

ICOLIS

2021

Intercontinental NMR Conference on Methods and Applications

ICONS₂₀₂₁

February 10-12, 2021

Time: 12:00-15:00 (Berlin/Paris, CEST)

Organised by:

Daniel Abergel, Gerd Buntkowsky, Konstantin Ivanov, P. K. Madhu



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Foreword

ICONS2021 is the second of a new on-line magnetic resonance conference series. It aims to cover recent topics in both NMR and EPR. The meeting is an off-shoot of the Intercontinental NMR Seminar Series that started on April 8, 2020. This seminar series enabled communication and dissemination of research ideas among the magnetic research community especially in the times of the COVID-19 pandemic. The seminar series also gave early-stage researchers an opportunity to give seminar talks and interact with colleagues from different countries. The success of the seminar series prompted us to introduce a new conference to highlight the recent research contributions from some of the leading groups in magnetic resonance. We target to reach a good cross-section of the community even despite the time-zone disparity. We sincerely hope that both the seminar series and the conference will prove to be beneficial to the magnetic resonance community and contribute to the growth of magnetic resonance science and help many of us to stay connected.

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Time/CEST/UTC	February 10 Wednesday	February 11 Thursday	February 12 Friday
12:00-12:45 11:00-11:45	Jeletzko	Prisner	van Doorslaer
12:45-13:25 11:45-12:25	Kagawa	Sato	Bucher
13:30-14:10 12:30-13:10	Ouari	Jannin	Hill
14:15-14:55 13:15-13:55	Griffin	Novikov	Matysik
15:00-15:40 14:00-14:40		Han	

February 10, 12:05-12:45 (CEST)

Nanoscale NMR enabled by diamond quantum sensors

Fedor Jelezko

Institute of Quantum Optics, Ulm University, Germany

A particularly interesting application of diamond based quantum sensing is the detection of nuclear magnetic resonance on nanometer scales, including the detection of individual nuclear spins or small ensembles of external nuclear spins. Single nitrogen vacancy (NV) color centers in diamond currently have sufficient sensitivity for detecting single external nuclear spins and resolve their position within a few angstroms. The ability to bring the sensor close to biomolecules by implantation of single NV centers and attachment of proteins to the surface of diamond enabled the first proof of principle demonstration of proteins labeled by paramagnetic markers and label-free detection of the signal from a single protein. Single-molecule nuclear magnetic resonance (NMR) experiments open the way towards unraveling dynamics and structure of single biomolecules. However, for that purpose, NV magnetometers must reach spectral resolutions comparable to that of conventional solution state NMR. New techniques for this purpose including technique that employs hyperpolarization will be discussed.

February 10, 12:45-13:25 (CEST)

DNP using photo-excited triplet electron spins

Akinori Kagawa

Osaka University, Osaka, Japan

Several methods such as para hydrogen, nitrogen-vacancy center in diamonds and optically pumped gases are studied as promising candidates to obtain extremely high nuclear polarizations. As the sources of high polarization in these methods are not thermally equilibrated electron spins, these techniques do not require high magnetic fields and/or cryogenic temperatures. DNP using photo-excited triplet electron spins (triplet-DNP) has also been carried out under low magnetic fields and relatively high temperatures. While triplet-DNP has advantages for the experimental conditions, it has to overcome several problems to become a versatile method such as dissolution-DNP. Recently, we have advanced this technique toward the application in NMR/MRI analyses. For example, eutectic mixtures and glassy host molecules have been investigated to increase the number of target molecular species to be polarized by triplet-DNP. In this talk, we discuss how to widen the range of triplet-DNP applications.

February 10, 1330-14:10 (CEST)

Mixing DNP, EPR and organic synthesis for a better (NMR) world

Olivier Ouari

University of Aix-Marseille, France

Microwave-driven dynamic nuclear polarization (DNP) is an active and fast growing area of research in magnetic resonance today. DNP is now a well-established method used to tremendously enhance nuclear magnetic resonance (NMR) signal intensities by transferring spin polarization from unpaired electrons to nearby nuclei. Thus, typical DNP experiments usually require doping the sample with exogenous free radical as polarizing agents. In magnetic fields of 9 or 18 T, there are several mechanisms that might lead to polarization transfer, but currently the most efficient at 100 K is the cross effect (CE). The cross effect requires two dipolar coupled unpaired electrons to fulfill a condition where the difference in Larmor frequencies of the two electrons matches the Larmor frequency of the nucleus. There is much interest in designing radicals for high resolution, high sensitivity ssNMR DNP. By correlating data from EPR, radical structures and DNP, a series of key steps to make cross-effect transfer more efficient at 9 T but also at higher field (up to 21 T) and faster MAS will be presented and limitations as well as further extensions will be discussed.

February 10, 14:15-14:55 (CEST)

Time domain dynamic nuclear polarization

Robert G. Griffin

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In the last few years microwave driven dynamic nuclear polarization (DNP) using CW microwave sources (mainly gyrotrons) has emerged as the method of choice to enhance signal intensities in a variety of magic angle spinning (MAS) NMR experiments. In particular, because of the large signal enhancements, it is used to address a variety of important chemical, biological and physical questions that are otherwise inaccessible. Despite the success and wide applicability of DNP, there remain a number of areas where the methodology and instrumentation can be improved. In this presentation we explore one of these, namely time domain or pulsed DNP experiments, with the goal of providing higher polarization enhancements at high fields. In particular, we review results of the “gold standard” lab frame-rotating frame NOVEL experiment and show how it can be improved with alternative pulse experiments. These solutions are based on the frequency swept integrated solid effect (FS-ISE), the newly observed stretched solid effect (SSE) and the recently reported time optimized pulse DNP (TOP DNP) and the adiabatic solid effect (ASE). To date these experiments have been constrained to low microwave frequencies (9-95 GHz) where it is possible to generate microwave pulses. Thus, we also discuss the instrumentation under development to perform phase, amplitude and frequency modulation of the microwaves and to generate high power microwave pulses with a gyroamplifier.

February 11, 12:05-12:45 (CEST)

Investigation of flexible molecules with rigid spin labels using pulsed EPR spectroscopy

Thomas Prisner

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Goethe University Frankfurt am Main, Germany*

Pulsed EPR dipolar spectroscopy (PDS) can be used to determine distances in the 1-10 nm on biomolecules. This is achieved by determining the size of the magnetic dipole-dipole interaction between two covalently attached spin-labels. Typically MTSL spin labels with a rather flexible linker are used for this type of experiments in proteins, which limits the accuracy of the distances to about 0.3 nm. Here I will show how spin labels rigidly incorporated into nucleic acid molecules substantial increase the accuracy in distance determinations. Additionally measurements with such rigid spin labels allow to obtain information on the mutual orientation between both spin-labels. I will show how this information can be combined with NMR restraints and directly compared to MD simulations to give an overall picture of the conformational dynamics of RNA and DNA molecules in solution and to compare results obtained in-vitro with results of in-cell measurements.

February 11, 12:45-13:25 (CEST)

Spin Manipulation Technology based on Pulsed ESR with Arbitrary Waveform Microwave Pulses

Kazunobu Sato

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Molecular spin quantum control is one of the challenging issues for realizing quantum computing and quantum information processing. Pulsed NMR techniques have been applied to molecules to implement elementary quantum algorithms, demonstrating the usefulness of pulsed magnetic resonance techniques as quantum spin technology. We have applied pulsed ESR techniques to molecular spin systems for manipulation of electron spin qubits in molecules [1-3]. A pulsed ESR spectrometer with an arbitrary waveform generator (AWG) has been introduced to sophisticated ESR measurements, expanding research fields in spin science and technology. We have implemented electron spin technology with AWG for the precise manipulation of molecular spins. Microwave pulses generated by AWG have been utilized for exciting electron-spins in molecular spin systems. I will present the AWG-based spin technology which enables us to manipulate molecular spins. The AWG technology has been applied to typical molecular spin systems for demonstrating the spin excitation underlying quantum control. I will also discuss a complicated microwave-GRAPE (GRAdient Ascent Pulse Engineering) approach which is promising for global control of spin qubits in molecular spin systems.

[1] S. Nakazawa, K. Sato, Y. Morita, T. Takui et al. *Angew. Chem. Int. Ed.* **2012**, *51*, 9860-9864.

[2] S. Yamamoto, K. Sato, T. Takui et al. *Phys. Chem. Chem. Phys.* **2015**, *17*, 2742-2749.

[3] K. Sato, E. Bagryanskaya, T. Takui et al. *J. Phys. Chem. A* **2019**, *123*, 7507–7517.

A Hyperpolarized Journey: from the electron to the MRI scanner

Théo El Daraï,¹ Samuel Cousin,¹ Quentin Chappuis,¹ Morgan Ceillier,¹ James Kempf,² Dmitry Eschenko,² Roberto Melzi,² Marc Schnell,² Laurent Gremillard,¹ Aurélien Bornet,³ Jonas Mllani,¹ Basile Vuichoud,¹ Olivier Cala,¹ Damien Montarnal,² and Sami Jannin¹

¹University of Lyon, France, ² Bruker Biospin, Switzerland, ³ École polytechnique fédérale de Lausanne, Switzerland

More than fifteen years after its invention, dissolution dynamic nuclear polarization (d-DNP)[1] had apparently settled into well-defined technologies and methodologies, and it was mostly believed that d-DNP needed to be performed at the point of use. However recently, a series of advances have shaken foundations of d-DNP. For the first time, it was demonstrated that d-DNP could potentially be performed remotely, off-site,[2] thus without the need of a polarizer on-site.

In our group, we have in the past years, merely been working at improving efficiency,[3] compatibility,[4] and repeatability[5] of d-DNP. Our candid objective basically was to enable (or at least to improve) applications; nonetheless it has led us to develop a new concept i) to dramatically extend hyperpolarization lifetimes from minutes to days and, ii) to enable transport to far distant MRI or NMR sites.[2]

We are now generalizing this new concept to a broad range of systems, such as neat endogenous tracers, mixtures of metabolites, or amino acids, by developing new hyperpolarizing solids such as our silica-based HYPISO materials, or more recently hyperpolarizing porous polymers (HYPOP). These can be impregnated with arbitrary solutions that are then hyperpolarized efficiently and stored and transported over hours, before being melted and released. We will in particular present a new epoxy-based polarizing material. We'll show how the porosity and morphology of this material can be tuned, and we will present DNP results on the very first generation of these new materials.[6]

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- [2] Ji, X. *et al. Nat. Commun.* **8**, (2017). Capozzi, A. *et al. Nat. Commun.* **8**, 15757 (2017).
- [3] Bornet, A. *et al. J. Phys. Chem. Lett.* **4**, 111–114 (2013). Bornet, A. *et al. Chem. Phys. Lett.* **602**, 63–67 (2014). Bornet, A. *et al. Phys. Chem. Chem. Phys.* **18**, 30530–30535 (2016).
- [4] Gajan, D. *et al. Proc. Natl. Acad. Sci. USA* **111**, 14693–14697 (2014). Cavaillès, M. *et al. Angew. Chemie Int. Ed.* (2018). doi:10.1002/anie.201801009. Vuichoud, B. *et al. J. Phys. Chem. B* **118**, 1411–1415 (2014).
- [5] Bornet, A. *et al. Anal. Chem.* **88**, 6179–6183 (2016).
- [6] El Daraï, T. *et al.* <https://doi.org/10.21203/rs.3.rs-123790/v1> under review.

Spotting magnetic bistability with paramagnetic NMR spectroscopy

Valentin Novikov

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Transition metal complexes possessing magnetic bistability are searched for their ability to switch between two magnetically-nonequivalent states useful in high density data storage, molecular spintronics, switching, sensing and quantum information processing. They are usually either single-molecule magnets (SMMs), the term referring to chemical compounds that keep their magnetization in the absence of an external magnetic field, or spin-crossover (SCO) compounds that switch between low-spin (LS) and high-spin (HS) states in response to an external stimulus (such as temperature, pressure, light irradiation, electric or magnetic field).

For identification of these two types of molecular magnets among many possible transition metal complexes, magnetometry is often used, as it directly probes the spin states and the magnetic relaxation times. The applications of this method are, however, limited to bulk solid samples of chemical compounds that need to be thoroughly isolated and purified – a task that is not always easy to achieve. While many spectroscopic techniques (such as EPR, MCD, UV-Vis absorption and luminescence spectroscopies) have been shown to provide invaluable information on the SMM and SCO behaviour, NMR spectroscopy, which is arguably the most common tool for a synthetic chemist, is mostly ignored by molecular magnetism community.

In my lecture, I will show how NMR spectroscopy helps to spot potential SCO and SMM compounds, based on a simple analysis of the temperature dependence of their chemical shifts. Only demanding a correct assignment of at least some of the signals in the NMR spectra, this approach is potentially applicable to mixtures of different compounds, including those obtained *in situ* in an NMR tube. The possibility to probe the spin-state switching and slow magnetic relaxation for many compounds simultaneously may provide a huge advantage in high-throughput screening of transition metal complexes for potential SCO and SMM applications and in fine-tuning their magnetic properties by proper chemical modifications to the ligands.

This study was supported by RSF (project 19-73-10194) and CPRF (grant MD-1935.2020.3).

Role of electron spin dynamics and coupling network in dynamic nuclear polarization

Songi Han

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The direct transfer of polarization from an isolated electron spin to a surrounding nucleus is inefficient at high B_0 . It is now well understood that utilizing coupled electron spins ($e-e$) can remedy this problem. Specifically, there are two distinct DNP mechanisms (Cross Effect (CE) and Thermal Mixing (TM)) that rely on $e-e$ couplings (1's-100's MHz) to induce triple-flip transitions between two coupled e spins and a hyperfine coupled nucleus. The resonance condition is satisfied when the difference of the EPR frequencies of the coupled electron spins matches the nuclear Larmor frequency, e.g. 400 MHz for ^1H at 9T. In diluted bis-nitroxides, this condition is met by its large g -anisotropies, where the CE is predominant and highly efficient at moderate B_0 such as 9T. However, contemporary NMR of biomolecules and quadrupolar nuclei entail studies at higher B_0 , routinely at 18 T, where DNP efficiency is an order in magnitude lower than expected. Here, I will present the basis for utilizing TM DNP that exploits a strongly coupled electron spin network, in which the difference of the EPR frequencies of the coupled electron spins matching the ^1H Larmor frequency is generated from dipolar and exchange coupling between the electron spins.

I will present our recent discovery of highly efficient ^1H TM DNP with Trityl-OX06, as well as BDPA, as polarizing agents (PAs). These PAs have propensity to form clusters at high concentrations, leading to a strongly coupled electron spin network with broad ~ 1 GHz, EPR line-width. We could verify using pulsed EPR the co-existence of isolated and clustered species of BDPA and the build-up of a polarization gradient exceeding the linewidth of BDPA. TM DNP of these systems was completely unexpected but is intriguing given its promising DNP performance at high magnetic. In fact, concentrated BDPA-based PAs has been reported recently to lead to the highest reported DNP enhancements at high magnetic fields (900MHz) and/or fast MAS (~ 65 kHz). I will share pulsed EPR and ELDOR studies under DNP conditions that helped uncover that TM is the effective and dominant mechanism and, not the initially hypothesized Overhauser DNP. However, the implementation of the TM DNP concepts requires a better understanding of the spin dynamics of the coupled electron spin clusters that, to date, has evaded direct probe and manipulation.

Challenges in hyperfine spectroscopy

Sabine Van Doorslaer

BIMEF Laboratory, Department of Chemistry, University of Antwerp, Belgium

Hyperfine spectroscopy is a cluster name for EPR-based techniques that target the detection of the interaction of the electron spin (S) with the magnetic nuclei (I_i) in its vicinity. More specifically, they aim at identification of the type of nuclei through the *nuclear Zeeman interaction*, detection of the *hyperfine interaction* revealing information on spin-density distribution, $S - I_i$ inter-spin distance information and knowledge on the bonding types, and detailed knowledge on the *nuclear quadrupole coupling* for $I_i > 1/2$. Hyperfine techniques can reveal information that is of use in or complementary to NMR experiments (paramagnetic NMR, DNP, quadrupole NMR, ...).

The vast majority of the hyperfine techniques are pulsed EPR techniques. While some techniques, such as ESEEM (electron spin echo envelope modulation), EDNMR (ELDOR detected NMR, require the use of microwave pulses only, ENDOR (electron nuclear double resonance) techniques make use of a combination of microwave and radiofrequency pulses.

The talk will target at giving a brief overview of the most important hyperfine techniques, including recent developments in the use of shaped microwave pulses in this field and discuss the potential, but also the many challenges of hyperfine spectroscopy, both in detection and simulation of the hyperfine spectra as well as in interpretation of the experimental hyperfine and nuclear quadrupole interactions. A bridge will be made to developments in NMR, quantum chemistry and machine learning.

February 12, 12:45-13:25 (CEST)

NMR spectroscopy with NV-centers in diamond

Dominik Bucher

TU Munich, Germany

Recently, optically probed nitrogen-vacancy (NV) point defects in diamond have emerged as a new class of quantum sensors allowing the detection of magnetic fields on unprecedented length scales. The technique is based on optical detected magnetic resonance of the NV electronic spins, which can also be used to detect NMR signals from smallest sample volumes down to a single molecule. In the first part of this talk, I will introduce the concept of quantum sensing with NV-centers and how NMR signals can be detected. In the second part, I will report about recent progress in enhancing the sensitivity of this approach with hyperpolarization methods. In the concluding part, possible applications as well as remaining obstacles for a general tool in biology and chemistry will be discussed.

Probing electron-nuclear spin interactions via broadband pulsed EPR

Stephen Hill

*Department of Physics and National High Magnetic Field Laboratory, Florida State University,
Tallahassee, FL32310, USA*

This talk will highlight recent efforts at the US National High Magnetic Field Laboratory (NHMFL) focusing on electron-nuclear spin interactions in magnetic molecules using broadband pulsed EPR methods. This work is of both fundamental and practical interest in areas of research ranging from coordination chemistry to quantum information science. I will begin by summarizing recent technique developments, particularly those centered around our high-power quasi-optical 94 GHz (W-band) spectrometer, HiPER [1], developed at the University of St. Andrews. I will emphasize applications that take advantage of this instrument's considerable bandwidth, which enables pulsed excitation of relatively broad electron- and electron-nuclear magnetic resonance spectra. The first example involves two-dimensional electron-electron double resonance (ELDOR) measurements in which a frequency-pure saturation pulse is used to burn narrow holes in the inhomogeneously broadened EPR spectrum, followed by an electron-spin-echo detection sequence. The full spectrum can be collected either by scanning the frequency of the detection sequence [2,3] or, using an arbitrary waveform generator (AWG), it is possible to image the complete spectrum using chirped pulses followed by Fourier-transform detection [4]. Examples involving both approaches will be presented, where holes are generated at both the electron- and weakly-allowed electron-nuclear transition frequencies, thereby enabling rapid acquisition of NMR signals over a wide frequency range and with the advantages of EPR sensitivity. Time permitting, I will present recent experimental and computational work exploring the decoupling of electron and nuclear spins at so-called atomic-clock transitions [5,6], as monitored via electron-spin-echo envelope modulation (ESEEM) measurements. These transitions can be engineered in molecules containing transition metals and lanthanides via coordination chemistry, and the electron-nuclear decoupling is of importance for optimizing coherence for potential quantum technologies.

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- [2] S. M. Greer, C. M. Thomas, S. Hill et al., *Inorg. Chem.* **57**, 5870 – 5878 (2018).
- [3] X. Wang, S. Hill, J. R. Long, H. C. Dorn et al., *Chem. Comm.* **54**, 2425 – 2428 (2018).
- [4] J. Marbey, K. Kundu, S. Hill (in preparation, 2021).
- [5] A. Gaita-Ariño, F. Luis, S. Hill, E. Coronado, *Perspective in Nat. Chem.* **11**, 301 – 309 (2019).
- [6] J. Chen, C. Hu, J. F. Stanton, S. Hill, H.-P. Cheng, X.-G. Zhang, *J. Phys. Chem. Lett.* **11**, 2074 – 2078 (2020)

The solid-state photo-CIDNP effect

Jörg Matysik

Universität Leipzig, Institut für Analytische Chemie, Leipzig, Germany

One of the hyperpolarization techniques in NMR relies on the solid-state photo-CIDNP effect. The term “photo-CIDNP” (photochemically induced dynamic nuclear polarization) means that a photochemical process pumps nuclear spin-states and therefore the NMR signal. Not many systems are able to show this amazing and very strong effect.

In natural photosynthetic reaction center (RC) proteins under illumination, spin-correlated radical pairs occur and induce the solid-state photo-CIDNP effect improving the NMR sensitivity by a factor of several 10.000. Therefore, photo-CIDNP MAS NMR allows for perfect information at the atomic scale even in large photosynthetic units. We will ask for the origins of the functional symmetry break in purple-bacterial RCs as well as of the high quantum yield of light-driven electron transfer. Remarkably, all photosynthetic reaction centers studied have been demonstrated to undergo this light-driven pumping.

Recently, some flavoproteins were successfully probed paving the way for the design of artificial systems.