyl moiety (large J couplings between  $^1\text{H}$  and  $^{13}\text{C} \rightarrow$  well defined peaks)
- Using non-labelled allyl-acetate, the peaks in the low-frequency region, after MFC, are not well resolved from the noise  $\rightarrow$

### Plans for the future:

- Para-Hydrogenation conditions must be improved:
  - Parahydrogenation in a closed tube (pressurized with para- $\text{H}_2$  and shaken at high T) might optimize yield and singlet order transfer to the product.
  - $^{13}\text{C}$  labelled allyl-acetate can be used, in order to have larger  $^1\text{H}$ - $^{13}\text{C}$ J (between the methyl group and the  $^{13}\text{C}$  carboxylate).
- ZULF detection must be improved:
  - Perform measurements at the Commercial optically pumped magnetometer, the QZFM<sup>[1]</sup> at room temperature (minimize losses during hydrogenation at high temperature).

<sup>[1]</sup> John W. Blanchard et al, Journal of Magnetic Resonance, V.314, May 2020, 106723



# Relaxation measurements from zero to Earth's magnetic field

Piotr Put<sup>1</sup>, Danila Barskiy<sup>2</sup>, Szymon Pustelny<sup>1</sup>

<sup>1</sup> M. Smoluchowski Institute of Physics, Jagiellonian University, Łojasiewicza 11, 30-348 Kraków, Poland

<sup>2</sup> Department of Chemistry, University of California Berkeley, Berkeley, CA, 94720-3220, USA

**Abstract:** NMR relaxometry is an important tool for characterization of heterogeneous materials, porous media, and chemical mixtures. Its combination with portability and operation at ultra-low magnetic fields makes such incarnation of NMR an attractive tool for chemical characterization.

We present a novel ultra-low-field NMR setup enabling relaxometry in a magnetic-field range from Earth's magnetic field all the way to zero field. We demonstrate initial results on aqueous solution of glucose and propose research program aiming at low-field relaxation studies of blood and long-lived pyridine derivatives used as contrast agents.

## Related publications:

1. Ganssle, Paul J., et al. "Ultra-Low-Field NMR Relaxation and Diffusion Measurements Using an Optical Magnetometer." *Angewandte Chemie International Edition* 53.37 (2014): 9766-9770.
2. Jagtap, Anil P., Lukas Kaltschnee, and Stefan Glöggler. "Hyperpolarization of 15 N-pyridinium and 15 N-aniline derivatives by using parahydrogen: new opportunities to store nuclear spin polarization in aqueous media." *Chemical Science* 10.37 (2019): 8577-8582.



Piotr Put -1



## Challenge, approach and benefits

### Challenges

- Ability to measure relaxation properties in a large range of low magnetic fields
- Sensitive NMR detection not affected by an applied magnetic field
- Operation at close to room temperature (heating the sample can affect the relaxation properties)

### Our approach

- Use of atomic magnetometers as sensors for ultra-low field detection
- Operating sensors close to room temperature
- Use of a piercing solenoid stretching the whole length of the magnetic shielding: uniform magnetic field without affecting the sensor sensitivity

### Gains

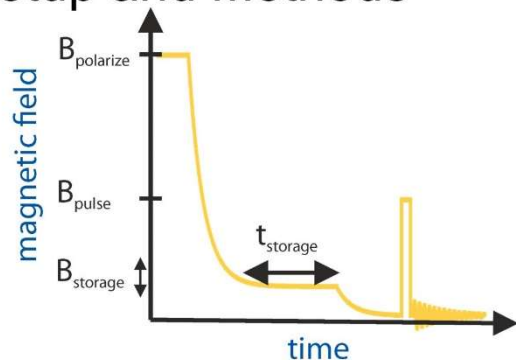
- High-resolution low- to zero field NMR spectra
- High spatial field uniformity
- Portability (field operation?)
- Access to magnetic field ranges not widely studied in relaxometry measurements (ultra-low field relaxation dispersion measurements)



Piotr Put - 2



# Setup and Methods

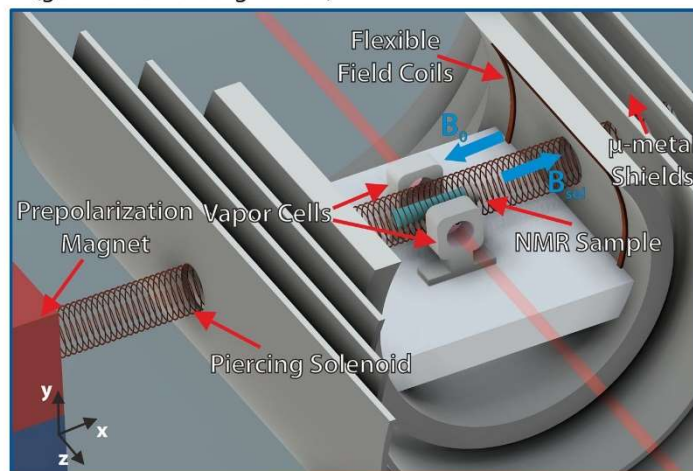


## Key stages of the experiment

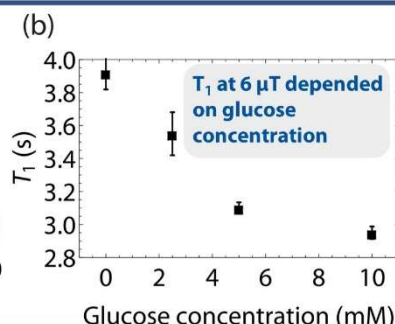
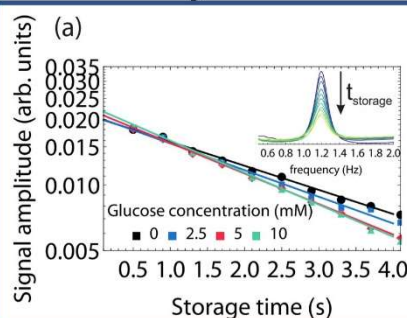
- ✓ NMR sample transported from a magnet to a shield inside a piercing solenoid
- ✓ Sample stored at a set field for a given storage time
- ✓ Pulse is applied and signal is observed (both zero- and low-field detection possible)

## Zero-to-ultra-low field setup based on atomic magnetometers

- ✓ NMR sample held inside piercing solenoid which field doesn't affect atomic magnetometer
- ✓ NMR signal is detected by a pair of atomic magnetometers (gradiometer configuration)



# Preliminary results and outlook



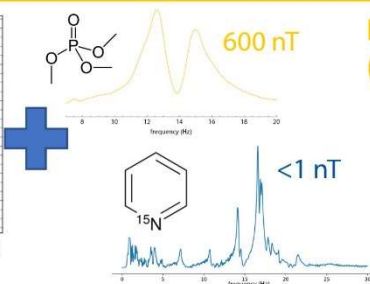
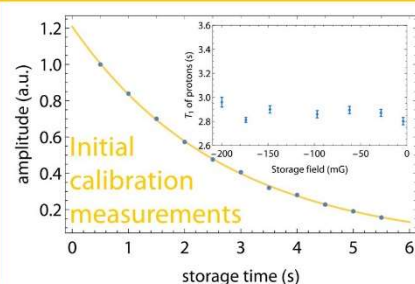
## Glucose concentration determination (blood test?)\*

- ✓ We demonstrated a dependence of low-field  $T_1$  on small concentrations of glucose in aqueous solutions.
- ✓ We adopted relaxometry measurement in a portable ZULF setup

### To do

- Dependence on the storage field
- Measurement in blood plasma/blood

\*This work done so far at UC Berkeley



## Relaxation dispersion measurements (long-lived contrasts?)

- ✓ We implemented a way to measure relaxation in a wide range of low-magnetic field
- ✓ We can measure both zero- and low-field NMR spectra (without affecting sensitivity)

### To do

- Measurement of pyridine derivatives contrasts for MRI



# NV center based super resolution nano-NMR

V S Anjusha<sup>1</sup>, D Cohen<sup>2</sup>, A Marshall<sup>3</sup>, C Findler<sup>1</sup>, J Lang<sup>1</sup>, J Scheuer<sup>3</sup>, P Neumann<sup>3</sup>, A Retzker<sup>2</sup>, GT Genov<sup>1</sup> and F Jelezko<sup>1</sup>

<sup>1</sup> Institute for Quantum Optics, Ulm University, Albert-Einstein-Allee 11, D-89081, Ulm, Germany

<sup>2</sup> Racah Institute of Physics, The Hebrew University of Jerusalem, 91904 Jerusalem, Givat Ram, Israel

<sup>3</sup> NVision Imaging Technologies GmbH, Albert-Einstein-Allee 11, D-89081, Ulm, Germany

**Abbreviated abstract:** NV center based room-temperature spectrometer is a promising tool for performing NMR in nanoscale volume at low field. However, poor spectral resolution is one of the major challenges in NV Nano-NMR. In this work, we try to investigate the correlation function of the temporal magnetic field noise induced by the diffusing spins at the NV centre and thereby understanding the line shape of the NMR spectrum. We show that the magnetic noise power spectrum can be deviated from the Lorentzian noise spectrum due to diffusion and this can lead to an improved resolution.

(1) D. Cohen, R. Nigmatullin, O. Kenneth, F. Jelezko, M. Khodas, A. Retzker, *Sc. Rep.* **10**, 5298 (2020)

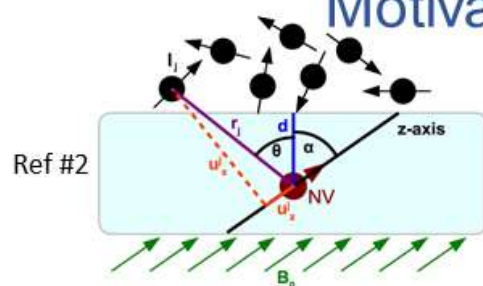
(2) Pham et. al., *Phys. Rev. B* **93**, 045425 (2016)



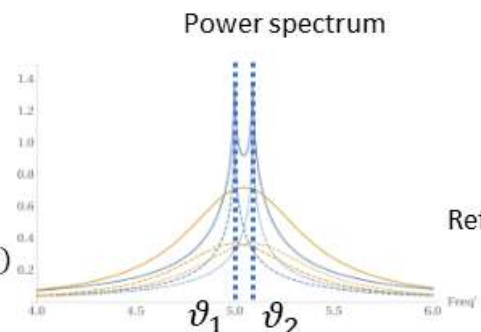
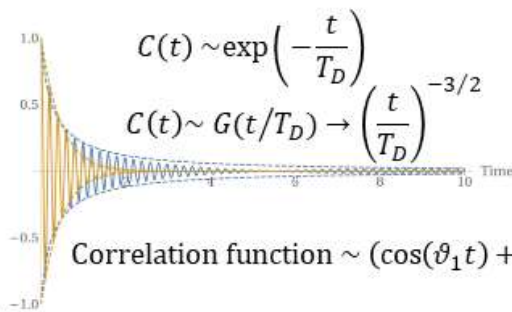
V S Anjusha - 1



## Motivation and approach



- During the sensing, spins are moving in and out of the detection volume due to diffusion
- Time to diffuse distance  $d$ ,  $T_D = \frac{d^2}{D}$ :  $D$  – Diffusion coefficient
- Theory claims deviation from Brownian motion and non-Lorentzian



Ref #1



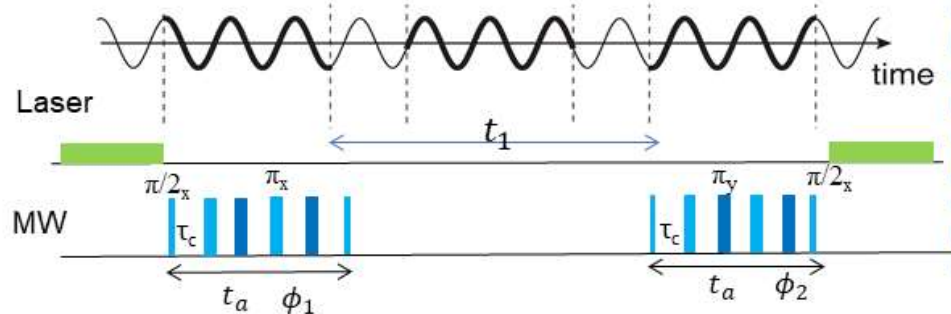
V S Anjusha - 2



# Techniques and methods

## Correlation Spectroscopy

Signal  $V(t) = V_m \cos(2\pi\theta t + \alpha)$



$$\phi = \gamma V_m t_a U(\theta, t_a)$$

$\gamma$  – Gyromagnetic ratio of the nuclear spin

$U(\theta, t_a)$  – Filter function of the DD sequence of length  $t_a$

$$\tau_c = 1/2\theta$$

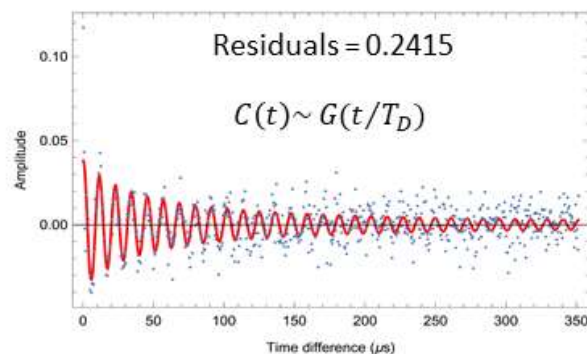
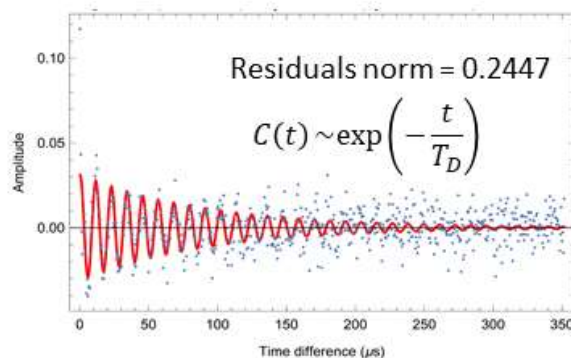
- The measurement outcome of the correlation spectroscopy,  $p(t_1) \approx 1/2 (1 - \phi^2 \cos(\alpha) \cos(\alpha + 2\pi\theta t_1))$  and this oscillate with signal frequency with  $t_1$



V S Anjusha - 3



## Preliminary results and future outlook



- The new model shows a slight improvement over Lorentzian model, but the difference is not statistically significant.
- **Outlook:** reduce noise, optimize the sampling to obtain the best SNR



V S Anjusha - 4





# Dissolution dynamic nuclear polarization-enhanced ZULF NMR (dDNP-ZULF NMR)

*R. Picazo-Frutos<sup>1</sup>, Q. Chappuis<sup>2</sup>, J. Eills<sup>1</sup>, S. F. Cousin<sup>2</sup>, Morgan Ceillier<sup>2</sup>, S. J. Elliott<sup>2</sup>, O. Cala<sup>2</sup>, John Blanchard<sup>1</sup>, D. Budker<sup>1</sup> and S. Jannin<sup>2</sup>*

<sup>1</sup> Helmholtz Institute Mainz, GSI Helmholtzzentrum für Schwerionenforschung, Mainz 55090, Germany

<sup>2</sup> Centre de Résonance Magnétique Nucléaire à Très Hauts Champs, 5 Rue de la Doua, 69100 Villeurbanne, France

**Abbreviated abstract:** Zero- and ultra-low field NMR is a modality of NMR experiment that do not require strong magnets with applications ranging from molecular spectroscopy and chemical-reaction monitoring to dark-matter searches and study of physics outside of the standard model. However, as any NMR experiment, it suffers from low sensitivity. In this work we combine a hyperpolarization technique called dissolution Dynamic Nuclear Polarization to enhance our signal and thus extend the reach of future applications.

## Related publications:

- Blanchard, J. W., & Budker, D. (2016). Zero-to Ultralow-Field NMR. *eMagRes*, **5**, 1395-1410.
- Jannin S *et al.* (2019). *J. Magn. Res.*, **305**, 41-50



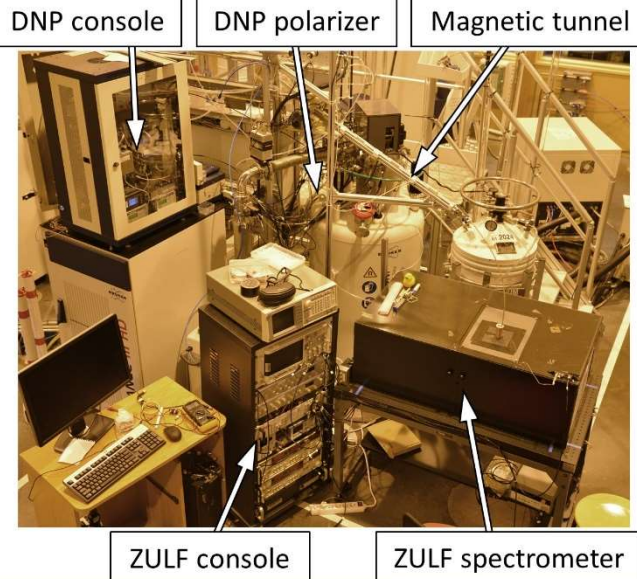
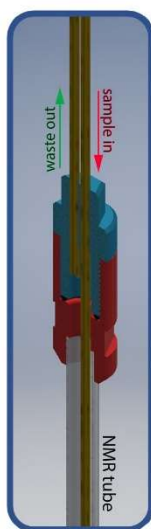
**HIM**  
HELMHOLTZ  
Helmholtz Institute Mainz

Picazo-Frutos & Chappuis - 1

**ZULF NMR**

## Previous work, challenge, and approach

- Hyperpolarize sample by dDNP (rather than thermal prepolarization at 2 T): expected enhancement of 100k
- Make portable a working zero-field NMR gradiometer setup and install it at HMRlab in Lyon, next to a dDNP polarizer
- Challenges: Time synchronization, lossless magnetization transfer, sample injection
- How to solve this: Software optimization, magnetic tunnel >4 mT, [home-built injector](#)



**HIM**  
HELMHOLTZ  
Helmholtz Institute Mainz

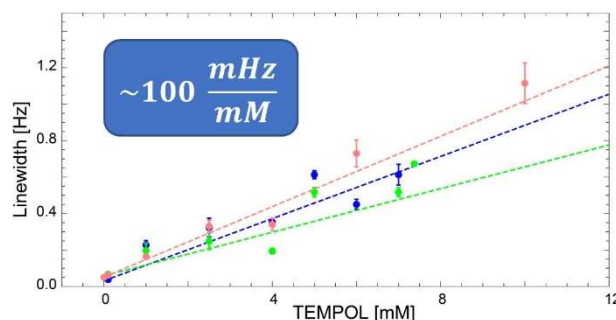
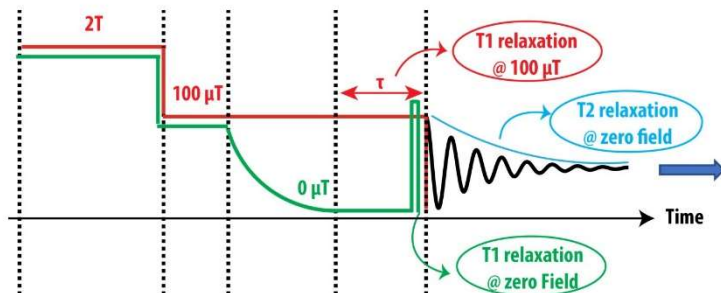
Picazo-Frutos & Chappuis - 2

**ZULF NMR**

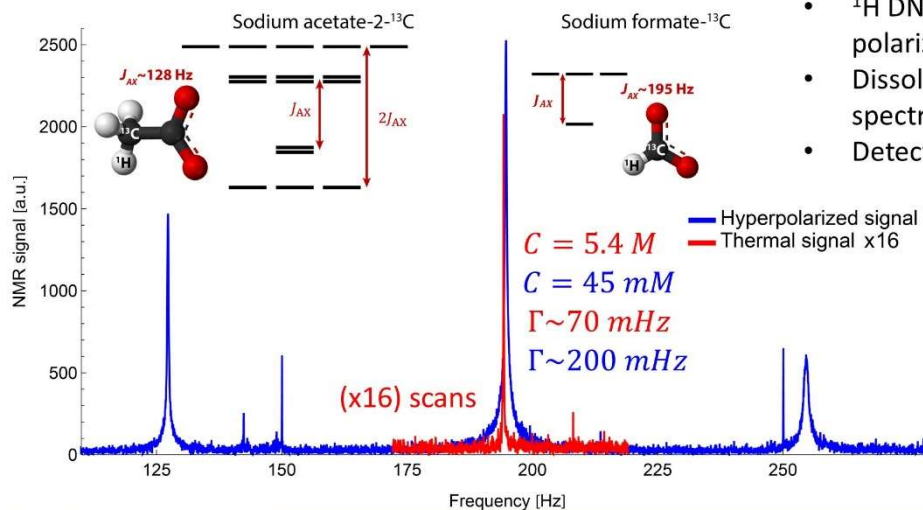
# Results I: Relaxometry at ZULF

- $d$ DNP produced hyperpolarized solution containing paramagnetic agents that can cause dramatic relaxation at ZULF
- Preliminary results at ZULF (without  $d$ DNP) show that hyperpolarization should survive despite the presence of TEMPOL: it causes a broadening of 100 mHz/mM at zero field

- $\bullet 1/\pi T_1^{\text{HF}}$
- $\bullet 1/\pi T_1^{\text{ZF}}$
- $\bullet 1/\pi T_2$
- $a [\text{TEMPOL}] + b, a=0.086, R^2=0.97$
- $a [\text{TEMPOL}] + b, a=0.060, R^2=0.92$
- $a [\text{TEMPOL}] + b, a=0.097, R^2=0.92$



# Results II: $d$ DNP-ZULF



## Methods

- Sample:  $[2-^{13}\text{C}]\text{acetate}$ ,  $[^{13}\text{C}]\text{formate}$  in "DNP juice"
- $^1\text{H}$  DNP at 1.2 K and 7.05 T using cross polarization to  $^{13}\text{C}$
- Dissolution and transfer to ZULF spectrometer at ~4 mT
- Detection at zero field

## Results

- Enhancement:  $\epsilon \sim 6k$
- Still some road ahead: Theoretical predicts  $\sim 100k$

## OUTLOOK: Applications

- Drug screening
- Chemical monitoring
- Dark matter searches

# Zero-field NMR J-Spectroscopy of Organophosphorus Compounds

*S. Alcicek, P. Put, V. Kontul, S. Pustelny*

*Institute of Physics Faculty of Physics, Astronomy and Applied Computer Science, Jagiellonian University, Krakow, Poland*

**Abstract:** Organophosphorus compounds are a wide and diverse class of chemicals often investigated in NMR. The interest is driven by their role in biology and medicine as phosphorus-31 ( $^{31}\text{P}$ ) is key element of such important molecules as nucleic acids, ATP, etc. Here we present our investigation of organophosphorus compounds using zero-field NMR. We report the results of theoretical and experimental studies on phosphorus-based organic compounds by analysing their J-spectra. We demonstrate a good agreement between measurements and simulations.

## Related publications:

1. Blanchard, J. W. & Budker, D. eMagRes 5, 1395–1410 (2016).
2. Tayler, M. C. D. et al. Rev. Sci. Instrum. 88, 13–15 (2017).



This project has received funding from the European Union's Horizon research and innovation program under the Marie Skłodowska-Curie grant agreement No. 766402.



*S. Alcicek - 1*

**ZULF NMR**

## Zero-field NMR in a Nutshell

These are **challenges** of zero-field NMR:

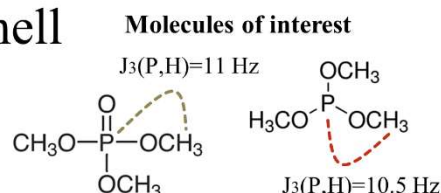
- Low thermal polarization
- Applicability to heteronuclear spin- $\frac{1}{2}$  compounds only
- Limited number of natural abundant spin- $\frac{1}{2}$  nuclei

This is **how we deal** with them:

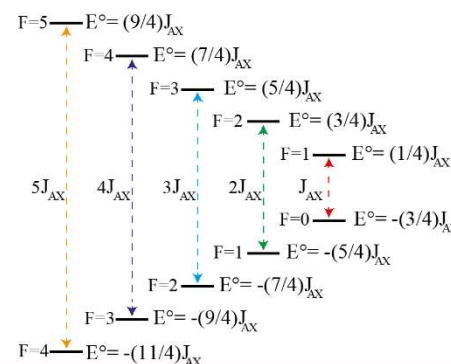
- Prepolarization in strong permanent magnet
- Indirectly infer homonuclear interaction
- Using compounds involving  $^1\text{H}$  and  $^{31}\text{P}$  of nearly 100% naturally abundance

This is **what we gain**:

- High resolution NMR spectra
- Direct access to spin-spin coupling
- Great agreement with simulations
- Straightforward sample preparation and experimental method



### Energy levels and transitions of $\text{XA}_9$ spin system



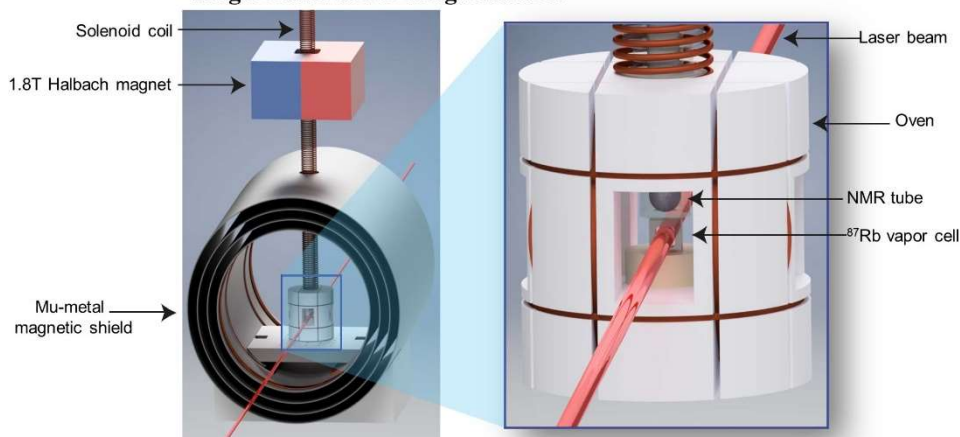
*S. Alcicek - 2*

**ZULF NMR**

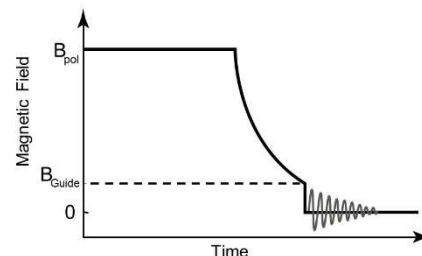


# Techniques and Methods

## Single Beam SERF Magnetometer



## Experimental procedure



Key elements of experimental setup.

- Liquid sample is polarized in strong permanent magnet.
- Sample is transported to zero field region (magnetic shield).
- Laser light traversing vapor cell measures magnetic field -NMR signal detection-

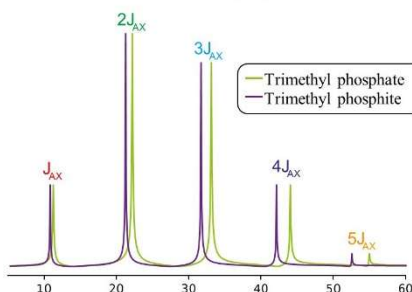


S. Alcicek - 3

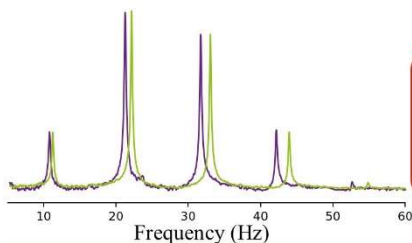
ZULF NMR

## Results and Conclusion

### Simulation



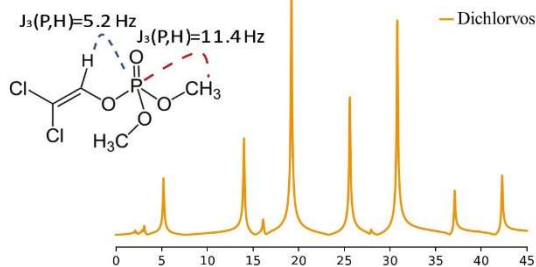
### Measurement



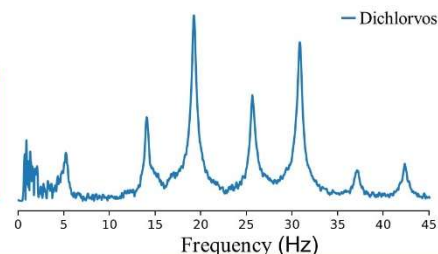
Distinguishable J spectra of compounds with identical spin system

Good agreement with simulation and experiment

### Simulation



### Measurement



Zero-field NMR J-spectroscopy is becoming a powerful tool in chemical analysis.



S. Alcicek - 4

ZULF NMR

# Real-time nanodiamond thermometry probing in-vivo thermogenic responses



Masazumi Fujiwara, Simo Sun, Alexander Dohms, Yushi Nishimura, Ken Suto, Yuka Takezawa, Keisuke Oshimi, Li Zhao, Nikola Sadzak, Yumi Umehara, Yoshio Teki, Naoki Komatsu, Oliver Benson, **Yutaka Shikano**<sup>1,2</sup>, and Eriko Kage-Nakadai

<sup>1</sup>Quantum Computing Center, Keio University, <sup>2</sup>Institute for Quantum Studies, Chapman University

**Abstract:** Real-time temperature monitoring inside living organisms provides a direct measure of their biological activities, such as homeostatic thermoregulation and energy metabolism. Here, using quantum nanothermometers based on optically accessible electron spins of nitrogen vacancy centers in nanodiamonds, we demonstrate in-vivo real-time temperature monitoring inside nematode worms. We developed a thermometry system that can measure the temperatures of mobile nanodiamonds inside the worms. Using this system, we determined the increase in temperature based on the thermogenic responses of the worms during the chemical stimuli of mitochondrial uncouplers.

## Related publications:

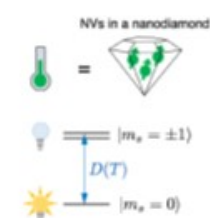
- M. Fujiwara et al, arXiv:2001.02844 (accepted for publication).
- M. Fujiwara et al, arXiv:2006.06901



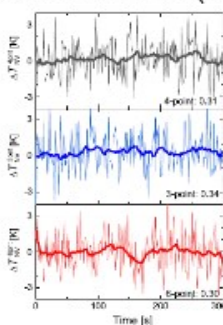
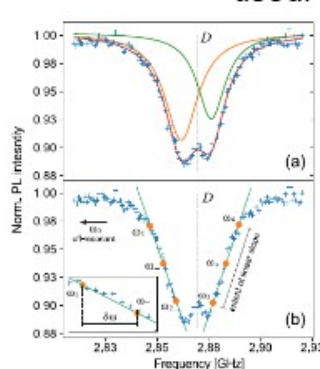
Y. Shikano - 1

ZULF NMR

## Nanodiamond thermometry via multi-points ODMR



Nitrogen-vacancy centers in nanodiamond are a promising candidate of the biological sensor. Due to the real-time temperature estimation with low intensity laser injection, the multi-points optically detected magnetic resonance (ODMR) technique is used.



Compared with 3-, 4-, 6-points ODMR, all accuracies are almost same. Depending on the situation, the multi-points ODMR should be properly used.

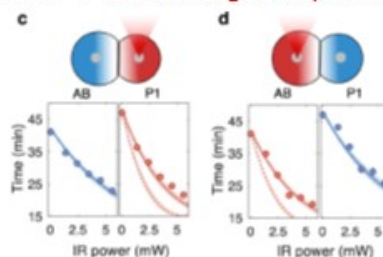
$$\Delta T_{NV} = \delta\omega \left( \frac{dD}{dT} \right)^{-1} \frac{(I_1 + I_2) - (I_3 + I_4)}{(I_1 - I_2) - (I_3 - I_4)}$$

## Development Biological Question solved by nanodiamond thermometry



Question:

Which temperature can cell division time be regulated? -> **Cell average temperature**



Dot Line : nucleus Line : Cell average

Lukin group, PNAS 2020



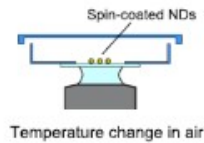
Y. Shikano - 2

ZULF NMR



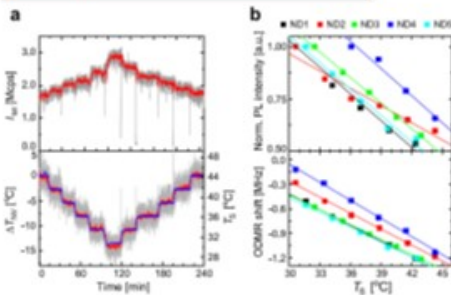
# Key Techniques

## Temperature Calibration

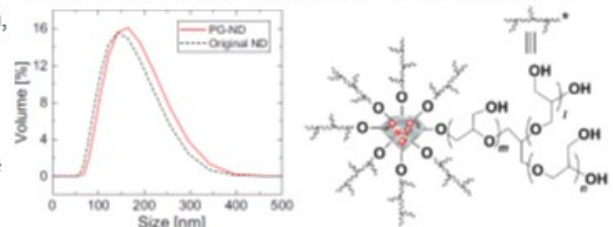


## Microinjection technique

We manually injected the polyglycerol (PG)-nanodiamond (ND) into distal arm of gonad. Site specification technique of the PG-ND has not yet established. The chemical termination of nanodiamonds is needed as the next investigation.

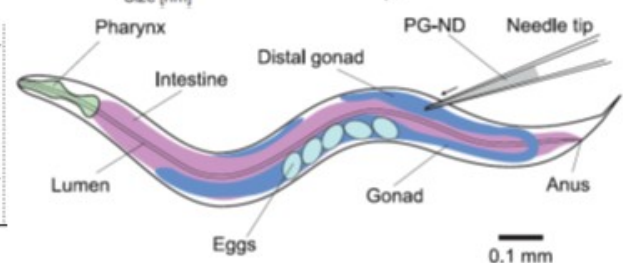
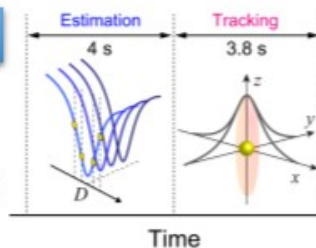


$dD/dT = -65.4 \text{ kHz/K}$  is calibrated. As next technological investigation, sample dependence and fluctuation should be understood. Also, the sample condition on a surface is important inside in-vivo biological sample.



## Real-Time Tracking Technique

In in-vivo biological sample, nanodiamonds are freely moved under microscope. The real-time tracking is needed. Tracking speed in our experiment is 80 nm/sec (maximum).

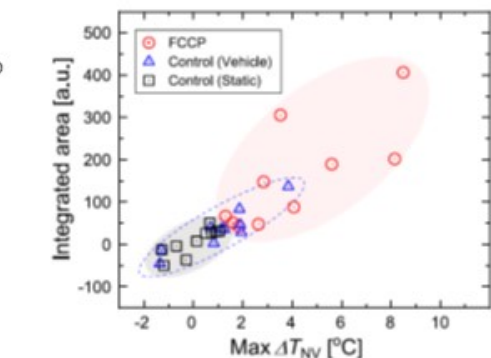
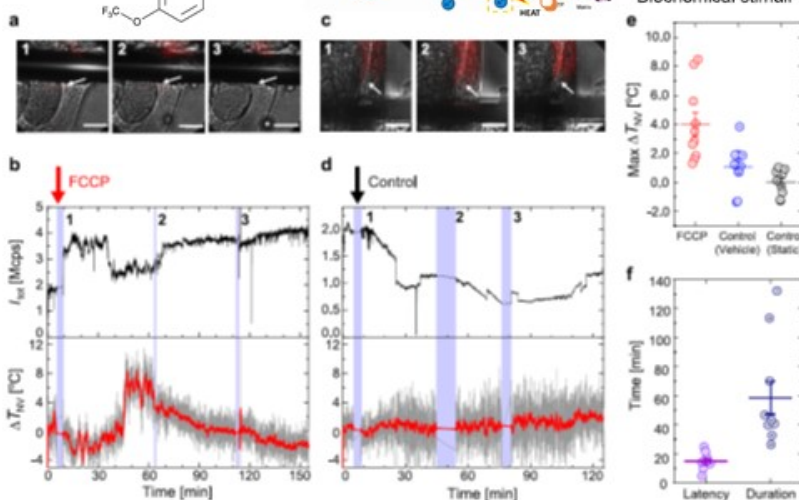
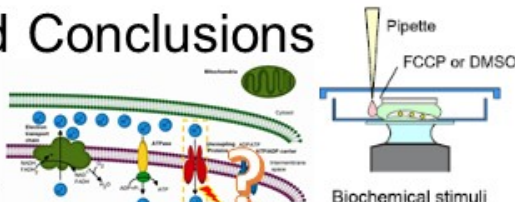
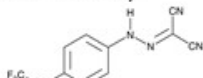


Y. Shikano - 3

ZULF NMR

# Results and Conclusions

Mitochondrial uncoupler (60uM FCCP)



Our question in Physiology: Biochemical-stimulated thermogenic response from *C. elegans*? -> **Yes.**

Nanoscale thermometer (= quantum sensor) should attack the biologically-driven questions. This may lead to open a field of nanothermal biology.



Y. Shikano - 4

ZULF NMR

# Optimising SABRE of amines via *in-situ* Earth's Field NMR

Aminata Sakho<sup>1</sup>, Fraser Hill-Casey<sup>2</sup>, Meghan E. Halse<sup>2</sup>, Simon B. Duckett<sup>1</sup>

<sup>1</sup>Centre for Hyperpolarisation in Magnetic Resonance, University of York, York, UK

<sup>2</sup>Department of Chemistry, University of York, York, UK

**Abbreviated abstract:** Amines have previously been successfully hyperpolarised by SABRE and detected using high-field (HF) instruments.[1] In this study, we report the detection of amine hyperpolarisation using an Earth's field NMR (EFNMR) instrument, where the catalytic activation process of SABRE has been followed *in situ*. The hyperpolarization level of these amines is increased by adding a co-ligand, dimethyl sulfoxide (DMSO). The effect of the addition of co-ligand on polarisation efficiency is studied herein. In parallel, the chemical exchange rate of the ligands (both amines and hydrides) and the corresponding thermodynamic parameters for these complexes have been explored at 11.7 T (500 MHz) to produce further insight into these processes.

## Related publications:

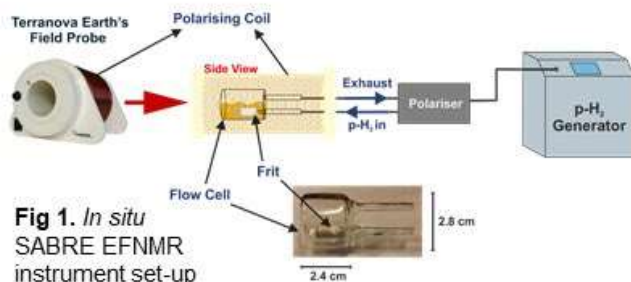
Hill-Casey F., *et al*, *Molecules*, 2019, **24**, 4126; Sakho A (*in prep*)



A. Sakho - 1



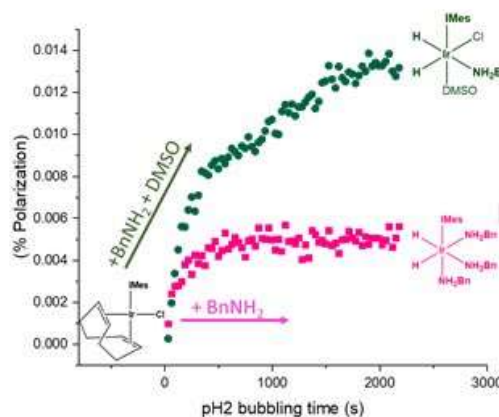
## Earth's field NMR with *in situ* SABRE



**Fig 1.** *In situ* SABRE EFNMR instrument set-up

- ❖ EFNMR spectrometer with integrated  $p\text{-H}_2$  generator for *in situ* SABRE experiments.
- ❖ The SABRE process takes place inside a flow reactor within the EFNMR probe.
- ❖ The pressure and flow of  $p\text{-H}_2$  through the cell is controlled by the polariser.

- ❖ Activation of SABRE catalyst is monitored via *in situ* SABRE-enhanced EFNMR



**Figure 2.** Increase in SABRE polarisation level during catalyst activation for benzylamine (pink) and benzylamine with DMSO as a co-ligand (green).

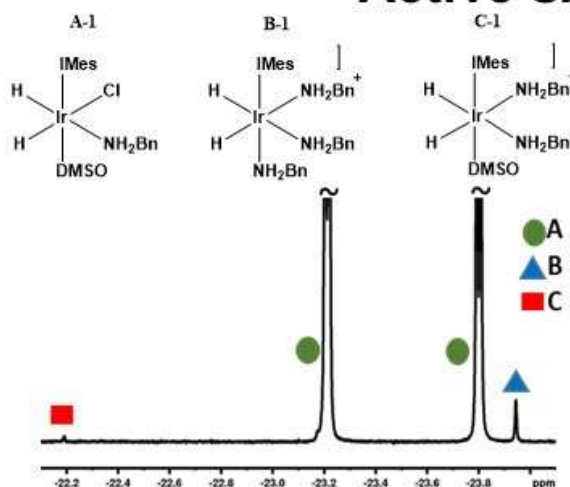


A. Sakho - 2





## Active SABRE complexes



**Figure 3.** Hydride region of a 500 MHz  $^1\text{H}$  NMR spectrum of 5.1 mM IMes pre-catalyst, 76.5 mM benzylamine, 76.5 mM DMSO- $d_6$  in  $\text{CDCl}_3$  following activation with  $\text{H}_2$ .

1.D. A. Barskiy, et al., *Prog. Nucl. Mag. Res. Sp.*, 2019, **114-115**, 33-70.

- ❖ The maximum observed polarisation level of benzylamine (BA) is significantly increased in the presences of the co-ligand, DMSO.
- ❖ Characterization at 500 MHz (Figure 3) shows the formation of three complexes A, B and C in the ratio 94%, 5% and ~1% respectively, in the presence of the co-ligand. The major complex A is likely to be the main driver of the SABRE hyperpolarization.
- ❖ Ligand exchange rates (for both hydrides and amines) measured at 500 MHz, show that the benzylamine exchange rate is increased from  $3.33 \text{ s}^{-1}$  to  $4.91 \text{ s}^{-1}$  by the presence of DMSO, which is close to the  $4.5 \text{ s}^{-1}$  optimal regime for pyridine<sup>1</sup>.



A. Sakho - 3

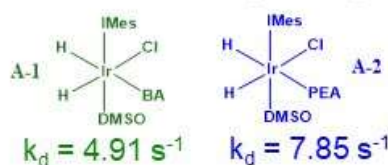
ZULF NMR

## Benzylamine (BA) vs Phenoxyethylamine (PEA)

Equivalent concentrations of BA and PEA (25 eq) compared to the pre-catalyst, produces different SABRE enhancements.

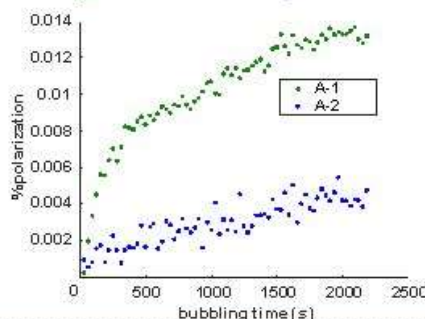
At 298 K, complex A-2 exhibits a disassociation rate of  $7.85 \text{ s}^{-1}$  compared to A-1 whose values is  $4.91 \text{ s}^{-1}$ .

A dissociation rate of  $7.85 \text{ s}^{-1}$  is above the value for optimal transfer on this basis.



Gibbs free activation energies are  $67.30 \text{ kJ mol}^{-1}$  for A-1 and  $68.08 \text{ kJ mol}^{-1}$  for A-2.

This data confirm that lower barriers to ligand loss promote more effective SABRE polarisation transfer.



**Figure 4.** Increase in polarization during activation of same concentration BA (green) and PEA (blue) at EFNMR

## Conclusions

Addition of co-ligand (DMSO) is shown to increase the BA exchange rate to a level which improves polarization transfer. Whereas for, PEA, the exchange rate is increased beyond the optimal polarization transfer regime.



A. Sakho - 4

ZULF NMR

# Applications of the NV centers in diamonds

D.Olivares-Postigo<sup>1,2</sup>, F. Gorrini<sup>1,2</sup> and A. Bifone<sup>1,2</sup>

<sup>1</sup> Center for Neuroscience and Cognitive Systems, Istituto Italiano di Tecnologia, Corso Bettini 31, 38068 Rovereto, Trento, Italy

<sup>2</sup> Department of Molecular Biotechnology and HealthSciences, University of Torino, Italy

**Abbreviated abstract:** Diamonds with nitrogen-vacancy (NV) centers provide intrinsic biocompatibility, robust chemistry within and on the surface of the diamond, combination of very high photostability, significant coupled magneto-optic properties, etc. that exceed the characteristics of other classes of fluorophores.

This exceptional combination of properties makes NV centers unique fluorophores with emerging applications in a variety of fields such as ultra-sensitive nanoscale metrology as temperature / electric field sensors or measuring the magnetic field of biological molecules, as a magnetic resonance contrast agents or in the field of bioimaging among many other more applications.

## Related publications:

[1] D. Suter *et al*, Progress In Nuclear Magnetic Resonance Spectroscopy, 98-99, 50-62 (2017)

[2] A. Ajoy *et al*, Physical Review X, 5(1), (2015)

[3] A. Ajoy *et al*, Science Advances, 4(5), (2018)



D.Olivares-Postigo - 1



## Introduction

- What makes diamonds unique are the defects they have within the structure that give them a different color (see Fig 1a). Specifically, more than 120 types of diamond defects are known. Currently for scientific applications, the most important defects within the diamond that are being used are the silicon vacancies (SiV) or nitrogen-vacancy (NV) centers.
- The NV centers consist of two adjacent places in the diamond lattice of carbon atoms where this carbon atoms are missing, one of them is replaced by a nitrogen atom and the other is empty (see Fig 1b). This new defect leaves bonds free within the diamond structure, with isolated electrons that are very sensitive to small variations in the environment such as variations in the magnetic or electric field, temperature, light-based, etc. [1]
- The electronic ground state has a zero-field splitting of  $m_s = 0$  and  $m_s = \pm 1$ . Preparation of the NV center into  $m_s = 0$  can be achieved with optical excitation, in which  $m_s = \pm 1$  undergoes an intersystem crossing to a long-lived singlet state ( $^1A$ ) that decays to  $m_s = 0$  ground state. Furthermore, state dependent fluorescence is used to determine the spin state (see Fig 1c).

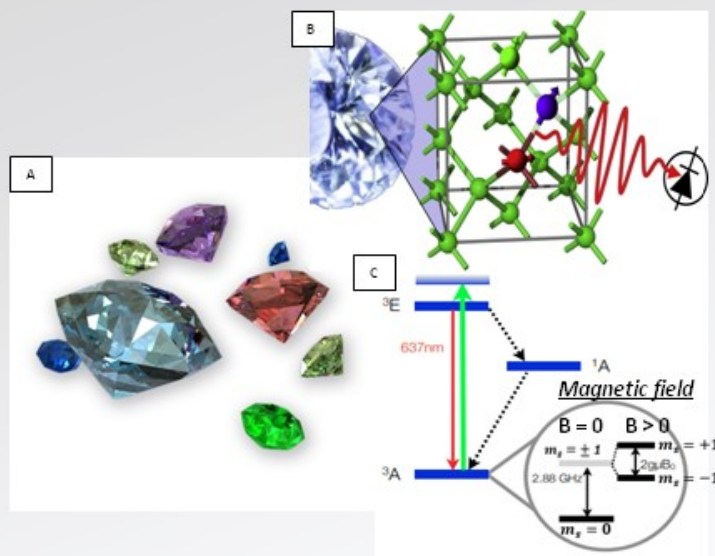


Figure 1 | a) Diamonds with different colors due to different defects in their structure. b) Structure of the NV center. The lone pair of the nitrogen (red color) is oriented towards that vacancy (purple color) and overlaps with the three dangling bonds of the carbon atoms located next to the vacancy (Reproduced from Ref. 1. © 2016 Elsevier B.V.). c) Energy level structure of the NV<sup>-</sup> center.



D.Olivares-Postigo - 2





## NV centers sensors

- These NV centers have been studied as small sensors to measure the temperature inside a living cell or the electric field from a single electron.
- They have also been used to measure the magnetism of a single protein [2]. For this, a biological molecule like a protein is placed on the surface of the diamond to determine its structure. When the NV centers are very close to the diamond surface around a few nanometers they can be used to detect the states of rotation of the particles within a molecule placed on the surface. In this way, the molecular structure could be revealed from the detection of the individual atoms. Specifically, when these diamonds are irradiated with a green laser and a combination of microwave pulses, the NV centers emit a red light that could be used to reconstruct spins from nearby particles, in this case from biological molecules
- They also have the advantage that these NV centers sensors can be used at room temperature, so they offer a great advantage over other techniques that require very low temperatures or even vacuum

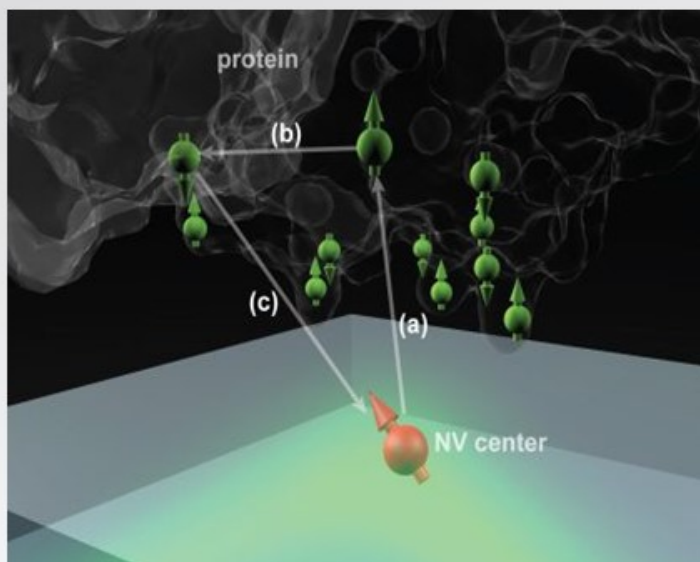


Figure 2 | NV centers could determine the structure of individual protein molecules that are on the diamond surface. (Reproduced from Ref. 2. © 2014 American Physical Society).



D.Olivares-Postigo - 3

ZULF NMR

## Hyperpolarization in NV centers

- One particularly interesting idea that has garnered much attention is the use of these NV centers in diamond as optical hyperpolarizing agents paving the way for using them as imaging contrast agents for biosensing or for the hyperpolarization of nuclear spins in arbitrary liquids that are in contact with the diamond surface.
- This hyperpolarization is achieved by applying a continuous laser and the frequency swept microwave at low background field  $B_{pol}$  to a powdered diamond (see Fig 3 a,b). The laser polarizes the NV centers of this diamond to  $m_s = 0$  sublevel and the microwaves transfers the polarization to the  $^{13}C$  nuclei. The bulk nuclear polarization is detected by inductive readout after rapid shuttling of the hyperpolarized powder to high field 7 T NMR and is compared against the corresponding Boltzmann polarization at 7 T [3].
- The end goal will be to flow a liquid like water through a device containing optically polarized diamond particles, thereby creating a polarized liquid (see Fig 3c). In this way, we could inject this polarized liquid into a human being creating an MRI image that could be 100 times brighter than conventional MRI. In this way, diamonds could be the key to a new low-cost technique that can cope with other expensive alternatives such as current medical imaging or drug delivery.

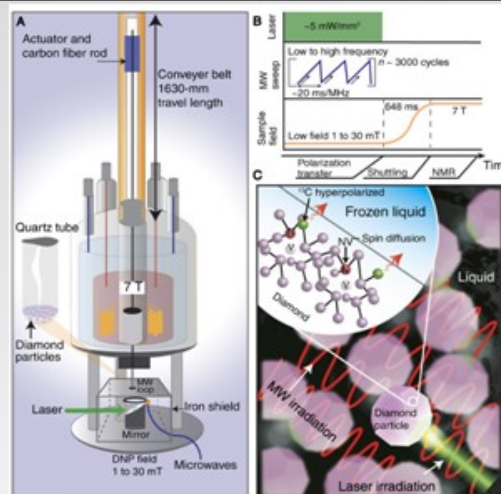


Figure 3 | a) Polarization transfer from optically pumped NV centers to  $^{13}C$  in diamond particles is carried out by microwave irradiation at low field magnetic field ( $B_{pol} \sim 1$  to 30 mT), after which the sample is shuttled rapidly for bulk inductive readout at 7 T NMR. The enhancement of the polarization signal in the diamond particles is compared with its 7 T thermal signal. b) Polarization transfer protocol: Laser light (532 nm) is continuously applied along with swept microwave (MW) irradiation across the NV center spectrum at a magnetic field  $B_{pol}$  to hyperpolarize the  $^{13}C$  nuclei. c) NV centers could optically polarize the  $^{13}C$  nuclei and thus transfer the polarization to a frozen liquid by spin diffusion, aided by the intrinsically large surface area of the nanoparticles. Rapid thawing of this liquid would allow enhanced NMR detection and thus open a new way to improve the MRI image. (Reproduced from Ref. 3. © 2018 American Association for the Advancement of Science).



D.Olivares-Postigo - 4

ZULF NMR



# Chemical reaction monitoring at zero magnetic field

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**Abbreviated abstract:** Herein, the kinetics of the two-step hydrogenation of dimethyl acetylenedicarboxylate with parahydrogen was studied by zero-field nuclear magnetic resonance spectroscopy. It was shown that heterogeneous/biphasic chemical reactions can be monitored with high spectroscopic resolution using ZULF NMR. Importantly, the reaction can be monitored even when it is carried out in a metal container.

## Related publications:

D. Burueva *et al*, Angew. Chem. published online, DOI: [10.1002/anie.202006266](https://doi.org/10.1002/anie.202006266) (2020)



D. Burueva - 1

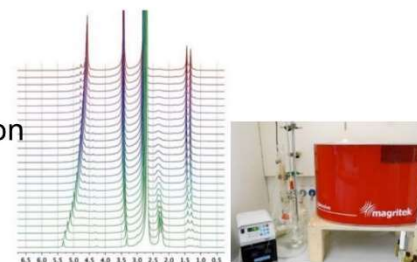


## Motivation

### Monitoring of catalytic reactions by HF NMR:

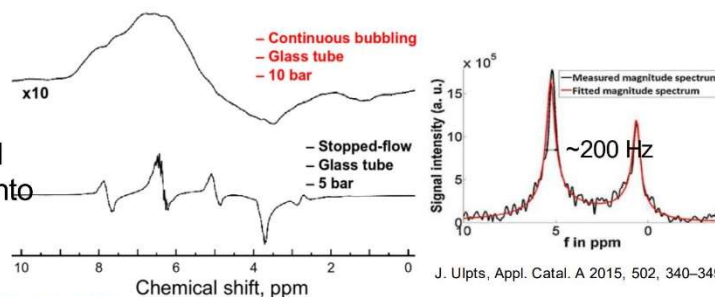
#### Pros:

- ✓ Quantitative analysis
  - ✓ Chemical specificity →
  - ✓ Non-invasiveness
- spatially and temporally resolved information that can be obtained:
- ✓ conversion and selectivity
  - ✓ mass transport (flow and diffusion)
  - ✓ adsorption processes
  - ✓ heat transport



#### Cons:

- ❖ line broadening from susceptibility gradients
- ❖ restrictions on catalytic reactor materials and catalyst nature due to limited rf penetration into conductive samples



J. Uilts, Appl. Catal. A 2015, 502, 340–349

### Promising alternative – NMR at zero magnetic field!

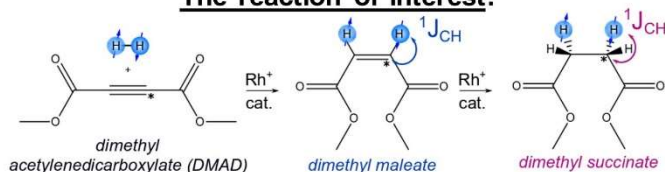


D. Burueva - 2

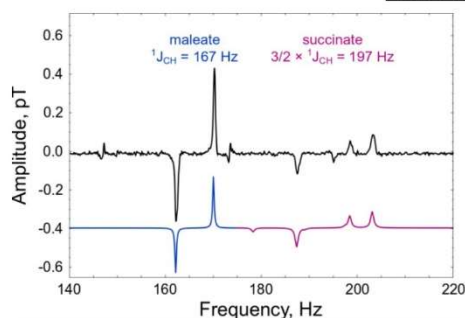


# Techniques and Methods

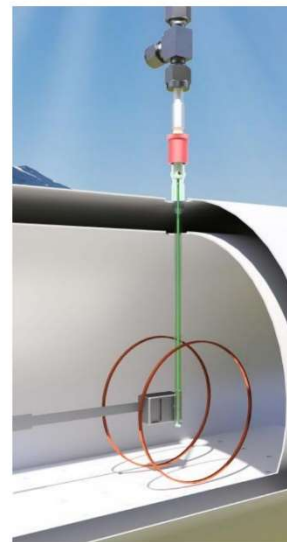
## The reaction of interest:



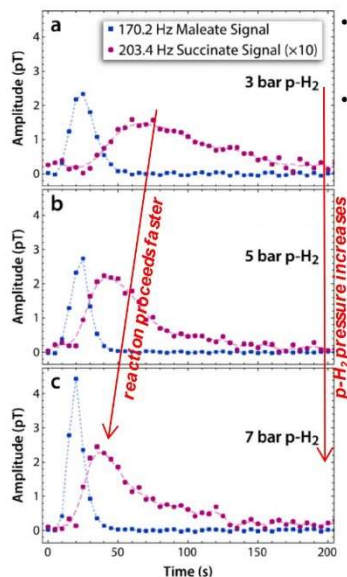
## Zero-field NMR spectra:



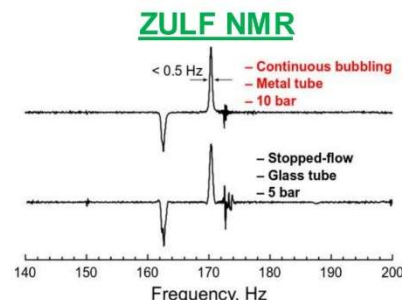
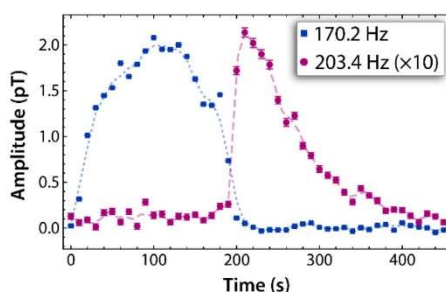
The two-step hydrogenation of DMAD with parahydrogen was studied by ZULF NMR using a commercial atomic magnetometer. The hydrogenation reaction was performed both in a glass tube and a titanium tube and was monitored by observing the NMR signals of the hydrogenated products (dimethyl maleate and dimethyl succinate) over time.



# Results and Conclusions



- The reaction timescale depends measurably on the availability of  $\text{H}_2$  in the system (at higher pressures it takes less time for the reaction to complete) – **oxidative addition of  $\text{H}_2$  is the rate determining step**
- The stronger binding of alkyne to metal complex (compared to alkene) allows it to outcompete the alkene in binding to the catalyst, which results in **high selectivity toward alkene** production even at high alkyne conversions.



The sample heterogeneity induced by bubbling parahydrogen during signal acquisition practically **does not** affect the spectral resolution in ZULF NMR! Importantly, ZULF NMR spectra can be acquired even when it is carried out in a **metal container**.