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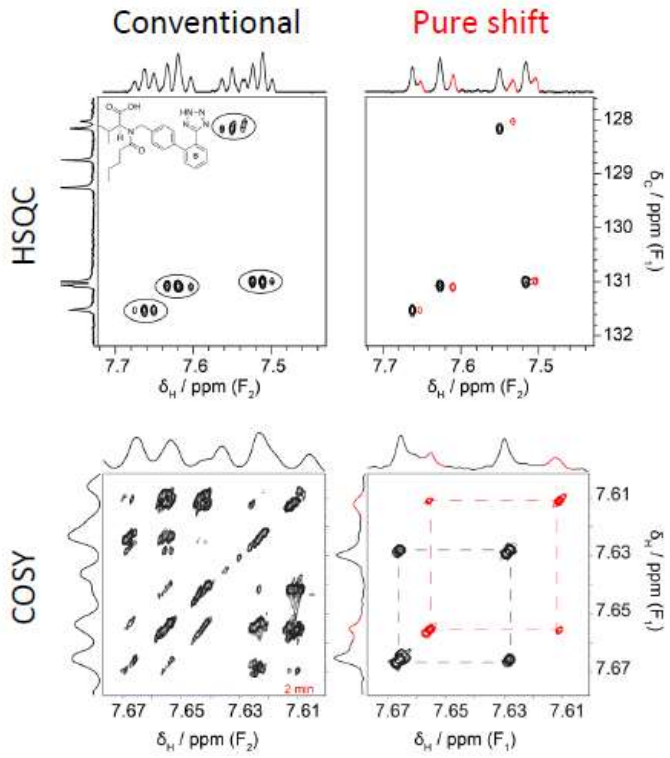
NMR Discussion Group



Postgraduate Meeting 2015

School of Chemistry

University of Manchester

25th June 2015

Local organisation and acknowledgements

Meeting coordinated by:	Yaroslav Khimyak, University of East Anglia
Local organisation coordinated by:	Mathias Nilsson, University of Manchester Ralph Adams, University of Manchester
Online registration coordinated by:	Stephen Byard, Covance

Thanks go to Gareth Morris (University of Manchester), Stephen Byard (Covance) and Yaroslav Khimyak (University of East Anglia) for acting as Judges for the prize giving.

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Posters

Posters should be mounted on the poster boards during the arrival period prior to the formal welcome and start of the program and should be attached to the board for which the poster number has been designated. Posters should be removed after the close of the meeting.

Programme

1000 – 1025 Arrival, registration, roster mounting and coffee
1025 – 1030 Welcome, Yaroslav Khimyak, NMRDG

Oral Presentation Session 1, session chair: Gareth Morris

1030 – 1110 **Mathias Nilsson,** University of Manchester
Pure shift NMR

1110 – 1130 **Jessica Bame,** University of Bristol
*Improved methodologies for nOe distance determination for small molecules***.**

1130 – 1150 **Hannah Davies,** University of Liverpool
Unpicking the early stages of amyloid aggregation using NMR

1150 – 1210 **Alex Heyam,** University of York
NMR studies of the microRNA biogenesis protein PACT reveal two states in slow exchange

1210 – 1230 **Karol Nartowski**, University of East Anglia
Controlled crystallisation in porous silicas: NMR insight into structure and self-assembly mechanism of confined organic crystalline phases.

1230 – 1250 **Catherine Smith,** University of Birmingham
Study of the molecular interactions of ionic liquid colloidal suspensions using rheometry and NMR

Lunch

1250 – 1330 Buffet lunch and mixing

Poster Session

1330 – 1400 Odd numbered posters manned
1400 – 1430 Even numbered posters manned

Oral Presentation Session 2, session chair: Yaroslav Khimyak

1430 – 1510 **David Middleton,** University of Lancaster
Adventures in biomolecular design (and solid-state NMR)

1510 – 1530 **Davy Sinnaeve**, University of Gent

Ultrahigh resolution ^{1}H-^{1}H coupling measurement

1530 – 1550 **Hannah E. Kerr,** University of Durham

Characterisation of molecular disorder in furosemide-isonicotinamide cocrystals

1550 – 1610 **Paula Sanz Camacho**, University of St Andrews
Investigating non-covalent interactions in crowded frameworks by ^{77}Se and ^{125}Te solid-state NMR

Close

1610 Tea and Coffee
1620 Award of Best Oral Presentation and Best Poster Presentation

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Abstracts of Contributed Talks

(Talk 01, Poster 04)

Improved Methodologies for NOE Distance Determination for Small Molecules

Bame, J.R.; Burns, M.; Essafi, S.; Bull, S.P.; Bain, E.; Dower, L.; Harvey, J.N.; Aggarwal, V.K.; Butts, C.P.

The quantitative use of the nuclear Overhauser effect for interproton distance determination has various applications for small molecules. Relative NOE intensities have been used to derive accurate NOE distances with errors as low as 3% by the Butts group.[1] These NOE-derived distances were used in the analysis of conformationally biased alkane products of a newly developed iterative homologation of boronic esters.[2] NOE distance analysis and ^{1}H-^{1}H and ^{1}H-^{13}C scalar coupling measurements profiled the conformation of the n-10 carbon chain and the all-syn alcohol ***1*** and the syn-anti MoM ether ***2*** were determined to take on helical and linear configurations respectively, as predicted by computation.

Recent work aims to improve accuracy of NOE-derived distances via perturbation of τ_c values through temperature. Decreasing temperature, increases τ_c which in turn affects overall NOE intensity[3] and also the accuracy of subsequently derived-NOE distances. This temperature-dependence has been tested on a selection of small molecules (quinine, camphor, erythromycin and clindamycin) of varying size and rigidity. This study aims to determine whether temperature-dependence of τ_c provides a tool to optimise the accuracy NOE-derived distances.

1. Butts, C.P.; Jones, C.R.; Towers, E.C.; Flynn, J.L.; Appleby, L.; Barron, N.J. *Org. Biomol. Chem.* **2011,** 9, 177-184
2. Burns, M.; Essafi, S.; Bame, J.R.; Bull, S.P.; Webster, M.P.; Balieu, S.; Dale, J.W.; Butts, C.P.; Harvey, J.N.; Aggarwal, V.K. *Nature* **2014,** 513, 183-188
3. Ley, S.V.; Neuhaus, D.; Williams, D.J. *Tetrahedron Lett.* **1982**, 23, 1207-1210

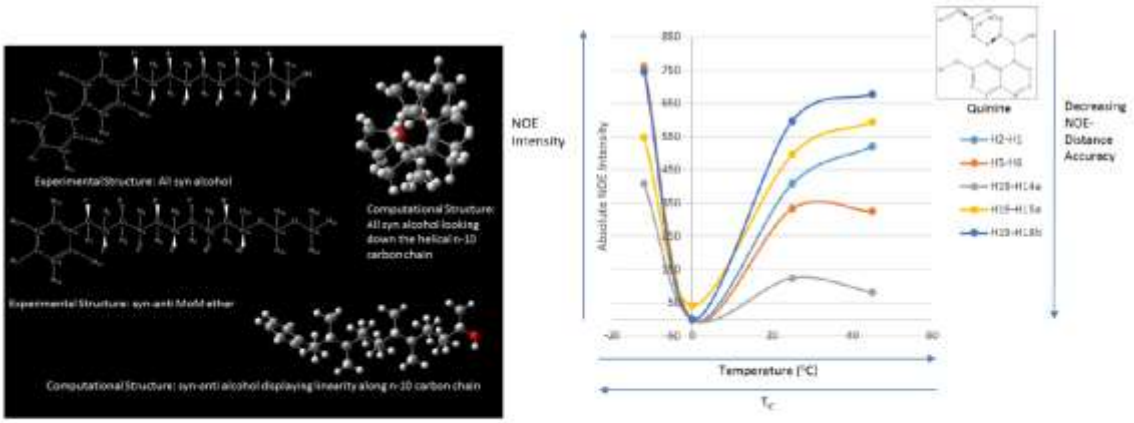

Figure 1: (Left) All syn alcohol and syn-anti MoM ether experimental and computational structures. (Right) Effects of Temperature on Rigid NOE Correlations in Quinine.

(Talk 02, Poster 09)

Unpicking the early stages of amyloid aggregation using NMR.

Hannah A Davies,[1] Marie M Phelan,[2] Sara B-M Whittaker,[3] and Jillian Madine.[1]
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[2]*Technology Directorate, Faculty of Health and Life Sciences, University of Liverpool.*
[3]*HWB-NMR, School of Cancer Sciences, University of Birmingham, Birmingham, B15 2TT*

Thirty-one proteins are known to form extracellular fibrillar amyloid in humans . Molecular information about many of these proteins in their monomeric, intermediate or fibrillar form and how they aggregate and interact to form the insoluble fibrils is sparse. This is because amyloid proteins are notoriously difficult to study in their soluble forms, due to their inherent propensity to aggregate . Medin is the key protein component of the most common form of localised amyloid with a proposed role in aortic aneurysm and dissection. Due to the rapid aggregation rate of this amyloid protein we used a combination of fast NMR techniques, band-selective excitation short transient (BEST) and band-selective optimized flip-angle short-transient heteronuclear multiple quantum coherence (SOFAST-HMQC) and denaturing conditions to assign this 5KDa protein (BioMagRes-Bank accession no. 25399) and transfer the NH assignment to more physiological conditions. This has enabled us to monitor the early stages of aggregation and identify key regions that seem to initiate amyloid formation. Furthermore we are now utilising 13-C direct-detected experiments collected with a 600 MHz TXO cryoprobe (Wellcome Trust-funded open access offered by HWB-NMR, University of Birmingham) to gain assignment of the C', CA, HA at different time points to enable more detailed analysis and CSI measurements. These spectra provide both insights into the aggregation mechanisms of this important amyloid protein and a methodology that could be applied to other transient protein species.

(Talk 03 and Poster 15)

NMR studies of the microRNA biogenesis protein PACT reveal two states in slow exchange

Alex Heyam,[1] Dimitris Lagos,[1,2] Michael Plevin[1]
[1]*Department of Biology, University of York, Wentworth Way, York, YO10 5DD*
[2]*Centre for Immunology and Infection, Hull York Medical School, University of York, Wentworth Way, York, YO10 5DD*

MicroRNAs are short RNA molecules that regulate mammalian gene expression, and are produced by a protein complex containing the ribonuclease Dicer and accessory proteins, including the RNA-binding protein PACT. PACT interacts with Dicer via its C-terminal domain (PACT-D3), which adopts a non-canonical double-stranded RNA-binding domain fold. PACT-D3 is homodimeric in solution, but is thought to interact with Dicer as a monomer, which may mean these interactions are incompatible.

We have characterised PACT-D3 homodimers using NMR, SEC-MALLS and analytical ultracentrifugation. Unusually, most peaks within the protein are doubled, indicating the presences of two distinct states. Exchange Spectroscopy shows the two states exchange on a timescale of approximately 600ms, and backbone assignment has revealed that the largest differences between the two states occur on the Dicer-binding interface. We are currently working to determine whether the two states represent different conformations of the dimer, or correspond to the two subunits of an asymmetric dimer.

(Talk 04 and Poster 21)

Controlled crystallisation in porous silicas: NMR insight into structure and self-assembly mechanism of confined organic crystalline phases

K. Nartowski[1],[1] D. Braun[2], L. Fábián[1], Y. Khimyak[1]

[1]*School of Pharmacy- University of East Anglia, Department of Drug Delivery and Pharmaceutical Materials, Norwich, United Kingdom*
[2]*Institute of Pharmacy- University of Innsbruck, Pharmaceutical Technology, Innsbruck, Austria*

Control over molecular self-assembly and crystallisation within drug delivery systems is of paramount importance for pharmaceutical industry as molecular alignment within a crystal determines its resulting physical properties. Recently, mesoporous silicas have attracted growing attention in drug delivery due to their controlled pore diameter, large pore volume and surface area. Determination and understanding of structure and dynamics of nano-size confined solids in complex materials is a significant analytical challenge due to lack of long range order or changes of the melting points. In this work we present solid state NMR molecular insight into the structures and transitions of confined materials, which are not accessible using another techniques.

Three poorly soluble drugs with significant differences in structural flexibility were chosen as model systems and loaded into porous solids. Firstly, crystallisation of indomethacin from amorphous state into the confined solvate and then into the stable form V were monitored inside the pores of ca. 30 nm. For the first time, using solid state NMR we observed transition of metastable tolbutamide form V into the stable form I^H inside the pores as small as 3 nm. Applying ^{19}F NMR and ^{19}F T_1 relaxation measurements we were able to gain a molecular level insight into the confined crystallisation mechanism through the formation of "molecular liquid-like" layer on the silica surface prior to the build-up of nano-crystal of flufenamic acid.

Such combined application of nano-size crystallisation and solid-state NMR spectroscopy is essential in directing molecular aggregation and answering fundamental questions on self-assembly of crystalline solids.

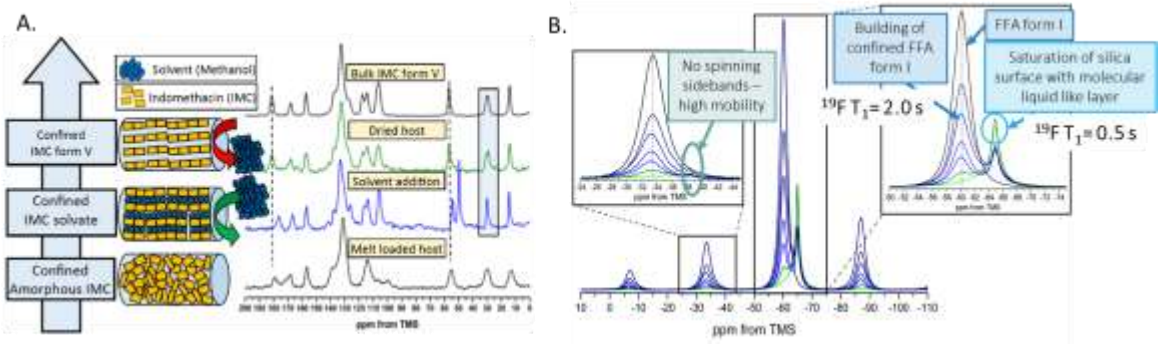


Figure 1. A. Formation of confined IMC form V from confined amorphous IMC; B. ^{19}F NMR in*sight into formation of nanocrystalline* FFA form I *confined in MCF porous host*.

Study of the Molecular Interactions of Ionic Liquid Colloidal Suspensions Using Rheometry and NMR

Catherine F. Smith, Melanie M. Britton
School of Chemistry, University of Birmingham, UK

Colloidal suspensions are of significant interest in many areas, including solar cells, solid state electrolytes and nanoparticles synthesis.[1] These can be formed in ionic liquids with the addition of nanoparticles.[1] Bulk rheological measurements are often used to investigate the dynamics and stability of these systems. Previous studies[2] have found that the nature of the ionic liquid has a large effect of the stability, and hence the rheometry, of the suspension formed. However, the precise nature of the interactions between the silica nanoparticles and the ions of the ionic liquids, and the molecular origin of their non-Newtonian behaviour is still unknown.

We have been studying[3] a range of imidazolium ionic liquids containing silica nanoparticles. Bulk rheological measurements (figure 1a) have been combined with NMR velocimetry (figure 1b) to understand the local rheology of these complex fluids. Using multinuclear relaxation (figure 1c) and diffusion measurements we have been able to better understand the interactions between the silica nanoparticles with the cations and the anions of the ionic liquid which underpins the non-Newtonian rheology observed.

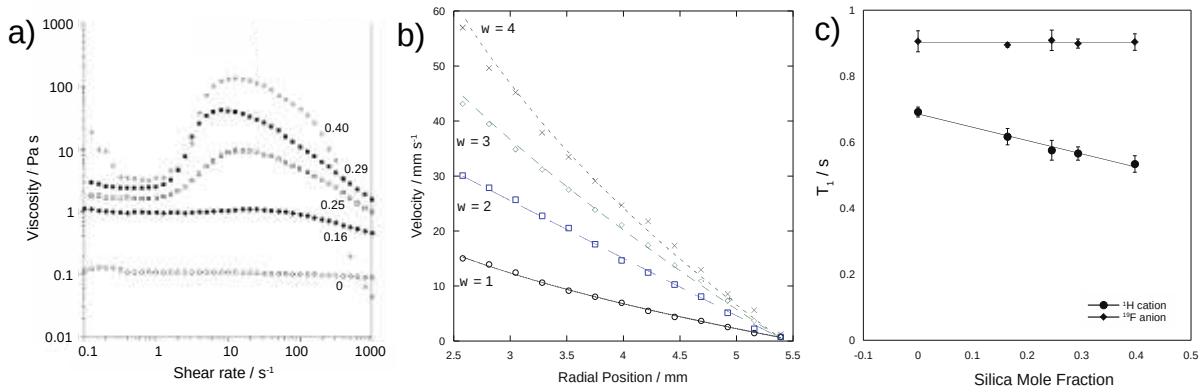


Figure 1: a) Plot of viscosity for [C_4mim][BF_4] with different mole fractions of silica; b) radial velocity profile for [C_4mim][BF_4] with 0.4 mole fraction of silica; c) ^{1}H and ^{19}F T_1 relaxation times for [C_4mim][BF_4] with different mole fractions of silica.

References:
1. A. Wittmar, D. Ruiz-Abad and M. Ulbricht, J. Nanopart. Res.,14 (2012) 651.
2. K. Ueno and M. Watanabe, Langmuir, 27 (2011) 9105.
3. J. Novak and M. M. Britton, Soft Matter, 9 (2013) 2730.

(Talk 06 and Poster 26)

Ultrahigh resolution ^{1}H-^{1}H coupling measurement

Davy Sinnaeve,[1,2] Mohammadali Foroozandeh,[1]
Mathias Nilsson,[1] and Gareth A. Morris[1]
[1]*School of Chemistry, University of Manchester, UK*
[2]*Department of Organic and Macromolecular Chemistry, Ghent University, Belgium*

Homonuclear scalar couplings are a double-edged sword. They deliver a wealth of structural information, but equally they are detrimental to spectral resolution, impeding their accurate measurement. One way to disentangle individual couplings from complex spectra is the SERF experiment, which delivers a 2D J-resolved spectrum containing only selected couplings.[1] A variant of this experiment, GSERF, uses the Zangger-Sterk pulse sequence element to deliver simultaneously all the individual couplings to one selected resonance.[2] Other recent variants incorporate band-selective and Zangger-Sterk pure shift acquisition.[3,4] However, all these methods can break down in crowded spectra, either because of signal overlap or because chemical shift differences between coupled spins are too small.

Here, we present the PSYCHEDELIC (Pure Shift Yielded by CHirp Excitation to DELiver Individual Couplings) experiment, derived from the PSYCHE pure shift method.[5] It delivers simultaneously all individual couplings to a selected proton, with minimal constraints on spectral overlap and chemical shift difference, with the usual high sensitivity and spectral purity of PSYCHE.

1. T. Facke and S. Berger, *J. Magn. Res. Ser. A*, **1995**, 113, 114-116.
2. N. Giraud et al, *Angew. Chem.*, **2010**, 49, 3481-3484.
3. J. E. H. Pucheta et al, *Chem. Commun.*, **2015**, 51, 7939-7942.
4. D. Pitoux et al, *Chem. Eur. J.*, **2015**, DOI 10.1002/chem.201501182.
5. M. Foroozandeh et al, *Angew. Chem.*, **2014**, 53, 6990-6992.

(Talk 07, Poster 18)

Characterisation of molecular disorder in furosemide-isonicotinamide cocrystals.

Hannah E. Kerr,[1] Lorna Softley,[1] Kuthuru Suresh,[2] Ashwini Nangia,[2] Paul Hodgkinson,[1] and Ivana Radosavljevic Evans[1,3]

[1] *Department of Chemistry, Durham University, Science Site, Durham DH1 3LE, U.K.*

[2]*Department of Chemistry, Hyderabad, India.*

[3]*Bragg Institute, ANSTO, New Illawarra Road, Lucas Heights, NSW, Australia.*

Solid-state NMR is shown to be a potential tool for the characterisation of disorder in molecular cocrystals by use in conjunction with first principles calculations to elucidate the nature of the disorder in the 2:1 cocrystal of furosemide-isonicotinamide. A variety of solid-state NMR techniques (both 1D and 2D as well as spin-lattice relaxation measurements) are used to determine whether the disorder is static or dynamic. The disordered sulphonamide group is found to be dynamic by variable temperature ^{2}H experiments as well as comparison of the experimental quadrupolar parameters with DFT-predicted values. ^{2}H spin-lattice relaxation times are used to characterise a two-jump model consisting of fast exchange of the sulphonamide NH_2 protons combined with a rotation of the whole sulphonamide group about the C–S bond. The furan rings of both the unique furosemide molecules are found to be dynamic by ^{13}C experiments, in contrast to the crystallographic model in which only one was modelled with split atomic sites while the other was successfully modelled with single atomic sites with elongated APDs. ^{13}C spin-lattice relaxation times are used to provide qualitative estimates for the energy barriers to rotation of the two furan rings and both are shown to have similar behaviour within the error of the model used.

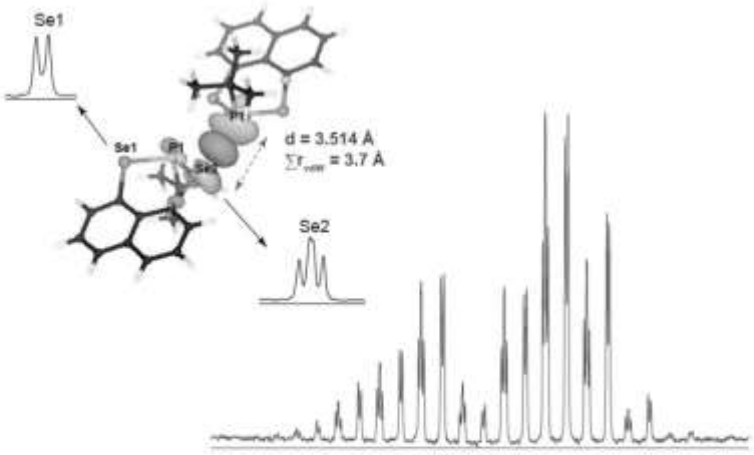
Investigating non-covalent interactions in crowded frameworks by ^{77}Se and ^{125}Te solid-state NMR

Paula Sanz Camacho,[1] Fergus R. Knight,[1] Kasun S. Athukorala Arachchige,[1] Daniel Dawson,[1] Alexandra M. Z. Slawin,[1] Jonathan R. Yates,[2] J. Derek Woollins,[1] and Sharon E. Ashbrook.[1]

[1] *School of Chemistry, EaStCHEM and Centre of Magnetic Resonance, University of St Andrews, North Haugh, St Andrews, Fife, KY16 9ST, UK*
[2] *Department of Materials, University of Oxford, Oxford, OX1 3PH, UK*

Non-covalent interactions are not as well studied as strong covalent and ionic bonding, and are still the focus of some controversy. However, these interactions are important as they can affect thermodynamic stability, molecular geometry, crystal packing, reactivity etc..., of the compounds in which they occur. Naphthalene and acenaphthene systems provide good models for studying this type of interaction, as two large heteroatoms are constrained in the *peri*-positions of a rigid organic backbone. In this situation, in order to stabilize the steric hindrance that occurs between the heavy atoms, a weak interaction and/or distortion of the geometry is often observed.[1]

In this work, we investigate not just intramolecular interactions between mixed *peri*-substituted acenaphthenes, shown in solution and in the solid-state by ^{77}Se and ^{125}Te solid-state NMR,[2] but also unusual *intermolecular* interactions that occur between two molecules (novel chalcogen-phosphorus heterocycles) that are packed such that the Se-P and P-P distances are smaller than the van der Waals radii.[3] ^{77}Se, ^{125}Te and ^{31}P results will be shown, together with DFT calculations, to understand the origin of these interactions. Furthermore, analysis of many of the compounds reveals significant polymorphism, not noticed in the original single-crystal diffraction data. The nature of the polymorphism present is then confirmed by a combination of solid-state NMR experiments, high-throughput "robot-based" crystallography of a number of single crystals and first-principles calculations.



1. Aschenbach, L. K.; Knight, F. R.; Randall, R. A. M.; Cordes, D. B.; Baggott, A.; Bühl, M.; Slawin, A. M. Z., Woollins, J. D. *Dalton Trans.* **2012**, *41*, 3141.
2. Stanford, M. W.; Knight, F. R.; Athukorala Arachchige, K. S.; Sanz Camacho, P.; Ashbrook, S. E.; Bühl, M.; Slawin, A. M. Z.; Woollins, J. D. *Dalton Trans.* **2014**, *43*, 6548.
3. Sanz Camacho, P.; Athukorala Arachchige, K. S.; Slawin, A.M.Z.; Green, T. F. G.; Yates, J.R.; Dawson, D.M.; Woollins, J. D.; Ashbrook, S.E. *J. Am. Chem. Soc.* **2015**. *in press.* DOI: 10.1021/jacs.5b03353

Abstract of Posters

(Poster 01)

Application of DOSY-NMR to probe TIPS-pentacene aggregation in solution

A.M. Alharbi, Péter Király, John.J. Morrison, Mathias Nilsson, A.B. Horn, S.G. Yeates

Abstract:
Over the last several years organic field-effect transistors (OFETs) have been extensively studied due to their potential impact in a wide range of electronic applications, such as drivers for flat-panel displays,[1–4] complementary circuits,[4–2] and various sensors. Solution-processed OFETs are particularly attractive for the realization of large area, cost effective, and pervasive printable electronic applications. However, pentacene has a very short half-life in solution under the influence of light; this behaviour can be attenuated markedly by derivatisation at 6- and 13- positions. As a consequence, materials such as TIPS-pentacene are becoming popular replacement for pentacene in electronic devices. TIPS-pentacene does still decay in solution by a photochemical process involving a reaction of its excited singlet state with O_2, which results in an endoperoxide with unfavourable electronic properties. This process has been shown to be concentration-dependent, with greater stability at higher concentrations. This is largely due to de-excitation of the singlet species by a second TIPS-pentacene molecule (which produces two triplet species which do not react further). It has been suggested that this de-excitation process is due to the formation of aggregates at higher concentration. In this poster, we present DOSY-NMR evidence that this is not the case over the technologically-relevant 10^{-5} – 10^{-2} M concentration range, so other explanations are needed.

(Poster 02)

Thermal Modification of Functionalised Polymers

Daniel Albrighton,[1] Rob Evans,[1]
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Poly(neo-pentyl styrene sulphonate) has shown to have electronic properties[1] and so has potential use in organic electronics. The neo-pentyl group can be removed on thermal treatment of the polymer, forming the sulphonate[1], and giving a large change in the properties of the polymer. It has been reported that during this thermal treatment, the neo-pentyl group can rearrange, attaching onto the benzene ring [2-3].
A range of NMR techniques have been used to determine the structure and kinetics of the reaction. In particular, diffusion NMR has been used to study the extent of the re-arrangement. In diffusion NMR, the diffusion coefficient obtained is directly related to the size of the species producing the signal in the NMR signal. Diffusion NMR , we found that the diffusion co-efficient for the neo-pentyl group was different to the polymer chain, suggesting that re-arrangement had not occurred.

1- 1- I, F Domínguez, J Kolomanska, P Johnston, A Rivatona, and P D. Topham. Polym Int (2014)
2- Li et al. J. Mater. Chem. (2011)
3- K,Y BAEK. Journal of Polymer Science: Part A: Polymer Chemistry, Vol. 46, 5991–5998 (2008)

(**Poster 03)**

Investigations into Quantitative Cross Polarisation Magic-Angle Spinning NMR

Sophie Ayscough,[1] Pedro M. Aguiar[1]
[1]Department of Chemistry, University of York, Heslington, York, YO10 5DD, UK

Cross-polarisation (CP) is used in NMR for signal enhancement, reducing experiment times and together with MAS has been vital to the proliferation of solid-state NMR for materials characterisation. The signal enhancement obtained for any given carbon under CP is highly dependent upon the local environment (proximity of hydrogens) obviating quantitative analysis. Johnson and Schmidt-Rohr recently proposed a multi-CP experiment to obtain quantitative CPMAS experiments of organic solids (JMR, **2014**, 44-49). The multi-CP technique consists of multiple cross polarisation periods alternating with ^{1}H spin-lattice relaxation periods that repolarise protons. The aim of our work was to expand on this and establish a determined set of parameters with which quantitative ^{13}C solid state spectra could be collected in minimal time. Compounds were chosen to investigate a range of carbon environments. It was found possible to achieve multi-CP NMR spectra to within 10% accuracy of relative integrations for all samples investigated; glycine ethyl ester, glycine, D,L-tryptophan, poly-galacturonic acid and sucrose. The insight gained from these model systems was applied to the analysis of the analysis of esterification levels in fruit pectin samples. The degree of esterification obtained via multi-CP spectra for these samples correlated well with the manufacturer's reported degree of esterification obtained by double-titration, showing that ^{13}C multi-CP MAS could be a promising method for the analysis of less-soluble pectins obtained from plant waste rather than food sources.

(**Poster 05**)

Solid-State NMR Characterisation of ^{17}O- and ^{29}Si-Enriched UTL-Derived Zeolites

Giulia P. M. Bignami, Daniel M. Dawson, Valerie R. Seymour, Paul S. Wheatley, Russell E. Morris and Sharon E. Ashbrook
School of Chemistry, EaStCHEM and Centre of Magnetic Resonance, University of St Andrews, St Andrews, UK

The vast success of zeolites has brought the elusive goal of targeting new framework types to the forefront of research. The ADOR (assembly-disassembly-organisation-reassembly) method[1] represents a feasible approach to be followed to achieve such a goal, transforming the way new, stable and active materials can be synthesised. In this contribution, we report the ADOR synthesis of ^{17}O- and ^{29}Si-enriched UTL-derived zeolitic frameworks and their subsequent characterisation through ^{17}O and ^{29}Si solid-state NMR.
Exploiting the different stages characterising the ADOR process, the final products have been successfully ^{17}O- and ^{29}Si-enriched. Specifically, either a natural abundance Ge-UTL or a ^{29}Si-enriched Ge-UTL has been synthesised, used as the parent zeolite and then disassembled employing 41% ^{17}O-enriched $H_2{}^{17}O$ in a low-volume HCl-catalysed hydrolysis reaction.
^{17}O NMR was able to demonstrate the success of this enrichment process and it has also been possible to selectively enhance the signal from Si-OH interlayer species in cross-polarised 1D spectra. Moreover, to resolve the intrinsically broad ^{17}O spectral lineshapes, MQMAS and ^{17}O-^{29}Si correlation experiments were carried out. Furthermore, ^{29}Si NMR spectra have been usefully employed to track structural changes in silicon sites depending on hydrolysis conditions.
In conclusion, we show how ^{17}O and ^{29}Si NMR-based structural investigation proves extremely helpful to gain insights into the ADOR mechanism, shedding light on the way new and targeted zeolitic structures could be achieved.

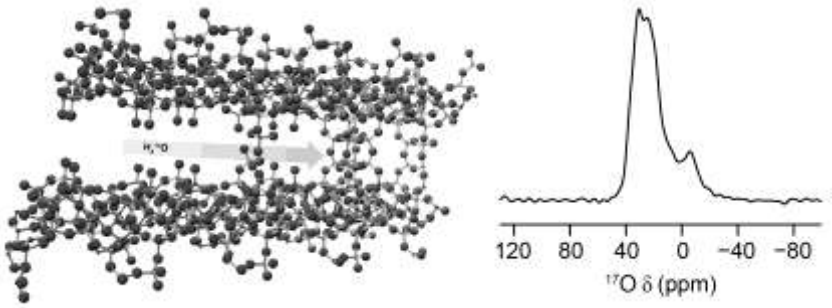

*Figure 2**. Sketch of the hydrolytic process occurring within the UTL layers (left). ^{17}O NMR MAS spectrum (20 kHz, 20.0 T) of the doubly-enriched hydrolysed UTL sample (right).***

[1] Roth et al., *Nat. Chem.* **2013**, 5, 628

(**Poster 06)**

The structure of the type III connecting segment (IIICS) of fibronectin

Eve Blumson[1,2], Matthew Cliff[1], Martin Humphries[2] and Jon Waltho[1].
[1] *University of Manchester, Manchester Institute of Biotechnology, Princess Street, Manchester, M1 7ND*
[2] *University of Manchester, Michael Smith Building, Dover Street, Manchester, M13 9PL*

The type III connecting segment (IIICS) domain of fibronectin (Fn) is able to facilitate the adherence and spreading of leukocytes and melanoma cells, highlighting the potential for therapeutic agents based on the IIICS structure, which could be used to block melanoma metastasis and reduce inflammation. Fn is mainly composed of three repeated domains, FI, FII and FIII, with the IIICS located between the 14th and 15th FIII domains ($FIII_{14}$ and $FIII_{15}$). The full-length IIICS contains two integrin binding sites and proteoglycan binding site, which are able to facilitate the cell binding properties.

The structure of the 13kDa IIICS is unknown, with it having no sequence homology to any of the repeated domains. The structure of $FIII_{15}$ is also unknown, but it is predicted to be unable to form a typical FIII fold. In order to investigate the structures and potential interactions of these domains, a range of constructs containing the IIICS flanked by $FIII_{15}$ at the C-terminus and one or more FIII domains ($FIII_{12\text{-}14}$) at the N-terminus have been expressed and analysed using NMR.

From triple resonance experiments on one of these constructs, almost complete backbone assignment of the IIICS and $FIII_{15}$ domain was possible. The dynamics of the construct were investigated through ^{15}N relaxation experiments, with this data showing the IIICS to have increased flexibility compared to the $FIII_{15}$ domain. Data analysis suggests that $FIII_{15}$ forms a unique FIII fold independently of both the IIICS and $FIII_{12\text{-}14}$ domains.

Further experiments will involve refining the structure of $FIII_{15}$ through the collection of NOE restraints. The flexibility of the IIICS will be further investigated using paramagnetic relaxation enchancement (PRE) experiments and ligand binding studies.

(**Poster 07)**

NMR Crystallography of Pharmaceutical Solids

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In the pharmaceutical industry there are various ways in which the API can be delivered, such as salts, amorphous forms and cocrystals. Pharmaceutical companies can engineer different ways of delivering the API and cocrystals are increasingly being utilised. Cocrystals are two or more different neutral molecules in the same crystal lattice. They interact via non covalent interactions such as hydrogen bonding, van der Waals and pi-pi interactions. This results in the cocrystal having physical and chemical properties which differ from the individual constituents. The excipient therefore can enhance the effect of an API.

Hydrogen bonding interactions in cocrystals have been explored which contain citric acid as the excipient. Investigations have involved a range of 1D and 2D magic angle spinning experiments which have the aim of determining intermolecular and intramolecular interactions and their distances in the cocrystal under investigation. Experiments have included: ^{13}C Cross Polarisation with Magic Angle Spinning (CP MAS), ^{14}N-^{1}H Heteronuclear Multiple Quantum Coherence (HMQC), ^{1}H-^{1}H Double Quantum with Magic Angle Spinning (DQ MAS) and ^{1}H-^{13}C Insensitive Nuclei by Enhanced Polarisation Transfer (INEPT).

Chemical shift information gained from experiments was compared with chemical shieldings calculated using the gauge-including projector-augmented wave (GIPAW) method [1,2]. Simulations were conducted to see the differences between the citric acid on its own and as a cocrystal. Hydrogen bonding interactions are interpreted in terms of changes in the chemical shift.

1 C. J. Pickard and F. Mauri, Phys. Rev. B: Condens. Matter, 2001, 63, 1-13.
2 J. R. Yates, C. J. Pickard and F. Mauri, Phys. Rev. B, 2007, 76, 1-11.

(**Poster 08)**

The FAM-N method for signal improvement in MQMAS: Description and applications under various conditions

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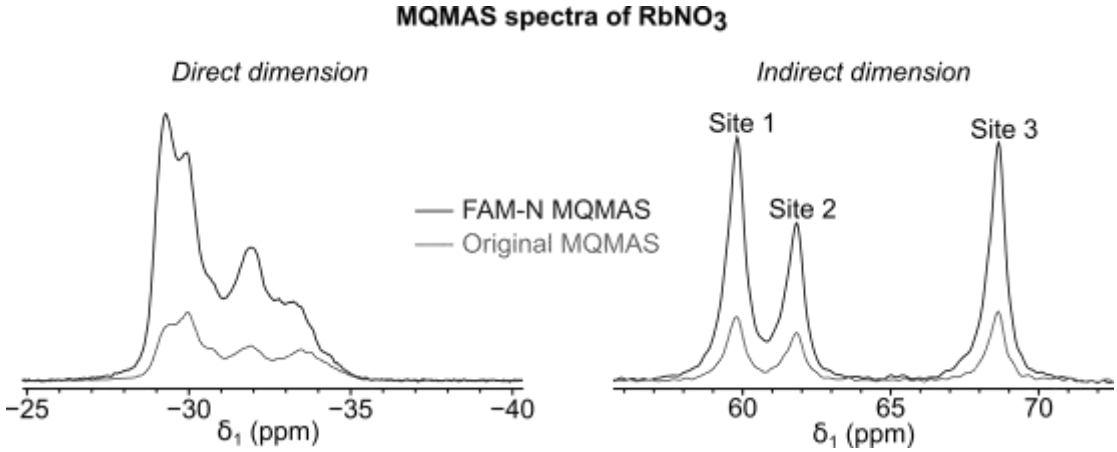

Quadrupolar nuclei comprise 75% of all NMR-active nuclei, yet their study is more challenging than spin I = 1/2 nuclei, owing to the presence of second-order quadrupolar broadening, which cannot be removed completely under magic-angle spinning (MAS). The introduction of the multiple-quantum (MQ) MAS technique[1] provides a convenient and efficient way to investigate quadrupolar nuclei through the separation of each component of the signal according to their respective quadrupolar coupling constants and isotropic chemical shifts. However, this method often suffers from inherently poor sensitivity, which decreases significantly as the MAS rate increases.[2] An MQMAS experiment consists of at least two pulses: one to excite multiple-quantum coherence and the other to convert these to observable single-quantum coherence. It has been established that this second conversion using a single pulse, as proposed in the original MQMAS experiment, has poor efficiency and numerous alternative conversion pulses have been proposed in the literature, e.g. the FAM[3] method.

We have recently developed an alternative approach using computationally pre-optimised composite pulses, termed FAM-N (FAM with N components), which consists of a succession of N subsequent and oppositely phased pulses optimised independently using a program built on MATLAB and SIMPSON. We have recently introduced FAM-N, its optimisation procedure, theoretical investigations and applications on model samples at standard MAS rate.[4] We have now explored various experimental conditions such as spins above I = 3/2, fast MAS, low-γ or strong quadrupolar interaction.

References

1. Frydman, L.; Harwood, L. *J. Am. Chem. Soc.* **1995**, *117*, 5367.
2. Amoureux, J.; Pruski, M.; Lang, D. ; Fernandez, C. *J. Mag. Res.*, **1998**, *131*, 170.
3. Madhu, P. K.; Goldbourt, A.; Frydman, L.; Vega, *S. Chem. Phys. Lett.* **1999**, *307*, 41.
4. Colaux, H.; Dawson, D. M.; Ashbrook, S. E. *J. Phys. Chem. A* **2014**, *118*, 6018.

(**Poster 10)**

Improving NMR methods to solve 3D molecular structure in solution.

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NMR spectroscopy has a wide application in the determination of three dimensional molecular structure and the use of 3-bond scalar couplings is common in solution-state NMR. Scalar coupling between nuclei separated by three bonds can be described empirically by homonuclear (^{1}H-^{1}H) [1] and heteronuclear (^{1}H-^{13}C) [2] Karplus equations relating the magnitude of the scalar coupling constant to the dihedral angle between the nuclei. Computational methods can also derive NMR properties such as chemical shift and scalar coupling constants for a given molecular structure [3].

In this report, methods of determining NMR properties computationally with Density Functional Theory (DFT) and the performance of several empirical equations relating coupling constants to structure are evaluated. The application of these to $^nJ_{HC}$ (n≥1) are compared to accurate experimental values – specifically those derived from coupled ^{13}C spectra, and further compared to a 2D experimental method (EXSIDE) to explore the accuracy of the latter. These techniques were applied to strychnine and methyl piperidines and are found to show that there is room for improvement in both experimental and computational approaches to $^nJ_{HC}$ determination.

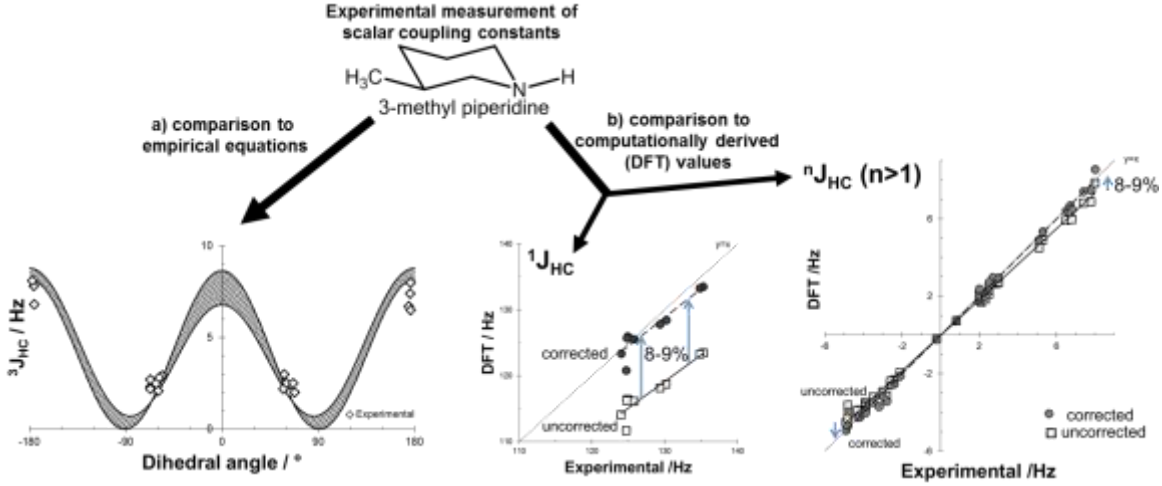

***Figure**: Experimentally measured scalar coupling constants compared to the range estimated by empirical equations for $^3J_{HC}$ (a) and computationally determined values for $^nJ_{HC}$ (b).*

[1] Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. Tetrahedron 1980, 36 (19), 2783.

[2] Palermo, G.; Riccio, R.; Bifulco, G. J. Org. Chem. 2010, 75 (6), 1982.

[3] Di Micco, S.; Chini, M. G.; Riccio, R.; Bifulco, G. European J. Org. Chem. 2010, 2010 (8), 1411.

(**Poster 11**)

Using experimental NMR data to evaluate molecular dynamics forcefields: a novel benchmark system.

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NMR spectroscopy and molecular dynamics (MD) simulations are highly complementary techniques to probe both the structure and dynamics of proteins. Improvements in MD simulations have made all-atom simulations on millisecond time-scales accessible for small to medium sized proteins. This has facilitated systematic assessment of available force-fields which are continuously improved to correct for discrepancies between simulations and experimental findings. However, recent comparison data sets are often limited to well-folded proteins, intrinsically disordered proteins (IDPs) and peptides. Despite their biological significance, extended dynamic loops and local unstructured regions are largely neglected.

Here we compare five force-fields characterising the dynamic TIL'-E' domains of the essential haemostatic protein von Willebrand Factor, a system containing both a well-folded region and a long, flexible loop. We have compared trajectories to both recently solved NMR structural ensembles and experimental NOE and chemical shift data. Our results show that force-fields generally deal well with folded structures, whereas the flexible structural elements with fewer interactions are more challenging. There is a strong argument that optimising MD force-fields against only globular proteins and IDPs is limited and the development of more versatile force-fields should also consider flexible systems containing all facets of protein structure and dynamics.

(**Poster 12)**

On resonance phase alternated CWFP sequences for rapid and simultaneous measurement of relaxation times

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T_1 and T_2 relaxation times have been often used as probes for physical-chemical properties in several time-domain NMR applications (TD-NMR). T_2 measurements are usually achieved using the Carr-Purcell-Meiboom-Gill (CPMG) pulse sequence, a rapid and robust method. On the other hand, the traditional methods for determining T_1 require long measuring. This led us to develop simple methods for rapid and simultaneous determination of T_1 and T_2 using Continuous Wave Free Precession (CWFP) and Carr-Purcell Continuous Wave Free Precession (CP-CWFP) pulse sequences. Nevertheless, a drawback of these sequences is that they require specific adjustment of the frequency offset or the time interval between pulses (T_p). Here we present an alternative form of these sequences, named as $CWFP_{x\text{-}x}$, $CP\text{-}CWFP_{x\text{-}x}$, where a train of $\pi/2$ pulses with phases alternated by π make possible to perform the experiments on-resonance and independently of T_p, when $T_p < T_2^*$. Moreover, a CPMG type sequence with $\pi/2$ refocusing pulses shows similar results as CWFP when the pulses alternate between y and –y axis, $CPMG_{90y\text{-}y}$. In these approaches, the relaxation times are determined by the magnitude of the signals, after the first pulse $|M_0|$ and in the steady-state $|M_{ss}|$, as well as the exponential time constant T^* to reach the steady-state regime, as in conventional CWFP. $CP\text{-}CWFP_{x\text{-}x}$ and $CPMG_{90y\text{-}y}$ show the highest dynamic range to measure T^* among CWFP sequences and, therefore, are the best techniques to measure T_1 and T_2 because they are less susceptible to SNR and can be used for any T_1/T_2 ratio.

(**Poster 13)**

Phase Transitions and Disorder in Pyrochlore Ceramics: a Solid-State NMR and DFT study

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Recently, much attention has been focused on the use of pyrochlores ($A_2B_2O_7$) as components of ceramic nuclear wasteforms, with the ultimate aim being the long-term storage of actinide-bearing radioactive waste. Many ceramics are highly resilient and can accommodate high waste loadings. Pyrochlore materials are ideal candidates for the immobilization of radioactive actinides as the A site being able to accommodate larger cations in eight-fold coordination, *e.g.*, La^{3+}, while the B site contains smaller cations in six fold coordination, *e.g.*, Sn^{4+}. If r_A/r_B is between 1.46 and 1.78, the formation of a pyrochlore phase is favoured. Below this, a disordered defect fluorite structure (A_4O_7) is predicted to form.

A recent investigation on phase transitions between pyrochlore and defect fluorite phases has revealed how solid-state NMR is an excellent probe of the local structure of these materials, with first-principles density functional theory (DFT) calculations also used to aid interpretation of the composite lineshapes observed experimentally.[1] Additionally, previous ^{89}Y and ^{119}Sn MAS NMR has facilitated the investigations on disorder in ceramics.[2,3] Adopting a similar approach, a phase transition between defect fluorite and pyrochlore phases (in $Y_2(Sn,Hf)_2O_7$) and pyrochlore and monoclinic phases (in $La_2(Sn,Ti)_2O_7$) is carried out using ^{119}Sn and ^{89}Y MAS NMR. The end members, $Y_2Hf_2O_7$ and $La_2Ti_2O_7$,[4] are predicted to form defect fluorite and monoclinic structures, respectively. ^{17}O enrichment of such oxides has also been undertaken to probe the anion disorder in these materials.

[1] Ashbrook, S.E. *et al*., *Phys. Chem. Chem. Phys.,* **2015***, 17,* 9049–9059.
[2] Ashbrook, S.E. *et al*., *J. Phys. Chem. C*, **2009,** *113,* 18874–18883.
[3] Ashbrook, S.E. *et al*., *Phys. Chem. Chem. Phys.,* **2011**, *13*, 488–497.
[4] Harvey, J.E. *et al., J. Mater. Chem.,* **2006**, *16*, 4665–4674.

(Poster 14)

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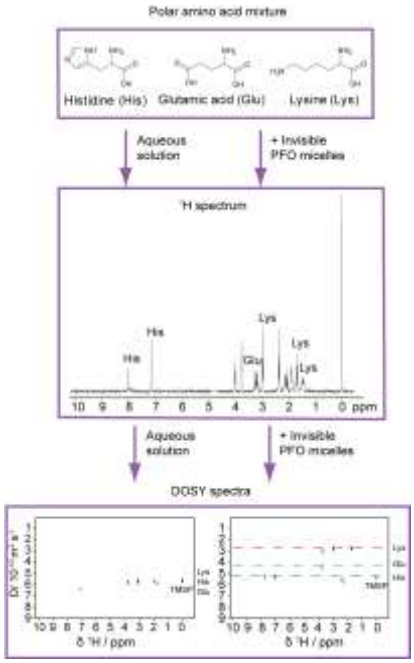
Diffusion-ordered spectroscopy (DOSY) is a family of NMR experiments for mixture analysis that disperse the resonances of different species into a second dimension according to their diffusion coefficients (*D*). However this is not effective for mixtures of species with similar rates of diffusion. A way to improve the DOSY dispersion in such systems is to add a co-solute to which the different species bind to different extents, thus perturbing their diffusion differentially.

This is known as matrix-assisted DOSY (MAD) [1], like chromatography, it exploits specific chemical interactions to drive the diffusion separation. A problem in MAD is that co-solutes introduce resonances that can overlap with signals of the species of interest. This can be avoided by using perdeuterated surfactants [2] that are almost invisible by ^{1}H NMR, or species with a very simple spectrum [3]. Here we report the use of sodium perfluorooctanoate (PFO) micelles that do not contribute any resonances to separate the ^{1}H signals of mixtures of amino acids.

The figure below shows that the addition of 100 mM PFO to a mixture of glutamate, histidine and lysine at pH 8 lifts the degeneracy in *D*, allowing the signals of the amino acids to be distinguished. Measurements of *D* as a function of pH for these and other amino acid mixtures can be modelled as equilibria between free and micelle-bound species in different protonation states, with binding significantly perturbing the ionization equilibria. Results show that binding is primarily driven by char-charge interactions but that amphiphilicity also plays a part.



References:

1. H. S. Evans Robert., Nilsson Mathias, Morris Gareth A., Analytical Chemistry, 2009, 81, 4548-4550.
2. M. E. Zielinski and K. F. Morris, Magnetic Resonance in Chemistry, 2009, 47, 53.
3. S. Huang, J. Gao, R. Wu, S. Li and Z. Bai, Angewandte Chemie International Edition, 2014, 53, 11592.

(**Poster 16)**

Multinuclear Solid-State NMR Study of Metallophosphates

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With network topologies analogous to zeolites, metallophosphates have potential applications in catalysis, ion exchange, gas absorption and separation.[1] Aluminophosphates (AlPOs) and gallophosphates (GaPOs) can adopt a large variety of structures, some unavailable to aluminosilicate zeolites. The catalytic activity of aluminosilicates arises from the Brønsted/Lewis acidity of the framework. The main drawback of pure $AlPO_4$ and $GaPO_4$ frameworks, in comparison to aluminosilicates, is their charge neutral framework and, hence, lack of acidic sites, which limits their use in heterogeneous catalysis. Framework charges can be incorporated by aliovalent substitution on either the metal or phosphate sites.

This work focuses on the chabazite-type frameworks, AlPO-34 and GaPO-34. We have synthesised the silicon-substituted AlPO, SAPO-34 and attempted to prepare the analogous Si-substituted GaPO, GaSPO-34. The synthesis of GaPO-34 is poorly understood and often yielded an impurity phase (termed GaPO-X). [2]

Here we present a multinuclear solid-state NMR study of two forms of GaPO-X prepared with methylimidazole and pyridine, which provides insight into the local structure of these materials. In addition we also investigate the local structure and disorder in Si-substituted AlPO and GaPO-34.

1. L. Han et al. J. Cryst. Growth, 2008, 311, 167.
2. C. Schott-Darie *et al. Stud. Surf. Sci. Catal.,* 1994, 84, 101.

(**Poster 17)**

Developing Models for the Earth's Core Formation through Multinuclear Solid-State NMR of High-Pressure Glasses

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Sharon Ashbrook [1]
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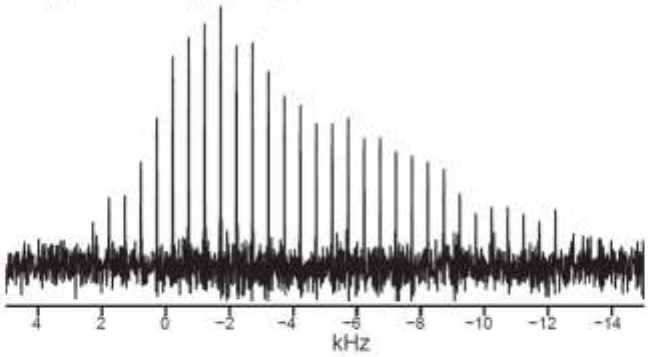
Magma has been involved in many important geological processes throughout the Earth's history: shaping landforms, transporting and concentrating metals, and enabling the Earth to segregate a metallic core and a silica-rich crust. Many of these processes occur deep in the Earth under high-pressure conditions. Minerals and melts reduce their volume under increasing pressure by changing their structure, for example, coesite $^{[4]}SiO_2$ changes to stishovite $^{[6]}SiO_2$ at pressures greater than around 9 GPa.[1] Understanding the structure and properties of magma at high pressure is necessary to fully understand these processes. The key to these processes is the knowledge of partitioning behaviour of elements between coexisting phases (*e.g.*, molten silicate and molten metal). Gradual changes in the coordination of cations such as Al and Si is well established,[2] however there have been very few studies of the coordination environment of trace elements in melts. In this work we have used multinuclear (^{17}O, ^{25}Mg, ^{27}Al, ^{29}Si and ^{71}Ga) solid-state NMR spectroscopy to investigate the changes in coordination of major elements (Si, Mg and Al) and a trace element (Ga), 3000 ppm in gallium-substituted calcium-magnesium-alumino-silicate glasses melted at different pressures. This has allowed us to understand whether the changes in coordination of trace elements is related to the changes in major elements and, hence, develop models for the Earth's core formation and the depths of magma origin.



^{25}Mg Natural abundance (14.1 T) CPMG-MAS (55 kHz) spectrum of glass sample melted at 6 GPa.

1 Zhang, J., Utsumi, W., Liebermann, R.C., 1996. *Phy. Chem. Miner.* 23, 1–10.
2 Allwardt, J.R., *Am. Mineral.*, **2005,** 90, 1218–1222.

(**Poster 19)**

Beyond Karplus; Using a quantitative method to determine stereochemistry from geminal coupling constants

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An equation designed to predict geminal carbon-proton coupling constants ($^2J_{CH}$) in organic molecules is being empirically derived using a large selection of $^2J_{CH}$ calculations (at the hybrid DFT MPW1PW91/6-311G(d,p) level). The equation takes the form of a Karplus-like curve and is designed to take into account any substituents that affect the ^{1}H-C-^{13}C coupling pathway, most importantly substituents on the α carbon (^{13}C), as these have been shown to produce a strong effect on $^2J_{CH}$, with the effect dependant on the dihedral angle (φ) between the substituent and the coupled proton. Using a set of ethane models, with various electronegative substituents (C,N,O,F,P,S,Cl,Br) in various substitution patterns and with φ being varied in steps of 30° between 0° and 360° a database of $^2J_{CH}$ values was generated and used to create a quantitative prediction tool. The equation will be tested against experimental results from a preliminary library of organic molecules to confirm its validity, with correction factors introduced to deal with any issues that are found. This tool will enable chemists to exploit $^2J_{CH}$ values in much the same way as $^3J_{HH}$ and Karplus are used currently, however it should be noted that there are many more $^2J_{CH}$ values in most organic molecules than $^3J_{HH}$ So we believe $^2J_{CH}$ could become an important tool in aiding the structural elucidation of molecules via NMR.

(**Poster 20)**

Structural Studies of Inflammation Receptor Integrin Mac-1 I domain by NMR Spectroscopy to Characterise Activation and Interaction with GPIbα

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In response to vascular injury, inflammation receptor Mac-1 is activated, enabling the firm adhesion of leukocytes to the newly formed blood clot. The arrest of the leukocytes on the clot is governed by the interaction between Mac-1 and the platelet counter-receptor glycoprotein Ibα (GPIbα). This interaction facilitates leukocyte migration into the peripheral tissue resulting in inflammation and therefore provides a novel molecular target for the treatment of vascular inflammatory diseases.

Within the Mac-1 heterodimer complex the major ligand-binding region is the I domain situated at the extracellular N-terminus of the α-chain. Integral to binding interactions is the Mg^{2+} bound at the metal ion adhesion site (MIDAS) located on the top face of the I domain.

3D NMR spectroscopy has been used to characterise the wild-type I domain, alongside a number of engineered low and high affinity structural mimics. Used in conjunction with additional methods including: selective amino acid unlabelling, perdeuteration and paramagnetic studies this has enabled the 80 % assignment of the ^{15}N I domain HSQC. This work has provided insights into the cation and ligand binding properties of the I domain following activation. Furthermore the preliminary mapping of the binding interface with GPIbα has been undertaken and further evidence of this interaction is also presented by SPR kinetic studies which have enabled the measurement of ligand affinity and demonstrated the MIDAS dependence of the interaction.

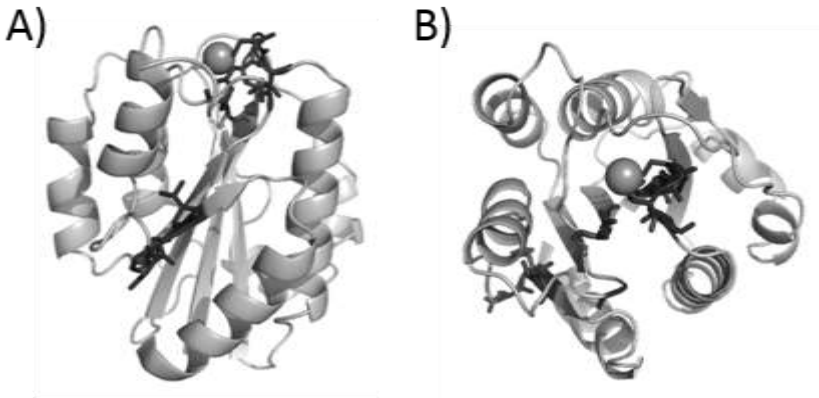

Figure 3:Mac-1 I domain residues located at the GPIba N-terminal domain binding interface are highlighted in dark grey, showing A) side view and B) top view

(**Poster 22)**

Extended Acquisition Time (EXACT) NMR

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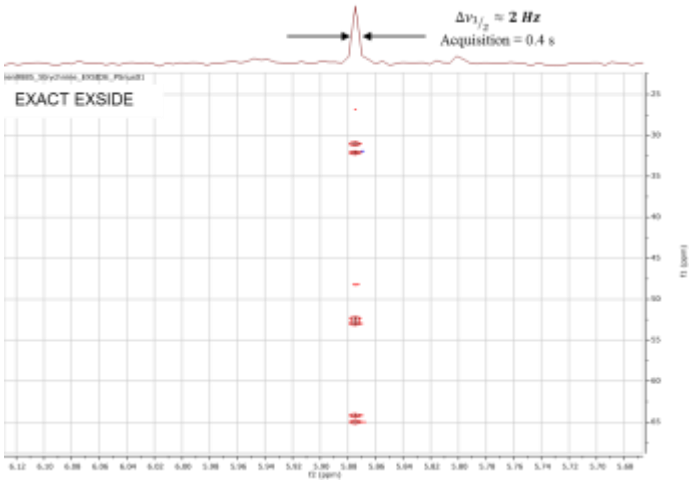
The overall duration of NMR acquisition time (AQ) is a function of the dwell time, DW (defined by the Nyquist condition) and the total number of specified data points, TD (AQ = DW*TD), which in turn defines the frequency resolution of the spectrum after Fourier transformation. The duration of acquisition time is, however, limited by relaxation. Recently, broadband decoupling techniques (^{1}H – ^{1}H and ^{1}H – ^{13}C or X) have become of significant interest to enhance the resolution and often the sensitivity of NMR spectra via removal of scalar couplings between coupled species. Excellent examples of this are the real-time decoupled HOBS (HOmonuclear Band-Selective[1, 2]) ^{1}HNMR and 'pure-shift' HSQC[3] where band- or isotope-selective pulses on the target (active) and coupled partner (passive) spins are applied during '*J*-refocussing' breaks in the acquisition period in order to refocus coupling. The downside of these methods is that data is not sampled during the *J*-refocussing breaks, which artificially shortens the acquisition time – leading to artificial line broadening in the spectrum. This is especially problematic when highly selective (and thus long) pulses are used in the *J*-refocussing elements.

Herein, we introduce a new method EXACT (**EX**tended **AC**quisition **T**ime) which not only retains the full length of the acquisition time but offers the flexibility of extending this period as well. The key here is to keep the active spins unperturbed during the *J*-refocusing period but achieving decoupling by pulsing on the passive spins. Data points (with zero intensity) are acquired during the *J*-refocusing period and these points are subsequently reconstructed to give an FID which reflects the 'true' T_2^* relaxation of the active species with enhanced resolution and sensitivity. Substantial improvements in linewidths can be made – with <2Hz lines achievable in most cases examined to date.



1. Castañar, L.; Nolis, P.; Virgili, A.; Parella, T., Full Sensitivity and Enhanced Resolution in Homodecoupled Band-Selective NMR Experiments. *Chemistry – A European Journal* **2013,** *19*, 17283-17286.

2. Castañar, L.; Saurí, J.; Nolis, P.; Virgili, A.; Parella, T., Implementing homo- and heterodecoupling in region-selective HSQMBC experiments. *Journal of Magnetic Resonance* **2014,** *238*, 63-69.

3. Paudel, L.; Adams, R. W.; Király, P.; Aguilar, J. A.; Foroozandeh, M.; Cliff, M. J.; Nilsson, M.; Sándor, P.; Waltho, J. P.; Morris, G. A., Simultaneously Enhancing Spectral Resolution and Sensitivity in Heteronuclear Correlation NMR Spectroscopy. *Angewandte Chemie International Edition* **2013,** *52*, 11616-11619.

(**Poster 23)**

(Very!) Broadband DOSY

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Broadband DOSY

A broadband DOSY Oneshot[4] sequence was built using the elements described below; uniform performance is achieved over almost a full 300 kHz bandwidth, with no loss in sensitivity, allowing DOSY to be performed over very wide spectral widths.

Broadband Excitation and Refocusing

In principle, a pair of chirp pulses of appropriate relative amplitude can be used to excite very wide bandwidths[2]. Unfortunately, phase errors build up towards the edges of the frequency range, reducing the bandwidth. A further problem is that the signal phase is extremely sensitive to B_1 with B_1 inhomogeneity causing large losses in signal. The double chirp sequence was, therefore, adapted (a) to compensate for B_1 error and (b) to correct phase errors. Uniform, constant-phase broadband excitation was achieved, allowing a 300 kHz bandwidth with 15 kHz RF amplitude, with no undue B_1 sensitivity and no loss in sensitivity. Broadband refocusing can be achieved using an adiabatic composite 180°180°180° chirp pulse[3].

References

(1) Bohlen, J. M., M. Rey and G. Bodenhausen, *J. Magn. Reson.* **1989,** 84, 191-197.
(2) Hwang, T. L., P. C. M. van Zijl and M. Garwood, *J. Magn. Reson.* **1997,** 124, 250-254.
(3) Pelta, M. D., G. A. Morris, M. J. Stchedroff and S. J. Hammond, *Magn. Reson. Chem.* **2002,** 40, S147-S152.

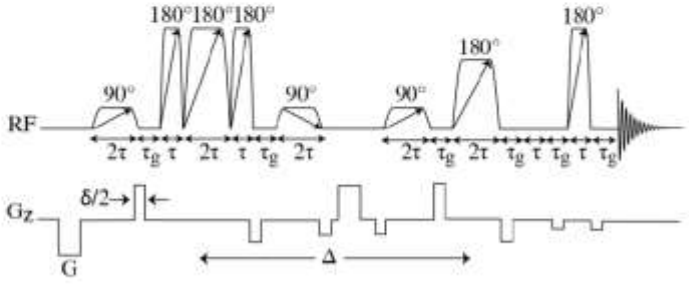

Fig.1. Broadband Oneshot pulse sequence.

(**Poster 24)**

Understanding Nanoscale Organisation of Tailored Supramolecular Hydrogels using NMR Spectroscopy

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Low Molecular Weight Gelators form complex 3D supramolecular structures held together by non-covalent interactions that are able of entrapping high contents of water. Despite having a wide range of applications in advanced drug delivery and tissue engineering, the mechanism of formation of such organized fibrous networks is not fully understood. The aim of this project is to investigate structure and dynamics of thermoreversible hydrogels through the detection of rigid, semi-solid and mobile parts of the supramolecular network using a combination of solution, solid state and HR-MAS NMR techniques.

Gelation process of single and multi-component amino acid based hydrogels was investigated to correlate different levels of self-assembly with local structure and molecular mobility. ^{13}C NMR spectra obtained using ^{1}H-^{13}C Cross Polarisation (CP) and ^{13}C Direct Excitation enabled us to distinguish between solid parts of the gel network and gelator molecules entrapped between gel fibrils. Furthermore, application of ^{1}H-^{13}C HSQC in solution and HR-MAS NMR enabled differentiating between co-gelator molecules incorporated in the solid network of the hydrogel (Figure 1), and co-gelators that remained fully solubilised in water. Finally, changes of dynamics of the system upon gelation were verified through variable temperature ^{1}H T_1 relaxation measurements and saturation transfer experiments.

In conclusion, complementary techniques of NMR spectroscopy have proven to be a powerful method to investigate dynamics and different organisation levels of complex heterogeneous materials essential in the design of tailored supramolecular hydrogels for advanced drug delivery.

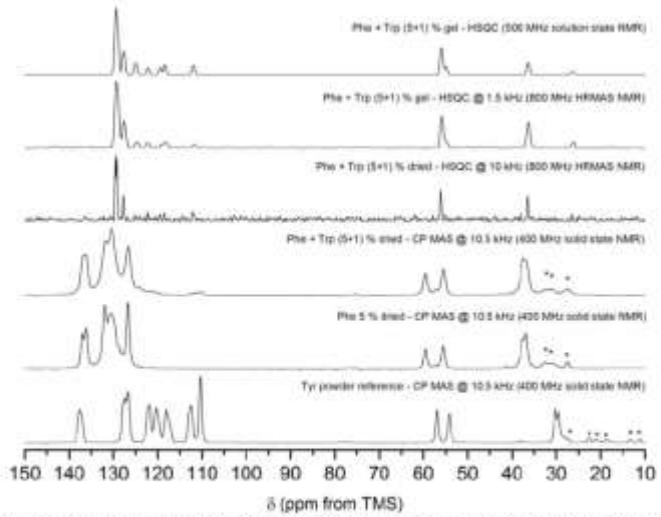

Figure 1. ^{13}C spectra of wet and dried samples of the hydrogel of Phe + Trp (5+1) % in D_2O (50 mg mL^{-1}) acquired in solid state Bruker Avance III 400 MHz, HRMAS Bruker Avance I 800 MHz and solution state Bruker Avance I 500 MHz NMR spectrometers.

(Poster 25)

Solid-State NMR Investigation of Supported Metal Catalysts: Probing the Metal-Support Interaction

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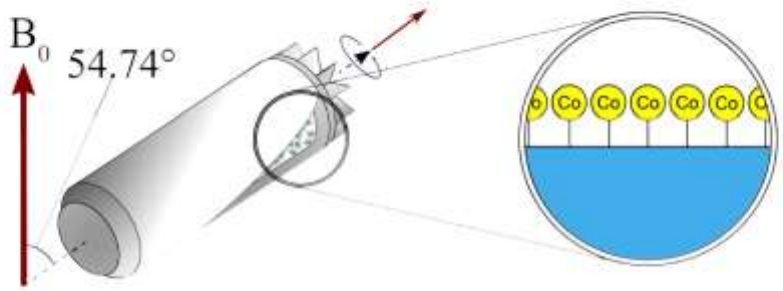
Heterogeneous catalysis plays a key role in several industrial processes. One of the most prominent is Fischer-Tropsch (F-T) synthesis, which involves the conversion of syngas to hydrocarbons, and is an important technology in regions where oil is not abundant. F-T synthesis reactions are catalysed by iron, cobalt or ruthenium loaded onto oxide supports such as TiO_2, SiO_2 and Al_2O_3. Co-based catalysts are generally favoured for F-T synthesis due to their high activity and high selectivity for linear hydrocarbons.



The metal-support interaction (MSI) was first identified by Tauster *et al.* in 1978 for group 8 noble metals supported on TiO_2. It was found that after a catalyst was subjected to high-temperature reduction, CO and H_2 sorption significantly decreased. This was not due to metal agglomeration, but instead formation of bonds between the metal and support atoms/cations. MSI has also been described for transition metals supported on SiO_2 and Al_2O_3.

Solid-state NMR is an effective probe of the local structure of materials, with no need for long- or short-range order. Element specificity and lack of restriction based on crystalline size also make NMR a powerful complement to diffraction-based techniques.

A series of model catalysts and catalyst supports were prepared via different preparation methods and conditions, with parameters such as metal loading and crystallite size distribution being varied. ^{1}H and ^{27}Al solid-state NMR experiments were used to study the interfacial relationships in these model samples, in order to probe the underlying properties affecting the formation and extent of the metal-support interaction.

List of delegates

1.	Dr Ralph Adams	University of Manchester
2.	Ahmed Alharbi	University of Manchester
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5.	Jessica Bame	University of Bristol
6.	Dr Juraj Bella	University of Edinburgh
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12.	Gemma Candy	University of Warwick
13.	Prof Timothy Claridge	University of Oxford
14.	Henri Colaux	University of St Andrews
15.	Dr Matt Cude	Royal Society of Chemistry
16.	Azzedine Dabo	University of Warwick
17.	Dr Adrienne Davis	University of Nottingham
18.	Hannah Davies	University of Liverpool
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24.	Arantxa Fernandes	University of St Andrews
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29.	Kenneth Inglis	University of Liverpool
30.	Prof Graham Jackson	University of Cape Town
31.	Nasima Kanwal	University of St Andrews
32.	Dr James Keeler	Cambridge University
33.	Hannah Kerr	University of Durham
34.	Dr Alan Kenwright	Durham University
35.	Dr Peter Kiraly	University of Manchester
36.	Prof Yaroslav Khimyak	University of East Anglia
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50.	Dr John Parkinson	University of Strathclyde
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57.	Dr Davy Sinnaeve	University of Gent
58.	Emma Thompson	University of Birmingham
59.	Dr Linda Trivoluzzi	University of Manchester
60.	Dr Sandra van Meurs	Bruker UK Ltd
61.	Dr Neil Wells	University of Southampton
62.	Dr Huw Williams	University of Nottingham
63.	Dr Corinne Wills	University of Newcastle