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20th edition of YBMRS

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SCIENTIFIC PROGRAM

Monday, November 25th

9:15 *Registration, welcome coffee*

10:20 *Opening*

10:30 ***Tutorial 1:*** **Magnetic Resonance Imaging**
Prof. **Chantal Tax** (University Medical Center Utrecht) – Chair: Luca Fusaro

11:20 ***Tutorial 2:*** **EPR to study structure and dynamics in paramagnetic materials**
Prof. **Josef Granwehr** (Forschungszentrum Jülich GmbH, Germany)

12:10 **Lunch break**

13:10 ***Tutorial 3:*** **SOPs for the metabolic analysis of large cohorts of samples**
Prof. **Oscár Millet** (CIC bioGUNE, Spain)

14:00 ***Oral Session 1*** **-** Chair: Samara Medina Rivero
Ziyou Yu (KULeuven) - Multinuclear Solid-State NMR and Spectroscopic Analysis of Fe-Bearing Alkali-Activated Slags: Insights into Iron Oxidation State and Polymerization

14:20 **Indiana Ternad** (UMons) - Exploring the Radiosensitizing Potential of Iron Oxide Nanoparticles

14:40 **Wiktor Adamski** (University of Lille) - Fast access to protein dynamics using ultra-selective ^{15}N-^{1}H spectroscopy

15:00 **Flash presentation of posters**

15:10 ***Poster Session 1***, odd numbers - coffee break

16:30 ***Plenary Lecture 1:*** Diffusion MRI with strong gradient hardware
Prof. **Chantal Tax** (University Medical Center Utrecht) – Chair: Dimitrios Sakellariou

17:20 ***Oral Session 2*** **-** Chair: Rodrigo de Oliveira Silva

17:40 **Barbara Mathieu** (UCLouvain) - Noninvasive discrimination between mitochondrial ROS and cytosolic ROS in solid tumors using in vivo EPR spectroscopy

18:00 **An Vanduffel** (KULeuven) - Improving medical material imaging with 3D-printed MRI passive shims

18:20 **Jennifer Theissen** (UHasselt/KULeuven) - Beware of the structure: Insights into the Phosphorus Dynamics of post-synthetically modified NU1000 in the presence of water

18:40 ***Break/Meeting***

19:00 ***Reception***

20:00 ***Dinner and party***

SCIENTIFIC PROGRAM

Tuesday, November 26th

9:00 ***Plenary Lecture 2:*** Investigating materials, components and devices for electrochemical applications using NMR and EPR – Prof. **Josef Granwehr** (Institute of Energy Technologies, Julich, Germany) – Chair: Sabine Van Doorslaer

Oral Session 3 - Chair: Elien Dervaux, Universiteit Hasselt

9:50 **Ilias Vandevenne** (UAntwerpen)- Electrical detection of magnetic resonance on a Chip (EDMRoC): A low-cost and sensitive characterization tool for defects in SiC MOSFETs

10:10 **Robine Cleirbaut** (UAntwerpen) - Characterization and incorporation of heme proteins in mesoporous titania materials for biosensing applications

10:30 ***Poster Session 2***, even numbers, coffee break

11:40 ***Oral Session 3 continued***

Jesus Alejandro De Sousa Rodriguez (UAntwerpen) - Detection of triplet excitons on open-shell (6,5)-SWCNTs-PTM• using Optically-Detected Magnetic Resonance

12:00 **Anthony Morena** (UNamur) - Characterizing the Acidity of Silica-Based Materials through ^{31}P ssNMR: TMP as a Probe for Lewis and Brønsted Acid Sites.

12:20 ***Group Picture &***

Lunch Break

13:50 ***Plenary Lecture 3:*** A molecular definition of metabolic syndrome as investigated by NMR-based metabolomics – Prof. **Óscar Millet** (CIC bioGUNE, Spain) – Chair José Martins

Oral Session 4 – Chair: Anthony Morena

14:40 **Yoanes Vianney** (UGent) - Structural Basis of Testosterone Recognition by a DNA Aptamer

15:00 **Ewoud Vaneeckhaute** (ULyon/KUleuven) - Boosting ^{1}H and ^{13}C NMR signals by orders of magnitude using benchtop DNP

15:20 *Coffee break, poster removal*

16:00 *Awards session and closure*

16:20 *End*

The book of abstracts can be downloaded on the conference website: www.ybmrs.be

ABSTRACTS TUTORIALS AND PLENARY LECTURES

Magnetic resonance imaging

C. Tax

University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

This tutorial provides an introduction to MRI, focusing on the fundamentals of spatial encoding and image reconstruction. Participants will learn how magnetic gradients are used to encode spatial information and how signals are transformed into detailed images of anatomical structures.

EPR to study structure and dynamics in paramagnetic materials

Josef Granwehr

Forschungszentrum Jülich GmbH, Germany

To be announced

SOPs for the metabolic analysis of large cohorts of samples

O. Millet[1]

[1] *Precision Medicine and Metabolism Laboratory, CIC bioGUNE, Derio, Spain*

Standardized operating procedures (SOPs) are critical for ensuring reliability, reproducibility, and comparability in NMR-based metabolic analysis, particularly when analyzing large cohorts of samples. We will present a comprehensive SOP framework designed to optimize NMR-based metabolomic profiling in high-throughput settings, addressing challenges such as sample preparation, spectral acquisition, data processing, and quality control. We will focus on minimizing variability through consistent sample handling, calibration protocols, and automated spectral analysis pipelines. By implementing these SOPs, we aim to establish a robust workflow that enhances sensitivity and specificity in detecting metabolites, enabling high-fidelity metabolomic profiling across extensive sample sets. Our protocols are validated through the analysis of a large cohort, demonstrating significantly reduced intra- and inter-run variability and improved reproducibility. These SOPs provide a valuable resource for large-scale studies aiming to utilize NMR metabolomics for biomarker discovery, population health studies, and personalized medicine applications. The framework can be adapted and refined for different biological matrices and metabolomic study designs, underscoring the importance of standardization in advancing metabolomics research on a broad scale.

Diffusion MRI with strong gradient hardware

C. Tax

University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

This talk will focus on diffusion NMR and MRI, which sensitises the signal to the molecular motion of water molecules. This technique can provide endogenous contrast to the microstructure of tissue. Diffusion encoding is done through applying additional field gradients, and the last decade has shown key developments in gradient hardware for more efficient encoding. The opportunities and pitfalls of strong-gradient diffusion MRI will be discussed.

Investigating materials, components and devices for electrochemical applications using NMR and EPR

Josef Granwehr

Forschungszentrum Jülich GmbH

To be announced

A molecular definition of metabolic syndrome as investigated by NMR-based metabolomics

R. Gil-Redondo[1], A. Ibañez-Opakua[2], R. Conde[1], A. de Diego[1], B. González-Valle[1], N. Embade[1], O. Millet[1,2]

[1] *Precision Medicine and Metabolism Laboratory, CIC bioGUNE, Derio, Spain.*

[2]*ATLAS Molecular Pharma, Derio, Spain.*

Metabolic syndrome (MetS) is a cluster of medical conditions and risk factors correlating with insulin resistance that, when occurring together in an individual, increase the risk of developing life hazardous cardiometabolic health problems. The specific criteria for diagnosing MetS are challenging and vary among different medical organizations but are typically based on the evaluation of abdominal obesity, high blood pressure, hyperglycemia, and dyslipidemia. In this context, an independent estimation of the risk of MetS based on quantitative biomarkers is highly desirable. We used NMR-based metabolomics on a large cohort of donors (n= 21,323) to investigate the diagnostic value of serum or serum combined with urine to estimate the MetS risk. Specifically, we have determined a plethora of circulating metabolites and the lipoprotein composition in serum samples and this information has been integrated with metabolic profiles extracted from urine samples. We have developed MetSCORE, a metabolic model of MetS that combines serum lipoprotein and metabolite information.[1] MetSCORE discriminate MetS patients (independently identified using the WHO criterium) from general population with an AUROC of 0·91. This continuous model can quantitatively stratify risk factors according to their contribution to the development of MetS. We believe that MetSCORE may be an insightful tool for early intervention and lifestyle modifications, potentially preventing the aggravation of metabolic syndrome.

[1]Gil-Redondo, R *et al*. *Cardiovas. Diabetol*. **2024**, 23, 272-280.

ABSTRACTS ORAL CONTRIBUTIONS

Multinuclear Solid-State NMR and Spectroscopic Analysis of Fe-Bearing Alkali-Activated Slags: Insights into Iron Oxidation State and Polymerization

Z. Yu[1], Alexios P. Douvalis[2], R. de Oliveira-Silva[1], Qifeng Shu[3], Y. Pontikes[4] and D. Sakellariou[1]

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Understanding the detailed structure of Fe-bearing alkali-activated slags (AASs) is crucial for assessing the role of iron in influencing their macroscopic properties. However, the local structure and polymerization degree of Fe-bearing AASs remain inadequately understood, largely due to the challenges posed by the limited use of solid-state NMR in materials with high iron content. In this study, we employ multinuclear solid-state NMR techniques, including both 1D MAS and 2D 3QMAS experiments, to investigate the effects of iron oxidation state in the slag precursors on the polymerization behavior of synthesized AASs. These techniques allow us to probe the molecular structure of AASs with greater detail than previously possible.

In addition to NMR, we use complementary ^{57}Fe Mössbauer spectroscopy and Raman spectroscopy to gain further structural insights into the iron-bearing components. The slag samples studied were not commercially available iron-rich slags but were synthesized with controlled Fe content below 10 wt% to ensure sufficient resolution in the NMR spectra. This approach minimizes the paramagnetic interference typically caused by high concentrations of iron, allowing for more accurate characterization of the slag structure.

Our results demonstrate that, after 7 days of curing, AAS synthesized from slag containing Fe^{2+} exhibits a less polymerized structure compared to AAS synthesized from slag containing Fe^{3+}. After 1 year of storage, the Fe^{2+}-bearing AAS shows a higher degree of polymerization, forming a chain-like structure. The paramagnetic effects on the NMR signals are discussed, with the deconvolution of NMR spectra allowing quantification of the silicate tetrahedra fractions, as all silicate species experience uniform signal broadening. Furthermore, we propose possible roles for Fe^{3+} based on NMR analysis, suggesting its incorporation into the Al^{VI} site in hydrotalcite or as a charge-balancing cation near the Al^{IV} site in bridging positions.

This research highlights the potential of NMR in advancing our understanding of Fe-bearing AASs.

Exploring the Radiosensitizing Potential of Iron Oxide Nanoparticles.

I. Ternad[1], D. Stanicki[1], T. Vangijzegem[1], V. Lecomte[1], H-F.Renard[3], L. Larbanoix[2], R.N. Muller[1,2], S. Laurent[1,2]

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Introduction

This study investigates the potential of magnetic iron oxide nanoparticles (IONPs) as radiosensitizers to enhance radiotherapy efficacy. IONPs are of particular interest due to their dual functionality in radiotherapy and magnetic resonance imaging. Traditionally, the radiosensitizing effect of nanoparticles has been attributed to physical mechanisms, such as secondary electron emission, but recent research suggests a significant role for biochemical mechanisms [1]. Interestingly, a correlation has been identified between the detoxification enzyme in cells treated with gold nanoparticles (GNP) and the strength of the radiosensitizing effect [2]. Given these elements, our aim was to explore if a similar inhibition pattern can be shown for different iron oxide nanoparticles (IONPs).

Results/Discussion

Through synthesis and characterization, various IONPs were evaluated for their cytotoxicity, cellular uptake, and radiosensitizing properties *in vitro*. The results indicate a strong correlation between AF and TrxR inhibition. The most active IONPs showed an AF of 17% after 48 hours of incubation, with macropinocytosis identified as the predominant uptake pathway. Confocal microscopy confirmed IONPs' lysosomal localization, where acidic degradation releases ferric and ferrous ions capable of disrupting TrxR activity.

Conclusion

In summary, our investigation into the radiosensitizing potential of various IONPs has revealed a consistent relationship between AF and TrxR inhibition for cells treated with IONPs. The most active one exhibit an AF of 17 % and are mostly uptaken by cells through the macropinocytosis pathway.

References

[1] S. Penninckx, *et.al.* « Gold Nanoparticles as a Potent Radiosensitizer: A Transdisciplinary Approach from Physics to Patient ». *Cancers* 12, 2020: 2021.
[2] S. Penninckx, *et al.*« Thioredoxin Reductase Activity Predicts Gold Nanoparticle Radiosensitization Effect ». *Nanomaterials* 9, 2019: 295.
[3] I.Ternad, *et al*. « Advances in the Mechanistic Understanding of Iron Oxide Nanoparticles' Radiosensitizing Properties ». *Nanomaterials* 13, 2023 : 201.
[4] F. Tyckaert, *et al*. « Rac1, the Actin Cytoskeleton and Microtubules Are Key Players in Clathrin-Independent Endophilin-A3-Mediated Endocytosis ». *Journal of Cell Science* 135, 2022: jcs259623

Fast access to protein dynamics using ultra-selective ^{15}N-^{1}H spectroscopy

W. Adamski[1,2], F-X. Cantrelle[1,2], G. R. Levy[1,2] and D. Sinnaeve[1,2]

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[2] Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, UMR 1167 - RID-AGE - Risk Factors and Molecular Determinants of Aging-Related Diseases, F-59000, Lille, France.

Spectral congestion in 2D protein NMR spectra is a ubiquitous problem. The usual strategy to overcome this issue is by adding further dimensions to the experiment or increase the number of time-increments in the existing indirect dimensions, but this results in longer experimental times. This problem is exacerbated in zz-exchange experiments, where additional exchange cross peaks are present, and especially in relaxation measurement experiments, where multiple experiments have to be acquired in order to sufficiently sample the signal decay. Especially for intrinsically disordered proteins, which often feature very congested spectra and limited sample life times, the required experimental time becomes impractically long. An alternative approach is to use selective experiments that target particular ^{1}H-^{15}N correlations, allowing the use of simple 1D experiments as a readout. Selective Hartmann-Hahn coherence transfer has been previously proposed for this purpose, but the selectivity of these experiments was limited (1,2).

Here, we propose a scheme that provides clean 1D spectra with an improved selectivity of 15-20 Hz in ^{15}N and ^{1}H with only a modest cost in sensitivity. Our approach uses an alternative scheme for selective polarization transfer that, to the best or knowledge, has been neglected until now (1). This is combined with improved purge elements based on ^{15}N and ^{1}H selective excitation (2). We will first demonstrate these principles by quantifying the exchange rates between two slowly exchanging conformers of the SH3-GL3 protein. The forms display very similar chemical shifts in the ^{1}H-^{15}N HSQC, but the new selective zz-exchange experiment successfully resolved the cross and diagonal peaks. Next, we introduce new selective R_1, R_2 and hetNOE experiments to quantify the dynamics along a 16-residue poly-glutamine (polyQ) stretch within a huntingtin exon 1 protein fragment, the causative agent for Huntington's disease. The severely overlapped polyQ signals until now precluded such relaxation measurements. We demonstrate, for the first time, the gradual increase in conformational dynamics from the N- to C-terminal ends of the polyQ using NMR relaxation and without requiring site-specific isotopic labeling schemes (3).

Our novel pulse sequences provide access to slow, intermediate or fast protein dynamics in a fraction of the experimental time required using non-selective (pseudo-3D) experiments (4), and are a substantial improvement compared to previously proposed selective Hartmann-Hahn schemes (5). The new experiments provide sufficiently selective and clean spectra at acceptable sensitivity, and will be very valuable for studies of dynamics of any biomacromolecule featuring highly crowded heteronuclear 2D spectra.

References

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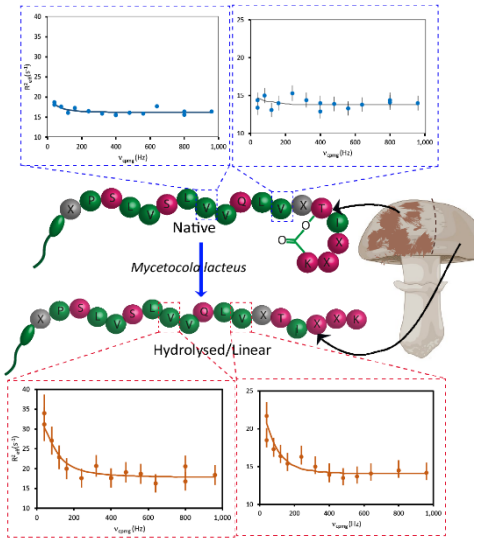
Structural and Dynamic Insights into the Loss of Activity of Tolaasin I

D. Prasad[1], B. Kovács[1], D. Roelandt[1], N. Geudens[1], M. Hofte[2] and J. C. Martins[1]
[1] *NMR & Structure Analysis Unit, Dept. of Organic and Macromolecular Chemistry, and*
[2]*Laboratory of Phytopathology, Department of Plants and Crops, Ghent University, Belgium*

Cyclic lipodepsipeptides (CLiPs), secondary metabolites produced by non-ribosomal peptide synthetases (NRPSs), are found predominantly in *Pseudomonas*, *Bacillus*, and *Streptomyces* species. These compounds exhibit diverse biological functions, such as promoting bacterial motility and demonstrating significant antibacterial and antifungal activities(*1*). Due to these characteristics, CLiPs are being actively explored for two key applications: combating multi-drug resistant pathogens in clinical settings and serving as biocontrol and biostimulant agents in agriculture. Among these, tolaasin from *Pseudomonas tolaasii*, an 18 amino acid CLiP featuring a 5 amino acid macrocycle at its C-terminus, is known for causing brown blotch disease in mushrooms and for its inhibitory effects against fungi and Gram-positive bacteria(*2*). Notably, tolaasin's antagonistic properties can be neutralized by a cohabiting bacterium which is causes enzymatic hydrolysis of the depsi (ester) bond closing the macrocycle(*3*).

Given the significance for biological activity, we aim to investigate how the structure, conformational dynamics and membrane interactions of native and hydrolyzed tolaasin is affected by this change, using NMR spectroscopy in SDS micelles. By growing *Pseudomonas tolaasii* on minimal medium, we produce ^{13}C- and ^{15}N-labeled tolaasin, enabling multidimensional NMR analysis. The isotopically enriched hydrolyzed form was obtained through controlled alkaline hydrolysis. Following complete resonance assignment of both forms, we recorded 2D HNHA experiments to access backbone conformation dependant $^{3}J_{HNHa}$ scalar couplings, while long-range 2D HNCO experiments allowed to assess long-lived hydrogen bonds through $^{3h}J_{NC'}$ scalar couplings. This revealed significant differences in the hydrogen bond networks between native and hydrolyzed tolaasin. Additionally, ^{15}N relaxation experiments provided insights into peptide backbone dynamics, with order parameters (S^2) elucidating molecular motions on the ns-ps timescale, while relaxation dispersion experiments confirmed the existence of µsec dynamics. These findings allowed us to identify residues with distinct rigidity and flexibility profiles in both forms, guiding the 3D structure determination of hydrolyzed tolaasin using nOe data. The structure reveals that opening of the macrocycle through ester bond hydrolysis affects the native structure well beyond the macrocycle, introducing additional dynamics in the exocyclic residues.



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Noninvasive discrimination between mitochondrial ROS and cytosolic ROS in solid tumors using *in vivo* EPR spectroscopy

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4. *Walloon Excellence in Life Sciences, and Biotechnology (WELBIO) Research Institute, 1300 Wavre, Belgium*

Mitochondria are major producers of ROS in cells. In healthy cells, mitochondrial ROS (mtROS) are maintained at stable concentration by antioxidant systems. When the balance is disrupted and lead to oxidative stress, mtROS are implied in cell death pathways. Yet, in cancer cells, mtROS are maintained at an intermediate level and promote cancer progression by triggering proliferation, angiogenesis and metastasis, key hallmarks of cancer. Electron paramagnetic resonance (EPR) spectroscopy allows detection of ROS in vivo but has never been used for specific mtROS detection in solid tumors.

ROS detection by EPR spectroscopy is based on the reduction of nitroxides (EPR detectable) to hydroxylamine (EPR indetectable) by ROS. Nitroxides are injected and the EPR signal decay is recorded over time[2,3]. To be specific of mitochondria, we used mitoTEMPO, a nitroxide accumulating in mitochondria, and worked in comparison with 3CP, a nitroxide non-targeting mitochondria. We modulated mitochondrial redox status with Antimycin A (ETC inhibitior) and we depleted cytosolic antioxidant GSH with L-BSO. We measured the signal decay rates of nitroxides over 3 days. To evaluate the impact of blood-wash out on the signal decay, we measured the concentrations of the nitroxide, and hydroxylamine form ex-vivo. To assess the specificity for superoxide we genetically modified cells to over-express SOD2.

MitoTEMPO signal decay rates in 4T1 tumors increased after 24 hours of treatment with Antimycin A but not with L-BSO. On the contrary, 3CP decay rates didn't change with Antimycin A but increased with L-BSO treatment. These data suggest a selectivity for mitochondria from mitoTEMPO and show the ability of mitoTEMPO to detect mtROS production in comparison with 3CP. The *ex-vivo* analysis showed that nitroxides are well converted into hydroxylamines but that the total concentration of product remaining in the tumors stays stable over time, indicating no impact from blood circulation on the signal decay. Finally, *in vitro*, the signal decay was lower in tumor cells over-expressing SOD2 than in wild-type cells. These results were confirmed *in vivo* where mitoTEMPO signal decay rate was lower. It shows that the method is partially selective for superoxide and confirmed that the method can detect changes in mitochondrial redox status. (See figure 2)

We propose a toolbox for the study of mtROS *in vivo* in solid tumors. We observed that mitoTEMPO is selective for mitochondrial redox modulation. The signal decay is not impacted by blood wash-out. The method is also partially selective for superoxide. Regarding these data, we can say that the use of EPR spectroscopy and mitoTEMPO allows dynamic measurements over time of mitochondrial redox status in response to therapeutic agents.

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Improving medical material imaging with 3D-printed MRI passive shims

A. Vanduffel(1), *H. Vanduffel*(1), *C. Parra*(1), *Q. Goudard*(1), *U. Himmelreich*(2), *D. Sakellariou*(1), *R. Ameloot*(1)
(1) cMACS, KU Leuven ; (2) MOSAIC, KU Leuven

Introduction: Magnetic resonance imaging (MRI) requires a highly homogeneous magnetic field (B_0) to produce clear, undistorted images. However, when a patient is placed inside the scanner, subject-specific features introduce local field inhomogeneities, leading to image degradation and geometric distortions. Magnetic fields can be corrected or shimmed to achieve the desired levels of magnetic field homogeneity. Current shimming techniques involve either active shimming using electric currents through coils or passive shimming through the strategic placement of magnetizable materials (ferro-, dia- or paramagnetic and metallic materials). [1] Passive shimming is typically labor-intensive, costly, and less effective at compensating for higher-order distortions induced by complex anatomy. We propose a novel approach for passive shimming using 3D printing to create shims tailored to magnetic field inhomogeneities caused by medical material (*e.g.* pedicle screws, teeth braces, etc.). Unlike traditional methods, increased geometric complexity in the design does not lead to higher manufacturing costs or extended production time. Our method employs powder-binder jetting (Fig. 1), allowing the precise deposition of varying concentrations of ferromagnetic material at predetermined locations to generate higher-order spherical harmonic terms to homogenize the magnetic field.

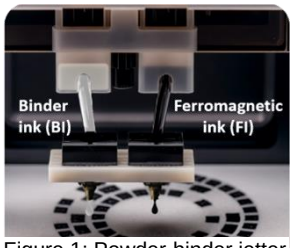

Figure 1: Powder-binder jetter

Methods: Field maps of medical material (*i.e.* pedicle screw) using a 3T Siemens MR scanner were obtained. These maps were used as inputs to homogenize B_0, by minimizing its standard deviation with a self-developed shimming algorithm in MATLAB. The algorithm solves the nonlinear problem with the help of the MEIGO optimization toolbox (fmincon solver) and calculates, as output, the concentration of ferromagnetic ink in each shimming voxel (Fig. 2 A,B). [2] The output was converted into a greyscale printable CAD design; and it was fabricated using an in-house modified powder-binder 3D printer (Projet CJP 660Pro). [3]

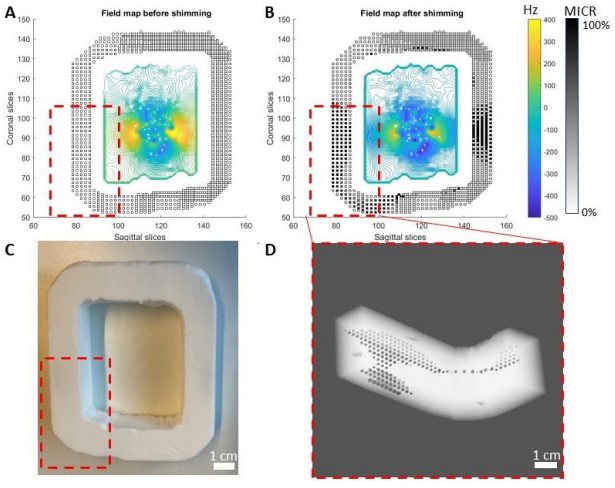

Figure 2: A) Unshimmed field map with voxel positions; B) Field map after shimming with amount of ink to be printed; C) 3D printed shim; D) CT scan of 3D printed shim

Results: 3D-printed (3DPed) passive shims containing ferromagnetic ink were produced (Fig. 2 C,D). Preliminary tests demonstrated that these 3DPed shims configurations could effectively manipulate the magnetic field towards a more uniform distribution, since our simulations showed a possible improvement in field homogeneity of around 20% (Fig 2).

Conclusion: Our results suggest that 3DPed passive shims can effectively shape the magnetic field within an MRI scanner. This technique shows promise for improving field homogeneity and image quality. Future research will focus on applying this method to ex vivo and in vivo specimens with complex anatomical structures to further evaluate its efficacy.

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Beware of the structure: Insights into the Phosphorus Dynamics of post-synthetically modified NU1000 in the presence of water

J. Theissen[1,2], E. Derveaux[2], R. Narvaez[3], S. Smeets[2], N. Gys[1], P. Adriaensens[2], W. Marchal[2], R. Ameloot[1]

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[2] *Institute for Materials Research (IMO-IMOMEC), Analytical and Circular Chemistry (ACC), UHasselt.*

[3] *General Chemistry (ALGC) - Materials Modelling Group, Vrije Universiteit Brussel.*

Understanding the structure and chemistry of materials at the atomic scale is essential to elucidate and rationalize their properties as a key step to boost their application in future technologies. Metal-organic frameworks (MOFs) are porous coordination polymers formed by the ensemble of metal ions or clusters and organic linkers, offering a large versatility and tunability in surface area, pore structure, chemical composition, and thermal stability. These properties are attractive for various applications, including gas storage and separation, catalysis and sensing [1]. These applications can be explored by introducing new organic functionalities into the MOF framework by metal node modification via solvent-assisted ligand incorporation (SALI). Phosphonic acids (PAs) are particularly appealing for such modifications, as they introduce Brønsted acid sites (P–OH/P=O groups) that can enhance catalytic activity and sorption properties. Their diverse binding modes to the Zr_6-node influence the acidity and functional behavior of the material. In this study, we investigate the post-synthesis modification of the Zr6 metal node in NU-1000 MOF through its reaction with phenylphosphonic acid (PhPA), yielding in the material NU-1000PhPA, with a focus on understanding and characterizing the binding modes of PhPA (Figure 1).

To probe the dynamic behaviour of this modified material in response to water, the material was stored under three different storage conditions and we performed solid-state ^{31}P-MAS NMR and two-dimensional dipolar heteronuclear correlation (HETCOR) experiments over an 8-week period. ^{31}P-MAS experiments provided valuable insight into the local phosphorus environment, enabling a detailed analysis of the evolution of the structure for different hydration degrees. It allowed us to distinguish between different phosphorus coordination modes and regions within the MOF where water and hydrogen bonding is either present or absent, depending on the loading of PhPA.

This study highlights the advantages of 2D dipolar HETCOR NMR techniques in elucidating the structural changes and coordination environments within MOFs, providing deeper insights into the role of water in modulating material properties over time.

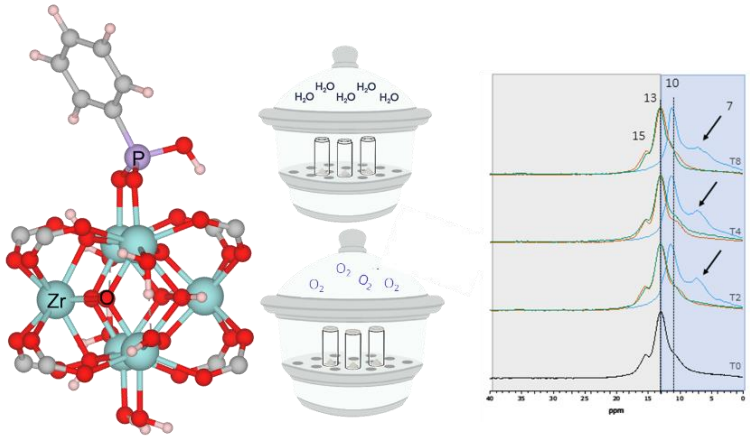

Figure 3: Graphical representation of the phosphonate grafting on the Zr_6 node of NU-1000 and solid state ^{31}P MAS NMR for different storage conditions, enabling the distinction of the chemical environment in correlation with water.

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Electrical detection of magnetic resonance on a Chip (EDMRoC): A low-cost and sensitive characterization tool for defects in SiC MOSFETs

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Recently, the integration of a microwave chip into an application-specific integrated circuit (ASIC) led to the development of so-called electron paramagnetic resonance on a chip (EPRoC), allowing for extremely compact and low-cost EPR instrumentation [1-2]. This method has recently demonstrated its potential for electrical detection of magnetic resonance (EDMR) in a thin a-Si:H solar cell, by detection of the EDMR signal through the change in conductivity in the photoactive layer [3]. Here, we extend EDMRoC spectroscopy to measurements of EDMR in lateral SiC MOSFETs, combining it with the powerful charge pumping (CP) characterization technique [4-5]. In CP, the gate voltage is periodically changed between inversion and accumulation so that a current can be extracted from the transistor channel region originating from recombination of charges at defect trapping sites. CP-EDMR has demonstrated the capability of identifying and quantifying charge traps within the transistor channel of SiC MOSFETs [6-7], but it requires advanced instrumentation and is therefore not generally applicable in fundamental and applied research as well as in industrial environments.

In this work [8], we present CP-EDMRoC as a versatile, fast, and sensitive technique to detect EDMR in SiC MOSFET devices. Figure 1 shows the experimental configuration of the device positioned in front of the microwave chip on the ASIC (permanent magnet not shown for clarity). The compact ASIC (total dimensions 6×12 cm) operates in a region around 13 GHz.

In contrast to conventional EDMR, in EDMRoC the microwave frequency is not fixed, allowing for scanning of either magnetic field or microwave frequency. Moreover, for sensitive detection, conventional EDMR uses magnetic field modulation, which induces currents in the device circuitry that yield a background signal, while in EDMRoC this can be avoided using microwave frequency modulation. A direct comparison of EDMRoC and cavity-based EDMR spectra, as well as between magnetic-field and microwave frequency scans, will be presented, showing very similar signal-to-noise ratio's for EDMRoC and cavity-based EDMR.

The authors acknowledge financial support of the Flemish Government and Flanders Innovation & Entrepreneurship (VLAIO) through the Baekeland project number HBC.2019.2171 as well as the fund for scientific research Flanders (FWO) for infrastructure funding for the EPR instrumentation.

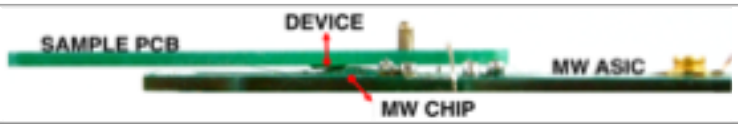

Fig. 1: Sample printed circuit board (PCB) with bonded MOSFET device positioned in close proximity to the microwave (MW) chip at one end of the ASIC.

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Characterization and incorporation of heme proteins in mesoporous titania materials for biosensing applications

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Biosensors based on heme proteins have shown to be promising for the detection of phenolic compounds[1]. The key in the development of this kind of devices concerns the immobilization of the proteins on suitable supports, with multiple factors influencing the efficiency of incorporation, such as temperature, pH, buffer type, support type and pore size, and the biochemical and biophysical properties of the protein itself. Mesoporous titania (TiO_2) has shown promise to be used as support material because of its biocompatibility and ability to generate reactive oxygen species[2].

The first focus lays on the characterization of the proteins. Initial experiments utilize commercial heme proteins, horse heart myoglobin and horseradish peroxidase (HRP), to establish baseline conditions. These will be used to evaluate B-class dye-decolorizing peroxidases from *Klebsiella pneumoniae*, which exhibit limited activity towards various substrates under current conditions[3]. A characterization of the proteins is therefore necessary. The scientific techniques used include Electron Paramagnetic Resonance (EPR), UV/Vis absorption spectroscopy, Electronic Circular Dichroism, Thermal Shift Assays, and electrochemical techniques to assess redox potentials, stability and enzymatic activity. While these techniques will be used for high-throughput analysis of the proteins in different buffer and salt conditions, advanced EPR techniques are also used to determine the electronic structure of the heme proteins, as will be exemplified for hemoglobin from *Lotus japonicus*.

Next, we zoom in on the incorporation part of the story. Conditions and compatibility of the proteins and mesoporous titania materials are probed using some of the same techniques as mentioned above. The mesoporous structure of titania not only mimics the natural environment of heme proteins but also may protect them from leaching. Additionally, the illumination of titania generates reactive oxygen species, which the peroxidases utilize in their catalytic cycle, circumventing the need for manual addition that could compromise sensor sensitivity[4]. An example of electrochemical detection of phenolic compounds using illuminated titania-HRP hybrids will be shown.

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Detection of triplet excitons on open-shell *(6,5)*-SWCNTs-PTM• using Optically-Detected Magnetic Resonance

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Single-wall carbon nanotubes (SWCNTs) are promising one-dimensional platforms for functional materials since the fine-tuning of their properties can be done by introducing different molecules in their interior or on their external wall.[1] Controlled sp^3-functionalization[2] of their wall has shown to shift the SWCNT emission to the NIR (by 100-300 meV) and drastically increase the efficiencies with at least an order of magnitude due to the increased lifetime of the trapped excitons.[3] The diversity of possible functional groups that can be introduced provides a playing room to create new functionalities. Recently, we decorated *(6,5)*-SWCNTs with the perchlorotriphenylmethyl (PTM) radical via diazonium chemistry (Figure. 1a).[4] PTM is a stable organic free radical with several interesting properties. This radical is paramagnetic, redox-active, fluorescent, and chiral.[5] Interestingly, the open-shell character of the PTM leads to a partial quenching of the emission from the sp^3 defects. A combination of photoinduced electron transfer and enhanced intersystem crossing (from singlet to triplet state) was previously proposed as the main responsible of the quenching.[4] Herein we expanded this study using optically detected magnetic resonance (ODMR) to directly investigate triplet exciton symmetry and yield. ODMR is an experimental technique that allows to monitor the transitions between triplet sublevels in an external applied magnetic field through the emission from the sample, combining the sensitivity of emission spectroscopy with the spin sensitivity of magnetic resonance.[6,7] Our experimental and theoretical calculations confirm a change of the exciton symmetry (due to the localized exciton trap) and an enhancement of the intersystem crossing by the presence of the radical which results in a higher intensity of the ODMR signal (Figure. 1b). Our results pave the way for exploiting sp^3-functionalization to tune intersystem crossing in SWCNTs toward highly efficient carbon-based optoelectronic devices.

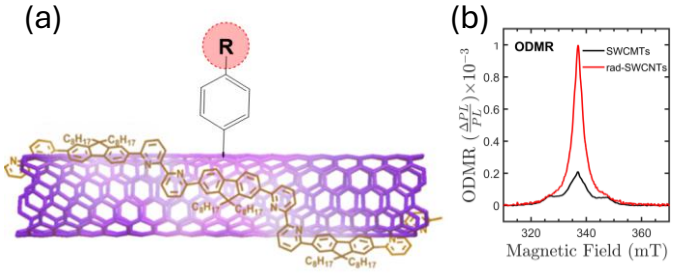

Figure 1. (a) Schematic drawing of a functionalized (6,5) SWCNT; (b) ODMR spectra of pristine (black) and radical-functionalized (red) SWCNTs showing the strong enhancement of the ODMR signal (thus ISC) and change in shape of the ODMR spectrum.

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Characterizing the Acidity of Silica-Based Materials through ^{31}P ssNMR: TMP as a Probe for Lewis and Brønsted Acid Sites.

A. Morena[1], O. Garot[1], L. Fusaro[1*], C. Aprile[1*]
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Acid catalysts are crucial in industrial processes, with homogeneous acids like H_2SO_4, H_3PO_4, and HF commonly used due to their strong acidity and good catalytic performances. However, they pose challenges like equipment corrosion, waste management issues, recyclability and toxicity.[1] To overcome these drawbacks, solid heterogeneous acid catalysts, including zeolites and functionalized silica, have been developed. These have been increasingly applied in many catalytic chemical processes due to their efficiency and improved safety. Heterogeneous solid acids typically exhibit two types of acidity: Lewis (L) and Brønsted (B). Among the various solid catalysts, silica-based materials are particularly popular due to their high specific surface area and well-distributed pore sizes. Another advantage of these materials is the ability to adjust the balance between Lewis and Brønsted acidity. This is done by either incorporating metal cations into the silica structure or altering the ratio between silicon and the chosen metal cation. As a result, the acidity of these catalysts can be fine-tuned for different applications. To better understand the acidic properties of heterogeneous catalysts, several analytical techniques have been developed. One common method involves the use of probe molecules, such as pyridine or ammonia, in combination with temperature-programmed desorption (TPD) or infrared spectroscopy (FT-IR).[2] These techniques allow researchers to study overall acidity and the behavior of acid sites in the material. More recently, solid-state nuclear magnetic resonance (ssNMR) has emerged as a powerful tool for examining more detailed characteristics of acidity, including the nature, concentration, and strength of acid sites. ssNMR is particularly useful when combined with a probe molecule containing an NMR-sensitive nucleus, such as ^{13}C, ^{15}N, or ^{31}P. Among the available probe molecules, trimethylphosphine (TMP) and its oxidized form, trimethylphosphine oxide (TMPO), are widely used in the field of acidity characterization. TMP and TMPO are advantageous because ^{31}P NMR offers a broad chemical shift range, allowing researchers to distinguish between different types of acid sites in the material. Additionally, ^{31}P is a highly sensitive dipolar nucleus, which makes it ideal for detecting subtle differences in acidity. Moreover, it is worth to say that TMP is a quite easily oxidable molecule. It will oxidize to TMPO in presence of oxygen. For that reason, it is required a proper experimental set up that allows to run the full analysis under inert atmosphere (Ar).[3] In this study, the Lewis and Brønsted acidity of various silica-based materials were characterized using TMP as a probe molecule. Initially, the study compared the acid properties of silica hollow nanospheres containing gallium (Ga) hafnium (Zr), gallium (Zn), and tin (Hf). Following this, the Ga hollow nanospheres were compared with their corresponding hollow nanotubes to investigate whether different morphologies influenced their acid properties. Finally, the oxidation of TMP to TMPO was performed through an air treatment, enabling a more precise examination of acid site strength across the materials.

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Structural Basis of Testosterone Recognition by a DNA Aptamer

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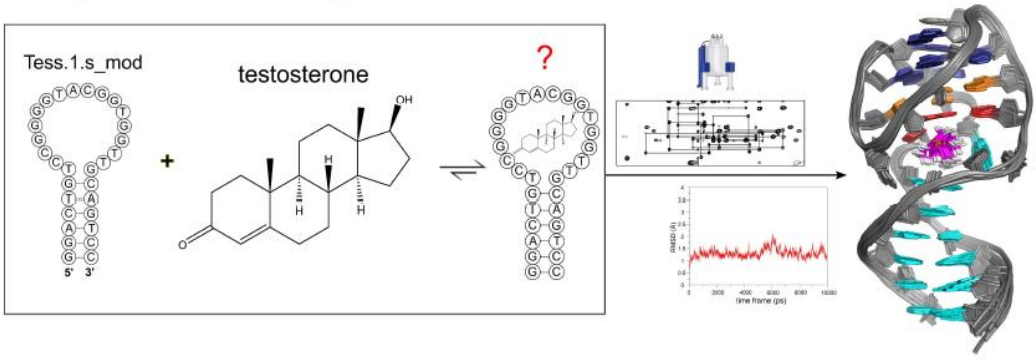
NMR and Structure Analysis Unit, Department of Organic and Macromolecular Chemistry, Ghent University

Nucleic acids, both DNA and RNA, are capable of adopting very diverse and complex arrays of three-dimensional folds. As such, nucleic acids have demonstrated many and varied technological and medical applications. In this work, we focus on the construction of aptamers. Aptamers are single-stranded DNA or RNA that fold into a unique 3D structure, mimicking antibody behavior in terms of their capacity for specific and selective binding to a particular target. The latter can range from ions, over small molecules, to proteins and even cells. The sensing approach relies on generating a detectable signal as a result of target binding. Aptamers display distinct advantages over antibodies for such applications because small molecules typically exert low immunogenicity preventing the generation of antibodies. Using SELEX (systematic evolution of ligands by exponential enrichment), nucleic acid sequences with high affinity and selectivity against a target of interest can be obtained from an initially randomized library of oligonucleotide sequences.1 To date, the de novo building of noncanonical DNA structure for aptamers still cannot yet be done and the tools to predict the endfolding of non-canonical nucleic acids are non-existent. Their future development relies on the availability of experimentally determined 3D structure models which are however left wanting, as only a very limited set of aptamer small molecule complexes have been solved to date.

Here, we used TESS.1, a testosterone aptamer, as a model system to study the basis of testosterone complexation by the DNA2. We already truncated the testosterone aptamer (TESS.1.s_mod) into a molecular size that is deemed convenient for NMR assignment, taking into account that the truncation did not change the binding behavior. Following full assignment, NMR-based structure calculation combined with restrained molecular dynamics simulation reveals the complex and novel scaffold of this testosterone aptamer. Testosterone, being nearly devoid of functional groups with hydrogen bonding potential, is simply located in a cavity formed by mutually hydrogen-bonded nucleotide bases, resulting from the folding of the aptamer. Molecular dynamics simulations reveal that maintaining the hydrogen bond network between the basis is important for the integrity of the recognition site. Base modifications are further done to test the importance of such interactions in order to devise guidelines for the rational design of steroid-sensing aptamers.



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Boosting ^{1}H and ^{13}C NMR signals by orders of magnitude using benchtop DNP

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Sensitivity poses a significant challenge in liquid-state nuclear magnetic resonance (NMR), often acting as a critical limitation. This problem is becoming even more pressing today with the fast-growing democratization of low-field benchtop NMR systems. Hyperpolarization by dissolution dynamic nuclear polarization (*d*DNP) [1] can address this sensitivity limitation. DNP uses the high spin polarization of electrons to hyperpolarize nuclear spins using microwave irradiation. However, for best performance it implies the use of complex cryogenic and highfield instrumentation.

We are presently working on the development of a widely accessible and recyclable hyperpolarized flow (HypFlow) DNP approach that can be installed on a bench. [2] It consists of replenishing the DNP hyperpolarization of a sample flowing through a closed loop, without dilution nor contamination. Hyperpolarizing silica-based solids (HYPSOs) are used as polarizing matrices [3] in a compact and helium-free DNP polarizer coupled to a benchtop NMR spectrometer for liquid-state detection. Hyperpolarization in such a simple benchtop polarizer, in combination with the use of HYPSOs may open the way to replenishable hyperpolarization throughout multiple liquid-state NMR experiments.

We introduce here the design and performance of the very first compact helium-free 1T benchtop polarizer as a simple and low-cost alternative to *d*DNP. It is equipped with a cryostat to perform solid-state DNP at 77 K with a double-tuned $^{1}H/^{13}C$ probe and a solid-state microwave source. After freezing and polarizing the frozen analyte solutions, we demonstrate proton enhancement factors of 100, with 1 second build-up times. The high polarization is subsequently transferred by $^{1}H \rightarrow ^{13}C$ cross-polarization (CP) to ^{13}C spins. The DNP performance in function of electron radical concentration and the polarization transfer mechanism from electron to nuclear spins are discussed. Finally, we show the current status of our efforts to freeze and melt the DNP sample using hot air convection, and what is required to reach our goal to melt in less than 1 second.

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ABSTRACTS POSTER CONTRIBUTIONS

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3	Opportunities for Active Site Identification and Activity Prediction of Zeolite Catalysts using MAS NMR	C. Vinod Chandran
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14	Click-to-release bioorthogonal tyrosine modification	Neeve Marien
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19	Application of NMR-based Metabolomics in the Evaluation of Anti-Osteoporotic Treatments	Arnaud Pinsart
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Please put up your posters in the board with your assigned number by lunch on Monday

Remove your poster during the final coffee break in the afternoon on Tuesday

Multi-diagnostic NMR + dielectric spectroscopy unveils the unconventional properties of nanoconfined water

A. F. Morais[1,2], S. Radhakrishnan[1,2], G. Arbiv[1,2,3], Vinodchandran C.[1,2], S. Meinert[4], M. Fröba[4], J. A. Martens[1,2] and E. Breynaert[1,2,3]

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Water is a key player in many chemical, biochemical and physical processes. The way it interacts with other molecules and materials defines solubility constants, reaction speed, reaction routes and supramolecular arrangement. At interfaces, where surface interactions strongly influence the intermolecular organization of the surrounding molecules, water presents unconventional properties. Near surfaces, water can form a low-density state with a high degree of hydrogen bonding frustration.[1-3] Stabilized by a high electrical potential barrier preventing reorientation of its dipole moment, water molecules tend to align parallel to the surface forming ordered (ice-like) phases.[2,4] Such ordered water exhibits very low polarizability, since the reorientation upon applying an electric field is limited by the surface interaction. This results in permittivity values as low as 2.[4] Confined in hydrophobic nano-pores ice melts at -65 °C.[5] This contribution discusses the properties of water confined in the pores of micro- and mesoporous silicate materials with tuned surface chemistry. In these materials, water adsorbs to defects and Brønsted acid sites, which is directly probed by NMR spectroscopy. Nanoconfinement also affects the hydrogen bonding properties of water, which in turn causes a drastic decrease in its dielectric permittivity and is reflected in the dielectric data recorded using the NMR probe head (**Figure 1**).[6] Water fractions occupying different positions inside the pores can also be observed via NMR and dielectric relaxation spectroscopy (DRS) spectroscopy.

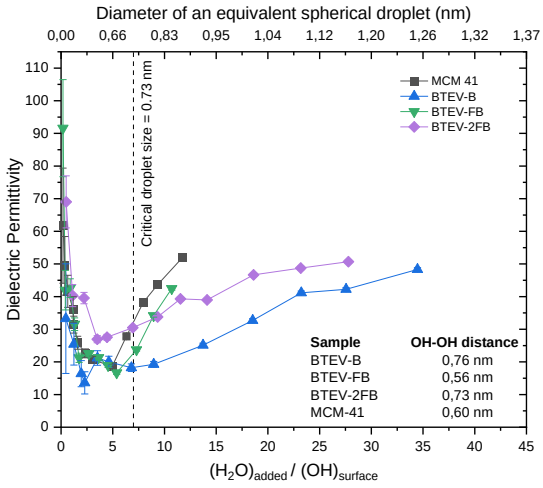

Figure 1: Dielectric permittivity of water confined in the mesopores of silicate materials of different surface chemistry. Different amounts of water - $(H_2O)_{added}$, in mol - were added to the sample. The amount of hydroxyl groups – $(OH)_{solid}$ - in the mesoporous solid was quantified using NMR.

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Mitochondrial dysfunction induced in human hepatocytes exposed to the fungicide kresoxim-methyl and to a mixture kresoxim-methyl/boscalid

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Fungicides are widely used in agriculture for crop protection. Succinate dehydrogenase inhibitors (SDHIs) and strobilurins inhibit mitochondria electron transport chain (ETC) in fungi, by blocking the complex II and complex III, respectively. Questions regarding their selectivity of action for fungi have been raised in the literature, and we previously showed that boscalid (SDHIs) alter the mitochondrial function of human hepatocytes. Here, we analyzed the impact of the exposure of human hepatocytes to kresoxim-methyl, a fungicide belonging to the class of strobilurins. Using Electron Paramagnetic Resonance (EPR), we observed a decrease in oxygen consumption rate (OCR) and an increase in mitochondrial superoxide levels after 24 hours exposure to 7 µM concentration. As a consequence, the content in ATP amount in the cells was reduced, the ratio reduced/oxidized glutathione was decreased, and a decrease in cell viability was observed using two different assays (Presto Blue, crystal violet) and an increase in cytotoxicity was observed using the LDH assay. In addition, as SDHIs and strobilurins are commonly associated in commercial preparations, we evaluated a potential "cocktail" toxic effect. We selected low concentrations of boscalid (0.5 µM) and kresoxim-methyl (5 µM) that did not induce a mitochondrial dysfunction in liver cells when used separately. In sharp contrast, when both compounds were used in combination at the same concentration, we observed a decrease in OCR, an increase in mitochondrial superoxide production, a decrease in the ratio reduced/oxidized glutathione, and a decrease in cell viability.

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Opportunities for Active Site Identification and Activity Prediction of Zeolite Catalysts using MAS NMR

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With their exceptional structures and versatile properties, zeolites have captivated both scientific communities and industries. These crystalline (alumino-)silicates, characterized by their unique porosity, high surface area, uniform pore size, and ion-exchange properties, are indispensable in numerous applications, playing pivotal roles in separation, catalysis, environmental remediation, and more. Advancing fundamental understanding of these processes and identifying active sites can drive innovation towards more optimized materials and processes.

This research aimed to develop solid-state NMR (ss-NMR) strategies, combining quantitative direct-excitation NMR spectra with homonuclear and multinuclear multidimensional NMR spectroscopy, as well as variable temperature (VT) NMR experiments to investigate (i) the mechanisms driving pore-filling adsorption of alcohols in high-silica zeolites,[1] and (ii) to create a predictive tool for catalytic activity of Cu-zeolites in the selective catalytic reduction of NOx.[2]

In the case of liquid-phase adsorption of C1–C5 primary alcohols on high-silica MFI zeolites (Si/Al = 11.5–140), the concentration of adsorbed molecules largely exceeds that of traditional adsorption sites, such as Brønsted acid and defect sites. Hydrogen bonding between the alcohol functional groups and the oxygen atoms of the zeolite's siloxane bridges (Si–O–Si) was shown to drive additional adsorption.[1] This mechanism coexists with chemisorption and physisorption on Brønsted acid and defect sites and may involve cooperative effects from dispersive interactions.

Cu atom mobility and dimerization, as implicated by computational chemistry, are key factors in the reduction of NOx to N_2 with Cu-zeolites. VT ^{1}H NMR revealed that Cu induces the generation of sharp ^{1}H resonances, with the onset temperature of these resonances showing a strong correlation with NH_3-SCR activity across a range of catalysts with varied frameworks, Si/Al ratios, and Cu contents.[2]

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Benchtop NMR system for Faraday and Gamma detection

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This work presents the construction of a benchtop MRI system designed to perform standard Faraday detection of nuclear magnetization and gamma emission detection of photons emitted by ^{131m}Xe atoms. The 50 mT magnet design includes a through-bore hole, allowing photon detectors to be positioned longitudinally, with a total gap of 16 cm between the pole pieces. A thermalization system, along with gradient and shimming coils, also featuring a 30 mm hole, was developed and integrated into the system. Additionally, a passive shimming layer was added to each pole piece, reducing the field homogeneity to 74 ppm (154 Hz) without active shimming. These advancements enabled the acquisition of ^{1}H images of phantoms, a carrot section, and a mouse head, as well as ^{129}Xe images from a spherical phantom containing Xe gas, using both traditional Faraday detection and gamma emission asymmetry from hyperpolarized ^{131m}Xe.

http://gamma-mri.eu/

AI-Driven Analysis of Multiparametric MRI for Evaluating Response to Targeted and Immune Therapies in Preclinical Melanoma Models

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Tumor heterogeneity is a significant driver of therapeutic resistance in advanced melanoma, limiting effective and durable treatment outcomes [1]. This study aims to assess tumor heterogeneity using multi-parametric MRI as a non-invasive marker for the early detection of treatment response. By integrating radiomics with deep learning, we seek to predict responsiveness or resistance to targeted therapies (e.g., BRAF/MEK inhibitors) and immunotherapies (e.g., anti-PD1). This approach addresses the limitations of conventional clinical criteria, such as RECIST, thereby advancing personalized treatment strategies in oncology [1].

We will employ syngeneic melanoma mouse models, specifically the BRAF/MEK-sensitive YUMM1.7 and the immune therapy-responsive YUMMER1.7. C57Bl6 mice will be inoculated with melanoma cells, and treatment will begin once tumors reach a size of 300±50 mm^3, utilizing a combination of the BRAF inhibitor vemurafenib, the MEK inhibitor trametinib, and anti-PD1 antibodies. Resistant models will also be used to validate imaging markers in non-responders, providing insights into the mechanisms of treatment resistance [1] [2] [3].

Longitudinal MRI scans will be conducted before treatment and at multiple intervals during treatment to monitor dynamic changes. Four MRI modalities will characterize the tumor microenvironment: anatomical MRI, diffusion-weighted MRI (DW-MRI), oxygen-enhanced MRI (OE-MRI), and hyperpolarized carbon-13 magnetic resonance spectroscopic imaging (^{13}C-MRSI).

After image acquisition, U-Net and E-Net deep learning models will be used to perform segmentation to accurately identify tumor regions from the anatomical images of the multimodal dataset [4] [5]. The segmented data, including regions of interest (ROIs), tumor volumes, and the entirety of the multimodal dataset, along with binary information related to drug administration, will be integrated into predictive algorithms designed to distinguish responders from non-responders based on multi-parametric MRI data. This study aims to develop a robust tool for monitoring tumor dynamics during therapy, ultimately enhancing the personalization of melanoma treatment and improving patient outcomes.

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Metafollow: one-year longitudinal follow-up to assess metabolites' variations in healthy subjects.

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In healthcare, almost all metabolomics' studies focus on pathologies by studying inter-individual variation of metabolites. But if we want to apply metabolomics to personalized medicine, we must first understand normal intra-individual variations of metabolites before preventively detect a pathological deviation. Our knowledge of the intra-individual « normal » variations of the metabolome is currently very poor and to expand our expertise, we have first to explore healthy people's metabolome over a certain period.

For this purpose, we selected 30 healthy volunteers that we followed for one year. According to gold standards of Clinical Chemistry, blood, urine and saliva samples were first collected each week for ten weeks and then each month for ten months. This work first focused on the blood NMR analysis. For the ten weeks' period, results showed that metabolites could be classified according to their variation, from the less to the most variable ones. The same approach has been applied to the monthly samples and have also highlighted a classification in the metabolites' variabilities very similar to the weekly ones. Metabolites were also linked to their metabolic pathways to identify the most variable networks.

The results obtained in this preliminary work make it possible to stratify blood metabolites according to their short and long-term variations. The subsequent urine and saliva analyses will complete our data and are expected to give a more complete overview of the normal human metabolome's variation, which is very important for the application of metabolomics in the context of personalized medicine.

Monte carlo simulations of the T_2 relaxivity induced by cubic shaped superparmagnetic nanoparticles

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Nanoscale materials have garnered immense attention in the scientific community for the past few decades due to their wide range of applications [1] and their unique properties. At this scale, magnetite and maghemite particles exhibit superparamagnetic behavior at room temperature in addition to a high surface area-to-volume ratio. SuperParamagnetic Iron Oxide Nanoparticles (SPIONs) are predominantly used as $\mathbf{T_2}$ and $\mathbf{T_2^*}$ contrast agents to detect tumors in Magnetic Resonance Imaging (MRI) [1]. When SPIONs are introduced inside a tumor by targeting methods, the associated $\mathbf{T_2}$ is decreased which darkens the tumor on the MR images.

Usually, SPIONs particles are synthetized in a spherical shape. However, over this last decade, some studies synthesized exotic-shaped particles [2] and measured a decrease in $\mathbf{T_2}$ by a factor 2 or even more compared to the usual spherical-shaped SPIONs. In our work, we propose to assess the impact of SPION's shape on $\mathbf{T_2}$ using relaxation simulation and an analysis of the stray field of a cubic-shaped SPION.

NMR CPMG sequences were simulated using a well-known Monte Carlo method considering cubic and spherical SPIONs under a very high magnetic field $\mathbf{B_0}$[3]. The magnetic stray field of a cubic particle is analytically derived from the demagnetization tensor field [4]. Proton diffusion is modeled by a random walk considering a water diffusion coefficient at 300°K. Each proton spin is represented by a vector in the plane perpendicular to $\mathbf{B_0}$.

Our results indicate that there are no significant differences between cubic and spherical shaped SPIONs when their diameters are larger than 30 nm, corresponding to the Static Diffusing Regime (SDR) and over 200 nm in the Partial Refocusing Regime (PRR). However, in the Motional Average Regime (MAR), i.e. for particle sizes smaller than 30 nm, a 10 to 20% decrease in $\mathbf{T_2}$ is observed for cubic SPIONs compared to spherical SPIONs. To quantitatively interpret these results, NMR relaxation models, which include an analysis of the field distribution, were applied to the two shapes [5] [6]. These models confirm our simulation results in the three regimes.

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Functionalized Silica Nanoparticles: Design, Characterization, and Multimodal Imaging Applications

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The association of magnetic resonance imaging (MRI) with optical imaging (OI) presents several advantages in the preclinical imaging field owing to the high spatial resolution of the former and the high sensitivity of the latter. The main objective of this project was to develop an efficient single MRI/OI probe by associating a gadolinium complex with a NIR-emitting compound within a nanoparticular matrix.

The encapsulation of a conventional Gd-complex (*i.e.* Gd-HP-DO3A) within silica nanoparticles (SNPs) has been performed by a reverse micro-emulsion process. To ensure the colloidal stability, the particle surface has been modified by the introduction of PEG chains. Carboxylic functions were introduced by mean of photochemical treatment in the presence of a carboxylated diazirine system. Afterwards, ZW800-2 dyes were grafted onto the particles surface using a classical EDC approach in order to obtain the desired fluorescent properties.

Stable paramagnetic/fluorescent nanoparticles were successfully prepared and characterized. PEG-coating procedure has allowed a long-term stability in physiological conditions. Besides, the presence of carboxylic groups onto fully PEG-coated SNPs has allowed the introduction of a fluorescent NIR-luminescent probe (ZW800-2 dye) to combine MRI to the benefits of OI within the in *vivo* optical window. In addition to the advantage of dye coupling, such modification allowed to design a prototype for multimodal imaging as a proof of concept for functionalization procedure.

The preparation of SNPs was particularly effective for the entrapment of Gd-HP-DO3A in their cores which improved efficiently the relaxometric properties in comparison with the free complex. In addition, modifications of the PEGylated particles using a carboxylated diazirine linker allowed the easy post-derivatization of the nanoplatform without affecting its colloidal stability. In future development, the as-proposed system will be modified with biological vectors for molecular imaging applications.

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Insights into the crystallisation behaviour of imidazolium-chloride by multinuclear NMR.

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Small organic molecules generally form simple supramolecular arrangements, producing crystal structures with relatively small unit cells. Recently, we observed that even a simple salt, such as fampridine hydrochloride can adopt incredibly complex self-assemblies in the solid state (ref).[1,2]

Here we report an investigation of the solid-state behaviour of another simple organic salt, imidazolium hydrochloride. This system is well known for its antifungal, antibiotics, and sedative properties, and is generally employed for producing stable ionic liquids.

We investigated its crystallisation from aqueous solution and water/acetone mixtures issued by liquid-liquid phase separation (LLPS). Multinuclear NMR experiments of ^{1}H, ^{13}C, ^{14}N and ^{35}Cl NMR were carried out in the liquid state as a function of the concentration until the crystallisation occurred. The samples were also investigated by 2D-ROESY and DOSY. The results are compared to classical Molecular Dynamics (MD) simulations, to understand the solute/solvents interactions better.

The characterisation involved an in-depth study of the solid-state phases by single-crystal X-Ray diffraction (SCXRD). Interestingly, the solid-state phases are characterised by (i) the presence of a large number of molecules in the asymmetric unit (z') and (ii) order-disorder phase transitions as a function of the temperature.

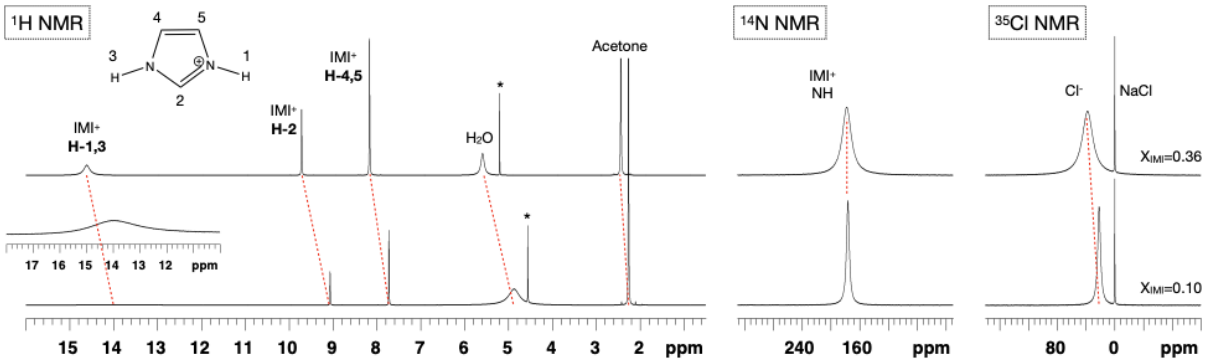

Figure 4. ^{1}H, ^{13}C, and ^{14}N spectra of imidazolium-chloride samples prepared by LLPS in water/acetone mixtures.

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NMR relaxometry to monitor in situ the loading of ion exchange resins with Ni^{2+} and Cu^{2+} ions during a column experiment

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Water pollution by heavy metals is a major environmental problem [1]. To address this issue, the removal of heavy metals from wastewater often requires the use of ion exchange resins or adsorbents. However, current methods for assessing ion exchange/adsorption efficiency are often indirect and destructive. Some heavy metal ions, such as Cu^{2+} and Ni^{2+} exhibit paramagnetic properties that influence the NMR relaxation times T_1 and T_2 of water protons. Benchtop NMR relaxometry was thus already used to monitor the removal of paramagnetic heavy metals by sorbents (alumina and activated carbon) and ion exchange resins [2,3]. These studies paved the way for the use of NMR relaxometry directly on the sorbent/resin in a column experiment, with the aim to monitor *in situ* the gradual loading of the resin with the paramagnetic ions. The setting up of such an experiment is of course much more complicated than for batch experiments, as is the interpretation of the obtained curves. In this work, we followed by relaxometry the loading of two ion exchange resins beds (Amberlite IR120 and Dowex Marathon) with Ni^{2+} and Cu^{2+} in a column which was directly inserted into an NMR device (Fig. 1).

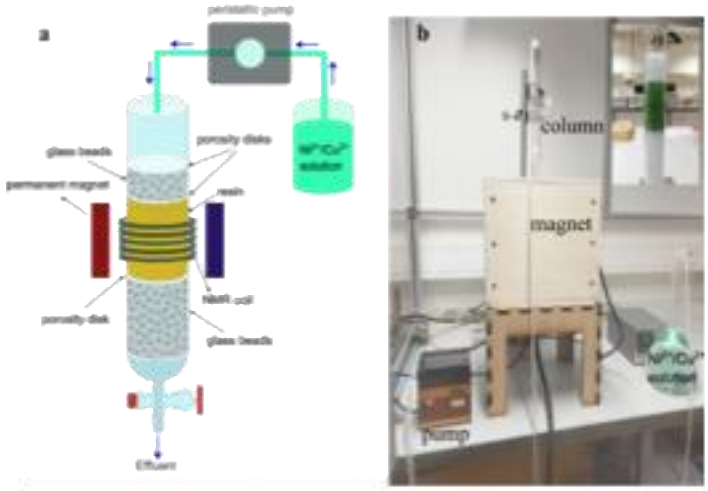

Fig. 1: (a) sketch of the experimental setup. (b) picture of the actual experiment, the inset shows a close-up of the column after saturation with Ni^{2+}

The measured transverse relaxation curves are clearly multiexponential. In a first approximation, we used a biexponential fitting. When looking at the evolution with time of the amplitude and transverse relaxation rate of the slow relaxing water fraction, a clear transition is observed at the end of the experiment. This is interpreted as the sign of a complete saturation of the studied zone of the resin bed with paramagnetic ions, which is confirmed by the quantification, at different times, of Ni^{2+} or Cu^{2+} in the effluent by AES Spectroscopy. Before and during the loading of the resin, the slow fraction corresponds to the treated water (without Ni^{2+} or Cu^{2+}) flowing between the resin beads. After the saturation, the slow fraction corresponds to the untreated solution (containing Ni^{2+} or Cu^{2+}) flowing between the resin beads already saturated with paramagnetic ions. This interpretation is consistent with the time evolution of the T_2 distributions obtained by inverse Laplace transform. In actual systems, the metal concentration of the feeding solution will be smaller and the experiment longer, which will imply to adapt the measurement sequence and the interpretation of the results.

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The Flemish Inter-University Ultra-High Field MRI Project (IN2U)

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7T in Flanders: a long standing dream to come true 7T MRI is commonplace worldwide, with over 130 installations[1], and our neighbour countries (NL, FR, DE) operate 16 systems. There is currently no 7T MRI installation in Flanders, and 1 system operational in Liège. Since 2012 there have been several attempts at acquiring funding for a 7T MRI system in Flanders, which resulted in a successful funding application in 2021. Part of the success is the fact that the project is supported by all Flemish university hospital radiology departments and all universities.

Mission and Vision The mission of the IN2U project is to bring 7T MRI to the clinic. Ultra-high field (UHF) MRI will have a clearly defined role in the management of several disease entities. By uniting the whole of Flanders, the consortium will be able to increase the number of subjects/patients to study and define the true value of UHF MRI for clinical decision making. But first, it will be crucial to this project to *unite experts in the field* to further develop techniques and to close the translational gap for a better diagnosis. A second key objective is to *educate future generations* of MRI scientists, clinicians, MR technologists and other interested parties, as the scientific MRI community is small in Belgium.

The IN2U Consortium promotors are the radiology department heads of Universitair Ziekenhuis Brussel, UZ Antwerpen, UZ Gent, and UZ Leuven, together with Universiteit Hasselt. Equally important is that each university (Vrije Universiteit Brussel, Universiteit Antwerpen, Universiteit Gent, and KU Leuven) is represented by a local senior staff member. All 9 parties have an equal share in the project.

The 7T Facility is located in Green Energy Park, Zellik, within close proximity of UZ Brussel. The scanner will be placed in an existing building that will be adapted to the specific research needs of a 7T MRI system by early 2026. General Electric (GE) Healthcare is chosen to be the supplier of its 7T Signa^{TM} system[2], initially with coils for neuro (^{23}Na/^{1}H), musculoskeletal imaging (^{1}H) and a ^{31}P/^{1}H surface coil. It will have the capabilities for *multinuclear spectroscopy*. The system will be open for pulse sequence development, application development, hardware development etc. A scientific committee will be installed that will oversee and evaluate scientific projects. One spokesperson per consortium member will be appointed to generate local UHF MRI projects.

We call on you! Improved spectroscopic imaging is one of the key advantages of a 7T MRI system. We especially call on the YBMRS community to join the IN2U scientific team and help to further advance 7T for clinical use.

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Homonuclear Decoupling combined with 2D-NMR experiments

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Commonly, NMR studies are conducted with the ^{1}H one-dimension (1D) experiment because of its simplicity, rapidity and quantitative aspects. However, ^{1}H 1D spectra have a relative low resolution due to several factors such as the number of signals, the homonuclear couplings and the relative narrowness of the chemical shift scale. These lead to peaks overlapping that can impede on the analysis of the spectra and can hamper the reliability of the data. Resolution improvement in terms of peak separation could decrease this overlapping and lead to an improvement of the data quality. Various solutions can alleviate this lack of resolution: higher magnetic field spectrometers, two-dimension (2D) experiments and Homonuclear Decoupling (HD).[1,2,3]

HD offers a gain of resolution by suppressing the homonuclear coupling interactions between active and passive spins. Only active spins are observed, and their signals become singlets with reduced signal widths. (Fig.1) That passive/active selection is essential and various techniques of HD exist and differ in the way that selection is obtained or in their combination with 2D experiments: an isotopic selection is used in BIRD and the combination of a magnetic field gradient with an adiabatic pulse is used in PSYCHE. Such selection suffers from a considerable loss of sensitivity, with only 1 to 10% of the protons being observed, which is a major drawback to the use of HD.[4,5]

Still, combination of HD with 2D-experiments can cumulate their respective resolution increase and can be useful in various domains. We are currently optimising 2D-HD protocols for the analysis of complex mixtures: bird-HSQC, psyche-TOCSY and psyche-DOSY.

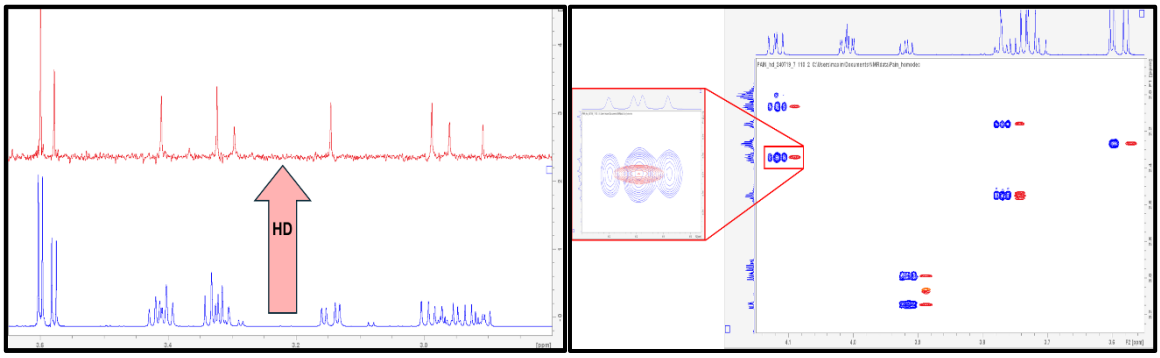

Figure 1 – Homonuclear Decoupling (red) and their corresponding conventional spectrum (blue) for 1D-^{1}H spectrum (left) and on 2D-TOCSY spectrum (right). The TOCSY spectrum present a small shift to allow a clearer view of the signals, and a zoom on one peak shows the gain in resolution obtained in both dimensions.

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In situ crystallization studies of zeolites and MOFs using static and MAS NMR

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Crystallizing zeolites with uniform properties is crucial for the chemical industry, but achieving this can be challenging due to the sensitivity of synthesis conditions. Although in-situ monitoring systems are essential, they are currently lacking. Nuclear magnetic resonance (NMR) spectroscopy has emerged as a versatile tool for studying crystallization kinetics. Static NMR provides quantitative, speciation-sensitive data on mobile and dissolved species, covering key elements such as H, Si, Al, Na, Cs, and C, and offers insights into Si-Al connectivity throughout crystallization stages. Additionally, MAS NMR enables the study of solid-phase evolution.

The transformation of hydrated silicate ionic liquids (HSIL) to pollucite was investigated using in-situ ^{27}Al NMR spectroscopy under both static and MAS conditions. Room temperature ZIF-8 formation was explored using direct excitation ^{1}H NMR in a static setup. The static experiments were conducted using a dedicated high-pressure cell design,[1] while the MAS experiments utilized commercial 5mm high-pressure MAS rotors designed by PNNL.[3] Crystallization profiles obtained from NMR were compared to moving electrode electrochemical impedance spectroscopy (MEEIS) and synchrotron measurements for pollucite, as well as light scattering for ZIF-8.

In-situ ^{27}Al NMR allowed for the detection of Al speciation and transformation within a hydrated silicate ionic liquid medium, tracking its removal from solution during the conversion into crystalline pollucite zeolite. Combined with ex-situ synchrotron X-ray diffraction and MEEIS data, this approach revealed that initial growth originates from Al-rich prenucleation clusters, leading to zoned crystals with an increased Si/Al ratio in their outer regions.

In-situ ^{1}H NMR, combined with harmonic light scattering, provided detailed insights into the crystallization mechanism of ZIF-8. This technique, inherently sensitive to structural changes, revealed molecular exchanges between particles and the solution. Initially, oligomerization forms small prenucleation clusters with an excess of protonated ligands in a pre-equilibrium state. When these clusters aggregate to form amorphous precursor particles, protonated ligands are released, resulting in an amorphous, charge-neutral structure that subsequently crystallizes into ZIF-8 through intraparticle reorganization. Later stages involve solution-mediated Ostwald ripening, where the growth mechanism shifts to the incorporation of monomers from the solution.

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Click-to-release bioorthogonal tyrosine modification

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Bioorthogonal chemistry is an emerging field that facilitates selective chemical reactions in physiological conditions. A particularly promising approach is tetrazine-isonitrile chemistry, noted for its ability to enable click-to-release reactions for phenols. This study presents the synthesis and NMR characterization of a tetrazine-modified tyrosine substrate and explores an isonitrile to induce a dissociative bioorthogonal reaction that liberates the unmodified substrate. This system holds potential for diverse applications in life sciences, including drug delivery and fluorescent labeling.

Unravelling the mysteries of black titania: A spectroscopic study on the reduction of titania with different crystal phases

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Titanium-dioxide materials are known semiconductors with many prospects in e.g. chemical catalysis, food industry and energy conversion. Most of these applications use the photocatalytic property of titania, which is mostly active in the UV part of the electromagnetic spectrum. By chemically reducing the white titania, we can alter its electronic properties and band gap. It then becomes active under visible light and acquires colour [1].

However, in literature there is a lot of contradiction on the most appropriate reduction process and its influence on the properties and photocatalytic activity of the coloured titania. In this project, titania was reduced using a thermal process with $NaBH_4$ as reducing agent [2]. It appeared that the reduction was sensitive to many different parameters of the process, explaining reproducibility issues in literature. Key aspects of reduction are the crystal structure and phase of the titania material, which are relevant for the photocatalytic activity, and the behaviour of the material during the reduction process. However, the reduction process also alters the properties of the titania crystal phases, which is an important parameter when looking at the photocatalytic activity of the black titania.

By characterizing different reduced titania materials with various spectroscopic techniques, amongst others electron paramagnetic resonance (EPR), XRD, X-ray photoelectron spectroscopy (XPS) and electron energy loss spectroscopy (EELS), it is attempted to create a clear overview on the influence of the different crystal phases of titania (anatase, rutile, brookite and amorphous) on the reduction and *vice versa*. EPR, as one of the key techniques, reveals insight in the nature of the Ti(III) centres formed upon reduction of the titania. XPS and EELS measurements complement the data on the conduction and valence band of the Ti centres in the reduced materials and give more information on the oxidation state of the Ti ions, while XRD provides understanding on changes of crystal structure.

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Toluene-induced Pluronic F127 micelles as templating agent for hollow silica nanostructures: an NMR study

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In the last two decades, various low-dimensional porous silica-based nanomaterials have been synthesized using sol-gel methods and micelle-templated approaches. Among these, hollow nanospheres and nanotubes (Fig. 1) have gained significant interest due to their high specific surface area and large pore diameters, making them ideal candidates for catalytic applications.[1] Additionally, the isomorphic substitution of Si with metal cations allows creating acidic heterogeneous catalysts.[2]

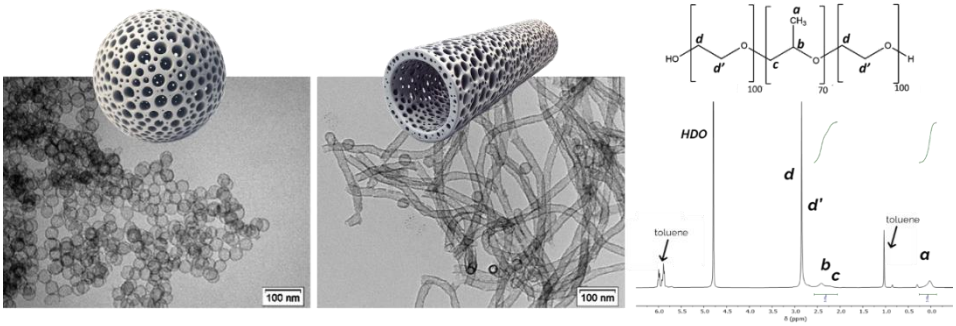

Figure 5*. TEM micrographs of silica hollow nanospheres (left) and nanotubes (center);* [1]*H-NMR of Pluronic F127 ((PEO)*$_{100}$*(PPO)*$_{70}$*(PEO)*$_{100}$*) in the presence of toluene (right).*

Interestingly, the synthesis protocols for silica nanotubes and hollow nanospheres are nearly identical, utilizing triblock copolymer (Pluronic F127) micelles as soft templates, along with toluene as a swelling agent. The key differences between the two processes are the stirring speed and the timing of the addition of the swelling agent relative to the silica precursor (tetraethyl orthosilicate, TEOS).[1] While previous studies suggested that hollow nanospheres form via nanotube fragmentation, our recent findings confirmed that the crucial factor in determining the morphology of the nanostructures is the amount of surfactant-stabilized toluene in the reaction mixture.[3] Contrary to the budding process hypothesis, the observed changes in pore diameters are consistent with a micelle rod-to-sphere transition, driven by the Hofmeister effect.[4]

In this study, ^{1}H NMR, 2D COSY, and diffusion NMR techniques have been employed to investigate how Pluronic F127 micellization is influenced by toluene concentration and temperature, and how these factors affect the formation of hollow nanospheres. 1D and pseudo-2D NMR experiments were performed varying experimental conditions to gather structural and dynamic insights. Additionally, tin-doped nanomaterials were synthesized and characterized using solid-state NMR of ^{29}Si and ^{119}Sn, alongside techniques such as N_2 physisorption and Transmission Electron Microscopy.

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High Temperature ^{1}H DOSY NMR reveals alteration of the molecular structure of water-extractable arabinoxylans during fermentation of wheat flour for sourdough production

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Arabinoxylans (AX) are important dietary fibers, predominantly encountered in wheat. They exist in water extractable (WE) and water unextractable versions and play a crucial role in human health. In food technology, especially the water-extractable arabinoxylans (WE-AX) are important due to their impact on viscosity and dough rheology. The production of sourdoughs is known to increase the WE-AX fraction, yet the underlying chemical mechanisms remain unclear. This study investigated the alteration of WE-AX during the fermentation of wheat flour for sourdough production using ^{1}H Diffusion Ordered SpectroscopY (DOSY) Nuclear Magnetic Resonance (NMR) at elevated temperature. This research aims to fill this gap by employing ^{1}H DOSY NMR to analyze the structural changes of WE-AX during fermentation with different lactic acid bacteria (LAB) strains.

1D ^{1}H and ^{1}H DOSY NMR experiments were performed at elevated temperatures to increase the applicability of these techniques for large biomolecular compounds. Deconvolution of the spectra also revealed vital information about the substitution patterns of the WE-AX samples. The results reveal a size reduction of the WE-AX compounds, indicated by an increase in mobility of the molecules by analysis of the diffusion coefficient as well as the transverse relaxation times. Increases in the solid residuals also indicate that fermentation might render larger WE-AX compounds no longer soluble, explaining aforementioned results. Deviations from the general trend might be due to a creation of exopolysaccharides by some of the LAB strains, although further research is necessary to confirm this.

This study provides insights into the impact of fermentation on WE-AX during sourdough production, offering potential applications for improving sourdough bread quality and its health benefits. Simultaneously it demonstrates that the use of elevated temperatures can greatly improve the applicability of DOSY NMR for larger biomolecular populations.

Simulation of transverse Nuclear Magnetic Relaxation Induced by superparamagnetic nanoparticles with a semipermeable coating

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Superparamagnetic iron oxide nanoparticles are characterized by a high magnetization when submitted to a high external field, and no remnant magnetization in zero field. Those properties make them suitable to be used as contrast agents in nuclear magnetic resonance imaging. Indeed, when present in a given tissue, they change the relaxation time of the surrounding water. This in turn changes the magnetic signal local intensity at any given time, and therefore make the area appear clearly in contrast to other surrounding tissues.

There is a variety of theoretical models which try to quantitatively explain the relaxation induced by those types of nanoparticles, depending on their physical parameters (in particular, their size and saturation magnetisation). In all those models however, high field transverse relaxation is caused by the progressive dephasing of the precession movement of water nuclear magnetic moments. Dephasing is caused by diffusion of the water molecules in the magnetic inhomogeneities created by the nanoparticles. As they diffuse, water molecules will experience varying magnetic fields which will alter their precession velocity, progressively dephasing [1]. Hence, relaxation times, and therefore contrast, are strongly linked to the diffusion coefficient of the water molecules.

The diffusion coefficient of water molecules therefore is an important parameter in describing those systems. However, due to their complexity, theoretical models are confined to modeling relaxation in a homogeneous medium, which is a very limiting hypothesis. In particular, the environment directly surrounding the nanoparticles is usually not homogeneous, as they are surrounded with a layer of coating. That coating is often a polymer and is therefore semi-permeable to water, with a lower diffusion coefficient as compared to bulk solvent. This is believed to affect experimental relaxation times [2], especially as this zone of slow diffusion is also a zone of high magnetic inhomogeneities, being directly around the nanoparticles.

This work aims at simulating the relaxation of water molecules, as induced by superparamagnetic iron oxide nanoparticles coated with a semi-permeable layer, with reduced diffusion coefficient. To that end, numerical simulations using Monte Carlo techniques, based on the random walk of water protons, and computation of the dephasing resulting from them, are developed. The goal of our work is, through those simulations, to evaluate if, for three different nanoparticle sizes, corresponding to three different relaxation regimes, slowed diffusion in the coating indeed impacts the relaxation times.

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Application of NMR-based Metabolomics in the Evaluation of Anti-Osteoporotic Treatments.

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Osteoporosis is a disease marked by bone mass loss and the degradation of bone tissue microarchitecture, primarily affecting the elderly and representing a significant public health challenge as populations age is increasing. Currently, clinical monitoring of osteoporosis relies on bone remodeling biomarkers like CTX, PINP, and b-ALP However, these markers have notable limitations; for example, CTX is influenced by circadian rhythms and fasting conditions. Additionally, poor patient adherence to anti-osteoporotic treatments increases fracture risk. To address these issues, our Clinical Metabolomics Group at the University of Liège conducted a longitudinal study to identify new osteoporosis-related markers, evaluate treatment impacts, and study patient compliance using a ^{1}H-NMR-based metabolomics approach.

In this study, plasma samples were collected from 53 osteoporotic patients at three intervals (baseline, 3 months, and 12 months). 42 metabolites/sample were identified and quantified by NMR and the obtained dataset was statistically analyzed. Patients were classified into four groups according to their treatment: no treatment, dietary supplements, bisphosphonates, denosumab, and teriparatide.

Various PLS-DA analyses were realised to compare the different treatments; no significant models were obtained, except for the separation between the "no treatment" and "teriparatide" groups which highlighted ornithine and histidine, both increased in the "no treatment" group.

Further, PLS modeling explored correlations between individual metabolomes and biomarker values (CTX, PINP, and b-ALP). Significant correlations were identified in the “no treatment” and “denosumab” groups for all three biomarkers, and a correlation between CTX and the metabolome of patients treated with teriparatide. However, no significant correlations were found for the “dietary supplements” and “bisphosphonates” groups.

Despite promising results, the study faces limitations, such as non-homogeneous treatment groups and non-standardized sample conditions (e.g., time of collection, dietary impacts). Future research would benefit from a more rigorously standardized metabolomics study, enabling detailed analysis of individual metabolomic changes across visits and reinforcing these initial findings.

The last missing interaction: Observation of ^{1}H-^{1}H J-couplings in solid-state NMR spectroscopy

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^{1}H-^{1}H J-couplings are yet to be observed in solids. Here we observe ^{1}H-^{1}H J-couplings in plastic crystals of (1S)-(-)-camphor in solid-state NMR at magic angle spinning (MAS) rates of 100 kHz and above. This is enabled when the intrinsic coherence lifetimes at fast MAS rates become longer than the inverse of the ^{1}H-^{1}H J couplings. As a result, we were able to record two-dimensional ^{1}H-^{1}H J resolved spectra that allow the observation and measurement of such ^{1}H-^{1}H J-couplings in powdered camphor.[1]

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Spin Magnetic Resonance and Time Resolved Spectroscopy of Molecular Qubits

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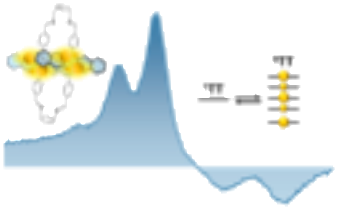
The search for smartly designed organic molecules that can operate as Molecular Qubits (MQBs) suitable for Quantum Information Science applications is a growing field. Research on MQBs has mainly focussed on electronically excited-state systems that demonstrate pure initial quantum states with long coherence times that behave as spin qubits even at room temeprature.[1, 2] Further, carbon-based molecules which demonstrate Singlet Fission (SF) have been investigated, in which a spin-correlated triplet pair ^{1}(TT) that can evolve to a quintet state ^{5}(TT) is photogenerated.[2] Both radical pair and ^{5}(TT) states fulfil the DiVincenzo criteria to constitute MQBs. Despite SF is a promising approach, it is still challenging to rationally achieve quantum coherence at room temperature, which requires precise control of the orientation and dynamics of triplet pairs.[3]

In this communication we show an example of how quantum coherence of quintet multiexcitons can be achieved at room temperature by conveniently arranging two pentacene chromophores within a macrocycle. The covalently linked pentacene dimer exhibits fast sub-picosecond SF and generates spin-polarized quintet multiexcitons with a coherence time as long as hundreds of nanoseconds even at room temperature.[4]

This macrocyclic parallel dimer strategy opens up new possibilities using molecular multilevel qubits in the excited state. Beyond them, ground-state organic MQBs will also boost the collection of molecules for future quantum applications, being organics diradicals the epitome of this group.



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Multi-harmonic EPR detection of melanin in skin melanomas: from mice to men

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Over the last decades, the incidence of melanoma has been continuously increasing. Today, melanoma remains the most aggressive skin cancer, significantly reducing survival rates for patients in its advanced stages. Therefore, early diagnosis remains the key to change the prognosis of patients with melanoma. The incidence of amelanotic and hypomelanotic melanomas being very low (with less than 2% of newly diagnosed melanomas each year [1]) justifies to mainly focus on pigmented melanoma. Eumelanin the main pigment present in melanomas, is paramagnetic and detectable by EPR. We previously described that images obtained using 9 GHz EPR imaging could be overlaid on histological images [2]. In parallel, ex-vivo measurements of human biopsies showed that the EPR signal in benign nevi was significantly lower than that in malignant melanomas and found a correlation between the EPR signal and Breslow depth (tumor thickness in the skin) [3]. This led us to succeed in detecting noninvasively the melanin signal from skin melanoma models in mice at low frequency EPR (1GHz) [4,5]. We performed a clinical study using a **whole-body EPR system** (*ClinEPR*), in patients on skin lesions suspicious of melanoma. EPR data obtained before surgery were compared with histopathology results. **The EPR signal of melanin was significantly higher ($p<0.0001$) in melanoma lesions (n=26) than that in benign atypical nevi (n=62)**. A trend toward a higher signal intensity (though not significant) was observed in high Breslow depth melanomas (a marker of skin invasion) than in low Breslow lesions [6]. Because the melanin signal recorded was at the limit of the noise, there was a clear room for boosting the sensitivity of the method through improvement in instrumentation.

Our clinical EPR system has been very recently upgraded with the capability to apply larger modulation amplitude and to record/analyze the EPR signal in **multi-harmonics** mode (*Novilet*) [7]. We have compared the melanin signal obtained on phantoms using classical CW-EPR (1st harmonic) and multi-harmonics mode. We observed a boost in sensitivity by a factor about 10. The same result was obtained when these phantoms were placed at the surface of human skin. In nude hairless mice (n=8) with implanted skin B16 melanomas, we observed a **boost in sensitivity *in vivo* similar to that *in vitro* with the capability to detect melanoma cells in the skin at an earlier stage of development**. **Multi-harmonic EPR was also able to detect non-invasively a signal coming from a lymph node tumor** (nude mice n=8) **as well as metastatic tumor in the lungs** (nude mice n=3). **The boost in the sensitivity compared to CW EPR was clearly significant.** We confirmed the improvement of multi-harmonic technology in signal acquisition for melanin *in vivo* and *in vitro* to be implemented in clinical studies for early melanoma diagnosis [8].

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From signals to insights: NMR-based metabolomics as a tool for lung cancer biomarker research

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Lung cancer is the leading cause of cancer-related deaths worldwide in both men and women. This high mortality rate is mainly due to delayed diagnosis as a result of the absence of symptoms in the early stages of the disease. Screening therefore aims to detect lung cancer before clinical symptoms occur. One of the main screening techniques is low-dose computed tomography (LDCT). Several studies, including the National Lung Screening Trial (NLST) and the Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON), have shown the effectiveness of LDCT screening in reducing lung cancer mortality in high-risk patients. However, the technique lacks the ability to discriminate between benign and malignant lesions, resulting in a high false-positive rate and ultimately unnecessary invasive diagnostic procedures. To overcome this challenge, researchers are searching for **early biomarkers** that can be used alone or in combination with existing screening techniques to provide a more accurate diagnosis in a non-invasive manner.

Biomarkers are defined as biological molecules found in body fluids, such as plasma, that indicate the presence or absence of a condition or disease. Metabolomics is an interesting platform for identifying potential early-stage biomarkers because metabolic alterations occur as soon as lung cancer develops. These metabolic alterations occur not only in the cellular environment but also in the extracellular environment, such as plasma, allowing the detection of altered plasma metabolite levels in lung cancer. Metabolite profiling can be performed using mass spectrometry (MS) or **proton nuclear magnetic resonance** (^{1}H-NMR). ^{1}H-NMR has several advantages over MS including a high reproducibility (>98%), short measurement time, and simple sample pre-treatment. There is already evidence for the use of ^{1}H-NMR as a tool to analyse the plasma metabolite profile, allowing the identification of potential plasma metabolite biomarkers for early-stage disease. Therefore, an overview of all the key breakthroughs achieved by our research group in this field will be discussed. This poster will first focus on the feasibility of lung cancer detection via blood plasma using NMR spectroscopy, followed by a discussion of further developments in preanalytical sample preparation and NMR measurement procedures, and finally a discussion of how plasma biomarkers can be used for early disease detection.

Conformational ensemble analysis of flexible peptides using residual dipolar couplings

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Today it is known that in biomacromolecules, structural flexibility is ubiquitously present and plays a fundamental role in function. Particularly in the case of intrinsically disordered proteins (IDPs), which are highly flexible proteins, this contrasts with the previous paradigm where function arises from a single, stable protein fold. While ordered or folded proteins can be accurately described using techniques such as X-ray crystallography or cryo-electron microscopy, IDPs require a different approach. NMR provides information dependent on a population-weighted average, and it reports conformational dynamics at atomic resolution, which makes it better for the study of flexible molecules. [1]

Residual dipolar couplings (RDCs) are NMR parameters that report on long-range conformational dynamics in both small and macromolecular compounds.[2] They have been used successfully to describe folded proteins and rigid small molecules, but their application for highly flexible molecules has proven to be a challenge. For this reason, we aim to use a recently developed approach known as MDOC[3] (molecular dynamics with orientational constraints) for the purposes of flexible molecule structure determination, which is a time-averaged restrained molecular dynamics simulation that accepts RDCs as tensorial restraints as a solution to this issue. We expect to obtain conformational ensembles from RDCs, but also using other structure sensitive data (ROEs, J-couplings).

As an initial case study, we have studied the insect neuropeptide proctolin (Arg-Tyr-Leu-Pro-Thr), the first structurally identified myotropic insect neuromodulator. Though a solid-state conformation obtained by X-ray crystal structure analysis has been reported[4], its structure in solution has not yet been proposed. Previous NMR studies of this peptide have been attempted[5] but did not deliver conclusive results due to the flexible nature. We have measured both easily accessible one-bond ^{1}H–^{13}C and ^{1}H-^{15}N RDC, as well as multiple-bond ^{1}H-^{1}H RDCs using pure shift-based methods to maximise the amount of independent orientational constraints.[6] We've used ROESY experiments to obtain interatomic distance data, better suited than NOESY for a molecule of this size. Our aim is to use this information as input for MDOC simulations to propose a full conformational ensemble of proctolin that can be used for structure-function analysis. This case-study would then serve as preparation toward studying larger flexible peptide fragments derived from disordered proteins.

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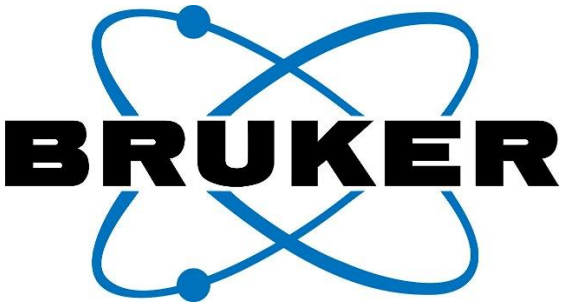
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