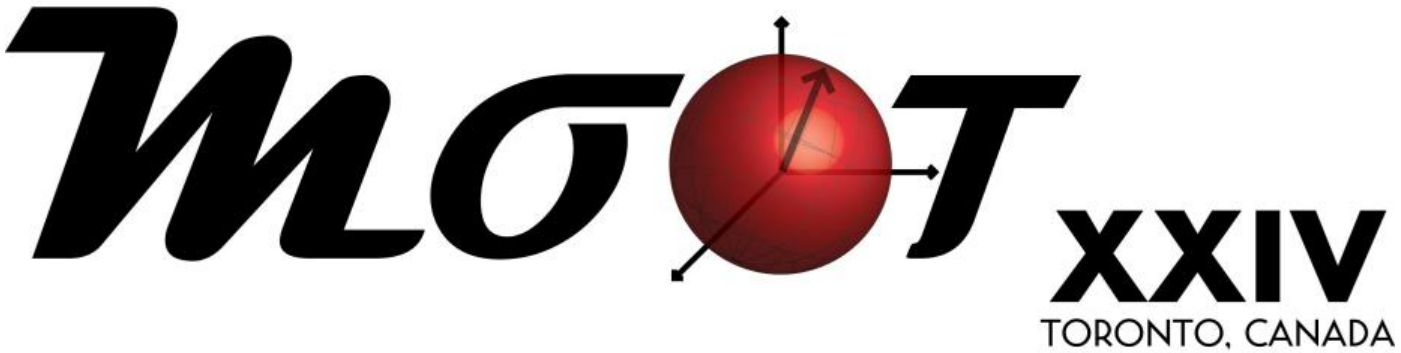

Conference Programme

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Conference Agenda

Friday October 21, 2011
University of Toronto, Sidney Smith SS2135

1:00-7:00 Agilent Users Meeting: hosted by Agilent Technologies and the University of Toronto Department of Chemistry

Saturday October 22, 2011
The Hospital for Sick Children, Hollywood Theatre (Room 1248)

8:00-8:45 MOOT XXIV Registration

8:45-9:00 Opening Remarks

9:00-9:40 Keynote Lecture – Lewis Kay

9:40-10:40 Morning Session I

10:40-11:00 Coffee

11:00-12:00 Morning Session II

12:00-1:30 Lunch

1:30-2:10 Tutorial Session – Glenn Facey, Solid State NMR for Newbies

2:10-2:50 Afternoon Session

3:00-5:00 Poster Session

6:30- Gala Dinner and Reception (Hart House, University of Toronto)

Sunday October 23, 2011
The Hospital for Sick Children, Hollywood Theatre (Room 1248)

9:00-9:30 Sunday Opening Lecture – Gillian Goward

9:30-10:30 Morning Session I

10:30-10:45 Coffee

10:45-11:15 Guest Session – David Weliky

11:15-12:15 Morning Session II

12:15-12:30 MOOT XXIV Closing Remarks

Abstracts

Opening Keynote: Lewis Kay – Saturday, 9:00-9:40

Morning Session I – Saturday, 9:40-10:40

Probing Human Serum Albumin - Alzheimer's Aβ Peptide Interactions by Solution NMR

Julijana Milojevic, Giuseppe Melacini
McMaster University

The aggregation of the Alzheimer's Aβ peptide is controlled by Aβ binding proteins, such as human serum albumin, which bind Aβ oligomers and prevent fibril formation (1, 2, 3). Recently we have investigated mechanism, stoichiometry and binding affinity of albumin-Aβ interactions to show that albumin selectively binds Aβ oligomers through binding sites that are evenly partitioned across the three albumin domains and with affinities in the 10-100 nM range (1). Furthermore, the interactions of albumin with the Aβ were investigated at subdomain and residues resolution, using the point and sub-domain deletion mutants of HSA domain 3 in combination with Saturation Transfer Difference (STD) and 15N-1H HSQC experiments. The results were used to assess possible competitions between Aβ and other endogenous HSA ligands as well as to design potent Aβ self-association inhibitor.

(1) Milojevic, J., et. al., 2011. Biophys. J. 100(1):183-92.
(2) Milojevic, J., et. al., 2009. Biophys. J. 97, 2585-2594.
(3) Milojevic, J., et. al., 2007. J. Am. Chem. Soc. 129, 4282-4290.

Thermodynamics and Kinetics of Monomer/Octamer Exchange in Prion Protein

M. Sameer Al-Abdul-Wahid, Karen Simonetti, Carlene Starck, Petro Czupiel, Simon Sharpe, R. Scott Prosser
University of Toronto

Prion diseases occur when naturally present proteins mis-fold into a diseased state; the mis-folded proteins eventually aggregate into macroscopic fibrils that occupy the neural tissues of the host. These misfolded proteins have been shown to form non-fibrillar oligomers which are cytotoxic and may be a key element of the aggregation pathway.

Recent studies of a protein fragment composing residues 90-232 of Syrian hamster prion protein (SHaPrP) indicate the non-fibrillar oligomers comprise eight mis-folded SHaPrP subunits, and are in exchange with mis-folded monomeric SHaPrP. What are the thermodynamics and kinetics parameters driving the formation of this disease-causing aggregate? How is the monomer/octamer equilibrium affected by pressure and temperature? In order to address these questions, we biosynthetically incorporated ^{19}F-tryptophan in place of the two tryptophan residues in SHaPrP, and explored the monomer/octamer equilibrium using solution-state ^{19}F NMR spectroscopy.

Owing to the high sensitivity of the ^{19}F chemical shift to local environment, we identify resonances associated with both monomeric and octameric SHaPrP. While ~50% of SHaPrP is in monomeric form at 25 °C, the octameric form is favoured at higher temperatures. In the temperature range 25 °C to 40 °C, octamerization is entropically favoured (> 250 J/mol K), but comes at an enthalpic cost (> 90 kJ/M). While we cannot detect monomer/octamer exchange at 25°C, increasing pressure results in increased exchange rates (up to 12.6 ± 1.5 Hz at 2000 bar), and broadened 19F resonances. We present results from our current work on SHaPrP, and discuss the thermodynamic and kinetic characteristics of monomer/octamer exchange at pressures ranging from 1 to 2000 bar.

Multinuclear Solid-State NMR of Magnus' Green and Pink Salts

Bryan E. G. Lucier, Michal D. Roslan, Robert W. Schurko
University of Windsor

Magnus' Green Salt (MGS), $[Pt(NH_3)_4][PtCl_4]$, is a stacked, highly insoluble 'double-salt' initially reported by Magnus in 1828.[1] The unique green colouring of MGS in comparison to the colours of its individual constituents, the colourless $[Pt(NH_3)_4]^{2+}$ cation and red $[PtCl_4]^{2-}$ anion, had puzzled chemists for over one hundred years, until it was characterized as a one-dimensional polymeric complex of square-planar Pt layers in 1957.[2] The unique colour of MGS is attributed to platinum-platinum metallophillic interactions between adjacent layers.[3,4] Interestingly, the synthesis of MGS may also generate a kinetically unstable co-product, Magnus' Pink Salt (MPS), which exhibits a faint pink

colour due to a longer Pt-Pt distance.[2] However, characterization of these remarkably insoluble complexes and, in particular, determination of the interlayer Pt-Pt distance in MPS, remains challenging.

Platinum has a receptive NMR-active isotope, ^{195}Pt (I = 1/2), which has a chemical shift interaction that is extremely sensitive to even the subtlest structural changes. Solid-state ^{195}Pt NMR (SSNMR) is an attractive option for the characterization of MGS and MPS, and in particular, for investigating the impact of Pt-Pt metallophillic interactions on the ^{195}Pt CS tensor. The square planar Pt(II) environments in both MGS and MPS result in powder patterns that are typically too broad to acquire using conventional SSNMR experiments (e.g., CP/MAS, etc.); as such, ^{195}Pt SSNMR studies of these compounds have not yet been reported.

Recently, we introduced the WURST-CPMG pulse sequence[5] for the purpose of rapid static acquisition of broad powder patterns with high S/N,[6] rendering these compounds plausible targets for ^{195}Pt, as well as ^{14}N and ^{35}Cl, SSNMR experiments. Multinuclear SSNMR of both MGS and MPS, along with complementary spectroscopic methods and DFT calculations, provide insight into the structure of MPS.

(1) Magnus, G. *Pogg. Ann.* **1828**, *11*, 242.
(2) Atoji, M.; Richardson, J. W.; Rundle, R. E. *J. Am. Chem. Soc.* **1957**, *79*, 3017.
(3) Pyykko, P. *Chem. Rev.* **1997**, *97*, 597.
(4) Pyykko, P. *Chem. Soc. Rev.* **2008**, *37*, 1967.
(5) O'Dell, L. A.; Schurko, R. W. *Chem. Phys. Lett.* **2008**, *464*, 97.
(6) O'Dell, L. A.; Rossini, A. J.; Schurko, R. W. *Chem. Phys. Lett.* **2009**, *468*, 330.

Morning Session II – Saturday, 11:00-12:00

BRAIN-CP: Using BRoadband Adiabatic INversion for Cross Polarization in Wideline SSNMR Spectra

Kristopher J. Harris, Bryan E.G. Lucier, Adonis Lupulescu, Lucio Frydman, Robert W. Schurko
University of Windsor

Cross-polarization (CP) is applied extensively in solid-state NMR spectroscopy because the moderate thermal polarization of low-gamma nuclei can be replaced with that of abundant, high-gamma nuclei.[1] The S/N gain of CP operation is often further enhanced by an increased repetition rate associated with the generally shorter T_1 values of the high-gamma nuclei. While CP is extremely useful for standard nuclei (^{13}C, ^{15}N, ^{29}Si, ^{31}P, etc.), there are many important nuclides for which large anisotropic interactions broaden the patterns well beyond the excitation bandwidth of CP. As the dilution of spectral intensity over large frequency regions is precisely the situation in which a S/N gain would be most valuable, a method for increasing the excitation bandwidth of CP is an important goal. Accordingly, we have begun investigating the use of frequency-swept adiabatic inversion pulses[2] for providing the CP matching condition.[1] Such pulses have been incorporated into a new sequence, referred to here as BRoadband Adiabatic INversion for cross polarization (BRAIN-CP), which can yield an approximately five- to ten-fold increase in the excitation bandwidth of CP. Experiments using ^{1}H nuclei to polarize ^{119}Sn, ^{199}Hg, ^{207}Pb, or ^{195}Pt nuclei with excitation bandwidths up to 0.5 MHz will be presented. Experimental considerations for applying BRAIN-CP will be outlined, as well as a brief explanation of the theory.

[1] S. R. Hartmann and E. L. Hahn *Phys. Rev.* **1962,** *128,* 2042–2053.
[2] E. Kupče and R. Freeman *J. Magn. Reson. Ser. A* **1995,** *115,* 273–276.

New Methods for Direct Detection of Solid-State ^{14}N NMR Spectra

Stanislav L. Veinberg, Chris R. Mireault, Zackary W. Friedl, Kris J. Harris, Luke A. O'Dell Robert W. Schurko
University of Windsor

^{14}N solid-state NMR (SSNMR) spectroscopy is not widely used, despite the high natural abundance of ^{14}N (99.63%) and the need for costly isotopic labelling with the spin-1/2 ^{15}N nuclide. This is due to the 'unfavourable' NMR characteristics of the ^{14}N nucleus (i.e., spin-1, low-γ [$\gamma = 1.93 \times 10^7$ rad T^{-1} s^{-1}] and a moderate nuclear quadrupole moment [$eQ = 20.44 \times 10^{-31}$ m^2]). Recent publications have demonstrated that the utilization of swept-frequency (chirped) pulses and CPMG echo train acquisitions enable the rapid acquisition of ^{14}N SSNMR spectra at intermediate and ultra-high magnetic fields.[1,2] Such spectra typically range from hundreds of kHz to several MHz in breadth, and cannot be obtained using conventional rectangular pulses and spin-echo experiments, due to both their breadths and very low S/N. Furthermore, the ^{14}N electric field gradients (EFG) that give rise to these broad patterns are extremely sensitive to the local nitrogen environments (e.g., hydrogen bonding) as well as dynamical motions at the molecular level.[2,3] We present an introduction to experiments involving the direct detection of ^{14}N NMR spectra. Experimental methodologies for obtaining high quality ^{14}N SSNMR spectra of model systems will be discussed, as well as potential applications of such methods to systems of increasing complexity. Correlations between nitrogen structural motifs and experimental findings are discussed with the aid of complementary first principles calculations of ^{14}N EFG tensors, which are conducted using linear augmented plane wave methods.

(1) O'Dell, L. A.; Schurko, R. W. *Phys. Chem. Chem. Phys.* 2009, **11**, 7069.
(2) O'Dell, L. A.; Schurko, R. W.; Harris, K. J.; Autschbach, J.; Ratcliffe, C. I. *J. Am. Chem. Soc.* 2011, **133**, 527.
(3) Mineva, T.; Gaveau, P.; Galarneaut, A.; Massiot, D.; Alonso, B. *J. Phys. Chem. C.* 2011.

Analysis of Lithium Ion Battery Materials Using Ex-Situ Quadrupolar Solid-State NMR
T. Leigh Spencer, Gillian R. Goward
McMaster University

The development of novel materials for lithium ion batteries has been a challenge for many years.[1] The introduction of electric and hybrid vehicles has been catalytic in this field, moving researchers forward with new challenges arising from the broadening scope of lithium ion batteries. With new cathode, anode and electrolyte materials being developed the methods of analysis of these materials has also been challenged. Solid-state NMR is a powerful method for the analysis of lithium battery materials, as it can "see" clearly the lithium ions with high sensitivity. In addition this method can be used to study these materials in the phase that is used in the battery. The combination of solid-state NMR and battery cycling is a fantastic tool for tracking the exact motional pathway of lithium through battery materials.[2-4]

^{6,7}Li solid-state NMR does, however, have its challenges. For diamagnetic materials, such as many solid-state electrolyte materials, the relaxation delays necessary can be lengthly.[5] This results in extraordinarily long experiment times. To circumvent this issue, researchers have used secondary nuclei to study structure and lithium dynamics in battery materials.

The use of quadrupolar nuclei with large quadrupole moments to study battery materials is a novel technique. This method is viable since many nuclei are quadrupolar in nature, and many battery materials usually contain a large quadrupolar nucleus. We have used ex-situ solid-state NMR to study the structure of several solid-state cathode and electrolyte materials, including $LaLi_{0.5}Fe_{0.2}O_{2.09}$, and the spinel family, $Li_2FeMn_3O_8$.

The garnet-like structure $LaLi_{0.5}Fe_{0.2}O_{2.09}$ is thought to conduct lithium ions through vacancy-mediated ionic hopping. The combination of solid-state NMR and electrochemical cycling gives an important method of investigating this mode of ionic motion in $LaLi_{0.5}Fe_{0.2}O_{2.09}$. This allows the possibility of tailor made materials with specific structural properties that take advantage of the different methods of ionic conductivity.

Similarly, the ^{6,7}Li MAS NMR spectra collected before and after electrochemical cycling of the spinel materials $Li_2CoMn_3O_8$ and family, can identify where lithium ions are being extracted from during battery discharge. This allows us to fully track the mobility of lithium through the spinel system.

(1) Goodenough, J. B.; Kim, Y. *Chemistry of Materials* **2010**, *22*, 587-603.
(2) Cahill, L. S.; Kirby, C. W.; Goward, G. R. *Journal of Physical Chemistry C* **2008**, *112*, 2215-2221.
(3) Davis, L. J. M.; Heinmaa, I.; Goward, G. R. *Chemistry of Materials* **2010**, *22*, 769-775.
(4) Bhattacharyya, R.; Key, B.; Chen, H. L.; Best, A. S.; Hollenkamp, A. F.; Grey, C. P. *Nature Materials* **2010**, *9*, 504-510.
(5) Kuhn, A.; Narayanan, S.; Spencer, L.; Goward, G.; Thangadurai, V.; Wilkening, M. *Physical Review B* **2010**, *83*.
(6) Cahill, L. S.; Chapman, R. P.; Britten, J. F.; Goward, G. R. *Journal of Physical Chemistry B* **2006**, *110*, 7171-7177.
(7) van Wullen, L.; Hildebrandt, L.; Jansen, M. *Solid State Ionics* **2005**, *176*, 1449-1456.
(8) Spencer, L., Coomes, E., Ye, E., Terskikh, V., Ramzy, A., Thangadurai, V., Goward, G.R. *Canadian Journal of Chemistry-Revue Canadienne De Chimie* **2011**.

Tutorial Session: Glenn Facey – Saturday, 1:30-2:10

Solid-State NMR for Newbies
Glenn Facey
University of Ottawa

Afternoon Session – Saturday, 2:10-2:50

Solid-State NMR and X-Ray Diffraction Analysis of Halogen Bonding Involving Thiocyanates and Selenocyanates
Jasmine Viger-Gravel, Ilia Korobkov, and David L. Bryce
University of Ottawa

Halogen bonding, RX-B, is the result of a non-covalent interaction between a halogen X and a negative site B (e.g., Lewis base or π electrons). The halogen, X, is part of an RX molecule where R can be another halogen, an organic or an inorganic electron-donating group.[1] Halogen bonds are of particular interest since they are widely used in crystal network engineering for the creation of new materials and are implicated in multiple biological processes such as molecular folding and recognition. In this work, solid-state nuclear magnetic resonance (SSNMR)

spectroscopy is used to study thiocyanate (SCN^-) and selenocyanate ($SeCN^-$) moieties which are halogen-bonded with iodine atoms in compounds of the form $(R_4NSCN)_x(p\text{-}C_6F_4I_2)_y$ and $(R_4NSeCN)_x(o \text{ or } p\text{-}C_6F_4I_2)_y$.[2] X-ray diffraction was used to elucidate their crystal structures. Correlations between the halogen bonding environment of the compounds and the NMR tensors of the nuclei involved directly and indirectly in halogen bonding, such as ^{13}C, ^{77}Se, and $^{14/15}N$, were determined. Results are compared with those for simple thiocyanate and selenocyanate salts. Also, density functional theory (DFT) was used to compute the molecular orbitals and shielding tensors of the synthesized compounds in order to corroborate experimental findings. We have found that the isotropic shift and the span, for some nuclei, will exhibit a clear change upon halogen bonding.[3] We interpret those results in the context of Ramsey's theory.

[1] Metrangolo, P.; Resnati, G. *Halogen bonding: fundamentals and applications*, Springer, Berlin, London, **2008**, 221 pp.
[2] Cauliez, P.; Polo, V.; Roisnel, T.; Llusar, R.; Fourmigué, M. *CrystEngComm* **2010**, *12*, 558-566.
[3] Viger-Gravel, J.; Korobkov, I.; Bryce, D. L. *Cryst. Growth Des.* **2011**, DOI : 10.1021/cg200889y

Structure determination of Anabaena sensory rhodopsin by solid-state NMR
Shenlin Wang, Lichi Shi, Izuru Kawamura, Kwang-Hwan Jung, Leonid S. Brown, Vladimir Ladizhansky
University of Guelph

Solid-state NMR (ssNMR) spectroscopy is emerging as a powerful tool for studying structure and dynamics of membrane proteins in lipid environment. Recent advances in ssNMR have demonstrated the feasibility of obtaining high-resolution 3D structures of large membrane proteins. In this presentation, I will show our progress towards an ssNMR structure determination and dynamic characterization of a 28 KDa lipid-embedded seven-helix transmembrane (7TM) photosensor *Aneabena* sensory rhodopsin (ASR). The structure will be determined by distance restraints derived from carbon-carbon spin-diffusion spectra of alternately labeled samples, together with dihedral angle restraints obtained from the chemical shifts. Procedures of sample preparation, the progress of spectroscopy toward structure determination and strategies on the data interpretation will be discussed. Also I will discuss the site-specific dynamic properties and the light-induced conformational changes of ASR as studied by ssNMR. The information obtained provided the structural-dynamic basis for the understanding of the photosensory function of ASR. Finally, this procedure can be applied to other 7TM proteins, i.e., those of the family of G protein–coupled receptors.

Poster Session – Saturday, 3:00-5:00

P-1 Mapping Allosteric Networks in the Regulatory Subunit of PKA Ialpha Through the NMR Chemical Shift Covariance Analysis (CHESCA)
Madoka Akimoto, Rajeevan Selvaratnam, Giuseppe Melacini
McMaster University

P-2 Structural Changes of Model α-helical Transmembrane Segments in the Presence of Detergents
Rohan Alvares, David V. Tulumello, Peter M. Macdonald, Charles M. Deber and R. S. Prosser
University of Toronto

P-3 Characterization of the Interaction between Parkin UbLD and Ataxin-3 UIMs.
Jane Bai, Gary S Shaw
University of Western Ontario

P-4 Optimization of Agglomerative Clustering (AC) used in Chemical Shift Covariance Analysis (CHESCA) of EPAC
Amir Bashiri, Rajeevan Salvaratnam, Giuseppe Melacini
McMaster University

P-5 Towards Understanding the Structural Basis of cAMP vs. cGMP Selectivity in Hyperpolarization-Activated Cyclic Nucleotide-Modulated (HCN) Ion Channels
Matthew Brown, Bryan VanSchouwen, Madoka Akimoto, Giuseppe Melacini
McMaster University

P-6 Structural Studies of the Tetherin Transmembrane Domain
Gregory Cole, Karen Simonetti, Irsa Ademi, Simon Sharpe
The Hospital for Sick Children

P-7 Basic Experimental Approaches to Differentiate Phases in Heterogeneous Samples Using Comprehensive Multiphase NMR Spectroscopy
Denis Courtier-Murias, Ronald Soong, Hashim Farooq, Hussain Masoom, James G. Longstaffe, Werner Maas, Brian Andrew, Michael Fey, Sridevi Krishnamurthy, Jochem Struppe, Rajeev Kumar, Martine Monette, Henry Stronks, Myrna J. Simpson and André J. Simpson
University of Toronto

P-8 Proton Dynamics in Sulfonated Ionic Salt Composites: Alternative membrane materials for Proton Exchange Membrane Fuel Cells
Nicole De Almeida, Mark Ma, Jason W. Traer and Gillian R. Goward
McMaster University

P-9 Novel modes of SH3-domain interactions of 18.5-kDa myelin basic protein
Miguel De Avila, G.S.T. Smith, M.A.M. Ahmed, J.M. Boggs, G. Harauz
University of Guelph

P-10 Rapid Parameter Optimization in Low Signal-to-Noise Samples: Application to Recycle Delays
Hashim Farooq, Denis Courtier-Murias, Ronald Soong, Hussain Masoom, Werner Maas, Rajeev Kumar, Martine Monette, Henry Stronks, Myrna J. Simpson and André J. Simpson
University of Toronto

P-11 A ^{14}N Solid-State NMR Study of Amino Acids and their Polymorphic Forms
Zack Friedl, Stanislav L. Veinberg and Robert W. Schurko
University of Windsor

P-12 Solution NMR Studies of a Family 32 CBM from Clostridium perfringens: Novel Insights into Ligand Binding and Dynamics
Julie Grondin, Chitayat, S., Ficko-Blean, E., Boraston, A.B. and Smith, S.P.
Queen's University

P-13 ^{6,7}Li Solid State NMR Studies of Lithium-Ion environment and dynamic process in $Li_2MP_2O_7$(M=Fe, Mn) as new serious of Cathode Material for Lithium-Ion batteries
Xuan He
McMaster University

P-14 A Study of Transition-Metal Organometallic Complexes using ^{35}Cl NMR, ^{35}Cl NQR and First-Principles DFT Calculations
Karen Johnston, Robert W. Schurko
University of Windsor

P-15 Cooked Flax Bolls: An Alternative Omega-3 Fatty Acid Source
Chris Kirby, JL McCallum, K Bernard, and B Fofana
Agriculture and Agri-Food Canada

P-16 Structural and functional correlation of the N-terminus and first transmembrane segment of the apelin receptor
David Langelaan, Aaron W. Banks, Graham Dellaire, Denis J. Dupré and Jan K. Rainey
Dalhousie University

P-17 Quantum Chemical Calculations for NMR Crystallography
Kevin Langendoen, Darren H. Brouwer
Redeemer University College

P-18 Reductive ^{13}C-deuteromethylation of Lysine Residues: Practical Implications for in vitro and in-cell Studies of Proteins by NMR
Sacha Larda, R. Scott Prosser
University of Toronto Mississauga

P-19 The pH-Dependence of the Interactions Between Environmental Xenobiotics with Humic Acid: An Investigation Using ^{1}H/^{19}F NMR Spectroscopy

James Longstaffe, James G. Longstaffe, Denis Courtier-Murias, Ronald Soong, and Andre J. Simpson
University of Toronto

P-20 Can a Single Spike Be Better Than a Whole Spectrum? Rapid Prediction of Experimental Run in Low Concentration "Multi-Day" Samples
Hussain Masoom, Courtier-Murias, D., Soong, R., Farooq, H., Maas, W., Kumar, R., Monette, M., Stronks, H, Simpson, M.J. and Simpson, A.J
University of Toronto

P-21 Isolation of Pure Active and Inactive Conformational States of the RIα Subunit of PKA in Solution for NMR Investigations
Nicholas McGregor, Madoka Akimoto, Giuseppe Melacini
McMaster University

P-22 Slice-Selection to Eliminate Curvature in PFG NMR Diffusion Decays Originating from Non-linear Gradients
Kaz Nagashima, Hannah H. Morales, Peter M. Macdonald
University of Toronto Mississauga

P-23 ^{35}Cl Solid-State NMR Studies of Hydrochloride Pharmaceuticals and their Polymorphs
Andrew Namespetra, Marcel Hildebrand, Robert Schurko
University of Windsor

P-24 ^{14}N Magic Angle Spinning Overtone NMR Spectra
Luke O'Dell, Christopher I. Ratcliffe
Steacie Institute (NRC)

P-25 Investigation of natural organic matter dynamics in glacial ecosystems by NMR Spectroscopy
Brent Pautler, Myrna J. Simpson, André J. Simpson, David M. Wolfe, Ashley Dubnick, Martin J. Sharp
University of Toronto

P-26 A Double-Rotation NMR Study of a New Hydrate of Deoxycytidine Monophosphate and Other Sodium Nucleotide Salts.
Frédéric Perras, David L. Bryce
University of Ottawa

P-27 Everything Old is New Again
D. Burns, R. Breton and W. F. Reynolds
University of Toronto

P-28 Conformational Analysis of a Designed S100 Protein by Residual Dipolar Coupling
Liliana Santamaria-Kisiel, Gary S. Shaw
The University of Western Ontario

P-29 Solid-State NMR Investigation of Bicelle Structural Organization and Peptide Interactions
Muzaddid Sarker, Ulrike Werner-Zwanziger, and Jan K. Rainey
Dalhousie University

P-30 ^{6}Li 1D Selective Inversion MAS NMR Studies of Monoclinic Lithium Vanadium Phosphate
Danielle Smiley, Linda J.M. Davis and Gillian R. Goward
McMaster University

P-31 Quebec/Eastern Canada High Field NMR Facility. Le Centre de RMN à Haut Champ du Québec et de l'Est du Canada
Tara Sprules, Kalle Gehring
QANUC/McGill

P-32 Structure and Dynamics of Syrian Hamster Prion Protein Beta-oligomers by Solid State NMR
Carlene Starck, Patrick Walsh, Karen Simonetti, Simon Sharpe
The Hospital for Sick Children

P-33 ^{19}F NMR Studies of Protein Unfolding by Temperature and Pressure
William Thach, Joshua Hoang, Juli Kitevski-LeBlanc, R. Scott Prosser
University of Toronto Mississauga

P-34 NMR solution structure of the monomeric aciniform spider silk and characterization by AFM
Marie-Laurence Tremblay, Lingling Xu, Paul X.-Q. Liu, Jan K. Rainey
Dalhousie University

P-35 Structure determination of Streptococcus suis type 14 capsular polysaccharide
Marie-Rose Van Calsteren, Fleur Gagnon, Cynthia Calzas, Guillaume Goyette-Desjardins, Masatoshi Okura, Daisuke Takamatsu, Marcelo Gottschalk, Mariela Segura
Agriculture and Agri-Food Canada

P-36 Synthesis and Structural Investigation of Layered Silicates
Nicholas VanHuizen, Darren Brouwer
Redeemer University College

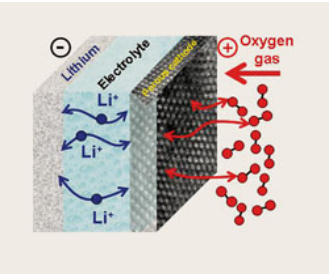
P-37 Role of Dynamics in the Autoinhibition and Activation of the Exchange Protein Directly Activated by Cyclic AMP (EPAC)
Bryan VanSchouwen, Rajeevan Selvaratnam, Federico Fogolari, and Giuseppe Melacini
McMaster University

P-38 Metal ion scavenging by crown ethers detected by PGSE NMR
Zhejia Yan, Bob Berno, Gillian R. Goward
McMaster University

P-39 Calix[4]pyrrole – A Solid State NMR Study
Z. E. M. Reeve, R. Jamieson, R. Webber, G.H. Penner
University of Guelph

Sunday Opening Session: Gillian Goward – 9:00-9:30

^{7}Li and ^{17}O NMR Studies of Reaction Mechanisms in Li-Air Batteries
Michal Leskes, Clare P. Grey, Gillian R. Goward
McMaster University



Lithium-air batteries are attracting attention within the electrochemical community, as they offer the potential for dramatic increases in the energy density of the device, as compared to traditional lithium ion batteries.[1] The theoretical electrochemical reaction is that between metallic lithium and molecular oxygen, with lithium peroxide as the sole product. It was discovered in the past two years that the forward reaction does not form Li_2O_2, but rather, the reactive oxide radical attacks the traditional carbonate electrolyte of the electrochemical cell, and spews out a number of possible organo-carbonate reaction products. This realization has lead to a focused search for compatible electrolyte materials that would enable the desired electrochemistry.[2]

Solid-state NMR is well placed to aid in the understanding of the electrochemical reaction mechanism. In particular, ^{17}O-NMR may offer the direct distinction between carbonate and peroxide products, due to the significant difference in the bonding environments of oxygen in each possible product. At the National Ultra High Field NMR facility in Ottawa, we have acquired natural abundance data sets for both lithium carbonate, and lithium peroxide. Both WUSRT-QCPMG and solid-echo experiments were performed. Additionally, further data was acquired at the UK 850MHz facility in Warwick, including DFS-solid-echo experiments on both Li_2O_2, and the first ^{17}O- enriched electrode materials. These studies have demonstrated that the C_q of the possible reaction products, Li_2O_2 and Li_2CO_3, are substantially different, in both spectral width and lineshape. Combining CASTEP calculations of the quadrupole parameters of the ^{7}Li and ^{17}O environments in Li_2CO_3 and Li_2O_2, with experimental results on electrochemically prepared cathode materials, we have demonstrated the ability to distinguish the oxygenated products. Thus, solid-state NMR is demonstrated to be an effective tool in evaluating candidate electrolytes for their stability to peroxide radical attack in the Li-air cell.

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(2) Bruce, P. G.; Freunberger, S. A.; Chen, Y. H.; Peng, Z. Q.; Griffin, J. M.; Hardwick, L. J.; Barde, F.; Novak, P. *Journal of the American Chemical Society* **2011**, *133*, 8040.

Morning Session I – Sunday, 9:30-10:30

Multinuclear Magnetic Resonance and Crystallographic Investigation of Phosphonium Halide Salts

Kevin M. N. Burgess, *Ilia Korobkov, David L. Bryce*
University of Ottawa

We present here the characterization of the quadrupolar halogen ($^{35/37}$Cl, $^{79/81}$Br, and ^{127}I) electric field gradient (EFG) and chemical shift (CS) tensors of phosphonium halide salts bearing the triphenylphosphonium moiety with solid-state NMR spectroscopy. This class of compounds has found multiple applications in chemistry as ionic liquids, phase-transfer catalysts, fertilizers, and anion receptors. Experiments were performed at magnetic fields ranging from 9.4 to 21.1 T under stationary and magic-angle-spinning conditions. Gauge-including projector-augmented-wave DFT calculations using the X-ray crystal structures of the studied compounds have provided insight into the relationship between the halogen NMR parameters and the different local halogen environments present in the phosphonium halides. For example, the bromine CS tensor span is strongly related to the Br–P distance in triphenylphosphonium bromides, a result which has possible applications in the growing field of NMR crystallography. Furthermore, the crystal packing was found to influence the nuclear quadrupolar coupling constant for bromine. The 21.1 T spectra were acquired at the National Ultrahigh-Field NMR Facility for Solids (www.nmr900.ca).

Tailoring ^{1}H spin diffusion in small molecules via super-cooled water? A promising approach for metabolite identification

Ronald Soong, *Hashim Farooq, Denis Courtier-Murias, Andre Simpson*
University of Toronto

The use of super-cooled water in conjunction with spatial correlations techniques, such as NOESY, has shown tremendous promise for metabolomics applications. Under super-cooled conditions, long-range spatial correlations in small molecule that are otherwise absent at room temperatures are readily observed. Importantly, the sign of the NOE switches, from negative to positive, indicating a cross over from the fast tumbling small molecular regime to the slow tumbling macromolecular limit, which facilitates proton spin diffusion process. Since rigid molecules experience limited internal motions, the efficiency of their spin diffusion process is intensified in super-cooled water due to a decrease in their overall correlation times, generating spin clusters representative of their overall structures. Therefore, super-cooled water provides an effective and non-perturbing medium to contrast different molecular dynamics for various water-soluble molecules. To illustrate its potential metabolomics application, we demonstrate the avenue in which nucleotides and/or nucleoside-based metabolites extracted from worm tissue can be identified and distinguished from each other based on our approach. Although significant spectral overlap is observed in our super-cooled water NOESY spectrum, the ability to extracts key metabolites from a biological mixture via this approach will advocates its incorporation into the current collection of NMR based metabolomics techniques.

Biophysical studies of the first nucleotide binding domain of SUR2A

Elvin de Araujo, *Claudia Alvarez, Jorge P. López-Alonso, Voula Kanelis*
University of Toronto

ATP-sensitive potassium (K_{ATP}) channels are found in various cell types, including vascular smooth muscle, heart, and pancreas. By sensing the cellular concentrations of ADP and ATP, K_{ATP} channels link cellular metabolism to membrane potential and excitability, leading to crucial roles in several biological processes. Cardiac K_{ATP} channels are comprised of four pore-forming Kir6.2 proteins surrounded by four regulatory SUR2A proteins. SUR2A belongs to the ATP-binding cassette (ABC) superfamily. ATP binding and hydrolysis at the SUR2A NBDs leads to opening of the K_{ATP} channel pore. Further, phosphorylation of specific serine and threonine residues in the SUR2A NBDs activates K_{ATP} channels, possibly by increasing the affinity of the NBDs for ATP and/or the rates of ATP hydrolysis at the NBDs. Mutations in the nucleotide binding domains (NBDs) of SUR2A that disrupt regulation of K_{ATP} channel gating are associated with several cardiovascular disorders, making studies of the NBDs essential in understanding regulation of K_{ATP} function. Currently, studies into the molecular basis by which various mutations in SUR2A cause disease are limited. Further, the molecular mode by which phosphorylation activates K_{ATP} channels is also not understood. This lack of molecular-level information on the SUR2A NBDs is primarily a consequence of poor solubility of the isolated SUR2A NBDs, as is typical for many NBDs from eukaryotic ABC proteins. By employing structure-based sequence alignments, predictions of disordered regions, and biophysical studies, we determined domain boundaries for SUR2A NBD1 that enabled, for the first time, NMR studies of NBD1. Our biophysical studies

demonstrate that the isolated SUR2A NBD1 is folded and exhibits ATP binding activity. Preliminary results suggest that phosphorylation of NBD1 results in changes in the conformation of the protein and altered protein dynamics. Additional studies are now possible to examine the effects of disease-causing mutations on structure, dynamics, and interactions of NBD1 and some of these data will also be presented.

Guest Session: David Weliky – Sunday, 10:45-11:15

Solid-state NMR structural studies of viral fusion proteins in membranes and in inclusion bodies in whole bacterial cells: Greatly improved sensitivity and resolution at 900 MHz with an E-free probe
Matthew J. Nethercott, Erica P. Vogel, Jaime Curtis-Fisk, Kelly J. Sackett, Scott D. Schmick, and David P. Weliky
Michigan State University

Enveloped viruses infect cells by joining their membrane with that of the target host cell. This process is catalyzed by a viral fusion protein and in particular by the fusion peptide (FP) region which binds to the host cell membrane. Solid-state NMR (SSNMR) has been used to determine high-resolution structures of the HIV and influenza virus FPs in membranes. SSNMR has also been used to measure distances between nuclei in the FP and nuclei in the lipid molecules in the membrane and it has been observed that there is a strong correlation between fusogenicity and depth of FP membrane insertion. Finally, SSNMR was used to quantitatively determine the population distribution of beta sheet registries for the membrane-associated HIV FP. There was a broad distribution of antiparallel registries and a good correlation between individual registry populations and their free energies of membrane insertion. A very different registry distribution was detected for the non-functional V2E mutant which binds to membranes but is not membrane-inserted.

Recombinant protein expression is often plagued by the production of inclusion bodies (IBs) which are insoluble aggregates of the expressed protein. Although little is known about the structures of IB protein, one model is amyloid beta sheet structure. Residue-specific conformation of three recombinant proteins in IBs was probed by SSNMR. The native conformations were predominantly helical. The ^{13}CO chemical shifts of individual residues in the proteins were measured and correlated with local conformation. Three types of samples were studied: (1) purified protein which had native structure; (2) whole unlysed hydrated cells; and (3) the hydrated pellet formed from the insoluble material in the cell lysate. The ^{13}CO signals from the latter two types of samples were predominantly from IB protein. All ^{13}CO chemical shifts in all samples correlated with helical rather than beta strand conformation. The data therefore suggest that much of the native fold is retained for these two proteins in hydrated IBs.

Spectra were obtained at both 400 and 900 MHz and there was greatly improved resolution and sensitivity at the higher field.

Morning Session II – Sunday, 11:15-12:15

Investigating the assembly of amyloidogenic peptides from Prion protein by solid-state NMR
Jason Yau, Simon Sharpe
Hospital for Sick Children

Fibrillar protein aggregates are characteristic of amyloidosis such as Alzheimer's disease and the mammalian prion disease. These diseases involve misfolded proteins self-assembling into β-rich structures as a pathological marker coincident with cell death. Many small peptide fragments from amyloid proteins demonstrate propensity to fibrillize, with amyloid characteristics similar to their full-length counterpart. This makes them excellent models to examine the cytotoxic mechanisms of amyloids. We have investigated three fibril-forming peptides from human prion protein to study the structure of cytotoxic fibrillar aggregates. Biophysical characterization by electron microscopy, fourier-transformed infra-red spectroscopy, and thioflavin T binding indicate that the peptides fibrillize and contain β-sheet secondary structure, but with differences that may correlate with cytotoxicity. SSNMR coupled with site-specific labeling has been used to determine the structure of the amyloid fibrils under MAS. Specifically, the constant-time PITHIRDS technique was used to determine backbone ^{13}CO internuclear distances, while the TEDOR and rotational resonance techniques were used to probe side-chain interactions. Our results showed that the fibrils assemble into in-register parallel β-sheets, but with intermolecular contacts observed in the NMR experiments suggesting variation in fibril packing between sequences. This presents a basis for further investigation of their biological properties and gives us insight into the role of local structure in determining cellular toxicity.

Chemical Shift Covariance Analysis (CHESCA): Principles and Applications to Allosteric Systems
Rajeevan Selvaratnam, Bryan VanSchouwen, Federico Fogolari, Mohammad T. Mazhab-Jafari, Rahul Das, Giuseppe Melacini

McMaster University

Allostery is a fundamental mechanism of regulation in biology. The end points of long-range allosteric communication are commonly identified by comparative analyses of structures and dynamics in apo and effector-bound states. However, the networks of interactions mediating the propagation of allosteric signals between the end points often remain elusive. Here we show that the covariance analysis of NMR chemical shift changes caused by a set of covalently modified analogs of the allosteric effector (*i.e.* agonists and antagonists) reveals extended networks of coupled residues. Unexpectedly, such networks reach not only sites subject to effector-dependent structural variations, but also regions that are controlled by dynamically driven allostery. The proposed chemical shift covariance analysis (CHESCA) identifies inter-residue correlations based on the combination of agglomerative clustering (AC) and singular value decomposition (SVD). AC results in dendrograms that define functional clusters of coupled residues, while SVD generates score plots that provide a residue-specific dissection of the contributions to binding and allostery. The CHESCA approach was validated by applying it to the cAMP-binding domain of the exchange protein activated by cAMP (EPAC) and the CHESCA results are in full agreement with independent mutational data on EPAC activation. Furthermore, CHESCA can also be used to map the effects of new mutations that have not yet been characterized. For instance, SVD was also employed to quantitatively gauge the extent of activation achieved by apo-EPAC mutants targeting key autoinhibitory determinants.[1-6] Overall, CHESCA is a generally applicable method that utilizes a selected chemical library of effector analogs and/or mutations to quantitatively decode the binding and allosteric information content embedded in chemical shift changes.

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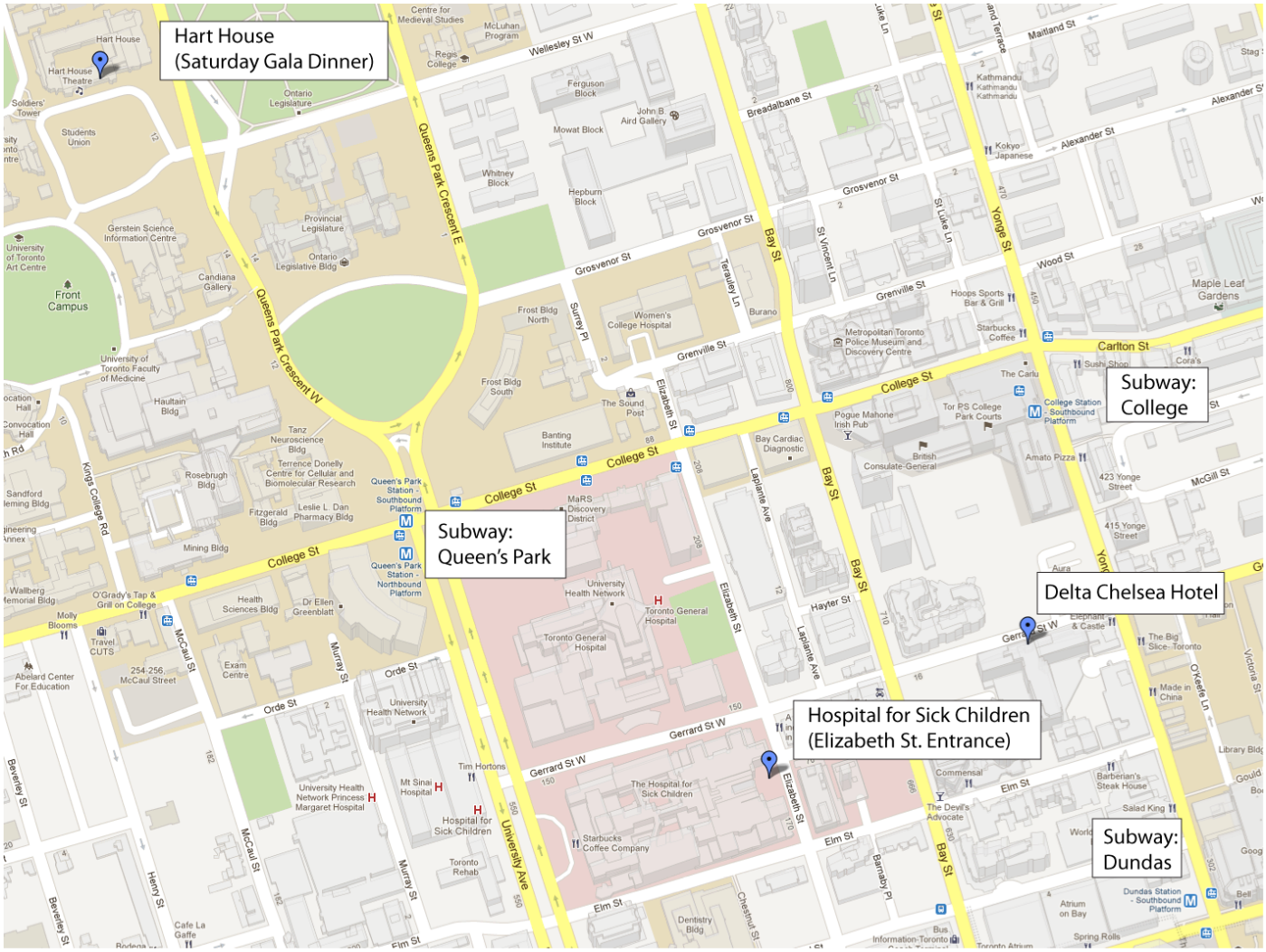
6. Selvaratnam, R., VanSchouwen B., Mazhab-Jafari, M. T., Das, R., Melacini G. *(2011).* J.Biol.Chem. **–** *Submitted*

Dynamics and Internal Structure of a Mixed-Surfactant Wormlike Micellar System Using NMR and Rheometry

Suliman Barhoum, Rolando Castillo, Anand Yethiraj
Memorial University of Newfoundland

We use complementary experiments - proton NMR diffusometry and relaxometry, deuterium NMR lineshapes and rheometry - to construct a picture of the microscopic structure of a mixed-surfactant wormlike micellar system composed of a zwitterionic surfactant and an anionic surfactant in brine which exhibits deviations from standard wormlike micellar behavior. From NMR relaxometry, we determined the overlap concentration. Deuterium NMR spectral lineshapes indicate the presence of orientational disordered domains with slow exchange between domains. Surfactant diffusion coefficients are seen to decrease with increasing diffusion time, consistent with restricted diffusion within a reptating micelle. Fitting the diffusion results to a simple model, the average end-to-end micellar distance was estimated to be in the 1 μm range and only weakly dependent on concentration. Self-consistently, the wormlike micelles obeyed simple polymer-like scaling behaviors with a crossover from Zimm-like (diffusion) to Rouse-like (rheology) exponents.

The Hospital for Sick Children is located on the South side of Gerrard St. between University and Elizabeth.



The Hollywood Theatre is on the first floor of Sickkids, one floor above main, in the Black Wing near University Ave on the west side of the building, Room number 1248.

Access to the hospital on weekends is limited to the main doors on Elizabeth Street.