20th National Magnetic Resonance Society Symposium cum Annual Meeting

NMRS

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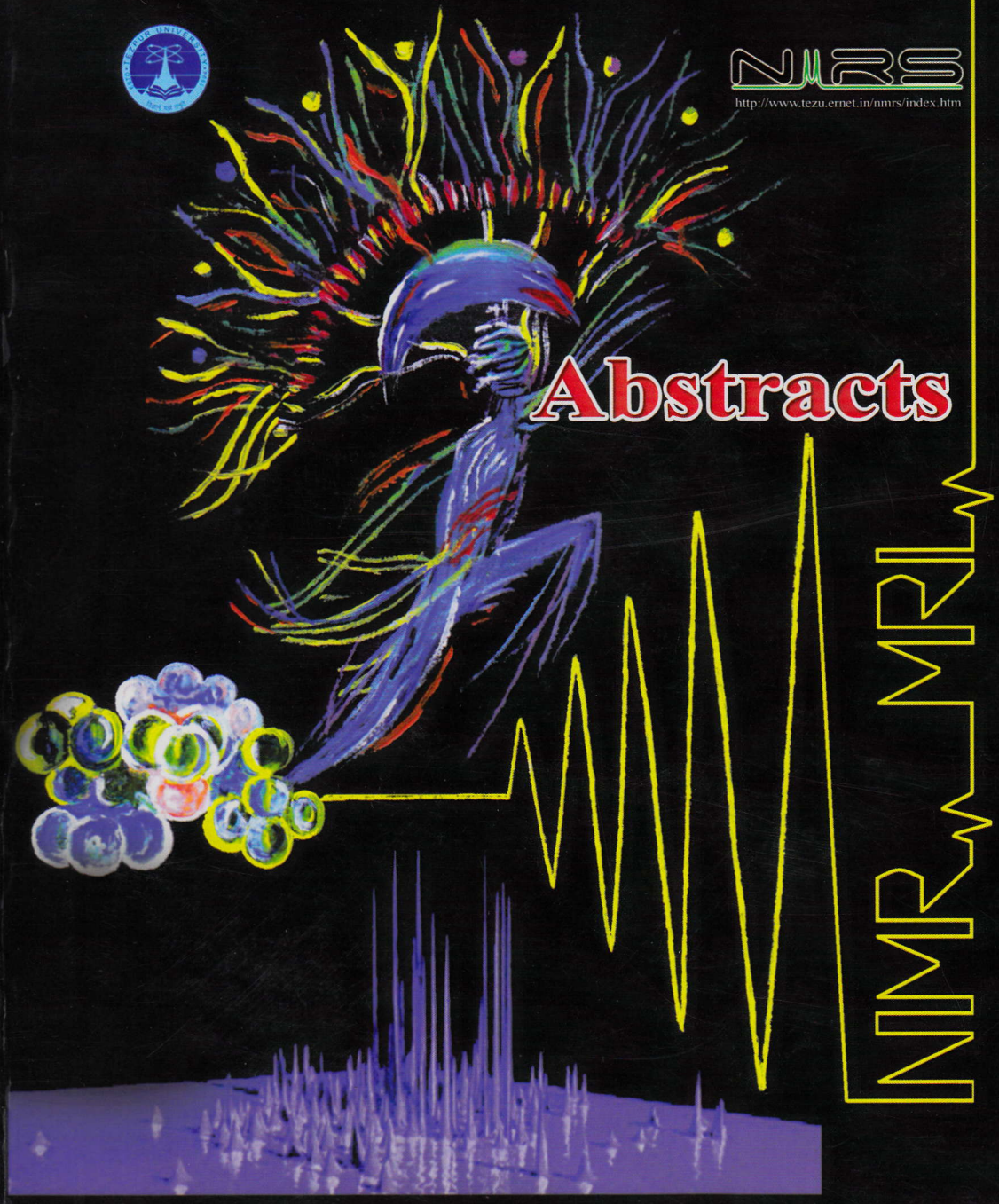

February 2-5, 2014

Organized by Department of Chemical Sciences, Tezpur University, India

National Magnetic Resonance Society (India)

20th National Magnetic Resonance Society Symposium 2014

NMRS-2014

February 2-5, 2014

Organized by

Department of Chemical Sciences

Tezpur University, Assam

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About National Magnetic Resonance Society

National Magnetic Resonance Society (NMRS) is a premier body which is providing a platform for scientific deliberations to the researchers/scientists/professionals working in the field of magnetic resonance. It gives me immense pleasure to share with you all that NMRS has successfully entered into the 20th year of its existence. During this period, the Society has expanded its horizon from national to international level and also its life membership is about to touch the number 1000.

The National Magnetic Resonance Society has made major contribution in enhancing the awareness and usefulness of magnetic resonance in various branches of science. Nuclear Magnetic Resonance (NMR) is most important spectroscopic technique. It becomes a primary tool for obtaining information about physical, chemical, electronic and structural aspects of small to bigger molecules. With the development of multi-dimensional NMR experiments, invention of portable NMR machines and advancement in the technology; NMR spectroscopy is a choice of scientists including chemical, biomolecular, material, pharmaceuticals, geological, biomedical etc.

The continuous and sincere efforts of all those concerned with NMRS has brightened globally the visibility and the activities of the Society. Along with providing 'Honorary Membership' to the distinguished scientists and Nobel laureates from all over the world, the Society is also making continuous efforts in identifying the young talent in the country and nurturing them as well. As a regular event in every NMRS meeting, a special session is devoted to young researchers and the best ones are honoured with awards. The Society has made provision for travel grant also so that the young students attend international conferences.

I welcome the delegates to the 20th Annual NMRS Symposium at Tezpur University, Tezpur (Assam). This Symposium will feature the talks and posters on various aspects of NMR encompassing methods, applications, imaging, metabonomics, and quantum computation. I thank the organizers for their excellent arrangement and I hope this Symposium will be a great success where the relevant issues of magnetic resonance would be discussed in its deliberations.

Prof. A. S. Brar
President
NMRS

Welcome to NMRS-2014 in Tezpur University, Assam

Greetings from Tezpur University

Magnetic resonance is one of the most widely studied and used, fascinating and versatile spectroscopic phenomenon. Due to the spectacular advancements, it has gone to such an extent that it now penetrates almost all fields of science thereby acts as a bridge among them. Now magnetic resonance opens up new vistas and opportunities as far as their applications are concerned. Hence, it is very important and great necessity to discuss and exchange knowledge in magnetic resonance and related phenomena in details among scientists, users, researchers, students, industries and academia. In order to facilitate that by creating a platform, it is our pleasure to inform you that Department of Chemical Sciences, Tezpur University organizes National Magnetic Resonance Society-2014 (NMRS-2014) symposium during Feb 2-5, 2014 at Tezpur University, the 20th one in the series. It is now well known that NMRS meetings play an important role in disseminating the knowledge in magnetic resonance and related phenomena. To our delight, this is for the first time that NMRS meeting is organized in the North Eastern region of India. It's a matter of great privilege and honour to host NMRS-2014. We were overwhelmed by the immense responses received from the participants.

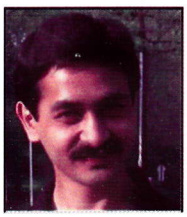
The supports and advices received from the President, secretary and members of National Magnetic Resonance Society in all respects are very commendable, we sincerely acknowledge that.

We are highly thankful to the peers in the area from India and abroad who are going to participate in the symposium.

The organizers want to express their gratitude to all the sponsors of this event for their generous support that make possible this event happen.

Our team of volunteers has done incredible amount of works for this event. Special thanks to this team.

On behalf of organizers of NMRS-2014 and Tezpur University, we extend our heartiest welcome to the participants of NMRS-2014. We are looking forward to a grand success of NMRS-2014 symposium.



Ashim Jyoti Thakur

Dr. Ashim J. Thakur

Bipul Sarma

Dr. Bipul Sarma

Conveners: Department of Chemical Sciences, Tezpur University, India

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CSIR-North-East Institute of Science & Technology, Jorhat, Assam, a constituent establishment of Council of Scientific & Industrial Research(CSIR), New Delhi has been engaged in multidisciplinary R&D work relevant to the North Eastern Region in particular and country in general.

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Following a Masters in Physics with an MBA, K.K. Bhagchandani has worked in the life sciences industry for 20 years. Having started his career in India working for pharmaceutical industry leaders Ranbaxy and Pfizer, he made a change in his career path with a move to software and IT. For more than a decade he has been involved in the Asian business world working for global IT-Software companies that provide enabling technologies for pharmaceutical and chemical R&D. In 2003 he joined ACD/Labs (a leader in software for Structure Characterization, predictive ADME-Tox, PhysChem, and nomenclature software; a company providing solutions for analytical data handling and chemical and analytical knowledge management). At ACD/Labs he is spearheading the Asian Business as Director of Asia and Pacific Operations. He has been a regular presenter at international scientific conferences and meetings, presenting tools that will help increase efficiency and productivity in R&D.

Abstract

It is almost a necessity that for any organic chemistry research to be complete a thorough characterization of the compound has to be done (and many times the related compounds also). NMR has been a key technique for elucidation / Characterisation of chemical compounds for ages and continues to do so. NMR by its nature contains more information about chemical structure as compared to other techniques, however, for complete elucidation one needs to work with several experiments from several analytical techniques. Modern tools now can handle multiple techniques and extrapolate the information one to another to facilitate elucidation. Often times, full characterization is not required; and scientists are sometimes just confirming the structures with the data to prove their hypothesis is correct for the structure. These tools can not only help in complete characterization but also in spectroscopically validating the chemical structures and dereplication to save time.

With ever increasing needs of regulatory requirements and quality consciousness; it is imperative for all companies to deal with the impurities in detail including the minutest details. The cost of either having an impurity or a wrongly identified impurity can be seriously high and can even shake the stock price of the company. Therefore one of the key aspect of this is complete structure

characterization of these impurities as early as possible and as conclusively as possible. Considering that impurities can be structurally related/similar to the pure compound the challenge is even more time consuming to work with them. This document is to share on how the **CASE** (Computer Assisted Structure Elucidation) can help researchers in reducing the time consumed and increase dependability of the characterization results.

This presentation is focused on sharing

1. Five different approaches to work with NMR data to resolve / confirm the chemical structure.
2. How much can software help in assisting elucidation
3. When to use dereplication approach and when to use confirmatory approach
4. How using these approach can expand the reach of thought process of an expert.

.....

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20th Symposium of National Magnetic Resonance Society, India; NMRS-2014

February 2 – 5, 2014

Tezpur University

National Magnetic Resonance Society (India)

Organizer: Department of Chemical Sciences, Tezpur University

Contact: Convenors, Dr. Ashim J. Thakur & D. Bipul Sarma; Department of Chemical Sciences, Tezpur University, Tezpur-784028, Email: nmrs2014attu@gmail.com

SCIENTIFIC PROGRAM

Sunday, February 2, 2014
Venue: KBR auditorium, TU

09.00 – 14.00	Registration
14.00 – 14.30	Inauguration Hon'ble Vice Chancellor Prof. M. K. Chaudhuri, Tezpur University, India Hon'ble Vice Chancellor Prof. A. S. Brar, Guru Nanak Dev University, India
	Session 1: Chair: Prof. C. L. Khetrapal, CBMR, Lucknow
14.30 – 15.15	**IT-1:** Claire Grey, University of Cambridge, UK **[ISMAR-NMRS Lecture]**
	Session 2: Chair: Prof. A. S. Brar, GND University, Amritsar
15.20 – 15.50	**IT-2:** T. S. Mahesh, IISER Pune [Prof. S. Subramanian's 60th Birth Day Lecture Award 2013] Multi-spin Quantum Control: Applications in NMR and Quantum Information
15.50 – 16.05	**OP-1:** Sachin R Chaudhari, IISc, Bangalore [Jharana Rani Best Student Award for 2013] **Extraction of Magnitudes and Relative Signs of $^{n}J_{HF}$ couplings: A Pure Shift and RES-TOCSY Methodologies**
16.05 – 16.35	Tea
	Session 3: Chair: Prof. Anil Kumar, IISc, Bangalore
16.35 – 17.05	**IT-3:** Daniel Huster, University of Leipzig, Germany **Molecular Dynamics of G Protein-Coupled Receptors in Membranes**
17.05 – 17.35	**IT-4:** Bernhard Blumich, RWTH Aachen University, Germany
17.35 – 18.05	**IT-5:** Nico Tjandra, National Heart Lung and Blood Institute, USA
20.00 – 10.00	Dinner Venue: Cafeteria, TU

Monday, February 3, 2014
Venue: Council Hall, TU

9.00-9.40	**PLENARY TALK: IT-6:** Robert G. Griffin, MIT, USA Chair Prof. K. V. Ramanathan

	Session 4: Chair: Prof. N. Suryaprakash, IISc Bangalore **Venue: Council Hall, TU**	**Session 5:** Prof. Gabriele Varani, University of Washington, USA **Venue: Seminar Hall, Dept. of Chem. Sc. TU**
09.40 – 10.10	**IT-7:** Asher Schmidt, Israel Institute of Technology, Israel **The interplay of phosphate and water in tuning ACC metastability - from stabilization to crystallization via a nano-scale solid-solid phase separation: A molecular NMR view.**	**IT-8:** Koichi Kato, Nagoya City University, Japan **NMR approaches for elucidating the functional roles of carbohydrate chains**
10.10 – 10.40	**IT-9:** Matthias Ernst, ETH Zurich **Optimized Proton-Driven Spin Diffusion by Tailored RF-Irradiation Schemes**	**IT-10:** Rolf Boelens, Utrecht University, The Netherlands **Structure and dynamics in gene regulation and DNA repair**
10.40 – 11.10	**IT-11:** Philippe Lesot, University de Paris-Sud, France **NMR using Chiral Anisotropic Solvents: Recent Methodological Advances and new Analytical Applications**	**IT-12:** K. V. Ramanathan, IISc, Bangalore
11.10 – 11.30	Tea Break	
	Session 6: Prof. S. K. Dolui, Tezpur University **Venue: Council Hall, TU**	**Session 7:** Chair: Bernhard Blumich, RWTH Aachen University, Germany **Venue: Seminar Hall, Dept. of Chem. Sc. TU**
11.30 – 12.00	**IT-13:** Thomas Szyperski, University at Buffalo, NY, USA	**IT-14:** Donghan Lee, Max Planck Institute, Germany **Molecular Recognition through Concerted Backbone and Side Chain Motion**
12.00 – 12.30	**IT-15:** Hanudutta Atreya, IISc Bangalore **New NMR methods for rapid data acquisition and analysis: Application to Metabolomics**	**IT-16:** Ashutosh Kumar, IIT Bombay, India **Native structure governs the amyloid formation and fibril reversibility of a short cyclic peptide hormone**
12.30 – 13.00	**IT-17:** Arindam Ghosh, NISER Bhubneswar **Are the wavelet based de-noising techniques necessary or optimum for NMR spectroscopy?**	**IT-18:** Nilamoni Nath, MPI, Germany **Probing supra-τ_c Dynamics on GB3 through $^{13}C_\alpha$–H_α Order Parameters**
13.00 – 14.00	Lunch Break Venue: Cafeteria, TU	
14.00-16.00	**Group Photo + Poster Session I + Tea Break** **Venue: Council Hall, TU**	

	Session 8: Chair: Dr. B. Jagadeesh, IICT Hyderabad Venue: Council Hall, TU	Session 9: Chair: Matthias Ernst, ETH Zurich Venue: Seminar Hall, Dept. of Chem. Sc. TU
16.00 – 16.30	**IT-19:** N. Suryaprakash, IISc Bangalore **Testing Enantiopurity by NMR Spectroscopy: Our Recent Strategies**	**IT-20:** Norbert Muller, Johannes Kepler University, Austria
16.30 – 17.00	**IT-21:** Bikash Baishya, CBMR Lucknow **"Perfect Echo" INEPT**	**IT-22:** Rama Jayasunder, AIIMS, New Delhi **NMR in validating Ayurveda**
17.00 – 17.15	**OP-2:** Shivanand M. P., IISc Bangalore **Accelerating 3D HSQC-DOSY with projection NMR spectroscopy and non-uniform sampling**	**OP-3:** Lokesh, IISc Bangalore **RES-TOCSY: A Simple Approach to Resolve Overlapped 1H NMR Spectra of Enantiomers**
17.15 – 17.45	**IT-23:** Hironao Sajiki, Gifu Pharmaceutical University, Japan. **Heterogeneous Platinum Metal-Catalyzed Deuterium Labeling Methods Characterized by the Simplification of NMR Charts**	**OP-4:** Veena Bansal, IOCL Faridabad **Solid State NMR Studies for Structural insights of Lignocellulosic biomass** **OP-5:** Nigel Crossley, Oxford Instruments India Pvt Ltd
17.45 – 18.00		**OP-6:** Rajagopal Bhaskaran, Claflin University **NMR Structural Studies on a Human Lymphatic Filarial Aspartic Protease Inhibitor**
18.30 – 19.45	**Cultural Program** **Venue: KBR auditorium, TU**	
20.00 – 22.00	**Dinner** **Venue: Cafeteria, TU**	

Tuesday, February 4, 2014
Venue: Council Hall, TU

09.00-9.40	**PLENARY TALK: IT-24:** Prof. Stephan Grzesiek, University of Basel, Switzerland
	Chair: Dr. A. C. Kunwar, IICT, Hyderabad
	Session 10: Chair: Prof. Robert G. Griffin, MIT, USA
09.40 – 10.10	**IT-25:** Lyndon Emsley, Universite de Lyon, France **Powder NMR Crystallography from Proton Chemical Shifts**
10.10 – 10.40	**IT-26:** Gabriele Varani, University of Washington, USA **NMR structures allow the design of pharmaceutically active and potent inhibitors of RNA**
10.40 – 11.10	**IT-27:** Lucia Banci, University of Florence, Italy NMR in Molecular Systems Biology: from structures to function
11.10 – 11.25	**Tea Break**

	Session 11: Chair: Prof. Nasreen Islam, Tezpur University **Venue: Council Hall, TU**	**Session 12:** Chair: Prof. Pradeep Phukan Gauhati University **Venue: Seminar Hall, Dept. of Chem. Sc. TU**
11.25 – 11.40	**OP-7:** Detlef Moskau, Bruker Biospin, Switzerland	**OP-8:** G. S. Kapur, IOCL Haryana
11.40 – 11.55	**OP-9:** Kavita Dorai, IISER Mohali **Explorations of multiqubit entanglement and decoherence mitigation on an NMR quantum computer**	**OP-10:** M. Srinu, IISc Bangalore **Characterization and Solution NMR Studies of Natural Compounds**
11.55 – 12.10	**OP-11:** Suresh Kumar Vasa, Max Planck Institute, Germany **Bactofilins β-sheet enriched bacterial cytoskeleton proteins**	**OP-12:** Pritam Deb, Tezpur University
12.10 – 12.25	**OP-13:** Virendra Kumar, AIIMS, New Delhi **In Vivo Quantitation of Metabolites using Proton Magnetic Resonance Spectroscopy of Brain at 3T in Obstructive Sleep Apnea**	**OP-14:** Harindranath Kadavath, MPI Gottingen **NMR Spectroscopy of Human Neuronal Tau Protein: Interaction of Different Isoforms with Microtubules**
12.25 – 12.40	**OP-15:** Amol S. Kotmale, NCL Pune **NMR Studies on a Synthetic Zipper Peptide Motif Orchestrated via Co-operative Interplay of Hydrogen Bonding, Aromatic Stacking and Backbone Chirality**	**OP-16:** Rajkumar Sharma, CBMR, Lucknow **Structural studies on major coat protein of bacteriophage M13 by solid state NMR spectroscopy**
12.40 – 12.55	**OP-17:** Shivam Dixit, Integral Bioscience, Delhi **qNMR - A quantitative tool for purity determination**	**OP-18:** Deepti Upadhyay, AIIMS, New Delhi **Abnormal metabolism in Celiac Disease: ^{1}H NMR study of blood plasma**
12.55 – 14.00	**Lunch Break** **Venue: Cafeteria, TU**	
14.00-16.00	**Poster Session II + Tea Break** **Venue: Council Hall, TU**	
	Session 13: Chair: Prof. Manoj Mishra, IIT Bombay **Venue: Council Hall, TU**	**Session 14:** Chair: Prof. Christian Griesinger, Max Planck Institute, Germany **Venue: Seminar Hall, Dept. of Chem. Sc. TU**
16.00 – 16.30	**IT-28:** Walter Kockenberger, University of Nottinghum, UK **Spin Diffusion and Solid Effect Dynamic Nuclear Polarization**	**IT-29:** Isabella C. Felli, University of Florence, Italy **Novel methods based on ^{13}C detection to study intrinsically disordered proteins**
16.30 – 17.00	**IT-30:** Ajith Kumar, NCL Pune	**IT-31:** B. Jagadeesh, IICT-Hyderabad **Real-time homodecoupled pure-shift NMR methodologies for**

		unambiguous analysis of organic molecules
17.00 – 17.15	**OP-19:** Christy George, IIT-Madras **Chemical shift resolved 'low' field ^{19}F NMR: DNP (OE) enhanced, diagonal suppressed correlation spectroscopy at X-band**	**OP-20:** Pravin Kumar Mishra, CCMB, Hyderabad **^{1}H-[^{13}C]-NMR study for understanding antidepressant effect of ketamine in social defeat model of depression**
17.15 – 17.30	**OP-21:** Harpreet Singh, IISER Mohali **Preserving quantum states in subspace and entangle state using super zeno effect on an NMR quantum computer**	**OP-22:** Jithender G. Reddy, TIFR Mumbai **Complete Backbone and DENQ Side chain NMR Assignments in Proteins from a Single Experiment: Implications to Structure – Function studies**
17.30 – 17.45	**OP-23:** Sai Chaitanya Chiliveri, CCMB-Hyderabad **On structural aspects of dsRBD containing proteins in the RNAi pathway across organisms**	**OP-24:** A. L. Susmitha, TIFR Mumbai
17.45-18.00	**OP-25:** Bappaditya Chandra, TIFR Mumbai Combining fast fluorescence and slow NMR techniques to determine the atomic level structure of transient toxic Amyloid beta oligomers	**OP-26:** K K Bhagchandini, ACD Labs
20.00 – 22.30	**Dinner (Banquet) Venue: Cafeteria, TU**	

Wednesday, February 5, 2014
Venue: Council Hall, TU

9.00-9.40 **PLENARY TALK: IT-32:** Prof. Christian Griesinger, Max Planck Institute, Germany.

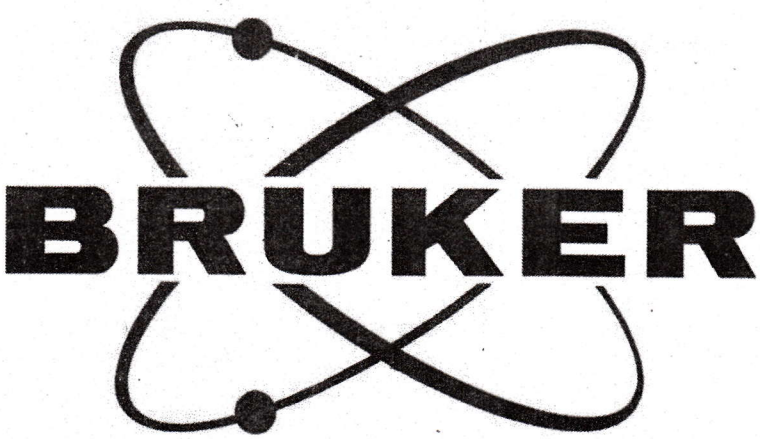
Chair: Prof. Stephan Grzesiek

	Session 15: Chair: Rolf Boelens, Utrecht University, The Netherlands **Venue: Council Hall, TU**	**Session 16:** Prof. Lucia Banci, University of Florence, Italy **Venue: Seminar Hall, Dept. of Chem. Sc. TU**
09.45 – 10.15	**IT-33:** Amir Goldbourt, Tel Aviv University, Israel	**IT-34:** Anant B. Patel, CCMB Hyderabad
10.15 – 10.45	**IT-35:** P. K. Madhu, TIFR Mumbai **Heteronuclear spin decoupling in solid-state NMR**	**IT-36:** Krishna Mohan Poluri, IIT-Roorkee **Structural Analysis of Chemokine-Glycosaminoglycan Interactions**
10.45 – 11.15	**IT-37:** Martin Billeter, University of Gothenburg, Sweden	**IT-38:** Hans Vliegenthart, Utrecht University, The Netherlands **NMR spectroscopy as a tool in carbohydrate and glycoprotein analysis**

11.15 – 11.45	**Tea Break**	
	Session 17: Chair: Prof. Ganesh Pandey, CBMR Lucknow **Venue: Council Hall, TU**	**Session 18:** Prof. Amir Goldbourt, Tel Aviv University, Israel **Venue: Seminar Hall, Dept. of Chem. Sc. TU**
11.45 – 12.00	**OP-27:** Arthanari Haribabu, Harvard University, USA **Solution structure of the Herpesvirus Nuclear Egress Complex Subunit Exhibits a Novel Fold**	**OP-28:** Kowsalya Devi Pavuluri, IISc Bangalore **Real Time Dissolution Monitoring using Spatial Encoding NMR**
12.00 – 12.15	**OP-29:** Kiran Kumar Singarapu, IICT Hyderabad **Solution structure determination of *Aedes Aegypti* Sterol Carrier Protein 2 Like2 (AeSCP2L2) and its complex with palmitate**	**OP-30:** B. V. N. Phani Kumar, CLRI, Chennai **NMR Investigations on Copolymer-Surfactant Interactions**
12.15 – 12.30	**OP-31:** Sudha M. Cowsik, JNU New Delhi **Molecular Recognition of Tachykinin Receptor Selective Agonists: Insights from Structural Studies**	**OP-32:** Kong Ooi Tan, ETH Zürich **Broadband double-quantum recoupling by combined continuous-wave and phase-alternating RF irradiation**
12.30 – 13.00	**IT-39:** Sujoy Mukherjee, IICB, Kolkata **Role of transthyretin's backbone conformational flexibility in amyloid fibril formation**	**IT-40:** G. Balasubramanian, MPI Biophys. Chemistry, Germany
13.10 – 14.30	**Lunch Break** **Venue: Cafeteria, TU**	
	Session 19: Chair: Prof. A. S. Brar, **Venue: Council Hall, TU**	
14.30 – 15.00	**IT-41:** Markus Zweckstetter, Max Planck Institute for Biophysical Chemistry, Germany **NMR studies of protein folding and misfolding**	
15.00 – 15.30	**IT-42:** Peter Guntert, Goethe-University Frankfurt, Germany	
	Session 20: Concluding ceremony, **Venue: Council Hall, TU**	
16.00 – 17.30	**High Tea & NMRS General Body Meeting** **Best Oral and Poster Awards Presentation**	

Legends: IT - Invited talk; OP - Oral presentation

Contents



High Frequency Dynamic Nuclear Polarization

R. G. Griffin

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Over the last few years we have developed cyclotron resonance maser (a.k.a. gyrotron) microwave sources that operate at frequencies of 140-527 GHz that permit DNP enhanced NMR (DNP/NMR) experiments in magnetic fields of 5-18.8 T (^{1}H NMR frequencies of 211-800 MHz, respectively). We review the instrumentation used for these experiments, which include new NMR probe designs and tunable gyrotron oscillators and a gyroamplifier based on a photonic bandgap cavity. Collectively, these advances in instrumentation have recently yielded significant improvements in the observed DNP enhancements.

In addition, we discuss frequency profiles of the electron-detected solid effect experiments obtained using trityl radical that show intense saturation of the electron at the usual solid effect condition. We also observe higher order solid effect transitions involving two, three, or four nuclei with surprising intensity, suggesting that higher order transitions are important primarily in the transfer of polarization to nuclei nearby the electron.

Third, we document the effects of nuclear signal quenching induced by the presence of a paramagnetic polarizing agent for conditions used in MAS DNP experiments on homogeneous solutions. Despite the substantial losses due to quenching, we find that four different polarizing agents all provide substantial gains in signal intensity, and in particular that the net enhancement is optimal for biradicals that mediate the cross effect DNP. We suggest that these effects could be mitigated with appropriately designed electron decoupling experiments.

Finally, using narrow line radicals (BDPA and sulfonated BDPA) we have recently detected Overhauser enhancements in insulating solids. Most previous investigations of the Overhauser DNP employed samples with mobile electrons — for example liquids, metals or conducting solids. Thus, this is the first example of Overhauser enhancements in insulators. The process is mediated by e$^-$-^{1}H hyperfine coupling and the experimental data show a field dependence that scales as ω_{0I} in contrast to the inverse field dependence associated with the cross and solid effects, ω_{0I}^{-1} and ω_{0I}^{-2} respectively.

Atomic details of protein folding, interactions and function revealed by NMR

L. Nisius, N. Vajpai, L. Skora, J. Habazettl, M. Gentner, H.-J. Sass, M. Wiktor, and ***S. Grzesiek***

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We extensively use residual dipolar coupling, paramagnetic labeling, scalar couplings and other NMR and non-NMR parameters to characterize folded and unfolded protein states in a quantitative manner. We will give several recent examples. Scalar couplings across hydrogen bonds (H-bonds), which report on the electronic overlap between donor and acceptor orbitals, present a highly sensitive measure of H-bond geometry. Using H-bond scalar couplings, we have recently mapped the pressure and temperature dependent deformation of ubiquitin's H-bond network.[1] We recently also obtained atomic details of the pressure-assisted, cold-denatured state of ubiquitin by high-resolution NMR techniques.[2] This state has structural propensities, which are very similar to ubiquitin's alcohol-denatured (A-) state. At non-denaturing concentrations of methanol, a complete transition from the native to the A-state can be achieved at ambient temperature by varying the pressure from 1 to 2500 bar. This method should allow highly detailed studies of protein folding transitions in a continuous and reversible manner. Abelson kinase (Abl) is an important drug target in the treatment of chronic myelogenous leukemia. We have characterized the solution conformations of the multidomain SH3-SH2-kinase c-Abl core in complexes with ATP-site and allosteric inhibitors. Our data provide detailed insights on the poorly understood combined effect of the two inhibitor types, which is able to overcome drug resistance.[3] Time permitting we will also give NMR structural and dynamical insights on multidrug recognition in the minimal bacterial multidrug resistance protein Tip A.

References:

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NMR of small and large Dynamic Systems

H. Sun[1], M. Schmidt[1], M. Müller[1], N. Schützenmeister[1], H. M. Ge[2], F. Hallwass[1], E. d'Auvergne[1], E. Whitson[3], C. M. Ireland[3], A. Navarro-Vázquez[4], J. Liu[5], R. X. Tan[2], U. M. Reinscheid[1], L. Russo[1], M. Maestre[1], L. Wong[1], S. Pirkuliyeva[6], J. Kühn[6], S. Ryazanov[1,7], J. Wagner[8], J. Levin[8], S. Shi[8], C.O. Fernandez[9], A. Fischer[7,10], N. Wender[7,10], N. Resaei Ghaleh[1,7], S. Eimer[7,10], A. Leonov[1,7], A. Giese[8], R. Benz[12], A. Lange[1], M. Zweckstetter[1,7], and C. Griesinger[1,7]

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NMR spectroscopy is especially suited for the investigation of structurally heterogeneous systems. In the presentation, several avenues towards the characterization of such disordered molecules will be given. First, the combination of NMR spectroscopy employing anisotropic parameters such as residual dipolar couplings and residual chemical shift anisotropies will be demonstrated in combination with chiroptical methods to provide absolute configurations of non-crystallizable molecules whose structures can only be described by ensembles. An interesting cases in which three independent enantioselective syntheses lead to the wrong absolute configuration will be presented.

In the B-cell antigen receptor, the largely intrinsically disordered protein SLP65 constitutively interacts with the multidomain protein CIN85 which is essential for its localization on the plasmamembrane. The structural insight allows to make minimalistic variants of this assembly that are still functional in cellular assays.

The aggregation landscape of α-Synuclein and other intrinsically disordered proteins leading to neurodegenerative diseases is explored and can be interfered with by small molecules. The latter cause novel species to arise whose structural assembly is being investigated with NMR as well as other biophysical techniques.

Compact NMR

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The first chemical-shift resolved NMR spectrum has been measured in1951 at Varian from ethanol with a 0.76 T electro-magnet at 0.1 ppm resolution.[1] Today NMR spectra are measured routinely at 31 times higher field (23.5 T) with an accordingly wider frequency range for the chemical shift and about 1000 times higher sensitivity. Why then would ^{1}H NMR at fields as low as 1 T be of interest? The lecture tries to answer this question with several examples from materials and chemical analysis with permanent magnets, whose field strength is effectively limited to values below 2 T. The examples include nondestructive testing, reaction monitoring in real time and chemical analysis for quality control. While the trend to smaller and more powerful NMR analyzers is documented with the recent advent of desktop spectrometers, it is left to speculation how small NMR spectrometers may become and what use they may have.[2,3]

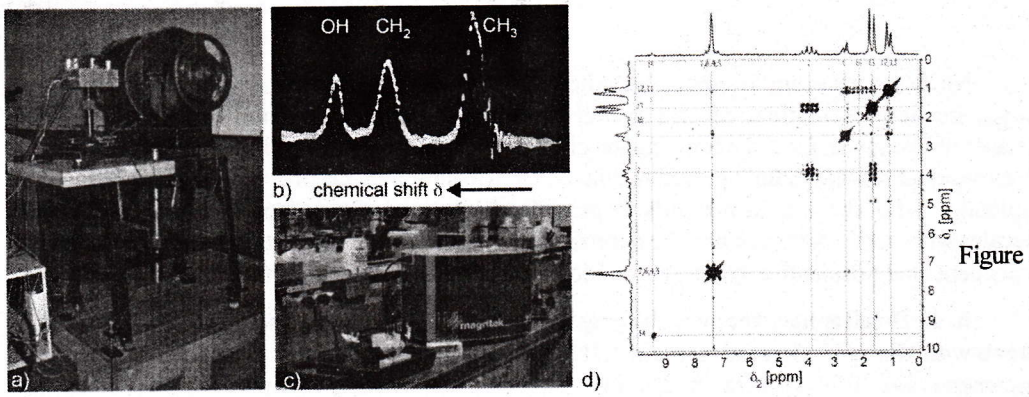

Figure NMR Hardware and spectra. a) Electro magnet of Walther Gerlach from LMU München now set up in Jena to demonstrate early NMR equipment. b) 32 MHz ^{1}H NMR spectrum of ethanol from 1951.[1] c) Permanent-magnet desktop NMR spectrometer for high-resolution Fourier NMR spectroscopy at 42 MHz. d) 2D COSY spectrum of Ibuprofen acquired in 8 minutes with the spectrometer shown in c).

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NMR structures allow the design of pharmaceutically active and potent inhibitors of RNA

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RNA provides an inviting target for pharmaceutical intervention in both infectious and chronic diseases, but it has so far been impossible to identify drug-like molecules with sufficient potency for successful clinical applications. We will present how NMR structure-based drug design is used to optimize the activity of molecules that bind to RNA. The first application is the development of a class of structurally constrained cyclic peptides that target the interaction between the HIV-1 transactivator protein Tat and its response element TAR, which plays an essential role in viral replication. The designed inhibitors of the Tat-TAR interaction have pM binding activity, discriminate between even closely related RNAs, have no cytotoxicity and inhibit viral replication with potency comparable to current antivirals. The same design strategy has been applied to other protein-RNA interactions, and we have used NMR to design new inhibitors of microRNA maturation that partially abrogate the production of oncogenic microRNAs. The new molecules we have identified allow us to investigate whether the inhibition of the biogenesis of specific microRNAs has pharmaceutical benefits and to generate more active drug-like inhibitors of microRNA function.

Molecular Dynamics of G Protein-Coupled Receptors in Membranes

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The recently determined crystal structures of several class A and class B GPCRs represent a breakthrough in our understanding of the complex biochemical processes these molecules undergo in their course of action. However, crystal structures typically represent static lowest energy structures. Once reconstituted into fluid bilayers, these molecules show a fascinating and comprehensive molecular dynamics on several time scales including large amplitude motions. I will provide an overview on recently carried out solution and solid-sstate NMR experiments on the human neuropeptide Y receptor type 2 to characterize some of the motions these class A GPCRs feature.

NMR approaches for elucidating the functional roles of carbohydrate chains

Koichi Kato [1,2,3,4]

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The carbohydrate chains displayed on proteins and lipids play pivotal roles in various molecular recognition events on cell surfaces as well as in intracellular environments. The intermolecular interaction systems involving the carbohydrate moieties could be potential therapeutic targets for various diseases.[1] However, structural analyses of glycoconjugates remain challenging because of heterogeneous and flexible properties of the sugar chains. In view of this situation, we have been developing a systematic methodology to deal with glycoconjugates as target of structural biology.[2,3]

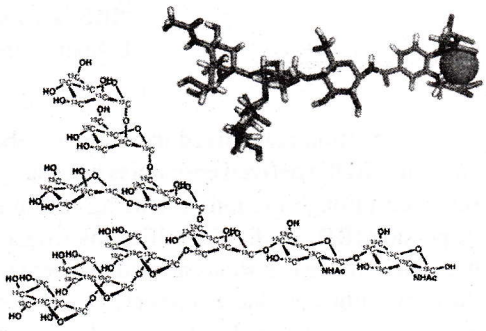

Fig.1 New NMR tools for characterizing dynamic conformational ensembles of oligosaccharides: Stable isotope labeling and lanthanide tagging.

In this presentation, I will outline our approaches for characterizing conformational dynamics and interactions of glycoconjugates using NMR spectroscopy in conjunction with other biophysical and biochemical techniques. To reap maximum benefit of NMR approaches, we have established techniques for overexpression of homogeneous oligosaccharides with isotope labeling, which were chemically tagged with paramagnetic probes as sources of long-distance information (Fig. 1). We demonstrate that lanthanide-tagging offers a new tool for experimental validation of dynamic conformational ensembles of oligosaccharides derived from molecular dynamics simulations. Our NMR approach is also presented for characterization of glycolipid clusters as unique platforms for interactions of amyloidogenic proteins associated with neurodegenerative disorders. These approaches will allow new possibilities for structural studies on glycoconjugates of clinical and pharmaceutical interests.

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Molecular Recognition through Concerted Backbone and Side Chain Motion

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Motion is involved in a large number of protein functions. For ubiquitin, residual dipolar coupling (RDC) derived ensembles have suggested it recognizes binding partners via conformational selection through motions occurring within the supra-τ_c (> 4 ns) range [1]. Subsequent relaxation dispersion (RD) studies identified microsecond fluctuations in backbone [2,3]. However, it has not been clear if these motions are independent or collective, and what role side chains play. To address those questions, we have conducted an in-depth RD analysis of the backbone and side chain methyl groups using recently developed high power $R_{1\rho}$ experiments [3]. In these RD experiments, not only microsecond fluctuations in the side chains have been observed but also motions in the side chain and the backbone have a common time scale. This result suggests that ubiquitin undergoes collective motion involving both the backbone and side chains.

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Principles of Efficient IgE Antibody response revealed by the structure of Grass Pollen Allergen Phl p 5a

Christoph Goebl[1], Margarethe Focke-Teijkl[2], Evelyne Schrank[1], Tobias Madl[1,3,4], Simone Kosol[1], Rudolf Valenta[2], Klaus Zangger[1], and ***N. Tjandra***[5]

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Seasonal allergic inflammation is a common and could be a chronic condition for a large number of populations in the world. The inflammation is due to the body immune response to allergens. The key physiologic event that is responsible for immediate allergic inflammation is cross-linking of mast cell and basophil-bound IgE (Immunoglobulin E) antibodies by allergens. We are interested in learning how some allergens can be more potent than others. Using Nuclear Magnetic Resonance (NMR) spectroscopy the three-dimensional solution structure of one of the most potent and frequent allergens, grass pollen allergen Phl p 5a, was determined. We find two structural determinants that describe increased allergenic activity: (i) the modular assembly of two flexible domains and (ii) the presence of repetitive sequential and structural epitopes. These are unique features in the family of the allergens and lead to the remarkably high allergenic activity of group 5 grass pollen proteins. The obtained structural and dynamical information allowed us to design peptides for SIT (allergen-Specific ImmunoTherapy). We found the efficiency of the peptides to induce blocking antibodies to be generally correlated with the lack of structure in the full-length protein and we identified excellent candidates for therapeutic development.

NMR using Chiral Anisotropic Solvents: Recent Methodological Advances and new Analytical Applications

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NMR spectroscopy in weakly orienting chiral liquid crystals (CLC) is a powerful, original and emerging methodology for analyzing chirality/stereochemistry of guest solutes as well as providing numerous useful molecular information such as the natural, site-specific (D/H) isotopic fractionation.

The growing success of this analytical approach in the (bio)chemist community clearly lies to: i) the continuous development of new multi-dimensional NMR experiments dedicated to the analysis of anisotropic spectra; ii) the discovering of new chiral liquid crystals showing efficient enantiodiscrimination properties; iii) and the multi-domain application of this technique to solve specific problems or provide alternative analytical strategies.

In this presentation, two aspects of these developments are proposed. In a first part, we describe the first experimental detections of ^{2}H-^{13}C isotopomers at natural abundance level (1.7×10^{-4}%, namely, one molecule over 580 000) in oriented systems by combining cryoprobe, high magnetic field (21 T) and optimised ^{2}H-^{13}C heteronuclear 2D experiments.[1] Interestingly, we show that ^{2}H-^{13}C enantio-isotopomers can be distinguished using 2D NMR in polypeptide, chiral aligned media, thus providing a new tool for the chiral analysis.

In a second part, we present a new analytical application of NMR in CLC using lyotropic DNA/water mesophases as orienting NMR solvents. Recently, the enantiodiscrimination properties of water compatible, DNA-based chiral mesophases using ^{2}H NMR to discriminate between enantiomers (chiral molecules) or enantiotopic directions (prochiral molecules) of natural alpha-amino acids have been experimentally demonstrated and reported.[2] Combining ^{2}H-{^{1}H} NMR and DNA mesophases, we experimentally demonstrate that the spectral monitoring of the enzymatic transformation of (*L*)-alanine-d_3 into its enantiomer (and *vice-versa*) by the alanine racemase (AlaR) is possible. The rate constants k_{catL} and k_{catD} of the enzymatic reaction determined by this method are similar to those observed by circular dichroism under slightly different conditions. The first results are very encouraging, and could provide shortly a promising alternative to classical, existing methods (CD, UV spectroscopy or chiral capillary electrophoresis).[3]

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The interplay of phosphate and water in tuning ACC metastability-from stabilization to crystallization via a nano-scale solid-solid phase separation: A molecular NMR view

Shifi Kababya,[1] Assaf Gal,[2] Keren Kahil,[2] Steve Weiner,[2] Lia Addadi,[2] and ***Asher Schmidt.***[1]

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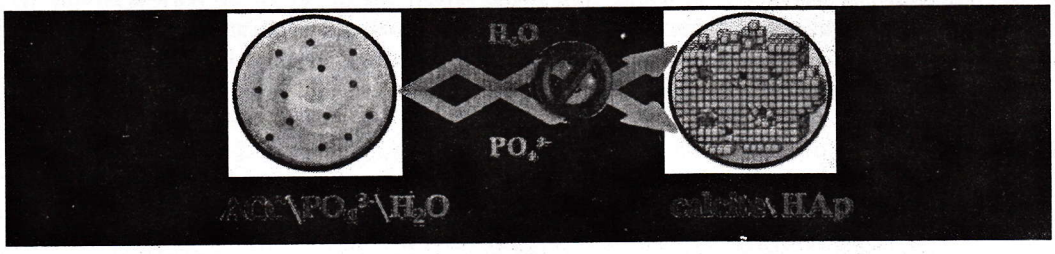
In biomineralization the thermodynamic metastability of amorphous calcium carbonate (ACC) is tuned to serve versatile functional purposes. When bioavailable calcium is required, ACC metastability is offset in vivo, its crystallization is prevented and a readily soluble form is maintained. In cases where crystalline structures are required, ACC is often casted as a metastable precursor that crystallizes via solid-solid phase transformation. ACC metastability is frequently regulated by incorporation of substantial amount of additives such as phosphate ions and water molecules. Their distribution and effect on ACC were studied in few biogenic and synthetic systems, however, the molecular mechanisms that govern ACC stability still remain unclear. Our earlier studies of the calcitic coccoliths and ACC gastroliths will be reviewed first. Following, our investigation - ^{1}H, ^{13}C, and ^{31}P solid state NMR, FTIR, XRD and electron microscopy, of the well-defined synthetic system of hydrous ACC precipitated in the presence of increasing concentrations of PO_4^{3-} will be described. The NMR identifies the interactions of phosphate and water with the CaCO3 matrix while stabilizing ACC and along its gradual phase separation and crystallization. This progression at ambient conditions may mimic the biomineralization process. Our study, by monitoring the intermolecular/ inter-ionic interactions between the different constituents (CO_3^{2-}, PO_4^{3-}, H_2O) and identifying the different phases, attributes ACC stabilization to these interactions and to the interplay between their abundances (levels of phosphate and water).



NMR in Molecular Systems Biology: from structures to function

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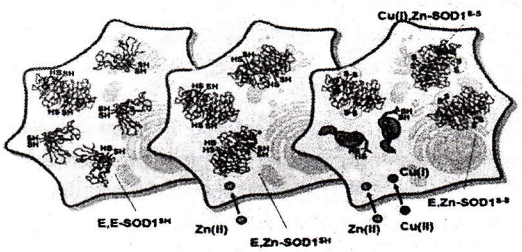
NMR spectroscopy constitutes an unique tool for describing functional biological processes at atomic level and in a cellular context. NMR is indeed suitable not only to characterize the structure and dynamics of biomolecules but, even more importantly, to describe transient interactions and functional events with atomic resolution. Metal transfer processes occurs through protein-protein interactions, with metal ion being transferred from one protein to the next, to the final recipient. The transfer is determined by metal affinity gradients among the various proteins, with kinetic contributing to the selectivity of the process[1]. Furthermore the presence of paramagnetic centers, such as iron-sulfur clusters, dramatically affects the NMR spectra, requiring tailored experiments also integrated with EPR spectra[2]. In cell NMR can provide the description of these processes within living cells[3].



SOD1 maturation steps depending on the presence or not of metal ions and/or of its CCS chaperone.

The power of NMR in describing cellular pathways at atomic resolution in a cellular environment will be presented for a few pathways responsible for copper trafficking in the cell and for the biogenesis of iron-sulfur proteins. New major advancements in in-cell NMR4 and in the characterization of highly paramagnetic systems5 will be also discussed within an integrated approach where, from single structures to protein complexes, the processes are described in their cellular context within a molecular perspective.

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Novel methods based on ^{13}C detection to study intrinsically disordered proteins

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Intrinsically disordered proteins (IDPs) are characterized by highly flexible solvent exposed backbones and can sample many different conformations. These properties confer them functional advantages, complementary to those of folded proteins, which need to be characterized to expand our view of how protein structural and dynamic features affect function beyond the static picture of a single well defined 3D structure that has influenced so much our way of thinking.

NMR spectroscopy provides a unique tool for the atomic resolution characterization of highly flexible macromolecules in general and of IDPs in particular. The peculiar properties of IDPs however have profound effects on spectroscopic parameters. It is thus worth thinking about these aspects to make the best use of the great potential of NMR spectroscopy to contribute to this fascinating field of research.

Recent progress in NMR instrumentation has stimulated the development of a variety of new NMR methods and, among them, exclusively heteronuclear NMR experiments based on ^{13}C direct detection now offer a valuable tool to address the peculiar features of IDPs[1], in particular approaching physiological conditions[2]. The experimental variants to improve the performance of ^{13}C detected NMR experiments to study IDPs include the design of multidimensional experiments, the exploitation of longitudinal relaxation enhancement, the design of experiments to alleviate the problem of extensive cross peaks overlap[2-6]. The new experiments are demonstrated on a paradigmatic IDP. α-synuclein.

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Optimized Proton-Driven Spin Diffusion by Tailored RF-Irradiation Schemes

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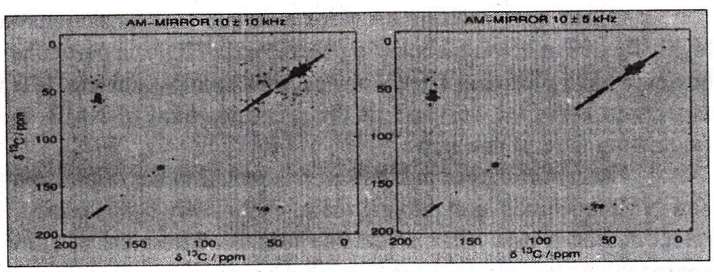
Experiments related to proton-driven spin diffusion are of great importance in solid-state NMR studies of bio-macromolecules. They give information about distances of spin pairs and are, therefore, an important source of short and long range distances, which can be used for sequential resonance assignment and structure calculation, respectively. However, the rate constants of the polarization transfer strongly depend on isotropic chemical shift differences and magic-angle spinning (MAS) frequencies. Irradiation of weak cw (DARR, MIRROR [1]) or phase alternating radio-frequency (rf) fields on the protons (PARIS, SHANGHAI, R-symmetry sequences [2]) lead to a broadening of the zero-quantum (ZQ) line or the generation of additional side bands in the ZQ spectrum and can thus increase the transfer efficiency. Floquet theory [3] allows to calculate position and intensity of these rf side bands. We use analytical expressions obtained from the Floquet analysis to design amplitude modulated (AM) irradiation schemes. The rf fields can be tailored in a way, that side bands of uniform intensity are generated in a specified chemical shift range. As the effective Hamiltonian is closely related to the MIRROR experiment, we call this sequence AM-MIRROR. The flexibility of AM-MIRROR to re-enable offset independent and band-selective spin diffusion even at fast MAS frequencies is demonstrated by numerical simulations and experimental data. We will discuss the properties of the new AM-MIRROR sequence and compare its performance to other existing sequences currently in use. In order to proof the experimental applicability, we recorded 2D AM-MIRROR exchange spectra of U-13C-15N-Ubiquitin at at fast MAS that clearly show the good performance of AM-MIRROR under these conditions.



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Powder NMR Crystallography from Proton Chemical Shifts

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A protocol for the *ab initio* crystal structure determination of powdered solids at natural isotopic abundance is used to determine the crystal structures of four small drug molecules: cocaine, flutamide, flufenamic acid, and theophylline. The method combines solid-state NMR spectroscopy, crystal structure prediction (CSP) and DFT chemical shift calculations. For cocaine, flutamide and flufenamic acid, we find that the assigned ^{1}H isotropic chemical shifts provide sufficient discrimination to determine the correct structures from a set of predicted structures by using the root-mean-square deviation between experimentally determined and DFT-calculated chemical shifts. In most cases unassigned shifts could not be used to determine the structures. This method requires no prior knowledge of the crystal structure, and is used to determine the correct crystal structures to within an atomic rmsd of less than 0.12 Å with respect to the known structures. For theophylline, the NMR spectrum is too simple to allow unambiguous structure selection. We show how the information contained in the NMR chemical shifts is complementary (and an independent measure) to powder XRD (PXRD). Combining ^{1}H NMR chemical shifts, CSP/DFT and PXRD leads to a very robust structure determination protocol, with no hypothesis. Likewise, we use this procedure to determine for the first time the crystal structure of a pharmaceutically pertinent molecule with previously unknown structure, where previous attempts by XRD alone had not been successful.

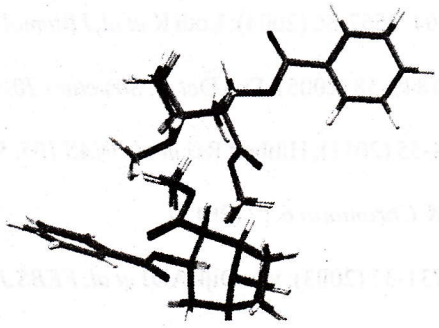

Fig.1 The crystal structure of powdered Cocaine determined by NMR, as compared to the known structure determined by X-ray diffraction on a single crystal sample.

Structure and dynamics in gene regulation and DNA repair

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NMR spectroscopy has developed to an invaluable tool to investigate the structure and dynamics of biomolecules. It provides unique detailed information on the interactions between biomolecules which can be weak and transient, that cannot be easily obtained by other methods. This progress is due to technical advances in NMR spectroscopy (3D double- and triple-resonance NMR, and high-field and sensitive NMR instruments), in protein production (high-throughput protein production and $^{13}C/^{15}N/^{2}H$ isotope labeling) and considerable advances in computing.

At Utrecht we use NMR spectroscopy to study structure and dynamics of protein-protein and protein-DNA complexes involved in DNA transcription and DNA repair. Studied examples are (i) E.coli Lac repressor,[1] (ii) the human XPF-ERCC1 DNA repair complex,[2] (iii) the Rad6-Rad8 ubiquitination complex[3] and (iv) nucleosome structure and dynamics.[4] $^{13}C/^{15}N$ isotope labeling was required for all NMR studies, and in several cases complemented with ^{2}H labeling. Several complexes were modelled using our docking procedure Haddock.[5] In many cases the NMR studies were complimented with biophysical data and results from complimentary structural biology techniques. The different examples demonstrate the strength and flexibility of NMR for studying the structure and dynamics of proteins and complexes involved in cellular regulation.

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NMR studies of protein folding and misfolding

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Protein folding and unfolding are crucial for a range of biological phenomena and human diseases. Defining the structural properties of the involved transient species is therefore of prime interest. Using a combination of cold-denaturation with nuclear magnetic resonance spectroscopy we reveal detailed insight into the unfolding of the homodimeric repressor protein CylR2. Seven three-dimensional structures of CylR2 at temperatures from 25 °C to -16 °C revealed a progressive dissociation of the dimericprotein into a native-like monomeric intermediate followed by transition into a highly dynamic, partially folded state. The core of the partially folded state appeared critical for biological function and misfolding.[1]

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Intercalation of large molecules into DNA: intermediates and mechanisms

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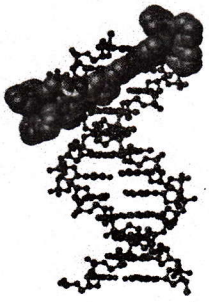
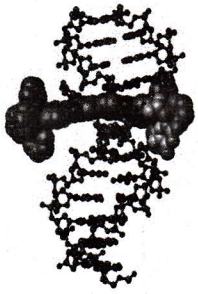
Implications of intercalative binding in DNA duplexes present a challenge ever since the discovery of aromatic molecules residing between base pairs. Typically, intercalation consists offlat rings sandwiched between nucleotide bases, but the steps leading to intercalationdepend on the ligand form: bulkygroups may temporarily require considerable DNA distortions, whichdetermine both the speed of the process (seconds to days; 1) as well assequence-specificity along the DNA. Rather than a wide opening of the DNA duplex, threading of a ligand through the DNA is likely to involve a series of tightly interacting intermediate complexes, where (aromatic) groups from both the DNA and the compound exchange interaction partners on the other molecule until the bulky group emerges in the other DNA groove, and most DNA base pairs are reformed. We probe intercalation by a chiral, chargeddimericRu complexcontaining planar phenazinyl moieties surrounded by bipyridines arranged in a propeller-like fashion (see figure). Several intermediates of the intercalation process are trapped, starting from an initial minor groove binding state (left figure; 2) until the final intercalated state (right figure); MD simulations complement the pathway mapping. Besides a better understanding of the roles ofintercalators, this studymay serve as an example for reactions involving a complex sequence ofintermediate, tightly interacting molecules, asoften found in other contexts, e.g. withDNA synthesis.





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Structural Analysis of Chemokine-Glycosaminoglycan Interactions

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Chemokines constitute the largest subfamily of cytokines that provide important regulatory cues in trafficking leukocytes. Glycosaminoglycans (GAGs) such as heparan sulfate are highly negatively charged linear polysaccharides. They are ubiquitously found on cell surfaces, and mediate a wide variety of biological functions. Though it is now well established that chemokine-heparan sulfate interactions regulate leukocyte recruitment, the structural basis and molecular mechanisms underlying these interactions are not well understood. CXCL1 (mKC) is a proinflammatory neutrophil activating chemokine, and exists in equilibrium between monomers and dimers (K_d = 36 ?M). NMR titration and diffusion studies of WT-CXCL1 (exists as a mixture of monomers and dimers) revealed that GAG binding to the monomer induces dimerization and that a minimum chain length of an octasaccharide is essential for dimerization. NMR and mutational studies using an engineered disulfide trapped CXCL1 dimer (dCXCL1) showed that GAGs bind orthogonal to the helical axis spanning the dimer interface.Residue level dynamics and stability measurements of apo- and GAG-bound dCXCL1 demonstrated GAGs enhanced chemokine's structural integrity. These data together indicate GAG-bound dimers regulate in-vivo neutrophil trafficking by multiple mechanisms including, defining the gradient formation and increasing the life time of 'active' chemokines on the endothelial cell surface for sustained recruitment.

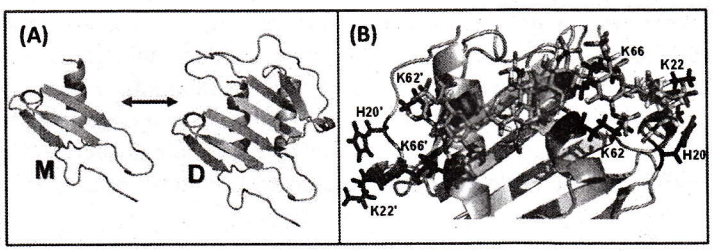

Fig1: (A) Structures of CXCL1 monomer-M and dimer-D; (B)NMR derived structural model for dimeric CXCL1-heparin octasaccharide complex.

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NMR spectroscopy as a tool in carbohydrate and glycoprotein analysis

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To define the structure of Carbohydrates and of Glycans derived from glycoconjugates completely, the determination of a number of structural parameters is required. This holds for the primary as well as for the three-dimensional structure. The obvious reasons for this feature are the following: *i)* diversity in constituting monosaccharides and non-carbohydrate substituents, *ii)* various types of linkages between monosaccharides, *iii)* the occurrence of branching and *iv)* intrinsic flexibility of carbohydrate chains. Furthermore, the absolute configuration of the constituents has to be established by methods that we have been developed.

For the determination of primary structures we derived the "structural reporter group concept" for the interpretation of ^{1}H-NMR spectra. We noticed that the chemical shifts of protons resonating apart from the bulk signal could be applied as identifiers for the structure in terms of type of monosaccharide constituent and glycosidic linkage. The structures could be deduced for a large library of compounds. The three-dimensional structure is much more difficult to define. Merely NMR spectroscopy even with the most advanced approach is not adequate. Combination with information from complementary methods is essential, because the glycan chains have a large flexibility. MM and MD calculations are often applied. For glycoproteins the interaction between glycan and protein are additional complications. A few examples of carbohydrates and glycoproteins will illustrate these aspects.

The glycans in glycoproteins have two functions: Intramolecularly by affecting the protein structure and intermolecularly by interacting with complementary molecules. The basis for productive interaction in the sense of biological function can be carbohydrate-protein interaction or carbohydrate-carbohydrate interaction. The latter feature will be illustrated for sponge cells. It is conceivable that for glycoproteins carbohydrate-protein as well as protein-protein interactions are needed to be effective. This principle of dual commitment has already been proven for glycolipids.

Heterogeneous Platinum Metal-Catalyzed Deuteriumu Labeling Methods Characterized by the Simplification of NMR Charts

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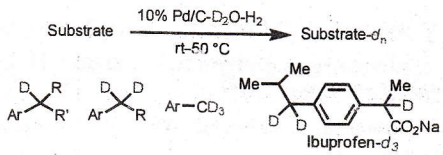
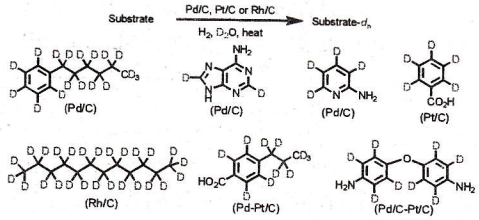
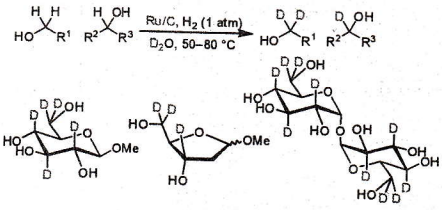
Deuterium (D) labeled Compounds are utilized in various scientific fields such as mechanistic elucidation of chemical and enzymatic reactions, preparation of new functional materials, tracers for microanalysis, D-labeled heavy drugs and so on. Although the H-D exchange reaction is a straightforward method to produce deuterated organic compounds, many precedent methods require expensive D_2 gas and/or harsh reaction conditions. A part of our leading research agendas are intended to the development of novel and functional heterogeneous platinum group catalysts and the reclamation of unknown functionalities of existing heterogeneous platinum group catalysts.





During the course of the study, the benzylic position of substrates was time-dependently and site-selectively deuterated under mild and Pd/C-catalyzed hydrogenation conditions in D_2O. Heat conditions promoted the H-D exchange reactivity of the Pd/C-H_2-D_2O combination and facilitated the H-D exchange reaction at not only the benzylic sites but also inactive C-H bonds and heterocyclic nuclei. It is noteworthy that Pt/C indicated a quite high affinity toward aromatic nuclei, and the H-D exchange reaction was strongly enhanced by the use of Pt/C as a catalyst under milder conditions. The mixed use of Pd/C and Pt/C or a novel bimetallic Pd-Pt on a support were also found to be more efficient in the H-D exchange reaction compared to the independent use of Pd/C or Pt/C. Furthermore, simple alkanes, which are inactive substrates by most definitions, could also be efficiently deuterated under Rh/C-catalyzed conditions. The use of Ru/C enabled the regiospecific and efficient D incorporation at the α-position of alcohols and the results were applied as a regio- and stereoselective



multi-deuteration method of sugars. H_2 gas is quite important as an activator of the zero valent metal of catalysts. The Pd/C-catalyzed *in-situ* conversion method of H_2 gas to D_2 gas in D_2O at room temperature was recently established in consequence of the detailed analysis of the deuteration mechanisms. It is possible to expand in application to the selective deuteration using the combine of these results and chemoselective heterogeneous catalyst developed by us. Therefore, these H-D exchange methodologies can contribute to a wide variety of chemistry fields as convenient and practical methods.

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1H-[13C]-NMR Study for Understanding Antidepressant effect of Ketamine in Social Defeat Model of Depression

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Depression is one of major causes of disability and suicidality worldwide. Most of the conventional antidepressants have long remission time and low recovery rate. Ketamine, an NMDA receptor antagonist, shows rapid antidepressant effect at sub-anesthetic dose but the mechanism of action is not clear[1]. In this study, we have evaluated the response of ketamine on glutamatergic and GABAergic neuronal metabolism in social defeat model of depression by using ^{1}H-[^{13}C]-NMR spectroscopy together with an infusion of [1,6-$^{13}C_2$]glucose. Depression was induced in 2 month old C57BL/6J mice by subjecting them to a social defeat (SD) paradigm for 10 consecutive days. Sucrose preference and Social Interaction test were performed to assess the depression like phenotype[2]. Ketamine (10 mg/kg, i.p.) was administered to control and depressed mice. The concentration and ^{13}C labeling of brain amino acids were measured in prefrontal cortex (PFC) extract using ^{1}H-[^{13}C]-NMR spectroscopy (Fig.1) on a 600 MHz NMR spectrometer (Bruker Biospin)[3]. Mice subjected to SD paradigm showed decrease in sucrose consumption and social interaction as compared with control which could recover to control level following acute ketamine treatment. The percentage ^{13}C enrichment of glutamate-C4, glutamate-C3,GABA-C2, glutamine-C4, and aspartate-C3 from [1,6-$^{13}C_2$]glucose was found to be significantly decreased (p<0.01) suggesting reduced glutamatergic and GABAergic neuronal metabolism in SD mice as compared with control. The reduced labeling of amino acids in depressed mice could recover to control value following an acute treatment of ketamine (Fig. 2). These data indicate that acute treatment with ketamine improved the excitatory and inhibitory neuronal activities in the PFC of depressed mice.

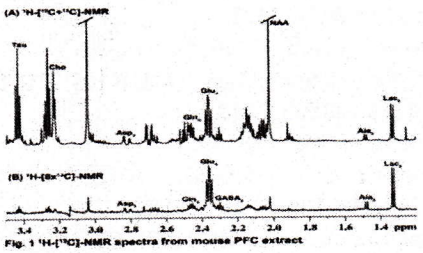

Fig. 1 ^{1}H-[^{13}C]-NMR spectra from mouse PFC extract

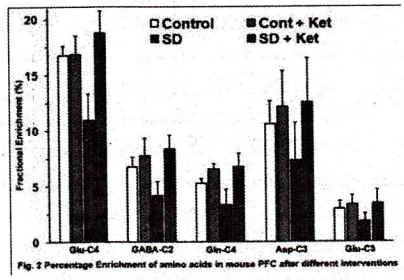

Fig. 2 Percentage Enrichment of amino acids in mouse PFC after different interventions

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Testing Enantiopurity by NMR Spectroscopy: Our Recent Strategies

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We have explored multipronged strategies for chiral-discrimination and measurement of enantiomeric excess in isotropic solutions, such as, design of novel chiral auxiliaries and one and two dimensional NMR experimental methodologies. The order sensitive NMR observables have been employed for differentiation of enantiomers by embedding the chiral molecules in the weakly ordered chiral liquid crystalline media. The new and weak chiral aligning media have also been introduced for such a purpose and numerous one and two dimensional experimental strategies have been developed to derive the anisotropic NMR parameters. In this presentation, I will discuss some of our recent results.

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New NMR methods for rapid data acquisition and analysis: Application to Metabolomics

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We have recently developed several new NMR methods which accelerate data acquisition and analysis. The methods combine the different fast NMR techniques such as projection NMR spectroscopy, non-uniform sampling and multiple NMR receivers to increase the efficiency and provide unambiguous assignments. Two such methods will be presented. The first one involve the use of dual NMR receivers to acquire three 2D NMR spectra in a single experiment. The three 2D experiments, namely, 1) GFT (3, 2) [^{1}H, ^{13}C] HSQC-TOCSY 2) [^{13}C, ^{1}H] HETCOR and 3) [^{1}H, ^{1}H] TOCSY provide complementary information for rapid assignments. The second approach involves the application of projection NMR spectroscopy to DOSY. The methodology speeds up the acquisition by replacing a series of HSQC spectra generally acquired by a single 2D constant time HSQC with the line widths encoding the diffusion rates. Application of these methods to some challenging systems studied in our laboratory will be presented.

Native structure governs the amyloid formation and fibril reversibility of a short cyclic peptide hormone

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Protein/peptide hormone storage and secretion in mammalian systems are intricately regulated. Storage of these hormones within sub-cellular compartments and their subsequent release is crucial for their native function. Recently, it was shown that peptide hormones form amyloid inside the secretory granule either in presence or absence of helper molecules such as glycosaminoglycans (GAGs). Here, we hypothesize that native structure and post-translation modification of protein/peptide may control its amyloid formation and subsequent monomer release. In this study, we investigated the role of disulfide bond in conformational dynamics, aggregation and fibril reversibility of a cyclic peptide hormone somatostatin-14, SST (disulfide bond between Cys3 and Cys14) *in vitro*. Here, we show that release of the disulfide bridge in somatostatin significantly increases its conformational flexibility and results in rapid amyloid formation. Furthermore, all-atom MD simulations probing self-association tendencies of the both the forms of peptide indicates marked differences in the intermolecular interaction patterns with greater contribution of hydrophobic interactions in case of non-cyclic somatostatin (ncSST). Interestingly, our results also indicate that almost all amino acid residues in both forms of somatostatin contribute to stable amyloid core, as suggested from our H/D exchange and proteinase K digestion experiments. Further, our results also show that ncSST fibrils possess greater conformational and thermal stability and also release monomers at a slower rate as compared to SST fibrils. Our data suggests that changes in native structure of the peptide hormone may alter its conformational dynamics and amyloid formation, which might have significant implications on its secretory granule biogenesis.

NMR Experiments for the Ordered Phases - Assignment, Structure and Dynamics

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The enormous success of solution state NMR in deciphering structures of molecules of chemical and biological interest has been largely due to experiments that could map proximities of atoms both through scalar and dipolar couplings. Similar approaches to study molecular structures in solids have been evolving and in recent years significant advances have been made for the case of several partially ordered and fully rigid systems. For such studies, it is necessary that the homonuclear dipolar couplings are eliminated while retaining chemical shifts and the heteronuclear couplings, requiring special techniques to be developed. Such studies can provide useful proximity information in the case of rigid and semi rigid systems, as the coherences can be generated through dipolar couplings. Here, we present our efforts in utilizing several correlation and recoupling experiments for the study of rigid powder samples of chemical and biological interest as well as static oriented liquid crystal samples. Correlations based on both scalar and dipolar couplings have been explored. The application of these techniques to liquid crystals oriented in a magnetic field as well to a few synthetic and natural peptides will be presented.

Spin Diffusion and Solid Effect Dynamic Nuclear Polarization

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The physics of the spin dynamics during solid effect Dynamic Nuclear Polarization (SE-DNP) can be modelled using a Liouville von Neumann master equation acting on a system density operator. Such simulations are restricted to relatively small spin systems due to the exponential growth of the Liouville space dimension, which is for spin 1/2 particles growing with 4^{n+1}, where 'n' is the number of nuclei. The simulations are limited to between 10 to 20 nuclear spins, and although they have provided an insight into the mechanism driving DNP for small systems [1], they cannot demonstrate phenomena apparent in larger systems. The quantum mechanical explanation of the transport of polarization away from the paramagnetic centres is not fully understood [2]. Simulations involving greater spin systems are necessary to gain more understanding of these processes that lead to the polarization enhancement of nuclei far away from the electron radical i.e. the 'bulk' nuclei of the system. We have recently developed a tool surpassing the limit dictated by this exponential barrier. It can be shown that all of the dynamics concerning the polarization build-up are contained in the Zeeman subspace of the full Liouvillian. Projection superoperators were used in order to project the SE-DNP dynamics into the zero-quantum subspace [3] and subsequently into the Zeeman subspace of the zero-quantum subspace. The outcome is a master equation perturbative to second order and applicable to spinsystems satisfying the following condition:

$$max\left\{|d_{kj}|^2, \frac{|\omega_A B_k|^2}{|\omega_I|^2}, R_1^2, r_{1k}^2\right\} \ll min\left\{(r_{2k}+r_{2j})^2, (R_2+r_{2k})^2\right\}$$

In effect, the dynamics are confined to a subspace of dimension 2^{n+1}. Using this strategy we show that all of the dynamics of such a master equation are contained on the diagonal of the density matrix, and thus the master equation itself is classical in form. We then show that the master equation can be rewritten in the Lindblad form, from which a set of Lindblad jump op- erators is obtained along with their respective effective rates. These effective rates provide direct insight into the underlying spin physics and can be used to explain the transport of polarization by spin diffusion. Such jump rates rely on the nuclear Larmor frequency, the conventional NMR longitudinal and transverse relaxation times, the strength of the microwave field, dipolar coupling strength parameters, electron thermal polarization, as well as several operator-valued coefficients. Thus it is shown that the whole of the SE-DNP dynamics involving polarization build-up can be described by a set of effective rates.

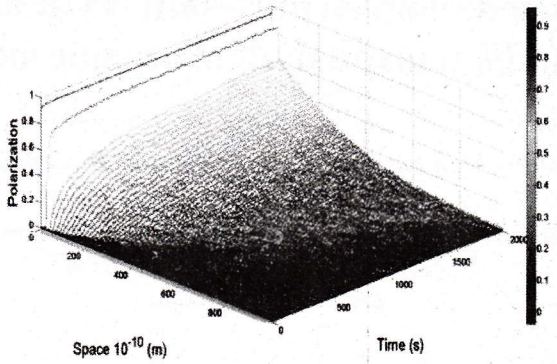

Figure 1: Polarization diffusion in a spin chain with 80 nuclei

The master equation in the Lindblad form can be solved by variable-time Dynamic Monte Carlo (DMC) [4]. The method relies on calculations of trajectories of the spin states, which are then averaged in order to approximate the polarization dynamics for each spin. The advantage is that the algorithm does not require vast amounts of memory, which is therefore no longer a limiting factor for the simulations. A stand-alone desktop enables simulations that involve an excess of 100 nuclear spins. The polarization transport was successfully demonstrated for long spin chains (fig. 1), the process was shown to resemble diffusive motion, and hence adiffusion constant can be obtained. The same projection method can also be applied to the cross effect (CE-DNP). Furthermore, we demo-nstrate that for certain parameter he spin dynamics of DNP can be described by a system of rate equations that depend on a first-order approximation of the master equation.

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Real-time homodecoupled pure-shift NMR methodologies for unambiguous analysis of organic molecules

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The recent strategic developments of experimental methods for the simplification of crowded ^{1}H spectra, TOCSY, HSQMBC and HSQC, by means of real-time homodecoupling has offered new possibilities for unambiguous analysis of complex molecules. In this regard, we will discuss the recent contributions from our laboratory: *viz.*, real-time pure-shift spin-echo, COSY, NOESY and ROESY and apply for organic molecules. The enhanced resolution allows to derive possibly more precise structural information than the conventional methods.

Heteronuclear spin decoupling in solid-state NMR

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Heteronuclear spin decoupling is very important in solid-state NMR experiments. The pulse sequence employed in decoupling determines the spectral resolution and magnitude of coherence decay times (T_2') in sequences with spin-echo blocks. We will present here outline of pulse schemes that can be applied for a wide range of magic-angle spinning frequencies, their properties with respect to resolution and T_2' values, and their dependence on various experimental parameters. We will also look into the commonality of some of the phase-modulated decoupling schemes.

Automated Assignment and the Information Content of NMR Data

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Resonance assignment constitutes the first and often very time-consuming step to a structure. The new FLYA algorithm for the assignment of backbone and side-chain chemical shifts has the reliability and flexibility to replace manual assignment procedures for most NMR studies of proteins.[1] The algorithm enables, in combination with the assignment of NOE distance restraints, the fully automated structure determination of proteins starting from raw NMR spectra, in favorable cases even without any "through-bond" spectra.[2] Applications to proteins and nucleic acids as well as from solution and solid state NMR will be shown.[3]

NMR protein structure determination relies primarily on NOE distance restraints for which a concise information content measure analogous to resolution in crystallography has been lacking. Here, we characterize the information content of NMR data for a structure calculation with a meaningful single number, the negative logarithm of the probability to fulfill the restraints by random structures, considering how much each restraint restricts the conformation space and how redundant it is with others.

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Multi-spin Quantum Control: Applications in NMR and Quantum Information

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Many interesting applications in NMR as well as in Quantum Information arise out of ability to control a large spin system. For example, a large star-topology spin-system allows a simple way to prepare NOON state - the highest multiple-quantum state. NOON states can have some interesting applications in NMR as well as in Quantum Information Processing. Here we describe some applications of NOON states, like in diffusion studies and in characterizing RF inhomogeneity. In the field of Quantum Information, control over large spin systems allows realization of larger number of quantum bits. We describe some of the recent and on-going experiments on the quantum simulations of single- and many-particle dynamics.

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Are the wavelet based de-noising techniques necessary or optimum for NMR spectroscopy?

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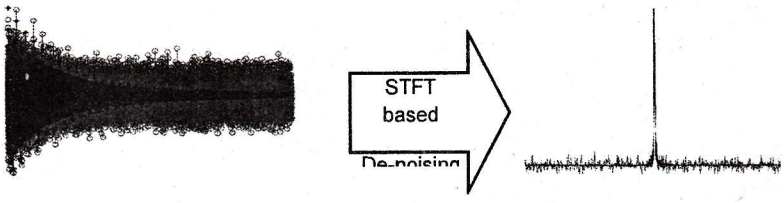
Nuclear Magnetic Resonance (NMR) based metabolomics or analysis of metabolites in body fluids is fast becoming an important and reliable technique in the medical diagnostic industry. For such analysis, often ^{13}C spectra are found to be advantageous over ^{1}H spectra due to their wide spectral range and hence less overlapping, J-multiplet free peak profile, narrow line-widths and possibility of further simplification of spectra using techniques like DEPT. However, the inherent insensitivity restricts ^{13}C based NMR from being extensively used for metabolomics as quantitative analysis based on noisy spectra becomes unreliable.

Recent developments in technology and methodology such as cryogenically cooled probes, high field magnets, dynamic nuclear polarization and digital signal processing techniques like 'spectral de-noising', however, are gradually preparing ^{13}C based NMR spectroscopy a sure candidate for quantitative analysis. Among different available de-noising techniques, the ones based on Wavelet Transform (WT) are the most popular and widely favored in almost all fields of signal processing, primarily because of their multi-resolution functionality.

Here we discuss, if the features which make WT de-noising so popular in other fields of science, are necessary or optimum for NMR spectroscopy. In addition, we demonstrate both qualitatively and quantitatively that de-noising techniques based on relatively straight forward Short Time Fourier Transformation (STFT) are good enough for all practical purposes and might be opted as an alternative for NMR as they are simpler to execute and relatively easier to incorporate in any spectrometer software interface.



Role of transthyretin's backbone conformational flexibility in amyloid fibril formation

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Transthyretin (TTR) is a 55 kDa thyroxine transporter protein that is responsible for a large number of amyloidoses. The wild type protein is implicated in senile systemic amyloidosis whereas its mutants are responsible for neuropathies, cardiomyopathy, ocular, leptomeningeal and other forms of amyloidosis.[1] Biophysical characterization of full length, wild type and mutant forms of TTR by various groups have revealed that protein aggregation is preceded by tetramer dissociation to monomers which then proceeds to form fibrils through a non-native or intermediate state. Mutations that destabilize the protein have higher fibril forming propensity and *vice versa*. Although conformational dynamics has been indicated to be a key factor facilitating fibril formation,[2] this has not been investigated in details before. Here, we probe the backbone dynamics of TTR spanning multiple time scales and combine them with molecular dynamics (MD) simulations to gain insights into the process of fibril formation. Results of backbone ^{15}N R_1, R_2 and $\{^1H\}$-^{15}N NOE spin relaxation measurements on wild type TTR at 40 ÚC and pH 5.8 suggests that the molecule remains a tetramer with an estimated rotational correlation time of 21 ns and an isotropic diffusion tensor. Estimation of modelfree order parameters suggests that most of the residues that are dynamic in this regime (i.e. ps – ns timescales) reside in the unstructured regions in the periphery of TTR's structure while the hydrophobic core is virtually intact and is in agreement with MD calculations performed in our group. In addition, we also probed the existence of slower timescale (~ms) motions using ^{15}N C.P.M.G. relaxation dispersion NMR on backbone amide spins of TTR. Here, we found that the dynamic residues are predominantly located in the β-strands of TTR's hydrophobic core that also forms the interface between multiple subunits. Fitting the set of contiguous, dynamic residues to a 2-site exchange model (3-ste exchange model did not significantly improve the fit), we found that approximately 10 % of the ensemble exists in chemical exchange with a minor conformer. Similar experiments on a set of stabilizing and destabilizing (pathogenic) mutants of wild type TTR has given crucial information in the modulation of backbone dynamics by these mutations and provide a model for the role of conformational flexibility in the initiation of fibril formation.

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"Perfect Echo" INEPT

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A "perfect echo" based INEPT experiment that demonstrates more efficient long range heteronuclear polarization transfer over conventional INEPT has been developed. The perfect echo INEPT suppresses undesired homonuclear ^{1}H-^{1}H *J*-coupling evolution and simultaneously allows desired heteronuclear *J*-coupling evolution to continue during INEPT transfer period. This leads to improvement of short range polarization transfer efficiency at longer INEPT transfer delays and also enhances the sensitivity of long range INEPT experiment drastically. This improvement is observed when loss of magnetization due to homonuclear ^{1}H-^{1}H *J*-modulation is more severe than that of T_2 decay. This is particularly true for long range INEPT experiment in small molecules where the long range heteronuclear couplings are comparable in magnitude to homonuclear ^{1}H-^{1}H *J*-couplings and T_2 of protons is longer. For shorter delays, its efficiency of polarization transfer is equal to that of conventional INEPT. Efficient polarization transfer is observed for small molecules dissolved in isotropic as well as weakly aligned media. Further, simulation results obtained using the full propagator and product operator analysis agree well with the experimental observation.

NMR in validating Ayurveda

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The growing interest in systems perspective is not only revolutionising cell biology but also providing the impetus for clinical medicine to shift from a reductionistic to a holistic approach for efficient disease management. This inevitably brings into focus one of the longest unbroken healthcare system in the world, i.e. ayurveda, indigenous to Indian subcontinent. The unique ability of NMR to study whole systems (*in vitro* and *in vivo*) and generate a wide range of information non-invasively makes it ideally suited to study holistic medicine like ayurveda. It offers a powerful non-invasive means to not only validate ayurveda but also to gain understanding of its concepts and translate them for use in modern healthcare. Different areas ranging from ayurveda's therapeutic use of medicinal plants to diagnosis, treatment efficacy and concepts of preventive healthcare can be studied and validated effectively through NMR, opening new vistas for expanding the role of NMR in healthcare. This presentation, while outlining the various applications of MR in ayurveda, will focus on NMR phytometabolomics to understand ayurvedic pharmacological use of medicinal plants and polyherbal formulations. The work also explores the potential of NMR to provide metabolosensory signatures, pushing the boundaries of NMR applications.

Visualizing Transient Structures in A-site RNA of the Ribosome[1]

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Dynamic changes in RNA structure drive many essential processes in living cells. Studies of RNA dynamics have focused on fluctuations about the dominant ground state at sub-microsecond timescales or large-scale transformations in secondary structure occurring at timescales slower than seconds. By using NMR relaxation dispersion and mutagenesis, we show that non-canonical regions of A-site Ribosomal RNA undergo transient excursions away from the ground state towards short-lived (μs lifetimes) and low populated (2%) excited states that feature local rearrangements in secondary structure and base-pair alignment in regions rich in non-canonical residues. A-site ribosomal RNA contains two highly conserved internal loop adenines A1492 and A1493, which serve to decode the mRNA message by looping out and stabilizing a codon-anticodon mini-helix when it is formed between mRNA and its cognate aa-tRNA. A-site is also known to bind to many antibiotics where drug binds the internal loop, flips the two adenines out and the adenines are forced to bind the codon-anticodon minihelix irrespective of correctness of tRNA. The excited state conformation we proposed is highly conserved and defines a new type of RNA switching that can be integrated into biological circuits. The A-site ES sequesters the A92 and A93 into base-pairs, such that they are no longer available for interacting with incoming tRNAs. Indeed, the C1407U mutation, which stabilizes the A-site ES has previously been shown to significantly increase the stop-codon readthrough and frame shifting, suggesting that the mutation weakens codon-anticodon interactions in the A-site and decreases the fidelity of elongating ribosomes.

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(Footnotes)

Probing supra-τ_c Dynamics on GB3 through $^{13}C_\alpha$"H_α Order Parameters

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The intramolecular dynamics of biomolecules are intimately connected to their biological functions. Residual dipolar couplings (RDCs) measured with nuclear magnetic resonance (NMR) spectroscopy provides detailed information concerning protein dynamics spanning the psec to msec time-scales (1a) and could be cast into an ensemble suggesting conformational selection of ubiquitin's promiscuous binding (1b). Determination of RDC-derived order parameters (S^2_{RDC}) is complicated as the actual magnitude of the alignment tensors are reduced due to dynamic averaging. In the past, Lipari-Szabo order parameters (S^2_{LS}), which describe dynamics occurring on time-scales up to the rotational correlation time ($\tau_c \leq$ low nsec), have been used as an upper bound for the scaling of S^2_{RDC}: $S^2_{LS} \geq S^2_{overall} S^2_{RDC}$ (1c). In a recent publication, we introduced an iterative method for the analysis of RDCs entitled Optimized RDC-based Iterative and Unified Model-free analysis (ORIUM) (2). We opened a new avenue for calculating $S^2_{overall}$ without S^2_{LS}, which exploits the fact that an inter-nuclear vector's motional variance cannot be negative by definition. For backbone amide vectors, this approach yields scaled S^2_{RDC} parameters that are below or within error of the parameters. Here, we have determined C_α"H_α parameters for the B3 domain of protein G (GB3) at ^{13}C natural abundance from the NMR parameters R_1, R_2, and hetero-NOE. In addition, measurement of [^{13}C,^1H]-TRACT (3) provides the residue-specific transverse cross-correlated relaxation rates (η_{xy}) between the chemical shift anisotropy and dipole-dipole relaxation. Subsequently, four experimentally determined parameters, R_1, R_2, hetero-NOE and η_{xy}, are used to fit for. With , we show that our approach for determining is also valid for the C_α"H_α vectors reducing the requirement for scaling.

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Testing Enantiopurity by NMR Spectroscopy: Our Recent Strategies

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We have explored multipronged strategies for chiral-discrimination and measurement of enantiomeric excess in isotropic solutions, such as, design of novel chiral auxiliaries and one and two dimensional NMR experimental methodologies. The order sensitive NMR observables have been employed for differentiation of enantiomers by embedding the chiral molecules in the weakly ordered chiral liquid crystalline media. The new and weak chiral aligning media have also been introduced for such a purpose and numerous one and two dimensional experimental strategies have been developed to derive the anisotropic NMR parameters. In this presentation, I will discuss some of our recent results.

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NMR Structural Studies on a Human Lymphatic Filarial Aspartic Protease Inhibitor

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In an intention to structurally understand the Filarial Infection, an aspartic protease inhibitor from human lymphatic filarial parasite, *Brugia Malayi* (Bm-Aspin) has been characterized for its interactions with human enzymes, Pepsin, Cathepsin D, Cathepsin E and Renin using UV Spectroscopy and Isothermal Titration Calorimetry. The results of these analyses suggest that Bm-Aspin inhibits the activities of all the four enzymes and indicate that the mode of protease inhibition by the Aspin is competitive for Pepsin & Cathepsin-E, non-competitive for Renin and mixed for Cathepsin-D. However, there was no structural information available on these inhibitors to explain the inhibition process from the structural point of view. Hence, for the first time, the Multidimensional NMR structural study has been initiated on the filarial protein. Initial NMR experiments suggested an aggregated sample conditions. We screened the sample under different solvent conditions with the use of detergents. The multi-dimensional NMR experiments that have been carried out on Bm-Aspin in SDS micelles indicate the feasibility to determine the solution structure by NMR and the backbone resonance assignment is in progress. With the available residue assignment, we could corroborate the results obtained by kinetic methods using NMR. In addition, the binding studies of the Aspin with the human proteases have been explained from the NMR titration studies.

Solution structure of the Herpesvirus Nuclear Egress Complex Subunit Exhibits a Novel Fold.

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Cytomegaloviruses, like other herpesviruses, both replicate their DNA and assemble their nucleocapsids in the nucleus. These nucleocapsids must then traverse the nuclear membrane in a fascinating process known as nuclear egress that has been thought to be unique to herpesviruses. In human cytomegalovirus (HCMV) these two proteins are a membrane protein, UL50, and a soluble protein, UL53. In murine cytomegalovirus (MCMV), the subunits are termed M50 and M53, respectively. We present here an NMR-determined solution-state structure of residues 1-168 of M50, which exhibits a novel protein fold (i.e., there is no known structural homologue). Using NMR methods, we mapped the binding of a segment of UL53 (highly conserved in mouse CMV), which is required for heterodimerization, to a region including a groove on M50. Single substitutions of UL50 residues corresponding to residues within the groove substantially decreased UL53 binding *in vitro*, and disrupted UL50-UL53 co-localization and caused lethal defects during HCMV infection.

Pseudo 5D NMR Experiment to Facilitate the Assignment of Backbone Resonances in Proteins Exhibiting High Backbone Shift Degeneracy

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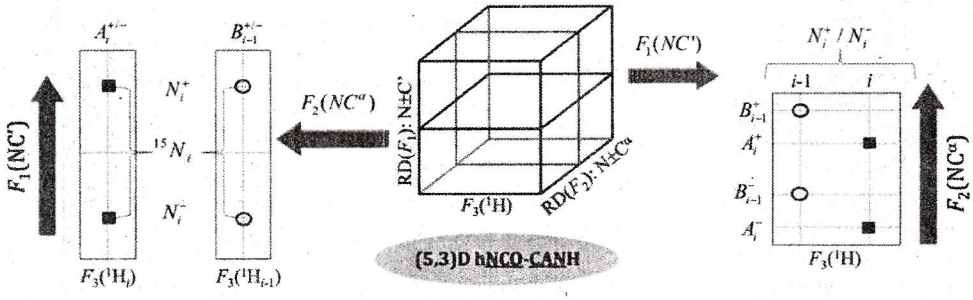
NMR assignment of backbone (^{1}H, ^{15}N, $^{13}C^a$ and ^{13}C') resonances forms the basis for variety of structural and functional studies of proteins by NMR. Most routinely, it is carried out using triple resonance three dimensional NMR experiments involving amide ^{1}H and ^{15}N resonances. However for naturally unfolded proteins, alpha-helical proteins or proteins containing several disordered fragments, the assignment becomes highly problematic because of high degree of backbone shift degeneracy. In this backdrop, a novel reduced dimensionality (RD) 3D NMR experiment –(5,3)D-hNCO-CANH referred here as pseudo 5D NMR experiment- has been presented here to facilitate (and/or validate) the sequential backbone resonance assignment in such proteins. The experiment exploits the linear combination of backbone chemical shifts along both the indirect dimensions -i.e. N±CO and N±CA, respectively, along the F_1 and F_2 dimensions- to resolve the ambiguity involved in connecting the NH(i) and NH(i-1) resonances for overlapping NH peaks. Additionally, the experiment provides five-dimensional chemical shift correlations in a three dimensional spectrum with significantly reduced spectral crowding and complexity. Taken together, the experiment -in combination with routine 3D triple resonance NMR experiments involving backbone amide (^{1}H and ^{15}N) and carbon ($^{13}C^a$ and ^{13}C') chemical shifts- will serve as a powerful tool to achieve the nearly complete assignment of protein backbone resonances in a very time efficient manner. The performance of the experiment and application of the method have been demonstrated here using a 15.4 kDa size folded tgADF protein (*Toxoplasma gondii* ADF, a 118 amino acid protein with an additional N-terminal 21 residue purification tag) and a 10 kDa size intrinsically unfolded culture filtrate protein (CFP-10) of *Micobaterium tuberculosis*.



Explorations of multiqubit entanglement and decoherence mitigation on an NMR quantum computer

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NMR quantum computers are a useful testbed for probing multi-partite quantum entanglement. It has been recently theorised that there exist a set of three qubit generic pure states which can be determined completely from their two-party reduced density matrices. On a three-qubit NMR quantum computer, we experimentally generate such a generic three-qubit state as well as the maximally entangled GHZ and W states. We produce a series of tomographs of the final density matrix including that of the three-qubit generic state and their two qubit subspaces. We experimentally demonstrate the preservation of a quantum state in a subspace on a two-qubit NMR quantum information processor, using the super-Zeno effect. The super-Zeno effect uses a set of inverting radiofrequency pulses punctuated by pre-selected time intervals for state preservation, and has been shown to be more efficient than the standard Zeno schemes. Our results have important implications for decoherence mitigation in multi-qubit entangled states.

Broadband double-quantum recoupling by combined continuous-wave and phase-alternating RF irradiation

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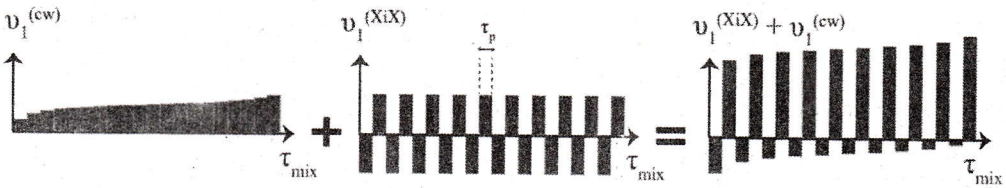
DREAM[1] is an adiabatic double-quantum dipolar-recoupling experiment that has been widely used in biological solid-state NMR for polarizations transfer, mostly for the assignment of chemical shifts. However, the transfer is not efficient if the chemical shifts difference becomes comparable to the spinning frequency, mainly due to high projection losses when the recoupling takes place in a titled frame. To circumvent this problem, we propose superimposing a phase alternating RF-irradiation scheme, i.e. XiX pulses[2] on the original DREAM sequence to make it more robust against chemical shift offsets, and call this sequence as XiX^{cw} DREAM. An infinite set of recoupling conditions can be found using a triple-mode Floquet[3] framework, and here we emphasize on a specific example in which the XiX modulation frequency and the RF fields of the phase-alternating part are set to match the spinning frequency. This double-quantum recoupling condition simultaneously recouples the spatial tensor components n=1 and n=2 without reintroducing the CSA, which is unavoidable in HORROR. Hence, the resulting transfer efficiency is higher than the theoretical limit of 73% in a non-adiabatic gamma encoded sequence. The performance of this broad-banded XiX^{cw} DREAM sequence was compared with DREAM experimentally on homonuclear 2D spectra of U-^{13}C-^{15}N ubiquitin, and it is evident that XiX^{cw} DREAM is a better offset-compensating sequence. The properties of the new sequence were also verified in numerical simulations.



Pulse sequence for XiX^{cw} DREAM

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NMR Investigations on Copolymer-Surfactant Interactions

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The self-aggregation dynamics and microstructure of PEO-PPO-PEO [poly (ethylene oxide)-poly (propylene oxide)-poly (ethylene oxide)] triblock copolymers viz., $E_{20}P_{70}E_{20}$, $E_6P_{39}E_6$ in the presence of aqueous sodium dodecylsulfate (SDS) were investigated using high resolution nuclear magnetic resonance (NMR) measurements.[1-3] Variable concentration and temperature data of NMR parameters like chemical shifts, spin-relaxation rates (R_1 and R_2) and self-diffusion coefficients yielded rich information on polymer-surfactant interactions. The observed NMR data were explained in terms of SDS-copolymer mixed micelle/aggregates and free SDS micelles. The salient features of the investigations include the synergistic effect of SDS in presence of the above copolymers.[1,3] The details of results will be presented.

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Molecular Recognition of Tachykinin Receptor Selective Agonists: Insights from Structural Studies

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This investigation deals essentially with the elucidation of structural features of Tachykinin family of neuropeptides, which are known to interact through three distinct GPCR subtypes, namely NK1 (Neurokinin 1), NK2 (Neurokinin 2) and NK3 (Neurokinin 3)receptors. In mammals, Tachykinins have been shown to elicit a wide array of activities such as powerful vasodilatation, hypertensive action and stimulation of extravascular smooth muscle and are known to be involved in a variety of clinical conditions including chronic pain, Parkinson's disease, Alzheimer's disease, depression, rheumatoid arthritis, irritable bowel syndrome and asthma. This broad spectrum of action of Tachykinins is attributed to the lack of selectivity of tachykinins to their receptors. All tachykinins interact with all the three-receptor subtypes with SP preferring NK1, NKA preferring NK2 and NKB preferring NK3. This lack of specificity can be accounted for by the conformational flexibility of these short, linear peptides. Hence, identification of structural features of the agonists important for receptor binding and biological activity is of great significance in unraveling the molecular mechanisms involved in tachykinin receptor activation and also in rational design of novel therapeutic agents. Understanding structure of the ligand-receptor complex and analysis of topography of the binding pocket of the tachykinin receptor is also crucial in rational design of drugs.

Bactofilins β-sheet enriched bacterial cytoskeleton proteins

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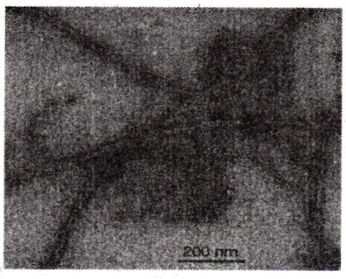
Bactofilins, a new class of bacteria-specific cytoskeletal proteins, are crucial for cell morphology, cell polarity regulation and cell motility[1,2]. Though bactofilin functions are bacteria specific, the underlying mechanism is not understood without the knowledge of structural information. Here, we have investigated the secondary structure and dynamics of bactofilin filaments by high-resolution solid-state nuclear magnetic resonance (ssNMR) spectroscopy. Moreover, these are also the first cytoskeletal proteins studied by ssNMR. Sequential analysis of residues from A39-137F was obtained for BacA filaments of *calobacter crescentus* bacteria. Secondary structure analysis suggests that bactofilins are enriched with a beta sheet core domain flanked by mobile N- and C-terminal. Confirming the previous biological studies, most of the residues from the polymerization module, DUF583 domain, are observed by ssNMR spectroscopy. STEM analysis for mass-per-length value excludes amyloid kind structure for bactofilins. Transmission electron micrographs also reveal lateral propensity of these filament to form rod/sheet structures. Moreover, 2D crystals like structure observation in combination with filaments suggesting the flexibility of bactofilins to adopt specimen-specific confirmation.

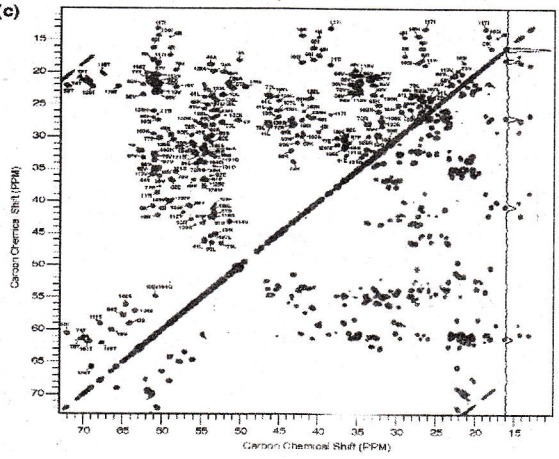
(a)

Bacteria	Bactofilin (no. of aa)
Calobacter crescentus	BacA (161), BacB(180)
Myxococcus xanthus	BacM (150), BacN(113) BacO (126), BacP(240)
Helicobacter pylori	CcmA(104)

(b)



(c)



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Characterization and Solution NMR Studies of Natural Compounds

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Identification of secondary metabolites produced by marine flora and has increased over the past two decades. Phenazines are redox-active nitrogen-containing aromatic compounds produced by a diverse range of bacterial genera. These compounds have broad spectra of antibiotic activitiy. The color of phenazine derivatives range from blue to red, depending on the ring substitution. The purified compounds were characterized by UV-Vis, IR and NMR spectroscopy and by Mass spectrometry. Compounds 1- 5 were obtained as a yellow-red, with molecular formula of mass 270 Da ($C_{14}N_2H_8O_4$), mass 240 Da ($C_{13}N_2H_8O_3$), mass 223 Da ($C_{13}N_3H_9O$), mass 249 Da ($C_{14}N_3H_{10}O_2$) and mass 360 Da ($C_{17}N_2H_{12}O_7$). The structural characterization of these molecules will be presented.

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Deciphering the functional role of Ca^{2+} in the beta/gamma crystallins by NMR spectroscopy

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The beta/gamma crystallin super family proteins are known for their existence along the entire hierarchy of evolution. Members of this group are structurally characterized by paired Greek-key motif arranged in single or multi-domains, and exhibit vast functional dichotomy in living cells. Some of the crystallins were shown to bind Ca^{2+} with millimolar to micromolar affinity however; the explicit relevance of the binding remained obscure. We present a methodical approach to delineate the conformational states accessed by a putative archeal beta/gamma crystallin, M-crystallin. NMR based approaches including selective labeling of residues and rapid acquisition methods, in conjunction with computational and biochemical approaches have been used to decipher and characterize thermo-sensory and ATPase function of M-crystallin.

qNMR - A quantitative tool for purity determination

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qNMR stands for "quantitative NMR", and refers to the use of NMR to determine the concentration of one or more chemical species in solution. This is so because the area of an NMR signal is directly proportional to its concentration. The qNMR method only requires that- (a) the sample dissolves completely in a deuterated solvent, (b)a standard of choice completely soluble in a deuterated solvent with the sample (c) the standard contains NMR-active nuclides has a resonance that does not overlap those of analyte,(d)that some care and attention is paid to data collection and processing. qNMR has already found wide acceptance as has been applied to a myriad substrates. These include (i) accurate determination of the purity levels of active pharmaceutical ingredients (APIs), and drug analysis, (ii) quantitation of natural products, (iii) quantitating pharmaceutical compound libraries,(iv) forensic analysis,(v) food sciences. The following method used to determine the analyte concentration and determination of a compound purity:

NMR Purity- It is frequently necessary to determine the purity of a chemical compound. This is important in the analysis of APIs and forensics.

Aim- In this work, the validity of qNMR has been tested with a CRM and the results compared directly to the reported purity.

Experimental and Results-

Accurately weigh 10-15mg of internal standard and analyte directly into the vial. (Prepare in duplicates).

Add 0.6 ml of deuterated solvent into the vial, and agitate to dissolve the sample. Ensure complete solubilisation of the sample. Transfer the solution to a new NMR tube. Acquire 1H NMR spectra for the duplicate sample preparations. Fourier transforms and manually phases all NMR spectra. Select an analyte peak whose identity is known, and that looks "clean" *i.e.* no shoulders, or other small peaks around it.

The 1H NMR spectra were acquired on 400MHz Varian NMR spectrometers, using Maleic acid as internal standard.

Sample Name	Purity (certified)	Purity (qNMR)
3-amino-4-methyl pyridine	98.00%	98.27%
Assay (% of Compound)	= (Area ratio / Molar ratio) x Purity of std = 98.27% (w/w)	

Conclusion- This work highlights the capability of qNMR spectroscopy for the evaluation of the quality and purity of organic reference materials.

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Abnormal metabolism in Celiac Disease: ^{1}H NMR study of blood plasma

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Celiac Disease (CeD) is an autoimmune intestinal disorder caused by ingestion of gluten present in cereals like wheat, rye, and barley in genetically predisposed individuals. The diagnosis of CeD is difficult due to widespread clinical presentations of the disease. Moreover, the disease has a direct impact on the metabolism. In this direction, metabonomics study of body fluids like blood plasma and urine provides an insight into the biochemistry of CeD.

In the present study, NMR based metabonomics was applied to study the blood plasma of CeD patients to determine the characteristic metabolites and investigate the biomarkers for differentiation of CeD from healthy controls (HC). Blood samples were collected from patients with CeD (n=21; mean age 28.6±10.4yrs) and HC (n=11; mean age 28.8±6.4yrs). An informed consent was taken and the Institute Ethics Committee approved the study. The diagnosis of CeD was made on the basis of European Society of Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN). All subjects were treated according to standard treatment regimen. After centrifugation, blood was subjected to ^{1}H NMR spectroscopy at 700 MHz. Assignment of resonances was carried out using 1D and 2D NMR and their concentrations were determined. Partial least squares-discriminant analysis (PLS-DA) was performed to study the disease pattern. A significantly higher concentration of glucose and acetoacetate was observed in blood plasma of CeD patients in comparison to HC which indicates the disturbance in energy metabolism in CeD patients (Fig1). Elevation in the concentration of glutamine in CeD suggests the role of glutamine in regulating the proliferation of T-lymphocytes and production of cytokines leading to pathogenesis associated with the disease[1]. The decrease in levels of creatinine in blood plasma of CeD patients as compared to HC may be due protein malabsorption. PLS-DA also showed significant difference in the metabolic profile of blood plasma between CeD patients and healthy controls (Fig2).

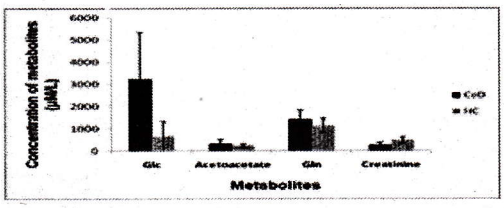

Fig 1: Metabolites in blood plasma of CeD & HC.

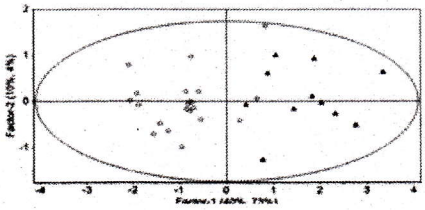

Fig 2: PLS-DA plot for CeD patient (o) & HC (Δ)

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Combining fast fluorescence and slow NMR techniques to determine the atomic level structure of transient toxic Amyloid beta oligomers

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As a class of Intrinsically Disorder Protein, Alzheimer's disease peptide -Amyloid beta (Aβ) is found to be one of the most aggregation prone peptides. The unique folding and aggregation features of this small peptide govern its functions. The monomers of Aβ appear to be random coils, while the aggregated fibrillar forms have cross beta architecture with a hairpin like shape. However how the conformational changes in the monomeric form leads it towards aggregation process, is still unknown. The initial oligomers of Aβ are believed to be the toxic species. The fibrils are rather well characterized through Solid-State NMR (ssNMR)(they have a ordered stable hairpin like structure); while the small oligomers are not because of their transient existence in physiological conditions. In smaller time scale we can characterize the small oligomers in terms of its size and conformation through optical spectroscopy. However, this does not lead us to atomic level structural information. Here we adopt a technique in which we characterize the size and the conformation of the transient small oligomers through Florescence Correlation Spectroscopy (FCS) and Florescence Resonance Energy Transfer (FRET), and follow it with rapid freezing and lyophilization. This leaves us with powdered Aβ which has a specific conformation and aggregation state frozen in. Now performing ssNMR with the powdered oligomeric Aβ sample gives us detailed structural insights compared to FRET or FCS. The ssNMR results with the oligomeric sample reveal the fact that the oligomer formation initiates with a hydrophobic interaction between the two hydrophobic parts of the peptide, which have a β sheet formation.

Chemical shift resolved 'low' field ^{19}F NMR: DNP (OE) enhanced, diagonal suppressed correlation spectroscopy at X-band

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^{19}F NMR is a powerful approach to study the physicochemical properties of fluorinated molecules. The ^{19}F isotope has 100% natural abundance and a magnetogyric ratio that is 94% of that of ^{1}H. However unlike ^{1}H, ^{19}F has a wide chemical shift range. This enables measurement of distinct chemical shifts even at moderately low field strengths, albeit with a corresponding penalty in sensitivity. The loss of sensitivity at lower fields could however be compensated by a variety of techniques. Dynamic nuclear polarization[1] is one of the earliest yet one of the most powerful techniques for sensitivity enhancement in NMR. In the early years, DNP-enhanced one-dimensional ^{19}F NMR measurements were performed in liquid state at low and moderate fields[1a,2], and chemical shift resolution was known especially at X and Q bands. After remaining dormant in the world of spectroscopy for a long period, DNP has now re-emerged both in solution state and in solid state at higher fields[3], evoking much interest among researchers. DNP in solution state is based on the electron nuclear Overhauser effect (OE) and is generated by microwave (MW) irradiation of the electron spin transition of a paramagnetic centre that has a fluctuating interaction with the nuclear spins of interest.

Here we present our work on DNP-enhanced ^{19}F NMR measurements on small fluorinated molecules in solution state at X-band, corresponding to a ^{19}F resonance frequency of *ca.* 13.8 MHz. It is shown that even at such a 'low' field, distinct chemical shifts could be clearly resolved, and differential DNP enhancements and build-up rates investigated; further, 'diagonal' suppressed homonuclear 2D correlation work could be successfully performed with our DNP-enhanced 2D DISSECT experiment. Our results on the distinct effects of various aliphatic and aromatic free radicals on DNP enhancements in perfluorinated and partially fluorinated aromatic and aliphatic molecules will also be summarized.

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Accelerating 3D HSQC-DOSY with projection NMR spectroscopy and non-uniform sampling

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Diffusion ordered spectroscopy has become routine to analyse mixtures, association and dissociation1. The analysis becomes complicated when there are overlapping peaks which leads to the average diffusion value of overlapping peaks of different molecules2. The overlapping peaks may resolve in high dimensional NMR spectra. To get a diffusion value from high dimensional NMR we have to record series of spectrum with different gradient values which is time consuming. Here we present pseudo 3D HSQC_DOSY where we obtain "diffusion information" in a single spectrum. The diffusion coefficient is extracted from the line widths in the indirect dimension. Using this method we were able to detect for the first time the presence of the intermediate of diphenylalanine in solution, enroute to the formation of nanotubes3.

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Solution structure determination of *Aedes Aegypti* Sterol Carrier Protein 2 Like2 (AeSCP2L2) and its complex with palmitate

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Aedes Aegypti is a mosquito species that spread Yellow fever, Chikungunya and Dengue viruses. As part of the development of insecticides to control these diseases, the mosquito genome and metabolism has been thoroughly studied and found that the absence of cholesterol biosynthesis enzymes resulted in inability of producing cholesterol in their body, which is required for their viability; instead, they derive it from host organisms through the diet. *Ae*SCP-2 (*Aedes Aegypti* Sterol Carrier Protein 2) genes have been shown to be involved in the cholesterol uptake in the mid gut in both larval and adult mosquitoes. More recently, it has also been shown that the mosquito SCP-2 proteins were specific for chemical inhibitors (SCPI) that are effective larvicides in *Aedes aegypti*, *Anopheles gambiae* and *Culex pipiens*, indicating that SCP-2 has functional similarity in different mosquito species. *Aedes Aegypti* Sterol Carrier Protein 2 (*Ae*SCP2) and its isoforms are ~13 kDa, proteins that have been shown to play an important role in the cellular lipid transport and cholesterol metabolism. Lack of sufficient structural information of *Ae*SCP2 has been one of the main reasons for poor understanding of their mechanism of action at molecular level. Therefore, we have planned to study the three dimensional structures of ligand free and palmitate bound SCP2L2 (SCP2-like2) in solution using NMR spectroscopy as a major tool. We have successfully prepared U-[^{15}N], U-[^{15}N, ^{13}C] labeled protein samples for structure determination. The details of the structures of apo-SCP2L2 and palmitate bound SCP2L2 will be discussed in detail. We believe that these structures provide indispensible evidence that will be useful to design, develop and screen the efficient inhibitors of AeSCP2.

Regulatory Issues of Radiopharmaceuticals as an Investigational New Drug Application

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Radionuclides in imaging technology and therapy proven as an important segment in modern diagnosis and chemotherapy Large number of radionuclide's such as iodine-131, phosphorous-32, yttrium-90 and I-131 MIBG have been in use for the treatment of many benign and malignant disorders and many more are filling regularly for investigational new drug application (INDA).

In early preclinical development, the sponsor's primary goal is to determine if the product is reasonably safe for initial use in humans and if the compound exhibits therapeutic or pharmacological activity that justifies commercial development. When a product is identified as a viable candidate and then clinical trials must submit an INDA to FDA in accordance with the regulations for further development to establish that the product. Internationally clinical applications of radiopharmaceuticals regulated by number of regulatory agencies including of U.S. Food and Drug Administration (FDA), International Atomic Energy Agency (IAEA), World Health Organization (WHO) and European Association of Nuclear Medicine (EANM). In *India,* Bhaba Atomic research centre is the regulatory agency of the radio pharmaceuticals and manufacture as per Radio pharmaceutical Committee (RPC) *guidelines. Moreover, exploratory INDA filling is a quick approach to getting the easily approval from FDA.*

Study of longitudinal relaxation time and suppression techniques in Amniotic fluid on 1.5 T in fetal MRI

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Purpose: Magnetic Resonance (MR) techniques like single shot Fast Spin Echo (ssFSE) have been used for acquisition by reducing the scan time.[1] T_2 Images look saturated due to longer TR which allows amniotic fluid to relax and produce a high intensity background. This problem is analogous to fluid suppression which is commonly used in MR imaging to suppress the signal from a tissue; this can be done by using Inversion Recovery (IR) pulse sequence, it is therefore imperative to understand the relaxation times of amniotic fluid to design strategies for suppressing amniotic fluid.

Methods: Experimental setup included sample of 100 ml amniotic fluid and a slab of meat (muscle) from a sheep placed in 1.5T Siemens MRI scanner. Study of T_1 mapping was carried out with the following acquisition parameters spin echo sequence; set of 9 images with varying repetition time (TR) of values 200-2000 ms; echo time (TE) set to 8.7 ms (min TE) and matrix size of 512 × 512; number of slices were 1; slice thickness of 5 mm. The study of longitudinal relaxation and IR was carried out, with the same imaging parameters mentioned above, but with inversion time (TI) fixed to 250 ms as determined. Experiment was carried out with TI value on different TR's to suppress the signal from amniotic fluid. Results obtained from mapping experiment with each mean pixel values of different TR's were computed. map was estimated by using this equation . Mean and standard deviation of intensity on map was computed to estimate the relaxation times of the amniotic fluid and the muscle.

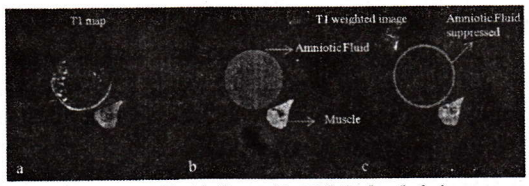

Fig 1: T1 map; T1 weighted images of Amniotic fluid and muscle of a sheep

Results: Figure (1) shows scanning results of amniotic fluid and muscle in a 1.5 T Siemens MRI scanner. Figure (1a) shows the map with Amniotic fluid value of 2.874 0.022 ms and muscle value of 0.805 0.00158 ms. The value of muscle, is found to be similar to previously published values [2]. Inversion recovery suppression study suggests that (Fig 1b) the resulting image of TR= 500 ms and TE= 8.7 ms signal from amniotic fluid persisted and correspondingly with same TR and TE but with TI= 250 ms, it was possible to nullify the signal from amniotic fluid (Fig 1c).

Conclusion / Future work: map obtained from amniotic fluid will be helpful in planning acquisition strategies for fetus and this work also shows acquisition with IR method that suppresses the signal from amniotic fluid (Fig 1c). Future work includes implementation of fast imaging sequences to reduce scan time, map characterization, TI based suppression techniques and implementation of spatial spectral pulses on amniotic fluid.

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In Vivo Quantitation of Metabolites using Proton Magnetic Resonance Spectroscopy of Brain at 3T in Obstructive Sleep Apnea

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Obstructive sleep apnea (OSA) is a major public health problem which may result into neurocognitive impairment, among other consequences. Common daytime symptoms of OSA include excessive daytime sleepiness and emotional deficits. Repeated episodes of apnea during sleep may damage neural structures and induce changes in cerebral metabolism. Earlier studies have reported use of *in vivo* proton magnetic resonance spectroscopy (^{1}H MRS) to assess brain metabolic changes in patients with OSA. However, most of the studies used metabolite ratios instead of absolute concentration of metabolites. In the present study we carried out ^{1}H MRS of brain to determine the absolute concentration of cerebral metabolites in patients with OSA at 3 Tesla for greater spatial and spectral resolution.

All MR investigations were carried out at 3T Achieva scanner (Philips Medical Systems). MR images in three orthogonal planes were acquired for the localization of MRS voxel. Single voxel proton MR spectra were recorded using point resolved spectroscopy (PRESS) pulse sequence with the following parameters: TR = 3000 ms; TE = 35 ms; NS = 64. Spectra were acquired from two different areas of the brain: namely, left frontal and left hippocampus. Absolute concentration of metabolites was estimated by Linear Combination Model (LC Model) program which allows deconvolution of spectra by using a basis set of reference spectra. The concentration of metabolites was expressed as millimoles per liter (mmol/l). Measurements of NAA (N-acetylaspartate), Glx (glutamine, Gln + glutamate, Glu), myo-inositol (mI), Choline (Cho) and Creatine (Cr) were assessed.

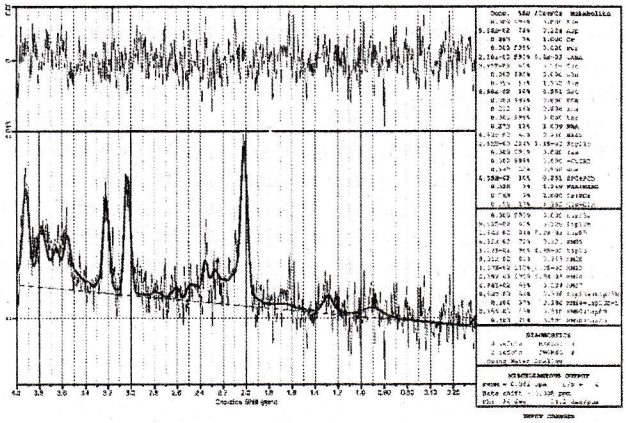

Fig 1. Proton NMR spectrum acquired at 3T from the left frontal area of brain of a 36 year male patient with obstructive sleep apnea.

Quantitative Amino Acid Analysis of Therapeutic Peptides by Using qNMR

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Ion-exchange chromatography with post column ninhydrin detection is one of the most common methods for quantitative amino acid analysis. As per the recent requirements from different Food Drug Administration (FDA), quantitation of individual amino acid mole ratio without breaking and altering the higher order structure of therapeutic peptide becomes most important for drug approval. Terlipressin Acetate salt H-Gly-Gly-Gly-Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Lys-Gly-NH2 is a (4-9 Disulfide bond) drug substance is an analogue of vasopressin used as a vasoactive drug in the management of hypotension.

By using qNMR (^{1}H-NMR) principle a quantitative method has been developed by using maleic acid as internal standard (IS) in deuterated water of 99.9 atom % D. The mole ratio of individual amino acid was calculated from peak areas of individual amino without altering the peptide structure by using qNMR principle. Simultaneously the entire amino acid residue can be identified as well as quantified individually without any reference material. The developed method is simple, non-destructive superior and quicker method in comparison to chromatographic techniques. Further it was well validated as per ICH guidelines, assessing its specificity, linearity, range, precision, accuracy, limit of quantification, limit of detection and robustness.

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Pulse design for parallel transmit MRI using SOMGA

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Purpose: Parallel transmit technology (pTX) has been used to demonstrate arbitrary volume selective excitation and employed to achieve performance optimization, increased B_1 homogeneity and subject specific fat suppression. Genetic Algorithm (GA) is a robust optimization method than Magnitude least squares method (MLSM) which is an approximate convex problem. MLSM cannot find the optimal solution of coefficients if the initial guess is not sufficiently near the ideal solution[1]. We propose an application to the spatial domain parallel excitation pulse design, where we use four channel excitation and employ GA known as Self Organizing Migrating genetic Algorithm (SOMGA) to improve excitation magnitude profile and optimize the obtained result.

Methods: RF pulses were designed to excite geometric shapes like cylinder and sphere. Design of spiral and multiple spiral trajectories is done[2] as shown in Fig 1 (a) and (b) and optimization was done using SOMGA for cylinder and sphere excitation[3].RF pulses are randomly generated by SOMGA and the converged solution is used to excite the desired pattern. Error minimized is given by, $E = (A_{full}B_{full} - M_{des})$ where $A_{full}B_{ful}$ is obtained magnetization profile, where A_{full}-matrix encoding coil sensitivities and Fourier transform, B_{full} - RF pulses and M_{des} - desired magnetization profile. Current work involved excitation of a cylinder and sphere using four transmit pulses B_1, B_2, B_3 and B_4 using SOMGA.

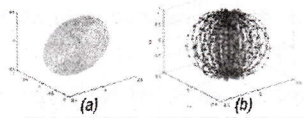

Fig 1: Trajectories a) Spiral b) Multiple spirals

Results and Discussion: Fig 2a shows excitation of cylinder by four RF pulses B_1, B_2, B_3 and B_4 which are excited along Mxy and Myz direction where a horizontal rod shape is obtained. Along Mzx direction a circle is observed. Fig 2b shows excitation of sphere by four RF pulses which are excited along Mxy, Myz and Mzx direction where a sphere is obtained. This allows the use of arbitrary *k*-space trajectories and is formulated as an optimization problem in the spatial domain. With increased k-space sampling magnetization profile and accuracy would improve and can be used to reduce errors further at the expense of longer k-space trajectory.

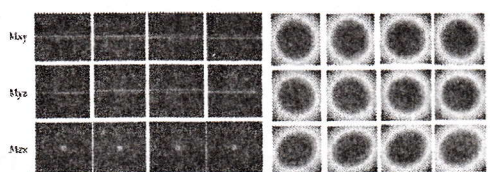

Fig 2a): Excitation of cylinder using four coils
Fig 2b): Excitation of sphere using four coils

Conclusion: We have verified the simulations of spiral trajectory and excitation of cylinder and spherical excitation of k-space using SOMGA for the first time. Current and future work is to reduce excitation error and balance the excitation error with the local Specific Absorption Rate by optimization of initialization parameters of SOMGA and application of these pulses on a MR scanner.

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Motion Tracking in volumetric Fetal MRI using Speeded-Up Robust Feature

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Purpose: Motion in fetal MRI is primarily caused by movement of fetus and mother which results in distortion in image quality (1). Current work involves motion correction being performed from a post-processing approach using motion tracking algorithms for single and/or multiple objects conventionally used in computer vision problems. Speeded-up Robust Feature (SURF (2)) is applied to detect the motion fields and to register images.

Method: From each subject, 8 volumes of fetal MRI data were acquired between 23-36 gestational weeks. Imaging parameters were: single shot Fast Spin Echo (ssFSE), TR/TE: 15000/140-180ms, slice thickness: 2.5mm and resolution of 1.176×1.76mm. Slices from two volumes of same subject having similar anatomy were considered. Simulations were performed by introducing a rotation of 45° and matching SURF feature vectors from both slices with and without rotation and then rotated image was registered with respect to reference image. Extending the same to fetal data acquired, where corresponding slices were identified in 9 pairs of volumes. SURF feature vectors were found from both reference volume's slice and slice from other volume were considered for matching and registration. In order to quantify the results root mean square error (RMSE) value was computed.

Results: Simulated result of a representative data set is shown in figure 1. SURF features in image A are indicated with red circles and green '+' indicate the SURF feature in image B and the yellow line indicates matched features between A and B is shown in D. Figure 2 shows the corresponding results of multi-volume fetal MRI data for a representative data set. In case of multi-volume data, SURF points are computed on the frame of reference volume and frame from the other volume are being mapped with respect to their SURF point displacement. It can be noticed that in the registered image motion has been reduced in both representative cases and has smoothening of edges. In multi-volume data due to less motion the blurriness of the edges is reduced. For all 9 cases RMSE values for simulated and real data are shown in figures 1(F) and 2(F) respectively.

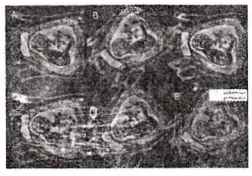

Figure 1: The original input image (A), The image in which rotation is introduced (B), Registered output image C, mapped feature are shown in D. The extent of the motion is indicated in the image E. The graph F shows the RMSE value of Simulated before and after registration(SBR and SFR).

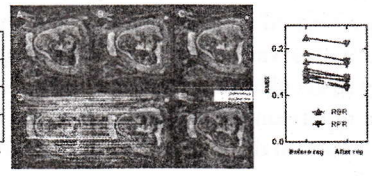

Figure 2: The original input image (A), The image to be registered (B), Registered output image C, mapped feature are shown in D. extent of the motion is indicated in the image E. The graph F shows the RMSE value of real data before and after registration(RBR and RFR).

Conclusion/Future work: RMSE values after registration were reduced compared to before registration values in both cases. Future work involves comprehensive volume-to-volume registration which would help in tracking of 3D rigid and non-rigid motion between different volumes for high resolution reconstruction (3).

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ROICS-PI: Combination of Region of Interest Compressed Sensing and Parallel Imaging for Arbitrary k-space Trajectories to Achieve Highly Accelerated MRI

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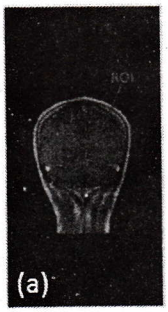

Introduction: Compressed sensing (CS) (1) and Parallel Imaging (PI) (2) are two well-known techniques to accelerate MRI. In this work, a recently developed technique developed by us called "Region of Interest Compressed Sensing (ROICS)" (3) is combined with PI to provide superior performance as compared to CS-PI. **Theory:** CS reconstruction algorithm can be represented by: $\min(\|F_u(m)-y\|_2+\lambda\|\Psi(m)\|_1)$ [1]. Here, m is current estimate of image, F_u is undersampled Fourier operator: $F(.)$* Undersampling mask, y is undersampled k-space measured by scanner, λ is regularization factor, Ψ is sparsifying transform operator and $\|.\|k$ is k-norm operator. Equation [1] can be solved for a particular ROI with data consistency evaluated in image domain and weighting the spatial data consistency term by a diagonal matrix W that results in $\min(\|F^{-1}(F_u(m)-y)*W\|_2+\lambda\|\Psi(m)\|_1)$ [2]. We can rewrite the equation [2] for each channel *'c'* with an arbitrary k-space trajectory to perform ROICS-PI: $\min(\|F_1^{-1}(F_{1u}(m_c)-y_c)*W\|_2+\lambda\|\Psi(m_c*W)\|_1)$ [3]. Here, F_1 is Non Uniform Fast Fourier Transform (NUFFT) for arbitrary k-space applied on image estimate m_c and y_c is the k-space of the c^{th} channel.

Methods: ROICS-PI technique was performed on 6 human brain datasets acquired using a 1.5 T Siemens scanner, as part of an ERB approved protocol, in coronal orientation and a SE sequence using 6 receiver coils (TR/TE = 410/8.7ms, matrix size=512 x 256) with no CS/PI during acquisition. ROICS was performed on each channel data with common ROI for all channels, k-space data was undersampled with a variable density spiral trajectory consisting of 64, 48, 32 and 16 interleaves corresponding to acceleration factors of 7.5x, 7.9x, 8.3x and 8.8x, using PI, CS+PI and ROICS+PI methods for comparison. Reconstruction errors for all 3 methods were quantified by Peak Signal to Noise Ratio (PSNR) at different interleaves/acceleration factors.

Results and Discussion: Sum of squares (SoS) of channels image with ROI chosen is shown in figure 1(a). Better performance of ROICS+PI can be observed from figure 1(b), (c), (d) and Figure 1(e) depicts the magnified ROI at 7.5x depicting aliasing artefacts that can be observed in the other 2 methods. Graph in figure 2 shows that PSNR value of proposed method is higher compared to the other two methods.

Conclusion and future work: Combination of ROICS and PI has been proposed and performed for first time and superior performance can be observed from figure 1 and 2. The technique has been implemented for arbitrary k-space trajectories and hence provides a general framework. Current and future work involves optimizing k-space trajectories to suit specific ROI shapes and identification of specific MR applications, integrating it in reconstruction framework.

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In vivo Proton MRS Study for Assessing Therapeutic Response in Breast Cancer Patients

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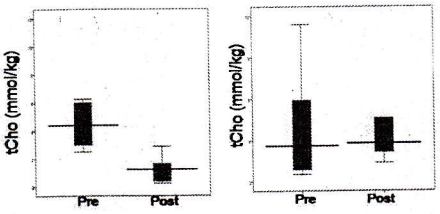
Neoadjuvant chemotherapy (NACT) is a standard treatment regimen for locally advanced breast cancer (LABC) and patients who respond to treatment show a reduction in tumor size following NACT. Monitoring of tumor response to therapy is important, especially to identify non-responders to initiate appropriate patient management. The objective of the present study is to investigate the potential of tCho concentration using in vivo proton MR spectroscopy (^{1}H-MRS) study in the assessment of early therapeutic response in patients with breast cancer.

In the present study 14 women with cytologically proven infiltrating ductal carcinoma (IDC; mean age=39.3 ± 8.6 yrs) were recruited. Clinical response to NACT was assessed using vernier caliper by measuring tumor size. Written informed consent was obtained and Institutional ethical committee approved the study. All MR investigations were performed at 1.5 T (Siemens, Avanto) scanner. A single voxel in vivo ^{1}H MRS was carried out using a PRESS sequence. The relative normalized integral was determined after spectral post-processing and the absolute tCho concentration was calculated. A statistically significant difference in tCho concentration was observed as early as 1st cycle which reduced further after 3rd cycle of NACT compared to pre-therapy values in responders (n=8). While, in non-responders (n=6) no significant difference in tCho values was observed at 1st and at the end of 3rd NACT cycle. The increased tCho concentration seen prior to treatment pertains to altered biochmemical pathways due to increased tissue cellularity and rapid growth rate of malignant tumors. Whereas, with the effect of NACT the mitotic count and tumor cellularity reduces leading to decrease in the tCho levels (which is an important constituent of cellular membranes) in patients who showed response to treatment regimen. The results obtained thus indicate that tCho might be used as an early indicator forpredicting clinical response in breast cancer patients.

Response status	Groups	tCho conc. (mean ± SD; mmol/kg)
Responders (n=8)	Pre-therapy *	5.02 ± 2.70
	After 1st NACT*	3.02 ± 1.20
	After 3rd NACT*	1.22 ± 0.90
Non-responders (n=6)	Pre-therapy	4.66 ± 2.74
	After 1st NACT	4.63 ± 2.58
	After 3rd NACT	4.58 ± 1.97



Preserving quantum states in subspace and entangle state using super zeno effect on an NMR quantum computer

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We experimentally demonstrate the preservation of a quantum state in a subspace on a two-qubit NMR quantum information processor, using the super-Zeno effect. The super-Zeno effect [1] uses a set of inverting radiofrequency pulses punctuated by pre-selected time intervals for state preservation and has been shown to be more efficient than the standard Zeno schemes. Efforts are underway to use these super-Zeno pulses to arrest the decoherence of a singlet state in a two-qubit system. We have successfully preserved quantum state in subspace. Our results have important implications for decoherence mitigation in multi-qubit entangled states.

Preserving quantum states in subspace

We consider a quantum mechanical system described by a two-dimensional Hilbert space $H = \{|00\rangle, |01\rangle, |10\rangle, |11\rangle\}$ which is a direct sum of two orthogonal subspaces *P* and Q. When the system is subjected to a very short duration external rf pulse we assume that the effect of the pulse can be represented by unitary operator *J*. If the system is initially in the state $|\psi\rangle$, after being subjected to the pulse, its state will change to $J|\psi\rangle$, J is the inverting pulse $J = P - Q$, where P and Q are the projection operators for the subspaces *P* and Q respectively. Clearly $J|\psi\rangle = -|\psi\rangle$, if $|\psi\rangle \in P$ and $J|\psi\rangle = |\psi\rangle$, if $|\psi\rangle \in Q$.

When the two-qubit NMR system is subjected to a sequence of n inverting pulses, the evolution operator is given by:

$$W_n(t) = U_o(x_{n+1}t \ldots\ldots\ldots J.Uo(x_2t).J.Uo(x_1t) \quad \text{where } U_o(t) = e^{-iHt}$$

If the initial state is $|\psi\rangle \in P$, then the effect of unitary operator $W_n(t)$ is to prevent the leakage of the quantum state in the subspace P to the subspace Q. We wish to achieve preservation of a general state within the subspace *P*, with the subspaces *P* and *Q* of the two qubit Hilbert space being $P = \{|00\rangle, |11\rangle\}$ and $Q = \{||01\rangle, |10\rangle\}$ respectively. As an example, we consider preserving the state $|\psi\rangle = \frac{1}{\sqrt{2}}(|00\rangle + |11\rangle)$ in subspace P. The inverting pulse for protecting $|\psi\rangle \in P$ is given by: $J = I - 2\left(|00\rangle\langle 00| + |11\rangle\langle 11|\right)$ and rf pulses takes the form: $W_4(t) = U_o(x_5t).J.\ U_o(x_4t).J$ $U_o(x_3t).J.U_o(x_2t).J.U_o(x_1t)$ where $\{x_k\} = \{\beta, 0.25, 0.5 - 2\beta, 0.25, \beta\}$ and $\beta = \frac{(3-\sqrt{5})}{5}$.

Preserving singlet state using super zero effect

If the initial state is $|\psi\rangle \in P$ is the only state in subspace P then the effect of unitary operator $W_n(t)$ is to prevent the leakage of the quantum state in the subspace P to the subspace Q and this algorithm act as state preserving algorithm. So we divided accordingly such that P contain singlet state only and Q contain other three triplet states and trying to see the effect of inverting pulses this work in process.

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NMR studies in crystal engineering: Detection of LSAM in solution

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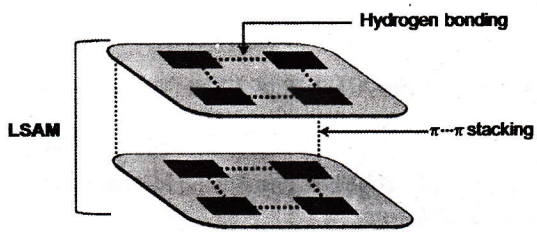
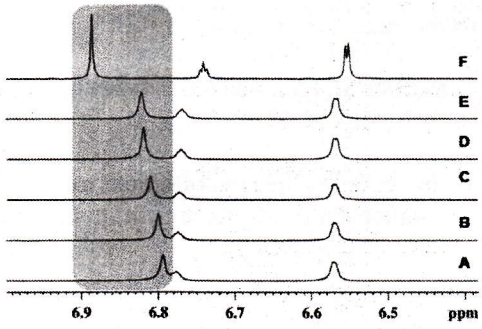
Supramolecular synthons[1] are the building blocks of any supermolecule. It has been shown recently that small synthons exist in solution[2]. In our studies of cocrystals (multi component solids) with predictable cell dimensions, the recurrence of larger synthons called as LSAMs[3] (Long range Synthon Aufbau Module) in many cocrystal structures provoked the possibility of presence of LSAMs in solution. In this context, we carried out dilution experiments which showed the presence of stacking in solution. Further studies based on advance NMR techniques were used to get a clearer picture towards the structure of synthons in solution. 1D-NOE experiments showed that the coformers are in close proximity in all dilution states which in other words can be equated with the presence of hydrogen bonding. T_1 inversion recovery and DOSY experiments, on the other hand, showed that the stacking is broken with increasing dilution. The stacking behavior was also probed by choosing 1,2,3-trichlorobenzene as a model compound. These results show a sequential dissociation of intermolecular interactions in solution which may be correlated with interaction hierarchy used in crystal engineering design strategies.





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Molecular dynamics simulations and magnetic field gradient spin-echo NMR studies of antioxidants diffusing in a phospholipid bilayer

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The diffusion behaviour of lipid-soluble antioxidants in a phospholipid bilayer (used as a membrane mimetic) has been studied using molecular dynamics simulations as well as pulsed-field gradient spin-echo and relaxation NMR experiments. Antioxidants curcumin and alpha-tocopherol were introduced into DPPC (Dipalmitoylphosphatidylcholine). The autoxidation of biological lipid membranes is prevented by lipophilic antioxidants but can occur in conditions of oxidative stress. It is hence important to understand the mechanism of penetration of the antioxidant into the lipid bilayer. Molecular dynamics was performed using the Martini coarse-grained force field in GROMACS. The results of simulation and experiments have been compared.

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Low frequency NMR studies on PAN-HTPB co-polymer based elastomers

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*Poly-acrylonitrile (*PAN)-Hydroxy terminated poly-butadiene (HTPB) co-polymers are being used for various elastomeric applications in industries. Polymerization in such elastomers has to be monitored to realize desired properties. Proton NMR relaxometry studies have been done on co-polymer of PAN-HTPB sample at low magnetic fields or studying polymerization. Spin-lattice (T_1) and spin-spin (T_2) relaxation data has been studied for monitoring curing process. Results on co-polymer samples with selective percentage of additives (chain extenders) were compared with pure elastomeric samples. Studies indicated proton NMR at low frequency is good tool for identifying cure state and polymerization process. Studies indicated that stiffness of polymer chains of elastomers is directly coupled with mobility of hydrogen nuclei-protons. NMR relaxation decay curves were studied for information about proton mobility in co-polymer samples. Cross-link density of samples with and without additives has been determined.

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Rapid NMR assignments in proteins with optimized amino acid selective unlabeling combined with 2D triple resonance experiments

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A novel strategy for rapid sequential assignment in proteins based on the methodology of amino acid selective unlabeling is presented. The method involves choosing a proposed optimal set of amino acid types in a given protein for selective unlabeling. Using this sample, sequential assignments are obtained in conjunction with a set of 2D triple resonance spectra. The experiments selectively detect resonances of labeled amino acid residues located in the neighborhood of the one being selectively unlabeled thereby aiding resonance assignments. In this approach, the spectra acquired are analyzed in a combinatorial manner yielding long stretches of sequentially linked residues which can be mapped onto the primary sequence. It is shown that a single sample with simultaneous unlabeling of multiple amino acid types chosen appropriately is sufficient for nearly 80% of sequential assignments in a given protein. The experiments are demonstrated on the intrinsically disordered central domain of the insulin-like growth factor binding protein-2 and ubiquitin are applicable to (per) deuterated proteins.

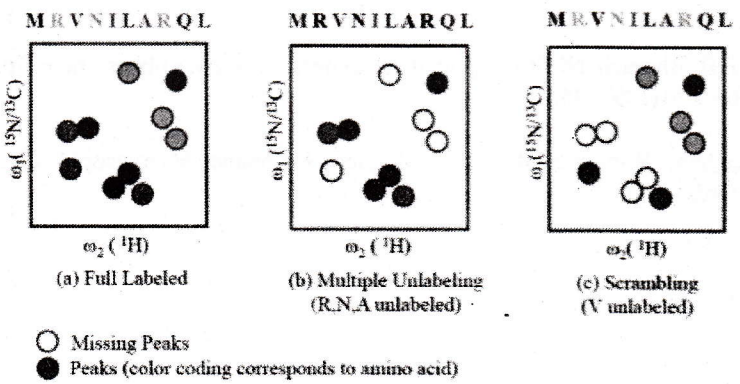

Figure 1: Schematic illustration of concept of multiple amino acids unlabeling and scrambling. Peaks in dashed box are unlabeled and missing. Peaks marked with arrow are getting crambled

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Tracking a Quantum System

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Can we completely characterize a given quantum system in an unknown state? Can we completely characterize a process (unitary or nonunitary) that is being applied to a quantum system? The answer is 'yes' for both of these questions, and in this talk, we describe the methods employed to achieve them. Quantum State Tomography (QST) is used to characterize the state of a quantum system at any instant of time and Quantum Process Tomography (QPT) is used to characterize the process acting on a quantum system. The standard methods of QST and QPT require a long series of independent experiments. Here we describe Ancilla-assisted QST (AAQST) which allows us to map the density matrix in a single experiment [1]. In particular, we describe the experimental AAQST of (i) a two-spin system in an isotropic liquid-state system and (ii) a three-spin system in a partially oriented system. We also describe a single-shot process tomography (SSPT) which alleviates the need for repeated applications of the process to be characterized. These techniques may be useful in tracking a dynamical quantum system.

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NMR studies of fluorinated drugs using PFG spin-echo experiments and cross-correlated spin relaxation

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^{19}F NMR is a very useful tool in medicinal chemistry. Fluorine plays an important role in estimating the binding affinity and potency of drugs. This work focuses on the study of fluoroquinolones which are used to treat bacterial infections such as respiratory and urinary tract infection. Quinolones target site is bacterial type II topoisomerases, generally DNA gyrase in gram negative bacteria and DNA topoisomereases IV in gram positive bacteria. These fluorinated drugs bind to these enzymes and inhibit their activity. DNA gyrase relives the strain of DNA double-stranded during the replication. ^{19}F chemical shift anisotropy (CSA) tensor is a useful tool in NMR to characterize biomolecules. This work focuses on characterization of CSA tensor in fluoroquinolone drugs using liquid state NMR cross-correlated relaxation experiments and quantum computational methods. The experiments are used to characterize the CSA tensor magnitude and its orientation, through measurement of cross-correlated spin relaxation rates between several different relaxation pathways in these molecules.

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Interaction Studies Of Regulatory And Catalytic Subunits Of Acetohydroxyacid Synthase (AHAS)

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Acetohydroxyacid synthase is a multisubunit enzyme that catalyses the first committed step in the biosynthesis of the branched chain amino acids viz., valine, leucine and isoleucine. The enzyme utilizes the cofactors Mg^{2+}, TPP and FAD. The molecular assembly consists of a large catalytic subunit (CSU) and a small regulatory subunit (RSU) that are expressed as independent polypeptide chains. Enterobacteria have three isoforms of AHAS viz. AHAS I (IlvBN), AHAS II (IlvGM) and AHAS III (IlvIH). The CSUs are ~60kDa in molecular size. The RSUs are distinct in size and sequence. While IlvN and IlvM are ~10kDa, IlvH is ~18kDa.

The RSU increases the catalytic efficiency of the enzyme substantially and binds to the branched chain amino acids to cause the feedback inhibition of AHAS. The structural basis and mechanism for this activation and feed- back regulation in the holoenzyme is not understood. The structure of IlvN in liganded form is known while that of the unliganded form has been partially characterized.

The present work involves further analysis of the mechanism and structural basis of interaction between the catalytic (IlvB) and the regulatory subunit (IlvN) of AHAS I using solution NMR methods. Full length IlvB has been expressed and purified. The solution NMR properties were analysed in the presence of the co-factors, FAD and TPP by one dimensional NMR studies. The effects of chemical modifications on the solution NMR properties of the unliganded form of ilvN are under investigation.

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Adaptations in cortical activations in early, Late Blind individuals during auditory task

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Introduction: Functional magnetic resonance imaging (fMRI) used to study the processes involved in phonological processing of noun pair antonyms and synonyms in early blind (EB) and late blind (LB) children.

Method: Twenty right handed subjects in the EB group (mean age ± SD 15.1 ± 3.6 years) and LB group (mean age ± SD: 12.9 ± 1.3 years), each from the clinics of our institute and ten sighted controls were recruited. Standard diagnostic and exclusion criteria were followed. BOLD sessions were carried out using 3T MR scanner (Achieva 3.0T TX, Philips, Netherlands). For Phonological processing: Patients were presented with antonyms and synonym noun pairs, through auditory cue with the help of E-prime and MR compatible headphone and microphones (NordicNeuroLab, Norway). Pre- and post-processing was carried out using SPM8 (Wellcome Department of Cognitive Neurology, London, UK). One sample t-test ($p<0.001$, cluster threshold 10) was used for group analysis.

Result: During synonyms task by LB subjects showed activation in bilateral fusiform gyrus, para hippocampal gyrus, primary and auditory association cortex, somatosensory association cortex, associative visual cortex (v3, v4, v5), premotor cortex and supplementary motor area. In EB activation was observed in bilateral superior frontal gyrus, left hemispheric cerebellum, middle frontal gyrus, para hippocampal gyrus, and right hemispheric cingulate gyrus and medial frontal gyrus. During antonyms task early activation in bilateral superior temporal gyrus, cerebellum and precuneus, right hemispheric lentiform nucleus, left inferior parietal lobule, para hippocampal gyrus, cerebral medial frontal gyrus, middle occipital gyrus, inferior frontal gyri. For antonyms task bold activation in LB was located in right superior, middle, inferior frontal gyri, para hippocampal gyrus, precentral and left activity in fusiform gyrus, inferior parietal lobule, lingual gyrus, medial frontal gyrus.

Discussion: Lexical semantic task, activate peripheral regions of visual cortex when subjects attended to sound due to there may be functional connections between auditory cortex and visual cortex to process language associated with sound sources.The involvement of Broca's area in phonological processing may be a function of task demands [2]. Semantically associated antonyms noun pair word evoked robust activity throughout visual cortical regions for blind people; The lexical semantic task elicited greater activity in medial cortical areas that have been possible due to participants may be covertly vocalized heard words when trying to remember common meanings or antonyms [1] Recently, it has also been suggested that the cerebellum is involved in purely sensory tasks, such as visual and auditory motion perception [3].

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Scaling of AC conductivity and electrochemical properties of ionic liquid based PVdF-HFP-MMT intercalated nanocomposite electrolytes

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Polymer electrolytes are the subject of intensive study worldwide mainly because of their shape versatility, flexibility, lightness and potential advantages in the continuing trend towards miniaturization.[1] In the present work novel polymer electrolytes have been prepared using 1-butyl-3-methylimidazolium bromide ionic liquid (IL), poly(vinylidene fluoride)-hexafluoropropylene copolymer [PVdF-HFP] and MMT nanoclay with varying concentration of MMT. Intercalation of PVdF-HFP into the layers of MMT has been confirmed from HRTEM micrographs as well as XRD analysis. The characteristic XRD peak of MMT shifts to lower angle side indicating increase in *d* spacing confirming intercalation. Ionic conductivity of the order of 10^{-3} S cm^{-1} at ambient temperature for the ionic liquid based nanocomposite electrolyte system has been obtained. Conductivity increases with increasing MMT content and becomes maximum for 5% of MMT content. Fig. 1 shows SEM micrographs of PVdF-HFP-MMT nanocomposite electrolytes containing different amounts of MMT. It is observed from Fig. 1 that with increasing MMT concentration porosity increases which allow more ionic liquid uptake resulting in increased ionic conductivity. Beyond 5 wt. % of MMT porosity decreases due to blocking effect leading to decrease in conductivity. The perfect scaling of AC conductivity depicts that ion concentration as well as ion diffusion length change with changing MMT concentration.[2] As PVdF-HFP intercalates inside MMT interlayers, chain conformation becomes more disordered increasing amorphicity. Due to increased amorphicity more ions become mobile leading to increase in ion concentration. Ion diffusion length also increases due to the free path created by the increased disordered conformation. The increased ion concentration and ion diffusion length enhance the ionic conductivity. Thermogravimetric analysis shows that nanocomposite electrolytes have high thermal stability with decomposition temperature at around 260 °C with slow decomposition rate.

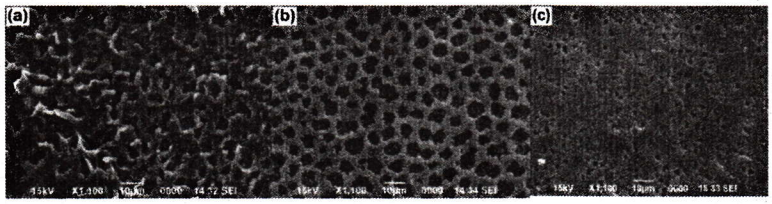

Fig. 1: SEM micrographs of PVdF-HFP-MMT nanocomposite electrolytes containing different wt. % of MMT where (a) 2.5%, (b) 5% and (C) 10%.

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^{13}C NMR Spectral study of Edible Oils, Mosquito Repellants and Incense Sticks that cause of Indoor Air Pollution

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During the recent times human society has experienced a lot of changes with respect to life style and food habits. Previously unknown products have become common household goods and various unhealthy practices have become commonplace. Along with these changes many new materials have entered in to our lives, like room fresheners, pest control devises and mosquito repellents etc.., which may be toxic when used excessively. More and more people are living in apartments where bed room, kitchen and bath room are very close. Any activity that emit gases in any room can disperse in to other rooms leading to indoor air pollution.

Human beings inhale an average of 6 liters per minute of air. Even, if the concentrations of toxic volatile organic compounds (VOCs) are about 1 ppb (1μg/L), since these VOCs are absorbed efficiently in the respiratory track, the total concentration will be around 3 ppm per day, which may affect the health of human beings.

To plan the experimental conditions for the Pyrolysis GC-MS analysis of the emitted gases, an idea on the nature of emitted gases is essential. The nature of emitted gases especially from mosquito repellents, incense sticks and edible oils which are burnt or heated to high temperatures in atmosphere depends on the nature of organic compounds present in these substances. So, the authors tried to assess the nature of the organic compounds present in raw materials of mosquito repellents, incense sticks and edible oils using C13 NMR spectra.

Using the 13C-NMRspectra, the aliphatic and aromatic moieties present in these materials along with other different carbon moieties have been understood. This information helped us to predict the nature of the emissions from these compounds and plan the experimental conditions for their monitoring. The 13C- NMR spectra of mosquito repellents, incense sticks and edible oils will be presented and discussed in this paper.

Non–haemolytic Gramicidin-S mimetics: Solution Conformational studies by NMR

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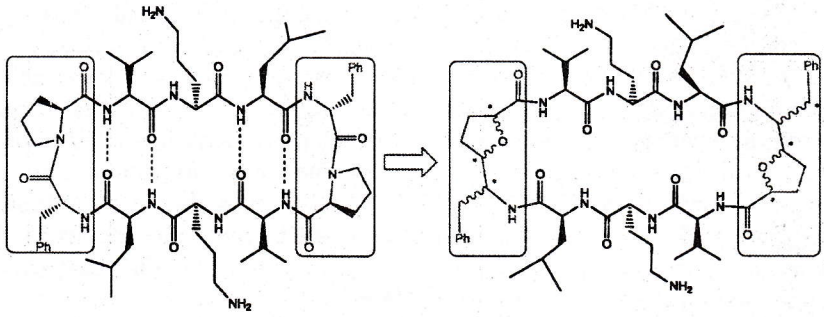
C_2-symmetric cyclic decapeptide Gramicidin-S has high potential against both Gram positive and Gram negative bacteria, but its therapeutic application is limited to topical usage owing to its haemolytic activity. Design and conformational studies were carried out on Gramicidin-S analogues containing Sugar Amino acid (SAA), a dipeptide isostere, which is placed in the position of D-Phe, Pro residues of Gramicidin-S. It was envisaged that such structural modifications would retain the antimicrobial activity while minimizing the haemolytic activity by taking advantages of the differences in architecture between the bacterial and host cell membranes. The experimental results suggested that the studied Gramicidin-S analogues displayed slight variations in the structures especially in the H-bonding pattern, compared to that of original Gramicidin-S. However, they showed excellent antimicrobial activity with negligible haemolytic activity makes them as promising to be potential leads. Conformational studies were carried out using conventional solution NMR techniques, which were further supported by restrained Molecular Dynamics (MD) studies.



Gramicidin-S Series of Gramicidin-S analog

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Study of reversibly self-assembled nanotubular structures of hIGFBP-2$_{249-289}$

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There is a great interest for developing biologics (>5000 Da) based therapeutics agents as they are composed of natural constituents, which is translated in to low toxicity, target selectivity, more efficient in protein-protein interactions and high potency1. On the other side Self-assembling peptides/proteins have gained increasing attention in the past several years as the promising drug delivery systems with an advantage of low toxicity over polymer based drug delivery system. Also, the most relevant and novel literature has been reported in the past decade regarding disulfide bonds in peptide/protein therapeutics, from their biological role in oxidative folding and Structure stability , to their capacity to enhance the pharmacological properties of peptides2. Furthermore, the disulfide bond containing protein/peptide which in turn enhances the cell permeability due to its reversible covalent linkages is considered as a novel therapeutic agent. Thus, a self-assembling protein/peptide (biologics) which also contains disulfide bonds serves as an efficient, excellent, novel and very promising therapeutic agent, owing to its high therapeutic demand.

Interestingly a report from our group describes a spontaneous and reversible in vitro self-assembly of the fragment of human Insulin-Like Growth Factor Binding Protein-2 comprising residues 249-289 (hIGFBP-2249-289) into long tubular structures of several micrometers length3. Moreover, the peptide fragment contains Cysteine residues and RGD motif (Cell adhesive epitope), which makes its relevance for applications in cancer cell imaging and therapeutics. Different mutants were generated to study the contribution of Cysteine residues in the formation of nanotube and for developing novel applications of IGFBP-2249-289. The recent studies of its applications in cancer cell imaging and binding studies of nanotube to the Cysteine containing peptide will be discussed. This binding study is useful to develop a novel application of hIGFBP-2249-289 nanotube in paramagnetic induced alignment experiment in NMR.

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Synthesis of pH and Solvent Responsive Smart Star Polymer by Atom Transfer Radical Polymerization

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A highly fluorescent fluorescein dye labeled core crosslinked star shaped random co-polymer with precise energy distribution was synthesized using Atom Transfer Radical Polymerization and Click Coupling method. Arm-first strategy was utilized to generate star architecture of the polymer. The synthesized polymer showed strong narrow fluorescence at hydroxylic solvents due to efficient energy transfer from AVS to fluorescein moiety. Also the synthesized polymer shows pH responsive fluorescence owing to a combined contribution from pH responsive acrylic acid moiety and fluorescin moiety in the main chain. Star shape of the polymer enhances its solubility and amphiphilic nature of the polymer enhances its applicability as a solvent responsive polymer. The structure of all the intermediate and final products was established through NMR spectroscopy, gel permeation chromatography, UV-visible spectroscopy and Fluorescence spectroscopy.
Keywords: ATRP, Fluorescence, pH and Solvent Responsive Polymer

Structural Characterization of Co-crystals by Solid-State NMR

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Co-crystals are systems constituted by two or more different molecules held together by supramolecular interactions. The study of structure-property relations of co-crystals is one of the active areas of the modern solid-state chemistry due to their important pharmaceutical applications. Solid-state NMR (SSNMR) is emerging as a fundamental tool for the structural identification and characterization of co-crystalline materials Accessing information on crystal packing, conformation and hydrogen bonding arrangements, which are the fundamentals in determining the final solid-state properties of a given form of co-crystal, is possible by newly emerged NMR techniques[1].Here we illustrate the combined use of two dimensional pulse sequences that exploit homonuclear and heteronuclear dipolar couplings for characterization of co-crystals. The molecular association is probed using both short- and long-range ^{1}H (FSLG) 6^{13}C CP HETCOR.^{1}H (DQ) 6^{1}H (SQ) experiments at fast MAS (30 kHz) have been used for achieving information on proton-proton proximities and thus on hydrogen-bond networks in the co-crystals. However, close proximities of N-H and aromatic protons hindered the full assignment of the ^{1}H spectra. To unveil this problem we are planning to perform ^{1}H (DQ) 6^{1}H (SQ) at ultra-fast MAS (~60 kHz) along with exploiting of more exotic spin pairs ^{14}N-^{1}H by ^{14}N-^{1}H heteronuclear multiple-quantum correlation (MHQC) experiment. The NMR methods utilized will be illustrated with some examples.

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On structural aspects of dsRBD containing proteins in the RNAi pathway across organisms

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Key stages in any RNA interference pathway are cleavage of dsRNA or pre-miRNA into siRNA/miRNA, loading of anti-sense strand to RISC complex and cognate mRNA silencing mediated by RISC complex. Two key enzymes, Dicer and Argonaute, are assisted by a variety of multiple dsRNA binding domains (dsRBDs) containing proteins (dsRBPs) to effect the pathway. Although the RNAi pathway appears highly conserved in higher eukaryotes, subtle differences in assisting proteins often alters the fate of this important post-transcriptional gene regulation pathway.

In organisms like *C. elegans* and *H. Sapiens*, only one Dicer and one or two dsRBDs are found to dictate both siRNA and miRNA biogenesis. Whereas, organisms like *D. melanogaster* have two separate sets of Dicer:dsRBPs for executing siRNA and miRNA pathway. In other extreme, *A. thaliana* represents four Dicers and four dsRBPs to carry out siRNA and miRNA driven gene silencing.

Interestingly, elementary bioinformatics analysis of sequences of these Dicer and dsRBPs show a variety of differences, e.g., the linker between RDE-4 dsRBDs (*C. elegans*) is composed of ~ 70 amino acids, whereas, in the majority of its counterparts the linker length spans only 5-10 amino acids. Several prominent changes in terms of C-terminal regions, dimerization etc. can be further noticed. Various Dicer domains are also seen to have many alterations, yet can perform their indispensible role.

For a conserved and ancient mechanism like RNAi, why would organisms need to alter key enzymes and proteins? At what stage, the key components have diverged? We explore answers to some of these questions through NMR driven solution structures of dsRBPs from *C. elegans* and *A. thaliana* and their interactions with dsRNA and minimal interaction domains of Dicer.

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Structure of RDE-4 dsRBDs, mutational studies and dynamics provide insights in the dsRNA recognition in RNAi pathway of *C. elegans*

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In *C. elegans*, RNAi pathway is initiated by the recognition of exogenous long dsRNA by RDE-4, a double stranded RNA binding protein (dsRBP). RDE-4 is a multi-domain protein with two dsRNA binding domains (dsRBDs) connected by a long linker (~60 aa) and a C-terminal domain that forms the dimer interface. Structural studies reveal a missing loop in both the domains that makes a contact with minor groove of dsRNA. Interdomain NOEs could not be identified and paramagnetic relaxation enhancement studies suggested a preferred orientation for the domains.

RDE-4 binds to dsRNA in a sequence independent way. NMR and ITC based titrations reveal that dsRBD2 is the key domain for the recognition of dsRNA and individual dsRBD1 fails to bind dsRNA. From structure and binding based mutagenesis, two tandem lysine residues (K217 and K218) were identified in dsRBD2 that are vital for dsRNA recognition. Additionally, our studies postulate a structural basis for the minimal requirement of linker and dsRBD2 for RDE-4's association with dsRNA and Dicer.

To understand the dynamics of RDE-4 (1-243), relaxation studies were performed at multiple fields and reduced spectral density analysis suggests that the first 35 residues and part of the linker are highly flexible, while rest of the protein is rigid. In addition, inter-domain dynamics will be studied by tagging a lanthanide on one domain and obtaining RDCs on other domain.

Preliminary studies on RDE-4C from ^{1}H-^{15}N HSQC, size exclusion chromatography and sedimentation velocity experiments suggests that RDE-4C undergoes concentration dependence association. This association may be required to enhance spatial proximity between two functional domains and thus augment RNAi efficacy in *C. elegans*.

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DFT-assisted RDC-NMR spectroscopy: Identification of synthetic epimers of Dinemasone-A metabolite

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The unambiguous structural determination of natural/synthetic organic molecules is crucial for employing in therapeutic applications. The recent developments of polymer gels as weakly oriented organic solvent media facilitate to record one-bond or two-bond orientational restraints, RDCs, that are superior over the conventional NOEs. The advanced method provides accurate determination of relative configuration, conformation, hydrogen bonding patterns of synthetic and natural organic molecules, and also gives access to identify the constitutional isomers of the intermediates. Herein, we discuss a simple scheme to distinguish two synthetic epimers of Dinemasone-A metabolite. The DFT-minimized structures of two epimers along with the experimentally derived RDCs (for both the epimers) have been subjected to SVD analysis, which has enabled to identify the Dinemasone-A and its epimer 6-epi Dinemasone-A.

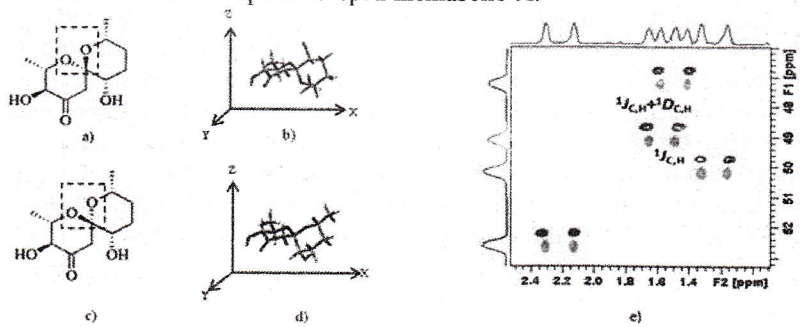

Figure 1: Schematic structures of Dinemasone-A (a) and 6-epimer of Dinemasone-A (c), the corresponding DFT minimised structures are shown in (b) and (d), respectively. The overlay of coupled HSQC NMR spectra of Dinemasone-A recorded in isotropic solvent medium ($^1J_{C,H}$) and anisotropic PDMS/CDCl3 gel medium ($^1J_{C,H}+^1D_{C,H}$) is shown in (e).

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Body mass index is associated with neurocognitive impairments in alcohol dependents

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Neuroimaging studies on alcohol dependent individuals have reported morphological and metabolic abnormalities along with a wide range of cognitive impairments[1]. Recent studies have also shown that these alcohol-related abnormalities appear to be adversely modulated by co-morbid conditions, namely, cigarette smoking, hypertension, coronary artery disease and type-2 diabetes, which are also associated with excess body weight. A growing body of evidence suggests that excess body weight is associated with abnormalities in brain neurobiology[2]. Taking this into consideration, we aimed at exploring the possible relationship between BMI (measure of body weight) and Psychological test measures (dysfunction scores).To that end, we performed a battery of neuropsychological tests(PGIBBD) on 25 alcohol dependent subjects and 20 healthy controls to assess various cognitive abilities. The dysfunction in any cognitive test was reported as Dysfunction rating score (Dys).The BMI for alcohol dependent subjects was in the range (20-38kg/m^2).On correlating BMI and Dys, we found a significant correlation between BMI and tests assessing the executive skills, memory and visuospatial skills. No significant correlation was observed between BMI and tests assessing the verbal skills. These finding suggests that brain injury is not solely mediated by effects of alcohol, but rather by a complex interplay among hazardous drinking levels and co morbid factors. These results reinforces the observation that a number of common co-morbid conditions, BMI in this study, can promote substantial variability in the pattern and magnitude of neurocognitive abnormalities observed in alcohol dependent individuals.

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Insight into functional regulation of IGFBP-2 by its intrinsically disordered linker domain

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The Insulin like growth factor (IGF) system is known for its role in growth and development of the human body. Dysregulation of the IGF system has been implicated in promotion and aggressiveness of various cancers. The bioavailability of IGFs is strictly regulated by a group of soluble, high-affinity IGF-binding proteins (IGFBPs). Thus IGFBP's pose as attractive therapeutic candidates for IGF mediated tumorigenesis.

The Insulin like growth factor binding protein-2—the second most abundant IGFBP in circulation known to form binary complexes with IGF—is 32 kDa in size with three distinct regions: the highly conserved *N* and C terminal region, and the intrinsically disordered linker domain (L-IGFBP2) with multiple cleavage sites. The presentation focuses on the insights gained about the structure and dynamics of the central intrinsically disordered domain of the human h-IGFBP2 and its interactions with IGFs by NMR and SPR. The IGFs bind L-IGFBP2 acting as allosteric activators to form a complex in which the dynamics but not the structure is altered in the bound form. The details of the study would be presented.

NMR based pharmacometabolomics of the response of chick chorioallantoic membrane to treatment with anti-angiogenic ayurvedic formulations

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Cancer is a leading cause of death worldwide and poses a huge health challenge. Many of the chemotherapy drugs used in cancer treatment are derived from natural products. Although single molecule drugs continue to be the focus of drug development, polyherbal formulations evoke interest since these are considered to have synergistic activity, low toxicity and multitargets[1]. NMR metabolomics can play an important role in evaluating the therapeutic efficacy of such formulations without the need to fractionate them. The present study has evaluated the anti-angiogenic potential of two ayurvedic polyherbal formulations using Chorio-Allantoic Membrane (CAM) assay[2] and assessed their response to treatment using high resolution NMR. The two formulations (labeled VK and GTK) in aqueous form were purchased from a GMP certified pharmaceutical company in India. Anti-angiogenic potential of the formulations was evaluated and compared with that of thalidomide (positive control) using CAM assay. Fresh fertile White Leghorn Chicken eggs (n = 180) were procured from KEGG Farms Pvt. Ltd., Gurgaon, India. These were divided into 3 groups of 60 eggs each, for studying three different concentrations (50, 75 and 100 µg/ml) of the formulations. Area of vascularisation was measured in CAM as an indicator of anti-angiogenic potential. The chorio-allantoic membranes treated with the formulations were removed from the chick embryos and extracted using perchloric acid. The membranes were lyophilized and redissolved in 600 µl of 100mM phosphate buffer (pH 7.0) prepared in 90% H2O-10% deuterated trimethylsilyl propionate (TSP). Water suppressed 1D proton spectra of the metabolic extracts of CAM were acquired on a 700 MHz NMR spectrometer (Agilent, USA) with the following parameters: spectral width - 12 ppm, relaxation delay - 4s, no. of scans - 64, data points - 32 K. Principal Component Analysis (PCA) was carried out using MATLAB programming platform. Of the 3 concentrations studied (50, 75 and 100 µg/ml), maximum anti-angiogenic activity was observed at 100 µg/ml. At this concentration, the inhibition of vascularisation was 63% for GTK, and 60% for both VK and thalidomide. Both the ayurvedic formulations showed significant anti-angiogenic activity comparable to thalidomide. Proton NMR spectra of CAM extracts after treatment with thalidomide and the two formulations showed significant reduction in choline, pyruvate, and lactate peaks compared to that from treated CAM. The reduction in choline peak was 50% for thalidomide, 60 % for VK and 40% for GTK. Treatment induced decrease in lactate (thalidomide - 90%, GTK - 40% and VK - 30%) and pyruvate (thalidomide - 50%, GTK - 20% and VK - 10%) suggest reduction of anaerobic glycolysis in CAM and reflects the positive response of CAM to treatment with all the drugs. NMR profiling is a quick and convenient method to evaluate the drug response especially of polyherbal formulations.

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NMR phytochemical profiling and evaluation of antiaging potential of medicinal plants

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Aging is a natural but inevitable process for all living organisms. During this process, generation of reactive oxygen species (ROS) is increased leading to the activation of elastase and collagenase, both of which contribute to skin aging. Plants as rich source of antioxidants possess the ability to reduce ROS and inhibit elastase, collagenase, hyaluronidase and tyrosinase activities[1]. In the present study, medicinal plants were analysed using NMR and also assessed for their antiaging properties using antielastase and antioxidant assays.

Authenticated medicinal plants (*Azadirachtaca indica* (AI), *Curcuma longa* (CL), *Emblica officinalis* (EO) *and Zingiber officinale* (ZO) were used for the study. The antiaging potential of the plants was estimated using antielastase assay with elafin/N-methoxysuccinyl Ala-Ala-Pro-Chloro (10μg/ml) taken as positive control. The antioxidant potential of the plants was estimated using DPPH (1, 1-Diphenyl-2-picrylhydrazyl) scavenging assay. Absorbance of the reaction mixture was measured at 517nm using a UV spectrophotometer and inhibitory concentration (IC_{50}) values were calculated. Sodium ascorbate was taken as the positive control. The samples were prepared as decoction and lyophilised for all the studies. 1D water suppressed proton spectra were obtained on a 700 MHz NMR spectrometer (Agilent, USA) using the following parameters: relaxation delay - 15 sec, no. of scans - 64, data points - 32 K, spectral width - 12 ppm. Deuterated trimethylsilyl propionate (TSP) in a coaxial insert was used as an external reference. Multivariate analysis of the spectral data was carried out using Principal Component Analysis (PCA) with MATLAB 2013b.

All four medicinal plants showed significant inhibition of elastase compared to the positive control. The percentage inhibition of elastase was 83.42 ± 0.09 (AI), 92.95 ± 0.08 (CL), 93.86 ± 0.09 (EO), 86.29 ± 0.09 (ZO), compared to that of positive control (95.03 ± 0.10). The inhibitory concentrations (mg/ml) of the medicinal plants in DPPH free radical scavenging assay are 2.3 ± 0.04 (AI), 0.79 ± 0.03 (CL), 1.92 ± 0.03 (EO), 6.96 ± 0.02 (ZO), in comparison to sodium ascorbate (0.02 μg/ml). Ascorbate, which is an antiaging metabolite was observed in all the four medicinal plants. In addition, antioxidant metabolites such as γ-amino butyric acid (GABA) and glutathione were also observed in the spectra. NMR could be a quick and robust method for phytochemical screening of medicinal plants with antiaging potential.

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NMR phytoanalysis and evaluation of anti-neovascularisation potential of medicinal plants

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Angiogenesis or neovascularisation is the sprouting of blood vessels from pre-existing ones. Cancer cells, by producing proangiogenic signals, induce vascularisation for their nourishment. Blocking of angiogenesis is thus an important therapeutic approach in the treatment of cancer[1]. In the last few decades, there has been an exponential growth in the field of plant-based medicines due to their pharmacological potential. The plants *Azadirachta indica* (AI), Piper nigrum (PN), *Tinospora cordifolia* (TC) and *Scindapsus officinalis* (SO), used in ayurveda for treatment of cancer, have been analysed in this study using NMR and also evaluated for their anti-neovascularisation potential. *Water suppressed 1D and 2D (COSY, TOCSY) proton NMR of lyophilised plant decoctions were acquired on a 700 MHz NMR spectrometer (Agilent, USA) using the following parameters: 1D (4s relaxation delay, 12 ppm spectral width, 64 scans, 32K data points) and 2D (2s relaxation delay, 12 ppm spectral width, 16 scans, 2K data points). Anti-neovascularisation potential of the formulations was evaluated* using ex-ovo chick Chorio-Allantoic Membrane (CAM) assay[2]. *Thalidomide was used as the positive control. Fresh fertile White Leghorn Chicken eggs (n = 180) were procured from KEGG Farms Pvt. Ltd., Gurgaon, India and were divided into 6 groups of 30 eggs each (Group1 - untreated, Group 2 to 5 - formulations and Group 6 - positive control). Data was acquired in five replicates at each concentration.*

The proton NMR spectra of the four medicinal plants showed in general, peaks from aromatic compounds, sugars, amino acids and metabolites such as choline, glycerol, inositol, β-hydroxy butyrate, indoxyl sulphate and p-hydroxy benzoic acid. However, differences were also observed. For instance, the observation of fumarate and lactate in AI, tyrosine and threonine in PN, fumarate and isoleucine in TC, and alanine in SO. A*nti-neovasculrisation activity as evaluated by CAM assay was 38.39 ± 2.87 mm² (AI), 36.11 ± 3.05 mm² (PN), 41.07 ± 4.28 mm² (TC), 36.4 ± 3.6 mm² (SO) and 36.4 ± 3.6 mm² (thalidomide at 10 µg/ml). Inhibition of vascularisation was 63% (AI), 60% (PN), 60% (TC), 60% (SO) and 60% (thalidomide). All the four plants showed significant anti-angiogenic activity comparable to thalidomide. Further studies are underway to correlate the spectroscopic findings with* anti-neovascularisation potential.

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Design of diastereomeric peptide foldamers containing APyC/β-Caa and study of enantiomeric handedness by NMR

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Earlier, our group designed and studied the (S,S)-APyC based α/β peptidic foldamers with right-handed 9/11-helices. The introduction of oxygen atom at β²-position on ACHC[1] provided additional stability by electrostatic interactions[2]. Further, the study was extended to the concept of accommodating left- and right-handed helices in a single peptide, generated from the enatiomeric parts from (S,S)-APyC and (R,R)-APyC. A new study was proposed on different series of peptide foldamers, which contain enantiomeric APyC's and diastereomeric β-Caa's. The foldamers made from alternating (R,R)-APyC and (R)-β-Caa (C-linked carbo-β-amino acid) show left-handed 12/10-mixed helix (Figure A), while peptides with alternating (S,S)-APyC and (S)-β-Caa show right-handed 12/10-helix (Figure B). These 12/10 mixed helical structures were further stabilized by 5-mr electrostatic interactions with pyran oxygen. In both the cases, the nOe NH(β-Caa(*i-1*))/NH(APyC(*i*)), supports the participation of 10-mr forward hydrogen bonding between NH(β-Caa(*i-1*))···O=C(APyC(*i*)), additionally the nOe NH(β-Caa(*i+1*))/CεH(APyC(*i*)) supports the electrostatic interaction with preceding pyran oxygen, whereas the NH(*i*)/CβH(*i-2*), supports the participation of 12-mr backward hydrogen bonding between NH(APyC(*i*))···O=C(β-Caa(*i-3*)). This study reveals the handedness can be tolerated by designing the peptides containing the constrained residues like APyC and diastereomeric residue β-Caa. Further studies on the generation of enantiomeric 12/10-helices in diastereomeric peptides are in progress.

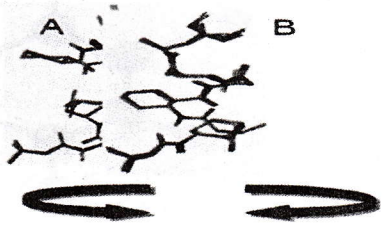

Figure A). A set of superimposition structures of left handed 12/10-mixed helix along with 5-mr electrostatic interactions. **B).** A set of superimposition structures of right handed 12/10-mixed helix along with 5-mr electrostatic interactions. side chains replaced with methyl's after calculations.

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Paramagnetic relaxation of Long-Lived Coherences in solution NMR

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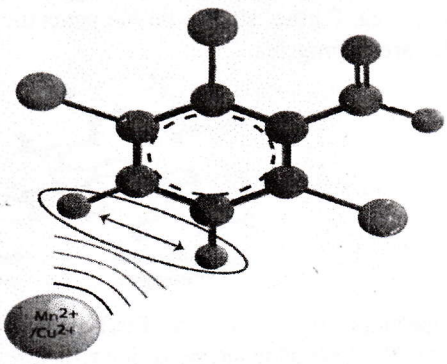
NMR spectroscopy, unlike other forms of spectroscopy, is characterized by the long lifetime of states and coherences. Long lifetimes result in narrower spectral lines, and so there is a constant pursuit to increase them. One promising technique where this was achieved recently in NMR involves a coherence between the singlet and central triplet state of a two-spin system called a long lived coherence (LLC). The excitation of LLC is generally symmetry forbidden, but can be induced by a specially designed pulse sequences in systems with two homonuclear scalar coupled spins I=1/2. The lifetime of LLC is much longer than the "normal" transverse spin coherence lifetime and is limited by the interaction of nuclei with other species, including that of unpaired electron spins. In this study we study the influence of paramagnetic ions Cu^{2+} and Mn^{2+} on the relaxation behavior of LLC in a two-spin system, 2,3,6-trichlorobenzaldehyde, and compare it with other common NMR relaxation rates[1]. It was observed that the presence of paramagnetic substances influence the relaxation rate of LLC more in comparison to transverse relaxation. In addition, the effect increases with the number of unpaired electrons[1]. A quantitative analysis of the effect of the paramagnet on the relaxation rate of the LLC is performed by modeling it as an external random field within the Redfield relaxation theory. This study shows that LLC is hypersensitive to these fluctuations. The results can be used in experiments involving contrast agents in MRI, which are paramagnetic.



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Low frequency NMR studies on PAN-HTPB co-polymer based elastomers

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*Poly-acrylonitrile (*PAN)-Hydroxy terminated poly-butadiene (HTPB) co-polymers are being used for various elastomeric applications in industries. Polymerization in such elastomers has to be monitored to realize desired properties. Proton NMR relaxometry studies have been done on co-polymer of PAN-HTPB sample at low magnetic fields or studying polymerization. Spin-lattice (T_1) and spin-spin (T_2) relaxation data has been studied for monitoring curing process. Results on co-polymer samples with selective percentage of additives (chain extenders) were compared with pure elastomeric samples. Studies indicated proton NMR at low frequency is good tool for identifying cure state and polymerization process. Studies indicated that stiffness of polymer chains of elastomers is directly coupled with mobility of hydrogen nuclei-protons. NMR relaxation decay curves were studied for information about proton mobility in co-polymer samples. Cross-link density of samples with and without additives has been determined.

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A Phosphorous Based Three Component Mixtures for Chiral Discrimination by NMR Spectroscopy

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A simple and efficient approach for NMR spectroscopic chiral discrimination of amino alcohols by using a three-component mixture employing the phosphorous based compound has been developed and applied to discriminate cyanohydrins and secondary alcohols. The Enantiopure chiral 1,1-binaphthyl-2,2-diyl hydrogenphosphate and 4-(dimethylamino)pyridine (DMPA) in $CDCl_3$ were incorporated as a chiral solvating agent. The simple mixing and shaking of amino alcohols with this solvating agent gave the well dispersed ^{1}H-NMR peaks not only for the α-proton of amino alcohols but also for other prochiral protons present in the molecule without any need for physical separation. This method also yields precise measurement enantiomeric excess.

Effect of sodium dodecylsulphate surfactant concentration on the formation of polypyrrole nanoparticles

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Conducting polypyrrole (PPy) has received much attention as functional materials due to their wide range of applications such as in sensors, actuators, polymeric rechargeable batteries, solid state devices, electro-chromic displays, drug and bio-molecule release, corrosion protection etc. [1]. The nanoparticles of PPy can be used in molecular electronics and microelectronic circuits. Chemical oxidative micro-emulsion method has been used to synthesis PPy nanoparticles in presence of ammonium persulphate (APS) as oxidant [2]. The effect of different molar concentrations of sodium dodecylsulphate (SDS) as surfactant cum dopant on the size and shape of the PPy nanoparticles are discussed in details. HRTEM micrographs show the formation of spherical PPy nanoparticles when SDS concentration is in between CMC-I (8×10^{-3} M) and CMC-II (0.2 M). At higher SDS concentration (> 0.2 M), elongated nanoparticles are formed. Also size of the PPy nanoparticles decreases with increasing surfactant concentration. XRD results show amorphous structure of PPy nanoparticles and crystallinity increases with SDS concentration. The higher value of electrical conductivity at higher SDS concentration correlates with the FTIR results which exhibit increased value of the effective conjugation length with increasing SDS dopant concentration. The thermal stability of PPy nanoparticles increases with increasing the dopant concentration which may be attributed to the ordered alignment of the polymer chains at higher dopant concentration.
Keywords: PPy nanoparticles, SDS surfactant, micro-emulsion, HRTEM, FTIR.

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DFT and NMR experimental evidences of formation of periodic γ-turns in unnatural α/β-hybrid peptides

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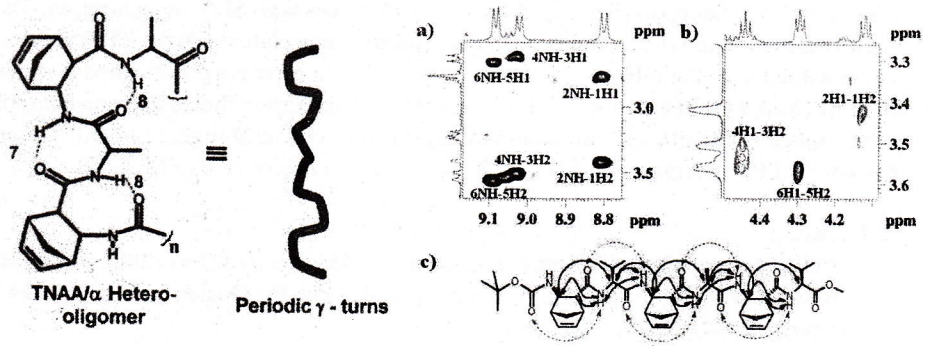
Residue based secondary structural control for γ-turns and extended conformations is explored in hybrid oligo-peptides. DFT and NMR studies on heterogeneous backbone oligomers comprised of *trans*-β-norbornene amino acid (TNAA) motifs and natural α-amino acid residues reveal a preferential formation of periodic inverse-γ-turns leading to extended ribbon-like structures in both polar and non-polar solvent media. These novel secondary structures are conformationally different from the other known α/β-hybrid peptides and serve as appropriate models for understanding antifreeze peptidic folding behaviour



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Study of structural, electrical and optical properties of polypyrrole nanotubes decorated with silver nanoparticles

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Polypyrrole (Ppy) is unique among conducting polymers in that its electrical properties can be reversibly controlled both by charge transfer doping and by protonation, which makes it a potential material for applications as chemical and biological sensors, actuators, antimicrobial agent, solar cell, light emitting diodes etc [1]. However, low processability and poor mechanical properties of Ppy has obstructed its potential applications. The incorporation of metal nanoparticles can effectively improve the electrical, optical, dielectric and antimicrobial properties of the polymer composites [2]. Nanocomposites of Ppy nanotube and silver nanoparticle (Ppy NTs/Ag NPs) have been synthesized by *in-situ* chemicalreduction of silver nitrate ($AgNO_3$) by sodium borohydride ($NaBH_4$) in presence of pre-synthesized Ppy nanotubes (Ppy /NTs). Four different compositions are prepared by varying the silver concentration from 6 to 15 wt % w. r. t. Ppy. These nanocomposites have been investigated by HRTEM, SEM, XRD, UV-vis spectroscopy, TGA, and impedance analyser. The incorporation of silver nanoparticles in the polymer matrix has been examined by HRTEMand XRD. The present paper reports the structural, electrical, optical and thermal properties of the Ppy NTs/Ag NPs decorated with silver nanoparticles.

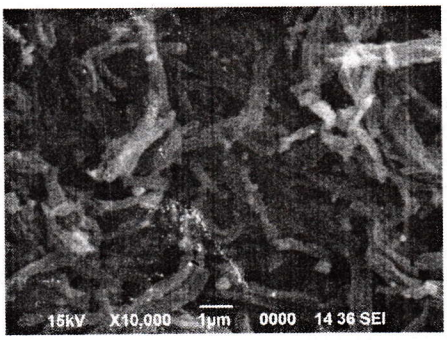

Fig. 1: SEM micrograph of Ppy NTs/Ag NPs nanocomposites.

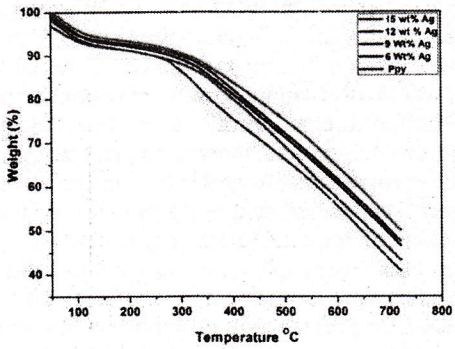

Fig. 2: TGA of Ppy NTs/Ag NPs nanocomposites with varying silver concentration.

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Language reorganization in chronic intractable epilepsy revealed by functional magnetic resonance imaging (fMRI)

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Purpose: Language functioning may be affected in patients with chronic intractable epilepsy foci in left hemisphere. BOLD contrast based functional MRI was used to map the cortical language network in patients of chronic intractable epilepsy prior to and after six months of surgery. **Method:** After obtaining the institute ethics approval, 15 consecutive patients with intractable epilepsy and 15 controls were recruited in the study. Thirteen patients underwent anterior temporal lobe resection (ATLR). FMRI was performed using single-shot echo planar imaging (EPI) sequence on 1.5T MR scanner (Avanto, Siemens, Germany) with 12-channel head coil. Design of the study involved meaningful word reading task, semantic judgment task, syntax reading task, comprehension syntactic-semantic task presented for a duration of (~ 500 s) using visual cues with MR compatible audio visual stimulus system during the active phase and black screen during baseline. The responses corresponding to semantic judgment task were recorded using 4-key button response pad. Data analysis and group comparisons were carried out using statistical parametric mapping (version SPM8).

Results: Preoperative data revealed less neural activity in IFG and STG in patients.Strong BOLD activation was observed post-surgery in left IFG, MFG and STG during lexical reading and semantic reading task in comparison to judgment and comprehension syntactic-semantic task. Clinical language assessment (IAB) demonstrated improvement in patients after surgery. **Discussion:** Disturbances in language network in intractable epilepsy patients, revealed by BOLD may be due to intractable seizure discharges and pathological abnormality. After surgery, specific language components (lexical, semantic, syntactic processing) were restored in TLE patients. However BOLD activation in MTG and STG involved in integration of semantic and syntactic information and is particularly responsive to meaningful sentences during semantic reading task [1,2]. We observedpatients who were affected hippocample sclerosis showed atypical language lateralization may suggest dominant hippocampus can be involve semantic and lexical information, and can raise questions regarding the specific roles of medial and lateral temporal cortex in targeted word retrieval [2].

Conclusion: Intractable epilepsy patients have atypical language lateralization with ipsilateral and contra lateral hemispheric lesions and pathological abnormalities. Important language components (lexical reading, semantic decision, semantic-syntactic processing) as measured by fMRI can guide surgeons for preservation of important brain areas during ATLR.

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A Solution Conformation Determination of an Abasic Lesion by 2D-NOESY

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Abasic lesions are the most frequently occurring lesions that may occur spontaneously, due to effect of radiations or as a transient intermediate by enzymatic process of repairing a modified or abnormal base. These sites may occur at a rate of 10000 per mammalian cell per day and may cause mutations or may be lethal if unrepaired. During replication process Adenine is placed fundamentally opposite to the abasic lesion during replication. We have proposed the study of an abasic lesion on 5'-d (CGGTCXCATCG)-3'.5'-(CGATGTGACCG)-3' for the sequence context. Here X denotes the furan abasic residue flanked by two Cytosine residues and a Thymine residue is placed opposite to the abasic site. The base and sugar proton resonances were assigned by NOESY in D2O and H2O. No major chemical shift differences were observed near the abasic lesion site while the sugar proton values for the sugar protons of the abasic site were shifted up field due the absence of base opposite to it. In H_2O NOESY, all the imino-imino protons connectivities were found in case of Control DNA oligomer, while the imino connectivities for G16-T17 and T17-G18 were not present in the modified DNA oligomer. This indicated a slightly extra helical geometry of unpaired Thymine residue present opposite the abasic lesion. Structural information provided by such structural studies would help in designing such molecules which specifically binds to Abasic sites and can act as anti-mutagenic agents.

Charge Assisted Assembling of Heterobimetallic Aggregates by Employing Magnetically Anisotropic Building Blocks

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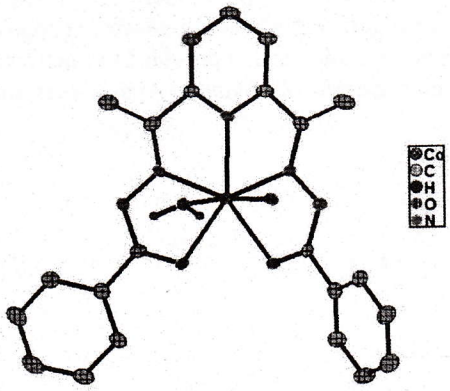
Significant efforts are being devoted to categorically enhance uniaxial magnetic anisotropy in molecular species owing to its relevance in raising the barrier of magnetization reversal in single molecular magnets. Due to geometric distortions, pronounced quenching of spin orbit coupling is observed in transition metal complexes and it confines the choice of significantly large *D* value to a handful of 3d ions e.g. Co^{2+}, Mn^{3+} etc (in O_h geometry).[1] Nevertheless modification of coordination geometry around the metal ion can overwhelmingly affect both the spin state and *D* parameter, thereby giving access to unprecedentedly large anisotropy in ions commonly regarded as magnetically isotropic.[2] For example significant enhancement of magnetic anisotropy is observed for Fe(II) ion in linear two coordinate geometry.[3]

Planer pentadentate acyclic ligands 2,6-diacetylpyridine bis (acyl/aryl hydrazone) are known to stabilize many transition metal ions in heptacoordinate pentagonal bipyramidal geometry. Several heptacoordinated first row transition metal complexes derived from these ligands are found to be highly anisotropic. The possibility to rationally assemble heterobimetallic aggregates by employing magnetically anisotropic pentagonal bipyramidal building blocks is being investigated. Salient features of this study shall be elaborated during this presentation.



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Assessment of Cranial Radiation Induced Acute Metabolic Alterations in Murine Model: A 1H NMR Spectroscopy Based Metabolomic Analysis

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The pathophysiology of radiation injury to CNS is not fully understood. Of all the brain regions, hippocampus is known to be very sensitive to radiation exposure, in particular CA1 and subgranular zone regions.Current knowledge on the early metabolic response of hippocampus for radiation exposure is still fragmented. The study is designed to look for comprehensive metabolic changes of acute radiation exposure effects on brain using NMR based metabolomic approach. A total of 18 strain 'A' male mice were taken and randomly divided into 2 groups of which 12 animals in the first group were exposed to single dose of 8Gy cranial radiation through Tele ^{60}Co irradiation facility unit, rest of the animals (n = 6) served as sham irradiated controls. Animals were sacrificed and hippocampus was dissected out carefully at day 5 and 10 post irradiation in radiation group. Control animals were also sacrificed and hippocampus was dissected out. The polar metabolite extracts of dissected hippocampus (50-70mg) was obtained based on acetonitrile extraction method. The tissue extracts were reconstituted in 480 µl of D_2O containing 1mM TSP as an internal NMR chemical shift standard and ^1H NMR spectra were acquired on a Bruker 400 MHz spectrometer at 300 K using 1D ZGPR pulse sequence.Each ^1H NMR spectrum from tissue was integrated into regions with equal width (0.04 ppm) using AMIX software package. The data set was normalized, mean centered and pareto scaled before performing the Principal component analysis (PCA) and Partial least square-discriminant analysis (PLS-DA) processing using Metaboanalyst 2.0.The metabolites observed in ^1H NMR spectra of hippocampus after 8Gy cranial irradiation compared to controls were mainly associated with energy metabolism, osmolytes, excitatory neurometabolites, N Acetyl Aspartate (NAA), ketone metabolism and membrane metabolites. Significant decrease in GABA, glutamine, glutamate, succinate, citrate, choline and GPE was observed in irradiated animals compared to controls at both the time points. On the other hand, aspartate, acetate, ketone and scyllo-inositol were strikingly elevated compared to controls both at day 5 and 10.The results indicate an overall decrease in hippocampal metabolic activity due to irradiation and provide strong evidence that hippocampus is metabolically responsive to irradiation.The significant decrease in the replenishment of some of TCA cycle intermediates and significant increase in ketone bodies post irradiation might be related to radiation induced poor glucose metabolism. Our present study supports that ketone bodies metabolism as an alternative energy source might have been permitted to meet the metabolic demand of brain post irradiation. The changes observed in hippocampus metabolism during acute phase of radiation injury might have long lasting effects on cognitive development and function

Assessment of Whole body Radiation Induced Early Delayed Changes in Mice Brain: A 1H MRS and Behavioral Evaluation Study

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As the threat of terrorism increases globally, the possibility of a radiological attack in a public place is of great concern. In the context of acute radiation sickness scenario, the role of Central nervous system has been underestimated. The susceptibility of CNS to radiation is high because of its low antioxidant pools, high metabolic rate and actively dividing cells in two discrete regions i.e hippocampal dentate gyrus and sub ventricular zone. Most of the studies suggest that acute injury is reversible whereas early delayed and late delayed injury is irreversible leading to metabolic and cognitive impairement. The present study is designed to observe early delayed effects of radiation during whole body irradiation leading to behavioral alterations and metabolic impairment if any. A total of 20 C57 male mice were taken and acclimatized for 48 hours in polypropylene cages under standard temperature, humidity conditions prior to group allocation and treatment. Out of 20 animals 10 animals were given 5Gy whole body radiation through Tele ^{60}Co irradiation facility (Bhabhatron II) with source operating at 2.496 Gy/min. The remaining 10 animals served as sham irradiated controls. The Behavioral and MRS experiments were carried out on 10 animals each at 3 months post irradiation. For behavioral experiments the spontaneous behavior activity in mice was evaluated using Opto-varimex 4 system. The working memory function was evaluated, the next day, using the novel object recognition test. For MRS, the voxel was localised in the cortex-hippocampus region of mouse brain. MR spectra were acquired using PRESS sequence and data (FID) was processed using LC model for quantitation.Behavioral studies showed locomotory and discrimination ratio impaired in irradiated group.1H MRS revealed significant decrease in Glutamine and significant increase in myo inositol in irradiated group compared to controls. The decline in cognitive function at 3 months post irradiation could be due to radiation induced persistent oxidative stress.In our study, increased mI and decreased cognitive function at 3 months post whole body radiation exposure reflect that whole body radiation exposure may have long lasting effect on the cognitive performance.Recently, glutamine has been reported to have a neuroprotective effect against DNA Damage, Beta-Amyloid and H_2O_2-Induced Stress. Reduced glutamine levels in our study might be associated for reduced cognitive functions as well. In the present study Behavior and MRS studies together were able to elucidate early delayed changes due to 5Gy whole body radiation in brain at cognitive and metabolic level. These findings can be valuable in evaluating the radiation induced persistent oxidative stress thus leading to cognitive dysfunction and metabolic impairment.

Characterization of keto-enol tautomers towards the synthesis of dibenzoxanthene derivatives via NMR techniques

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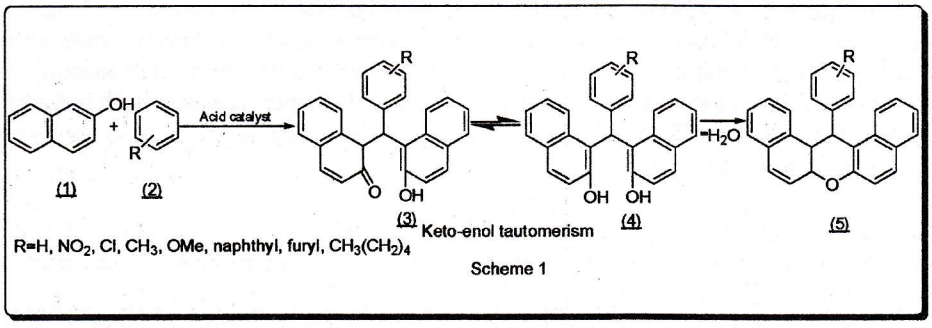
Dibenzoxanthene derivatives (5) are a class of heterocyclic compounds having varied applications both in pharmaceuticals[1] and material science[2]. The intermediates, bisnapthols (4) and keto-enol tautomers (3) that are encountered during their formation via the cyclocondensation of 2-naphthol (1) and aldehydes (2) (Scheme 1) also have potent uses in medicinal field[3] and organometallics. The keto-enol tautomeric intermediates have not yet been isolated till date. Versatile use of lewis acid can be implemented for the formation and isolation of these intermediates. The newly found intermediates have been confirmed by the extensive use of various techniques of Nuclear Magnetic Resonance (NMR) spectroscopy.



Scheme 1

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Structural, thermal and electrical transport study of polythiophene-Ag nanocomposite synthesized by *in-situ* chemical reduction method

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Modern technology continuously needs new materials having special properties. Nanocomposites formed by metal nanoparticles (NPs) dispersed in electrically conducting polymers, such as polyaniline or polythiophene, have received much attention in the last few years [1]. These hybrid nano-materials are expected to display several synergistic properties between the polymer and the metal nanoparticles, making them potential candidates for application in numerous fields such as catalysis, biosensors, memory devices, sensors, photovoltaic devices and solar cells [2-3]. In this work, polythiophene/silver nanocomposite has been successfully synthesized by *in-situ* chemical reduction method. HRTEM, XRD, FTIR, UV-Vis and TGA have been carried out to study the morphological, structural, optical and thermal characterization of the polythiophene/silver nanocomposite. HRTEM confirms the spherical nature of the synthesized nanoparticle. FTIR spectra confirm the formation of polythiophene. In case of nanocomposite the enhancement of band intensity in FTIR suggests the fruitful interaction between Ag and S atom of polythiophene. TGA has indicated an enhanced thermal stability of nanocomposite as compared to that of pure polythiophene. Dielectric and ac conductivity also show an increasing trend with increasing the wt.% of $AgNO_3$ in the nanocomposite. The increase of ac conductivity with increasing wt.% of $AgNO_3$ can be attributed to the increase of Ag nanoparticle concentration, which favors the better electronic transport. Imaginary part of modulus shows a relaxation peak and it shift towards higher frequency with increasing wt.% of $AgNO_3$. The shifting of relaxation peak towards high frequency suggests the enhancement of dc conductivity contribution.

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Three component synthesis of some new 5, 6- disubstituted cycloalkyl -3, 4-dihydropyrimidinone derivatives

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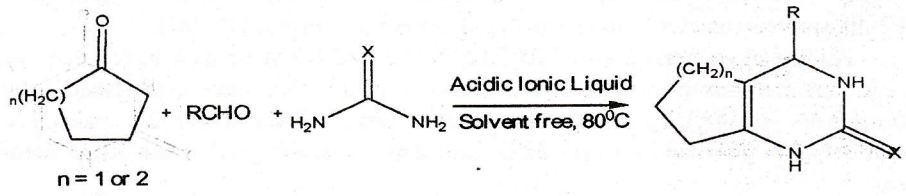
An operationally simple, one pot, three component method has been developed to afford some new 5, 6-disubstituted cycloalkyl-3, 4-dihydropyrimidinone derivatives **(A)** via Biginelli condensation[1] of cycloalkanone (1 mmol), aldehyde (1 mmol) and urea (2.5 mmol) (Scheme-1) in acidic ionic liquids at 80°C. Pyrimidinone derivatives exhibit some potent biological and pharmaceutical properties such as antiviral, antitumour, antibacterial and anti-inflammatory properties and also can behave as calcium channel modulators.[2]All the products were extensively characterized by various NMR techniques such as ^{1}HNMR, ^{13}C NMR, HETCOR, DEPTT and COSY spectra along with FT-IR and elemental analysis. Excellent yields, short reaction times, easy workup, reusability of the catalyst and green conditions are the most obvious advantages of this procedure



R=Alkyl or aryl
X=O, S

Scheme 1

A

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Solution structural characterization of RBP-42 from *T. brucei*

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RNA binding proteins (RBPs) have been known to play a significant role in the mRNA metabolism of many organisms such as *C. elegans, D. melanogaster, T. brucei etc.* RBPs have a modular structure and consist of multiple repeats that are built from a number of RNA binding domains, which bind to untranslated regions of mRNA. RBPs assist the processing and assembly of non-coding RNAs into ribonucleoprotein complexes, which mediate important cellular functions such as splicing and translation. RBPs are also essential for mRNA maturation, by addition of a 7-methylguanosine cap to mRNA-precursors, splicing of introns, editing, and the addition of a polyadenosine tail at the end of mRNA.

In *T. brucei*, a novel RNA binding protein named RNA binding protein 42 (RBP42) of ~ 38 kDa has been recently identified and has been hypothesized to play a major role in adaptation to different environment by regulating mRNA metabolism. RBP42 targets the coding region of mRNA that encodes proteins involved in cellular energy metabolism. RBP42 shows similarity with mammalian RNA binding protein, G3BP. The N terminal region has homology with the Nuclear transport factor (NTF2- like protein) and C terminal with the RNA recognition motif (RRM).

For the characterization of RBP42, NTF2 and RRM domain have been cloned using conventional methods in prokaryotic expression system. We have established solubilisation, purification and stability conditions for structural studies of RRM and NTF-2 domains. ^{15}N-^{1}H HSQC data show highly dispersed resonances in both dimensions suggesting that RRM domain is well folded.

We have performed NMR titration studies of RRM domain with target RNA mimics. Structural studies of RRM and NTF-2 domain of RBP42 and RNA titration data will be presented.

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Structural Characteristics of Conserved C-terminal Segment of Eukaryotic Acidic Ribosomal P2 proteins: Functional Implications

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Ribosome structure has been solved by X-ray crystallography several years ago, but to date, very little is known about the ribosomal stalk, which in the ribosome is a supramolecular assembly of proteins. During protein synthesis, the stalk is known to adopt different conformations at different steps of the elongation cycle. Eukaryotic stalk is much more complex than prokaryotic stalk. It consists of acidic proteins known as P proteins (P0, P1, P2), which are organized as a complex assembly, $P0(P1\text{-}P2)_2$. However, the individual proteins are known to self-associate under physiological conditions.

The P2 protein is quite conserved across several eukaryotic species, particularly, its C-terminal domain. Within the C-terminal domain also, the last 11 residues are even more conserved. It has been argued that multiple copies of this C-terminal sequence protrude outwards from the ribosome to the cytoplasm, function to fetch the elongation factors and draw them into GTPase-associated center. In order to understand structure function relationships of this domain, several constructs of the domain (5kDa) from different eukaryotic species (human, *P. falciparum, T. gondii*) were prepared. The constructs were expressed and purified. CD performed on these proteins shows that this domain is intrinsically disordered. NMR investigations show that this domain is not involved in self-association, and exists as a monomer in solution which is further confirmed by MALDI. The HSQC spectrum of these constructs shows all the expected 50 peaks. Fluorescence spectroscopy reveals that this domain interacts with GTP and elongation factor (eEF2). This domain also interacts with Trichosanthin, a ribosome inactivating protein and responsible for translation inhibition. Further investigations are in progress to unravel the details of the interaction.

Structure-Function Relationship of Crc, a Global Regulator in *Pseudomonas*

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Carbon Catabolite Repression (CCR) allows metabolically versatile free-living bacteria to selectively assimilate a preferred compound among a mixture of several potential carbon sources. CCR regulates metabolism, boosting the ability of bacteria to survive in their natural habitats. Crc (Catabolite Regulation Control, ~31kDa) is a global regulator protein in CCR in *Pseudomonas*. Crc triggers a repression process that inhibits the expression of genes involved in the transport and catabolism of non-preferred amino acids, while it indirectly favors the assimilation of preferred amino acids. A dissection of the molecular mechanisms underlying CCR is vital to know how metabolism is regulated and how compounds are degraded by this class of bacteria in the environment.

Crc acts by binding to target mRNAs at specific sites, generally containing NAA rich motifs located close to or overlapping with the translation-start site, and thereby inhibits the formation of a productive translation initiation complex. At the same time, in the absence of preferred substrates, Crc activity is regulated by small non-coding RNAs (e.g., *crcZ* and *crcY*),which bind to Crc thus preventing its binding to target mRNAs.Quite contrarily, several recent crystal structures of Crc could not identify a distinct RNA binding patch on the surface. Therefore, it is imperative to study the structure and RNA binding properties of Crc using solution-based techniques.

To this end, we have achieved >94% backbone and ~ 85% ^{13}C stereo-specific methyl chemical shift assignments of Ile (δ1), Leu and Val. The solution structure of Crc was calculated with a backbone RMSD of ~ 0.9 Å. The solution structure of Crc shows high degree of similarity with AP endonucleases and has ~2.7Å backbone RMSD with the homology model and crystal structure.

Electrostatic potential surface plot of Crc shows a positive patch on the side opposite to that involved in DNA-binding in its homologues. RNA binding site on Crc has been elucidated by titrating various RNA differing in length and structure. Chemical shift perturbations indicate that the site and mechanism of nucleic acid recognition is altered in Crc as compared to its homologues, hinting Crc's divergent evolution from AP endonucleases. Additionally, isothermal calorimetry titration studies suggest that Crc has μM affinity with small RNA. Further, site-directed mutagenesis studies are performed by biophysical and biochemical assays.

Evolutionary functional divergence of Crc and its structure-function relationship with regulatory and target RNA will be discussed.

Toxicological Effects of $CoCl_2$ Induced System Alteration in Multiple Rat Organs as Revealed by ^1H NMR Spectroscopy

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Introduction: Cobalt is a known heavy metal with multiple industrial applications but also results in a wide spectrum of toxicities. Oxidative stress is one of the main mechanisms involved in cobalt toxicity leading to the generation of reactive oxygen species (ROS), which in turn cause lipid peroxidation and protein oxidation in several tissues. Various research studies have reported the toxicity of cobalt at biochemical, enzymatic and genetic level, a comprehensive metabolome of cobalt toxicity remains to be elucidated.

Aim and Objective: Raturinary metabolic profilingfor acute toxicity induced by $CoCl_2$ using ^1H NMR spectroscopy.

Material and Methods: Male Sprague Dawley rats of 11 weeks of age (n = 5 in each group) were injected with $CoCl_2$ at a dose of 2.1 and 17mg/kg body weight intraperitoneally, controls were injected with 0.9% saline only. Urine samples were collected at 8, 24, 72 and 120 h post dose (p.d.) and placed at -80°C. 400µl of urine sample was added to 200 µl of deuterated phosphate buffer (pH= 7.4) containing 1mM TSP and transferred to 5mm NMR tube. ^1H NMR spectra were acquired at 400.13 MHz, Bruker-AVANCE 400 spectrometer at 298K. Peak assignment was determined according to previously reported literature[1]. In order to find out the dissimilarities between the control and $CoCl_2$ treated group multivariate analysis using metaboanalyst (http://www.metaboanalyst.ca/Metaboanalyst/faces/Home.jsp) was carried out.

Result and Discussion: The major metabolite changes corresponding to $CoCl_2$ toxicity are related to amino acids, osmolytes and energy metabolites. The energy metabolites, hippurate, DMA and BAA got altered as early as 8h p.d. in both the dose group. Most of the metabolites were recovered except citrate, DMA and hippurate at day5. NMR spectroscopy results of liver and kidney tissue extracts also showed changes in membrane metabolites, lactate and creatine till day 3 and reverted back to normal by day5. Our NMR findings suggested cobalt induced functional damage to renal and hepatic tissue which was well corroborated with histopathological and serum biochemical results. Our findings were also in tune with antioxidant parameters such as LPO, SOD, GSH and Catalase that showed oxidative stress induced by $CoCl_2$.

Conclusion: The present study demonstrates the potential of metabolomics in finding the putative metabolic markers for early prediction of risk of adverse effects by $CoCl_2$.

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^{1}H-NMR based Metabonomics study of tryptophan metabolism in *P. berghei* infected C57BL/6 mice model

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It's been more than a century when, for the first time, the cause of transmittance of *P. falciparum*, the major parasite that causes Human Malaria, has been discovered. Due to complexity in parasite's life cycle, we have not understood the disease completely so far. It has been known that there is an increase in uptake of tryptophan in RBC infected with *P. falciparum* but little is known about the organ specific tryptophan metabolism[1, 2]. In the present study, we have used the ^{1}H-NMR based metabonomics approach to understand the host response to tryptophan challenge in control and *P. berghei* infected C57BL/6 mice. The scores plots in PCA analysis clearly differentiates the control from the *P. berghei* infected group and also shows differences between the infected Trp-challenged and infected controls. These different groups further analyzed in pairs using OPLS/ O2PLS-DA and their corresponding loadings plots suggest that the tryptophan pathway is perturbed in malarial mice. The malarial mice has higher amount of Quinolinic acid (QA) and Kynurenic acid (KA) compared to controls as well as the ratio QA/KA is also higher in malarial mice matching with the earlier reports[2]. The further analysis is under process and we hope that these early results suggest that parasite favored QA pathway to make more and more NAD/NADP to use them in its glycolysis pathway. The enzymes of this pathway can be targeted by drug designers to curb the malaria.

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Extraction of Magnitudes and Relative Signs of $^{n}J_{HF}$ couplings: A Pure Shift and RES-TOCSY Methodologies

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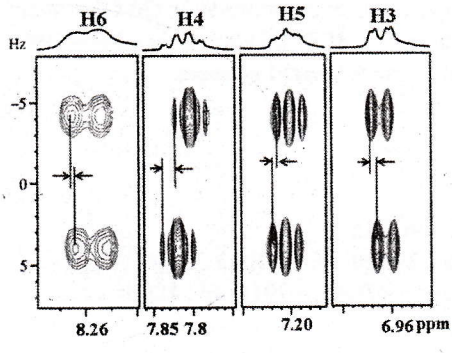
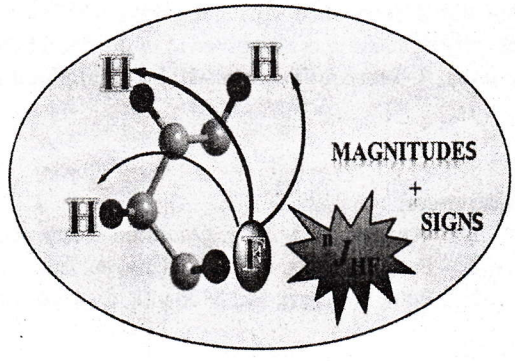
For the determination of constitution, conûguration and conformation of fluorine containing small organic, bio-molecules and natural products, the powerful long range heteronuclear coupling constants ($^{n}J_{HF}$) are employed. Unfortunately, the extraction of signs and magnitudes of such $^{n}J_{HF}$ is a challenging task, especially when the spectra are severely complex because of the presence of large number of short- and long- range homonuclear couplings ($^{n}J_{HH}$). In the present work an approach involving the utility of pure shift NMR[1] for the extraction of the $^{n}J_{HF}$ from the simple one dimensional ^{1}H-pure shift spectrum will be discussed. In addition the novel application of our recently introduced 2D RES-TOCSY[2] sequence, for the determination of relative signs and magnitudes of $^{n}J_{HF}$ will be discussed. The slopes of the displacement of F_1 cross sections of the 2D RES-TOCSY spectrum yield the relative signs of the couplings. The distinct advantage of the 2D experiment is the extraction of magnitudes of the couplings, which are hidden within the line widths.





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Electron paramagnetic resonance study of nanoscale Gd_2O_3 systems

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Rare-earth (RE) systems, and their oxides find profound interest in the deployment of high-performance luminescent devices, optoelectronic components, high-field magnets, sensors, and other functional devices, owing to their unique optical, electronic, magnetic, and physico-chemical properties arising from interlocked unpaired electrons, *4f–5d* carrier transitions and spin configurations [1]. Gadolinium, in either pure or oxide form, is highly stable against environmental degeneration [2]. In ambient environment, it exists in three polymorphic forms: hexagonal, monoclinic and cubic. Owing to environmental stability, thermal stability, low phonon energy, and ability to get easily doped with other lanthanide ions, Gd_2O_3 can have immense potential in a number of functional devices, including nano-bio interface applications. The structural and morphological characterizations of our synthesized nanostructured products were performed by x-ray diffraction and high resolution transmission electron microscopy; respectively.Considering oxygen vacancies as the major source of paramagnetic centers [3], and using electron paramagnetic resonance spectroscopy we explore spin states, resonance shift and *g*-values in both nanoparticles and nanorods of Gd_2O_3 systems. A special emphasis was also given to understand EPR response of 80-MeV Carbon irradiated nanorod systems. A comparative view will be highlighted for all these aforesaid systems.

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In Tube Approach for Testing the Enantiopurity of Chiral Amines and Amino Alcohols by ^{1}H NMR

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In tube approach involving a simple mix and shake method for testing the enantiopurity of chiral primary, secondary and tertiary amines, and their derivatives chiral amino alcohols by ^{1}H-NMR spectroscopy is developed. The procedure involves an *in tube* formation of chiral ammonium borate salt from the mixture of the C_2 symmetric chiral BINOL, trialkoxyborane and chiral amines. The proposed concept demonstrated convincingly on large number of chiral and pro-chiral amines and amino alcohols, also aids in the precise measurement of enantiomeric excess. The protocol can be accomplished in couple of minutes directly in the NMR sample tube, without the need for any physical separation.

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NMR Spectroscopy – A Versatile Tool to Investigate Structure and Activity of Peroxometal Macrocomplexes

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NMR spectroscopy has evolved into an important technique in research. It plays a crucial role in structure determination of macroligand incorporated metal peroxo complexes. In this work, we present the characterization of a number of series of macromolecular peroxo complexes of the metals V(V), Mo(VI) and W(VI), synthesized in our laboratory, by employing NMR technique (^{13}C, ^{51}V and ^{95}Mo) along with other analytical techniques.[1,2,3] In addition, ^{51}V NMR has been used to investigate the mode of degradation of monomeric as well as polymer anchored peroxovanadate complexes under the effect of reactive oxygen mopping enzyme (ROS) catalase.[1] Thus, the unique ability of this important spectroscopy tool to provide extremely valuable information has great significance in research.

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Design and Study of Mixed β-Peptides with Alternating Carbo-β-amino acids and β-hGly

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The biological functions of proteins and peptides are attributed to the compact three-dimensional structures that are adopted by them. 'Foldamers', which are referred to the oligomers of non-proteinogenic amino acids, form a variety of stable secondary structures, such as helices, sheets and turns, that are stabilized by non-covalent interactions. The oligomers, constructed from β-amino acids, form a variety of secondary structures like 14-helix, 12-helix,10/12-helix, 10-helix and 8-helix[1]. Earlier, it was reported that robust left-handed 10/12- and 12/10-helices[2] were observed in the mixed peptides with alternating (S)-β-Caa with D-xylose side chain and β-hGly. In continuation we proposed to study peptides with (S)-β-Caa with D-lyxose side chain, derived from D-mannose alternating with β-hGly to understand the effect of side chain on the β-peptides derived. Unlike the earlier study, the peptides displayed in Figure A & B, resulted in right-handed 10/12 mixed helix, supported by the characteristic nOe correlations CβH(2)/NH(4) & CβH(4)/NH(6), and weak NH(1)/NH(2), NH(3)/NH(4) and NH(5)/NH(6) in both the cases. This study reveals that change in the side chain influences a variation in the handedness of the helix. Further studies are in progress to understand this observation with peptides containing (R)-β-Caa.

Figure: A

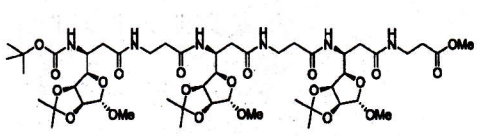
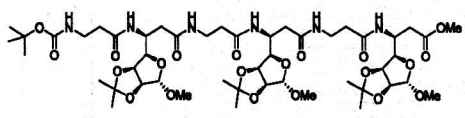


Figure: B



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Unraveling Multi-spin effects in Rotational Resonance NMR

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A quantum-mechanical model integrating the concepts of reduced density matrix (RDM) and effective Hamiltonians is presented to explain the multi-spin effects observed in rotational resonance (R2) NMR experiments. Employing this approach, the spin system of interest is described in a reduced subspace inclusive of its coupling to the surroundings. The analytic results obtained provide an accurate description/interpretation of R2 experimental results and could serve as a test-bed for distinguishing coherent/ incoherent effects in solid-state NMR.

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Spectroscopic metabolomics: A potential tool for studying nutraceuticals

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In healthcare, nutrition is now recognised to be as important as therapeutics and is gaining attention as a scientific discipline. In this context, plants as natural repository of nutrients are increasingly analysed from the perspective of nutraceuticals[1]. The aim of this study is to do a multitechnique spectroscopic analysis of nutraceutical plants and also assess their antioxidant potential, which has both nutraceutical and therapeutic roles. Twelve known nutraceuticals such as *Emblica officinalis, Cuminum cyminum* and *Piper nigrum* were studied using NMR, Fourier Transformed Infra-Red (FTIR) and Laser Induced Breakdown Spectroscopy (LIBS). The samples were prepared as 10% aqueous solution for all investigations. Water suppressed 1D NMR spectra were recorded in a 700 MHz spectrometer (Agilent, USA) using the following parameters: relaxation delay - 14 sec, number of scans - 32, spectral width - 15ppm and data points - 32 K. Principle Component Analysis (PCA) was performed on the spectral data, which were binned and bucketed at 0.04ppm intervals using MestReC and Unscrambler X10.2. FTIR 660 (Agilent, USA) was used to scan the sample in the 750-10,000 nm range in the Attenuated Total Reflection (ATR) mode. Elemental analysis was carried out using a 4-channel spectrometer (Ocean optics LIBS 2000+) in the 200-1100 nm wavelength region[2]. The antioxidant potential of the nutraceuticals was evaluated using DPPH (1,1-Diphenyl-2-picrylhydrazyl) assay. IC_{50} value was calculated for this assessment.

All the nutraceuticals showed antioxidant potential with the maximum and minimum activities shown by *Emblica officinalis* (IC_{50} - 1.92 mg/ml) and *Cuminum cyminum* (IC_{50} -13.11 mg/ml), respectively.(a) (b)

The NMR spectra showed resonances from primary metabolites such as carbohydrates and amino acids, and also secondary metabolites such as flavonoids, flavonol glycosides, polyphenols, although with varying intensities. PCA of NMR spectral data revealed antioxidant based clustering of nutraceuticals. The FTIR spectra exhibited the following functional groups: OH (1300-1420 cm^{-1}) and C=O (1661-1760 cm^{-1}) from carbohydrates, R-COOR (1773 cm^{-1}), R-NH_2^+ (2320-2380 cm^{-1}) from amino acids and alcohols/phenols (3594-3620 cm^{-1}). Groups such as OH, C=O and R-NH_2^+ are found in secondary metabolites, which are associated with antioxidant potential. Interestingly, the elemental analysis showed high levels of Mg and Ca in the antioxidant rich nutraceuticals. Spectroscopic profiling using a combination of techniques coupled with multivariate analysis can provide comprehensive and quick information on nutraceutical properties of plants. Further indepth studies are underway and in a larger sample size.

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NMR in sensory sciences

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Food supplements and nutraceuticals are increasingly being used as part of nutritional therapeutics. In this context, organoleptic property of taste is used as an important quality assessment parameter. The aim of this study is to evaluate the role of proton NMR spectral markers in identifying taste. Nutraceutical plants such as *Phoenix sylvestris, Vitis vinifera, Glycyrrhiza glabra, Agaricus campestris* and *Zingiber officinale* were analysed using NMR and correlated with the organoleptic property (taste), which was objectively evaluated using Electronic Tongue (E-Tongue).

The NMR studies were carried out using 700 MHz spectrometer (Agilent, USA). The following parameters were used to obtain 1D water suppressed proton spectra : TR - 14 sec, scans - 32 and data points - 32K. 2D NMR was carried out to assign the peaks. Parameters were : - 2 sec, scans - 16 and data points - 2K. The 1D spectral data was analysed using Principle Component Analysis (PCA), MestRe-C and Unscrambler X10.2. For this, the spectral region was binned and bucketed at 0.04 ppm intervals. Taste evaluation was carried out using a 16 autosampler E-Tongue (Alpha MOS, France), using a set of 7 sensors based on Chemical modified Field Effect Transistor (ChemFET) principle[1]. The NMR and E-Tongue data were correlated.

Although the proton NMR spectra showed a number of resonances from primary (carbohydrates, amino and organic acids) and secondary metabolites (polyphenols, flavonoids), there were differences as well. These were reflected in the PCA of the spectral data. The preliminary results showed similar clustering patterns for NMR and E-tongue data, indicating that NMR profiling could reflect the organoleptic property. Amino acids like alanine, glycine, tyrosine and phenylalanine could be spectral markers for taste. Further in-depth studies are underway to explore this in detail. With increasing interest in using organoleptic properties for quality assessment, NMR could open new vistas of application in sensory sciences.

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^{13}C NMR Spectral study of Edible Oils, Mosquito Repellants and Incense Sticks that cause of Indoor Air Pollution

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During the recent times human society has experienced a lot of changes with respect to life style and food habits. Previously unknown products have become common household goods and various unhealthy practices have become commonplace. Along with these changes many new materials have entered in to our lives, like room fresheners, pest control devises and mosquito repellents etc.., which may be toxic when used excessively. More and more people are living in apartments where bed room, kitchen and bath room are very close. Any activity that emit gases in any room can disperse in to other rooms leading to indoor air pollution.

Human beings inhale an average of 6 liters per minute of air. Even, if the concentrations of toxic volatile organic compounds (VOCs) are about 1 ppb (1μg/L), since these VOCs are absorbed efficiently in the respiratory track, the total concentration will be around 3 ppm per day, which may affect the health of human beings.

To plan the experimental conditions for the Pyrolysis GC-MS analysis of the emitted gases, an idea on the nature of emitted gases is essential. The nature of emitted gases especially from mosquito repellents, incense sticks and edible oils which are burnt or heated to high temperatures in atmosphere depends on the nature of organic compounds present in these substances. So, the authors tried to assess the nature of the organic compounds present in raw materials of mosquito repellents, incense sticks and edible oils using C13 NMR spectra.

Using the 13C-NMRspectra, the aliphatic and aromatic moieties present in these materials along with other different carbon moieties have been understood. This information helped us to predict the nature of the emissions from these compounds and plan the experimental conditions for their monitoring. The 13C- NMR spectra of mosquito repellents, incense sticks and edible oils will be presented and discussed in this paper.

^{15}N-NMR spectral data of selected Anti-Cancer Drugs

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Drug design is a process of selection of chemical molecules that are complementary in shape and charge to biomolecular targets and interact with them resulting in modification of their activity. Physico-chemical properties of the small molecules like structure, surface tension, viscosity, hydrophilicity, hydrophobicity, site of interaction and strength of the interacting site are very important in their functioning as drugs and in the design of new drugs.

In the list of drugs of small molecule category, out of a total of 4700 drugs, total 76.6% of drugs contain Nitrogen alone or Nitrogen with Oxygen, Sulphur, Phosphorous in different combinations and 55% of the drugs contain Nitrogen alone or Nitrogen with Oxygen. In most of these drugs, the active site of interaction in the drug is likely to be Nitrogen.

Development of NMR based approaches to screen small molecules is in progress [1]. Fesik et al [2] developed NMR based approach through ^{15}N- NMR chemical shifts of proteins (acceptors) to screen libraries of small molecules to identify and optimize high affinity ligands (donors). Beger, *et al.*, [3]have developed models to correlate ^{15}N- NMR and ^{13}C-NMR spectral data of small molecules with their biological activity. These models were then applied for prediction of cytochrome P 450 inhibition activity. ^{15}N- NMR spectral data of the identified drug molecules which have passed through several screening processes may help in identifying the actual site of interaction and its strength or reactivity in the drug. Since the drug molecules (donors) are smaller compared to the proteins (acceptors), obtaining natural abundance ^{15}N- NMR spectra of drug molecules is relatively easy. So, we selected several drugs in different categories i.e., Anticancer, Antiviral, Antihypertensive drugs for the ^{15}N- NMR study for identifying the active site of interaction and also for assessing its strength. In this paper, the ^{15}N- NMR spectral data of several anticancer drugs are presented and discussed.

List of Anti Cancer drugs studied:

1. Gemcitabine	3. Capecitabine	5. Imatinib	7.Altretamine	9. Docetaxel
2. Pemetrexed	4. Letrozole	6. Irinotecan	8. Amsacrine	10. Imiquimod

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Proton-Boron Correlation and Measurement of Distances in the Solid-State – Application to Borax and Other Boron Containing Compounds

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Boron containing compounds have a wide range ofapplications and are used inmaterials synthesis, organic reactionsand in neutron capture therapy treatments forcancer patients[1]. Given the utility of such compounds, an understanding of the structural andelectronic properties of these compounds is important. Solid-state ^{11}B NMR can provide valuableinformation about these properties.Rotational Echo Double Resonance (REDOR)[2] is anelegant technique vastly used in SSNMR for accurate measurementsof dipolar couplings (d) and hence the distances between heteronuclear spin-1/2 pairs.However application of REDOR technique for dipolar coupled spin half×6 Quadrupolar spin pairs often suffers due to large quadrupolar broadening. There are very few reports available in SSNMR literature on the distance measurement and the heteronuclear correlation (HETCOR) between ^{1}H (spin ½) and a quadrupolar nucleus such as ^{11}B.Moreover, ^{11}B signal is largely broadened by background signal from the NMR probe.Weimplemented ^{1}H {^{11}B} REDOR technique to estimate the B-H distance in borax ($Na_2B_4O_7 \cdot 10H_2O$) sample. The background signal of ^{11}B is removed by using Hahn echo technique. The REDOR dipolar dephasingcurves were prepared by recording both the controlled and dephased experiments at 33 kHz MAS (τ_r=30.30μs) and sampling at each n_{τ_r} (n is an integer). Fitting the experimentally obtained REDOR curves with SIMPSON[3] simulated curves; values of 'd' were estimated. In the SIMPSON[2(a)] simulation, the effect of ^{11}B quadrupolar coupling parameters of the two sites of borax were considered, which were determined from DM fit[2(b)] of the experimental ^{11}B spectra.The analysis of REDOR curves provided us the dipolar coupling values for two ^{11}B sites (d=4800 Hz). The calculated distances between 1H-11B atoms are matching well with the XRD reported values.^{1}H-^{11}B FSLG HETCOR experiments are also performed on this sample to know the proton chemical shifts and the nature of protons. Application of these methods to amine boranes is in progress and use of the methods presented here for determining molecular geometry and dynamics in the system will be indicated.

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Is sentence comprehension in adult bilinguals a conscious switching?

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Introduction: The language processing in bilinguals share same cortical areas for first (L1) and second language (L2) where L2 recruits greater activity from same regions [1] like left inferior frontal cortex [2]. Difference in bilinguals and monolinguals processing is that in bilinguals left middle temporal gyrus [3] and caudate [4] play role in conscious switching, monitoring and controlling the language used. In India Hindi as L1 that is phonetically transparent with subject object verb (SOV) word order and English as primary L2 that is phonetically partially opaque with SVO word order, whether influence the neural processing was targeted in the present study.

Methodology: After IEC approval pilot study was conducted on eight healthy multilingual subjects (age range 25 to 45 years) with standard inclusion criteria of right handedness, bilingual with proficiency in L1 and L2, given written consent and exclusion criteria any sensory impairment (hearing/ vision), neurological or psychiatric problems, any contraindication for MRI. Single-shot echo planar imaging (EPI) sequence on 3T whole body MR scanner (32 channel head coil) (Achieva 3.0T TX, Philips, Netherlands) was used for Blood oxygen level dependent (BOLD) data (slice thickness =5 mm, number of slices = 29, TR: 2000 ms, TE: 30 ms, flip angle = 90°, FOV = 230 mm, Dynamics: 360, Resolution: 64x64), overlaid on anatomical images using conventional T1-weighted 3D sequence. The visual text stimuli were presented using Eprime (version 1.1, Psychology Software Tools Inc, USA) and MR compatible LCD monitor (NordicNeuroLab, Norway). The two tasks comprised of 30 (15x2) syntactic events (in Hindi and English languages) where each event was of 10 sec duration. The paradigm included block of simple sentences of 3-4 words (6-9 syllables) in either language selected randomly and the response was oral reading. Duration of the fMRI data acquisition was 9 min 50 sec (590 sec).Pre- and post-processing was done using SPM8 (Wellcome Department of Cognitive Neurology, London, UK). The group data was analyzed by one-way ANOVA test ($p<0.001$, cluster threshold 5).

Results and Discussion: In all the subjects similar performance for auditory comprehension and in six subjects better speed and proficiency for L2 reading performance. The BOLD data showed that L2 recruited left hemispheric dominance of lingual gyrus, caudate and right dominance of middle temporal gyrus, middle occipital, fusiform gyrus (Table1) [1-4]. On comparison of English vs. Hindi significant BOLD activity was observed in left inferior frontal gyrus [3] and right lentiform nucleus (Table2).

Conclusion: The results indicate that in bilinguals there is conscious switching of language but not affecting the proficiency and reaction time. The study evidence the role of left caudate in second language use.

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Table1: BOLD activity during English sentences reading			
Clusters	Hemisphere	Areas	Brodmann Area
37	Left	Lingual Gyrus	BA18
5	Left	Caudate	
32	Right	Middle Occipital Gyrus	
22	Right	Fusiform Gyrus	BA19, BA20
7	Right	Lingual Gyrus	BA17
4	Right	Middle Temporal Gyrus	BA 19
Table2: BOLD activity comparing English vs. Hindi sentences reading			
24	Right	Lentiform Nucleus	Putamen
4	Left	Inferior Frontal Gyrus	BA 47

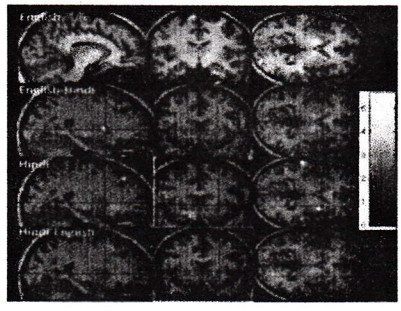

Figure: BOLD activation in Bilinguals during sentence reading overlaid on T1-3D anatomical

Study of Decoherence in Quantum Information Processing Using NMR

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In quantum information processing, the information of the quantum system encoded in the form of coherences of qubits inevitably undergoes irreversible transformations over certaintime-scales due to the omnipresent environmental interferences. This process, known asdecoherence, is a fundamental threat to quantum computation as well as quantum communication. Hence, preserving quantum information against decoherence is an importantarea of current research. Our work is an attempt towards a better study of decoherence bysubjecting the system qubits to engineered quantum noise, characterizing the artificialdecoherence by spectral density & quantum process tomography, and suppressing it usingdynamical Decoupling techniques using a two-spin NMR quantum information processor.

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Structural and functional analysis ofnovel Antimicrobial peptides from Chinese odorous frogs

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Antimicrobial peptides (AMPs) are small peptides with microbicidal properties, length varying from 6 to 50 amino acids. They are majorly cationic peptides having affinity to the negatively charged bacterial membrane which selectively interacts with it and eventually kills the bacteria[1]. AMPs derived from Chinese odorous frogs owe a potential therapeutic target[2]. These peptides can be a template to design synthetic analogue for antimicrobial agents to act against microbes which have already gained resistance over a wide array of antibiotics. Peptidomic analysis of purified AMPs reveals that the post-translational modification rarely happens in odorous frogs and thus helps to characterize AMPs by cloning techniques. While a number of peptides have been isolated till date, their mechanistic aspects remain unclear. In order to know the mechanism by which AMPs inactivate the host cell, it is essential to know their high resolution structures. This project aims at cloning a few selected genes of frog peptides in pET32a+ by recombinant DNA technology, *E.coli* C41 expression and purification, chemical synthesis of short length peptides, antimicrobial activity assays and mechanistic studies of AMPs. Isotope labeling of novel AMPs for structural characterization by solution NMR, these labeled peptides have been expressed in *E.coli* C41, purified by Ni-NTA column chromatography. Different 2D/3D NMR spectra have been acquired and spectral assignment is in progress. The solution structure of these peptides will aid in understanding the action of AMPs at a molecular level, enabling thus to develop peptides with enhanced anti-microbial activity.

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UltraFast Diagonal Peaks Suppressed Spin Echo Correlation 2D NMR Spectroscopy (UF-DISSECT)

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Multidimensional (*n*D) nuclear magnetic resonance (NMR) spectroscopy is one of the most popular and versatile analytical tools in modern research. Since its discovery it made a strong impact in organic chemistry, biological and material science, clinical and pre-clinical science *etc.* But *n*D NMR experiments are often time consuming owing to the standard mode of data acquisition. In general the complete data set is acquired by repeating the experiments for each increment of the spin evolution time in the indirect dimension, in N evolution steps. The data acquisition time is thus proportional to the product of the number of evolution increments in each virtual dimension. In the last few years several methods have been proposed to accelerate *n*DNMR acquisition. One of the most promising methods for fast *n*D NMR data acquisition is ultrafast (UF) NMR, originally proposed by Frydman and co-workers [1], inspired by EPI and chemical shift mapping by EPI [2,3]. This ingenious method modifies the $t1$-based temporal encoding of spin evolution in the indirect dimension into a spatial one and hence one can complete an *n*D NMR – or MRI experiment – in a single scan. Among several *n*D UF NMR methods UF COSY is most popular for its simple implementation [4]. But a major problem of 2DCOSY, also in UF implementation, is that diagonal peaks both from coupled and uncoupled spins may partly obscure informative cross peaks. Spin echo correlation spectroscopy (SECSY)is an alternative to COSY, where the mixing pulse is issued in the middle of the evolution period, and acquisition of signal commences from the echo top to explore the full J-connectivity in the molecule. The Ultrafast version of SECSY was reported recently and was found to be fruitful for applications in inhomogeneous media [5]. SECSY suffers however from mixed phase line shapes, besides what we may term 'pseudo-diagonal' peaks that are centered around$F1$=0.Here we present for the first time an ultrafast 2D sequence that suppresses 'diagonal' peaks from spin correlation spectra; we term this experiment as UF-DISSECT (Ultrafast Diagonal Suppressed Spin-Echo Correlation Spectroscopy). We demonstrate and bench mark the efficiency of diagonal suppression of our sequence with two different samples, measured on a standard high resolution NMR spectrometer system.

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^{129}Xe NMR Investigation of the Anisotropic Environment of Two Nematic Thermotropic Liquid Crystals of Opposite Diamagnetic Susceptibilities

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The anisotropic environment and Nematic-Isotropic phase transition of two nematic thermotropic liquid crystals 5CB and ZLI-1695 with positive and negative diamagnetic susceptibilities respectively has demonstrated using ^{129}Xe NMR studies. The temperature dependence of ^{129}Xe chemical shifts of xenon gas dissolved in 5CB and ZLI-1695 have shown clear signatures of the N-I phase transition. After applying pairwise additive model[1] to the present system, it was inferred that the variation of ^{129}Xe shielding with temperature in isotropic phase is mainly due to the change in density of the medium alone, whereas in the nematic phase in addition to the density of the medium, LC-xenon molecular pair correlation function plays a vital role. The effect of rigid confinement on the anisotropic environment and N-I phase transition of a nematic liquid crystal is also investigated and the results are analyzed by using pairwise additive model.

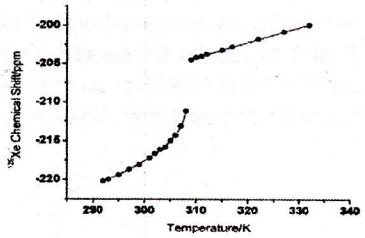

Fig-I: Variation of ^{129}Xe chemical shift of xenon gas dissolved in 5CB LC, with temperature

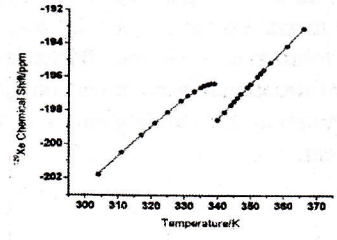

Fig-II: Variation of ^{129}Xe chemical shift of xenon gas dissolved in ZLI-1695 LC, with temperature

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Different Dynamic Properties of Proteins in Supra-τ_c Window

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Internal motions with diverse timescale (ps-ms) play crucial role to govern protein's function. Motions between the globular rotational correlation time (τ_c~4ns) and 40 μs, knows as supra-τ_c range, is proposed to play a decisive role in molecular recognition.[1] This previously hidden time window came into evidence from RDC-enhanced structural ensembles.[2]The very first experimental access of the kinetics within this supra-τ_c timescale was achieved recently by *Ban et. al* using a combination of NMR based techniques.[3] Here, to investigate the dynamic behavior of proteins in the supra-?$_c$ window we choose two small globular proteins: ubiquitin (8.5 kDa) and the third IgG-binding domain of protein G (GB3, 6.2 kDa). To get the time constant for conformational exchange, we performed rotating frame relaxation dispersion experiments on backbone amide nitrogen, amide proton and side chain methyl proton and methyl carbon that are sensitive down to 4 μs which is only recently accessible due to high power experiments on cryo probes. For GB3 and ubiquitin the experiments were carried out at 275.4K and 277K respectively. For both proteins side chain and backbone show motions with similar timescales. In GB3 backbone amide proton and side chain methyl proton shows a conformational exchange time constant of 9.3 μs, whereas for ubiquitin the time constant is 55 μs. To independently test this difference in timescale of motion, rate of conformational exchange for GB3 and ubiquitin were directly measured with dielectric relaxation (DR) in solution at 305K and 309K respectively. Peak frequencies for the sub-β relaxations, arising from conformational interconversion differ strongly. In GB3 the sub-β process is significantly faster than in ubiquitin. This finding nicely agrees with the results obtained from NMR relaxation dispersion experiments.

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Advanced spectroscopic characterizations of CdSe quantum dots with soy-extracted lecithin

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Use of semiconductor nanocrystals/quantum dots (QDs), in biolical systems, has emerged as an important aspect in fundamental biophysical areas of research as well as in nano biotechnology applications [1]. In this context, the interaction of QDs with the biological molecules has geared up significant research interest in recent times. In this report, we highlight the interaction of polyvinyl alcohol (PVA) dispersed CdSe-QDs with soyabean extracted lecithin. The work describes the synthesis of CdSe-QDs via aqueous route, extraction of lecithin [2-3] from soyabeen seed (model RKS-18) and adequate characterization to probe the QD-lecithin interaction mechanism. Different characterization techniques such as UV-Vis, FTIR, NMR, Mass spectroscopy (MS) were used to obtain optical, spectroscopic and structural information. The investigation of QD - lecithin interaction will largely help in understanding behavior of nanoscale materials in biological environment in general including artificial and natural semi-permeable bilayers.

Key words: Quantum dot; lecithin; ion channelPACS No.: 81.07.Ta; 87.14.Cc; 87.80.Jg

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NMR phytochemical analysis of cytotoxic medicinal plants

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Metabolomics provides a global assessment of metabolites within a biological system. Recent research has established NMR as an important technique for phytochemical fingerprinting and comparative analysis of medicinal plant[1]. Ayurveda, the traditional Indian medicine, has a long history of usage of medicinal plants for therapeutic purpose. Plants such as *Anethum graveolens* (AG), *Semecarpus anacardium* (SA), *Picrorrhiza kurroa* (PK) and *Plumbago zylanica* (PZ) are used in treatment of cancer in Ayurveda. The objective of this study is to combine NMR metabolomics, phytochemical colorimetry assays, and cytotoxicity assay to analyse medicinal plants.

1D and 2D (COSY and $_z$TOCSY) proton NMR data were obtained on 700 MHz NMR spectrometer (Agilent, USA) using the following parameters: 1D (spectral width - 12 ppm; relaxation delay -15 s; no. of scans - 64; data points - 32 K) *and 2D (2s relaxation delay, 12 ppm spectral width, 16 scans, 2K data points).* Deuterated trimethylsilyl propionate (TSP) was used as an external reference. The phytochemical assays such as Dragendorf test (alkaloids), Shinoda test (flavonoids), Molisch test (carbohydrates) were carried out to assess the presence of both primary and secondary metabolites. The cytotoxic potential of the medicinal plants was evaluated by MTT assay for the three time points (24, 48 and 72 hrs of treatment) on Human hepatocellular carcinoma (HepG2) cells. Chemotherapeutic drug paclitaxel has taken as positive control. Percentage cell survival and inhibitory concentrations (IC_{50}) were calculated.

Primary metabolites such as carbohydrates, amino acids were seen in general in all plans. However, there were also unique resonances for each of the plants, for instance, tryptophan in AG, acetate in SA, flavonoids in PK and polyphenols in PZ. The phytochemical evaluation by the colorimetry assays correlated well with the NMR spectral data. The spectra of plants which showed significant amounts of secondary metabolites such as flavonoids, flavonol glycosides, in the phytochemical assays also showed as resonances in the proton spectra. The medicinal plants also showed significant cytotoxicity in HepG2 cells and comparable to chemotherapeutic drug paclitaxel. *Semecarpus anacardium* and *Plumbago zylanica* showed maximum (101.93 ± 2.3 µg/ml) and minimum (158.63 ± 2.3 µg/ml) cytotoxicity respectively. Further in-depth analysis is underway to study the correlation of the phytochemical profiling with cytotoxicity.

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Synthesis and biological evaluation of amidine derivatives

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Some new amidine (**IIIa-i**) derivatives have been synthesized and characterized by ^{1}H NMR, ^{13}C NMR and GC-Mass. Synthesized compounds were screened for anticancer activity. Compounds **IIIc** and **IIIh** are showing good anticancer activity against ovary (PA-1) and liver (Hep G2).
Keywords: Amidine, Anticancer activity

Structural Characterization of Co-crystals by Solid-State NMR

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Co-crystals are systems constituted by two or more different molecules held together by supramolecular interactions. The study of structure-property relations of co-crystals is one of the active areas of the modern solid-state chemistry due to their important pharmaceutical applications. Solid-state NMR (SSNMR) is emerging as a fundamental tool for the structural identification and characterization of co-crystalline materials Accessing information on crystal packing, conformation and hydrogen bonding arrangements, which are the fundamentals in determining the final solid-state properties of a given form of co-crystal, is possible by newly emerged NMR techniques[1].Here we illustrate the combined use of two dimensional pulse sequences that exploit homonuclear and heteronuclear dipolar couplings for characterization of co-crystals. The molecular association is probed using both short- and long-range ^{1}H (FSLG) $6^{13}C$ CP HETCOR.^{1}H (DQ) $6^{1}H$ (SQ) experiments at fast MAS (30 kHz) have been used for achieving information on proton-proton proximities and thus on hydrogen-bond networks in the co-crystals. However, close proximities of N%H and aromatic protons hindered the full assignment of the ^{1}H spectra. To unveil this problem we are planning to perform ^{1}H (DQ) $6^{1}H$ (SQ) at ultra-fast MAS (~60 kHz) along with exploiting of more exotic spin pairs ^{14}N-^{1}H by ^{14}N-^{1}H heteronuclear multiple-quantum correlation (MHQC) experiment. The NMR methods utilized will be illustrated with some examples.

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Study on the interparticle interaction of superparamagnetic iron oxide nanoparticles for MRI contrast imaging application

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We report here the influence of interparticle interaction of iron oxide nanoparticles on their collective magnetic properties and their potential use in MRI imaging application. The particles which are observed superparamagnetic in individual form can show small ferromagnetic ordering due to strong dipolar and exchange interaction. We developed three nanostructure up- conversion assemblies; (i) oleic acid coated iron oxide nanoparticles IO@OA, (ii) Cetyl trimethyl ammonium bromide (CTAB) stabilized of IO@OA and (iii) Polyacrylic acid (PAA) surface modification of CTAB stabilized NPs. Atomic force microscopy (AFM) revealed the spherical cluster formation as the result of CTAB functionalization of oleic acid coated iron oxide nanoparticles, while for the PAA functionalized system the clusters were observed as reduced size and separated from each other. In addition, significant deviation from Curie law (χ_ 1/T) of filed cooling (FC) curve and shifting of zero filed cooling (ZFC) peak to higher temperature in the temperature dependent magnetization study can be correlated to the existence of strong dipolar and exchange interaction among the nanoparticles in clustered form. The saturation magnetization (Ms) and coercivity (Hc) were obtained higher for the assembled structures. These anomalous behaviours of bottom up structured assemblies will lead to promising application as MRI imaging probe.

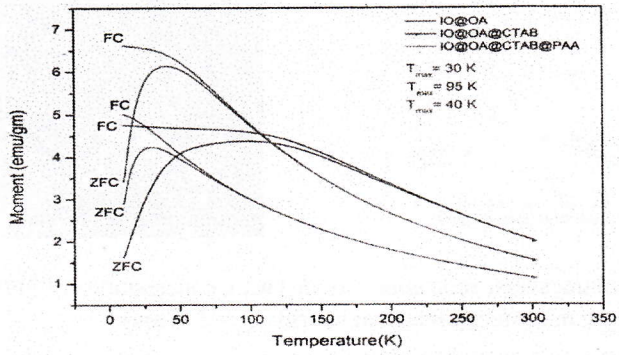

Fig. 1: M-T comparison of IO@OA, IO@OA@CTAB and IO@OA@CTAB@PAA

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Maglumino hybrid nanosystem as dual contrast agent for magnetic resonance and optical imaging

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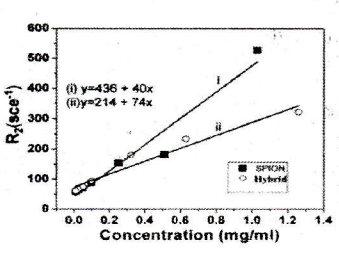
Assembling different nanoparticles into a single entity as a novel structural unit has the potential for the development of materials for simultaneous applications in biomedical imaging, detection or drug delivery. Maglumino hybrid nanosystems are the conjugation of magnetic and luminescent nanoparticles that integrate magnetic and fluorescent properties [2-3]. Mesoporous silica, when used as the template, adds additional functionality of loading efficiency to the maglumino hybrid nanosystems. In the present study, small angle scattering technique based investigation has been used to probe the constituent microstructures such as - super-paramagnetic iron oxide nanoparticles (SPION, size ~ 4.2 nm), luminescent quantum dots of (~3.2 nm) and mesopores (~15.2 nm), in controlled hierarchical architecture of the silica hybrid of size ~285 nm. Magnetic and optical characterization techniques are combined to investigate the persistency of the superparamagnetic and fluorescent properties of the individual components after hybrid formation. The applicability of the maglumino hybrid has been realized as T_2 contrast agent in magnetic resonance imaging (MRI). The transverse relaxivity of SPION is found to be 436 mg^{-1} mL sec^{-1} whereas that of the maglumino hybrid is found to be 214 mg^{-1} mL sec^{-1}. This along with the bright fluorescent property of the hybrid makes it a promising candidate as dual contrast agent.



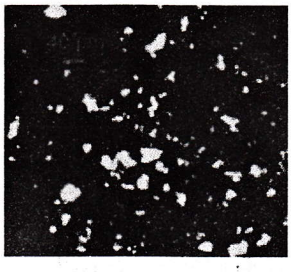


Figure 1 (a) Variation of transverse relaxation rate (R_2) w.r.t. concentration of SPION and hybrid and (b) Fluorescenee microscopy image of hybrid (λ_{ex} = 515 nm).

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Facile One Pot Synthesis of Hydrophilic Superparamagnetic FePt Nanoparticles for Molecular Imaging

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Recent advancement in nanomaterials preparation and their engineering has imparted a significant impact in the field of biomedical imaging[1, 2]. A new generation FePt nanoparticle (NP) based MRI contrast agent is developed here and characterized. We demonstrate here a facile one pot chemical route to fabricate hydrophilic monodispersed face-centered cubic (fcc) FePt NP and can be easily scaled up to produce multigrams of the NPs. The XRD pattern indicated fcc structure with (111), (200), (220) and (311) crystal planes. The surface characterization exhibits the -COOH group of TGA molecules projected outward from the surface which makes the NPs hydrophilic. The HR-TEM reveals the average NPs size as 6 nm. The EDX analysis confirm of Fe:Pt ratio as 1:1. The extensive room temperature and low temperature magnetic property studies have revealed low coercivity, high saturation magnetization and blocking temperature around 103 K. The Fe:Pt ratio makes the NPs superparamagnetic at room temperature

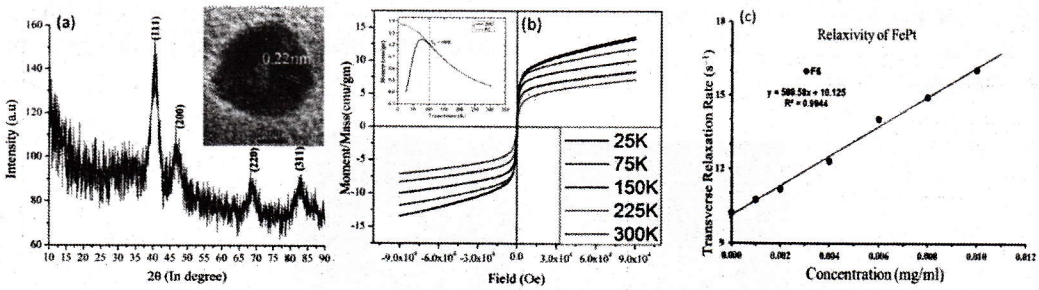

Figure: 1 (a) XRD pattern (inset HR-TEM) (b) M-H characterization at different temperature (inset M-T curve) (c) transverse relaxivity (r2) of the FePt nanoparticles.

The transverse relaxivity (r_2) was calculated (599 $mg^{-1}ml\ s^{-1}$)from the slope of transverse relaxation rate versus concentration graph[3] and has been observed promising for high T_2 relaxivity.

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MnO Nanoparticles Encapsulated with Mesoporous Carbon Shell as a Novel Biocompatible MRI Contrast Probe

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Mn^{2+} ion stands as a strong candidate to be used as MRI contrast agent due to its five unpaired electrons, suitable electronic relaxation time, labile water exchange and similar behaviour to Ca^{2+} ions in the body [1]. Besides, Mn^{2+} ion plays an essential biological role in the human body as a co-factor in many enzymatic reactions. Since Mn^{2+} is involved in mitochondrial function, it can be proved to be an excellent contrast agent for MR imaging of the mitochondria rich organs like liver and pancreas. Manganese oxide nanoparticle (MnO NP)s can be promising Mn^{2+} based MRI contrast agents [2]. But, overexposure to free Mn^{2+} ions can lead to a neurological disorder called "manganism". Coating of these NPs with a carbon shell can address this issue improving their stability, biocompatibility and relaxivity. Mesoporous carbon shell is more relevant as it allows easy access of surrounding water protons to the magnetic core leading to enhanced relaxation.

In this work, MnO NPs encapsulated in mesoporous carbon shell were synthesized with controlled microstructure and morphology. Various characterizations (microstructure, surface morphology, composition etc.) have been performed to ensure high quality product through this synthetic strategy. The magnetization corresponding to variation of field up to 9T and temperature up to 5K has been performed to identify magnetic phase and magnetic parameters. Distinct enhancement of relaxivity and contrast of MR images were observed by using this engineered contrast agent *in vitro*.

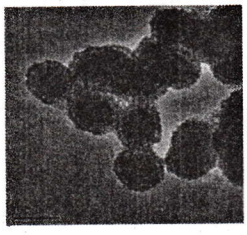

Figure 1 TEM of HCMSM sample

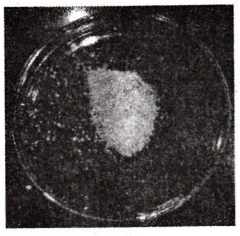

Figure 2 HCMSM sample

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Magnetoporous assembly of iron oxide nanoparticles for MRI molecular imaging

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Iron oxide nanoparticles synthesized with varying surface chemistry are widely exploited in biomedical imaging as they are benign in nature and exhibit greater sensitivity in the nano regime. Fine dimension magnetic iron oxide nanoparticles have found their use as MRI contrast agent owing to their spin-spin relaxation effects originating from the induced local field in homogeneities, which consequently results in shorter T_1 and T_2 relaxation times [1,2]. Herein we report the enhanced MRI contrast property of porous iron oxide nanospheres developed through a gentle chemistry route. The controlled assembly of iron oxide nanosystems lead to uniform mesoporous spherical architecture of dimension R~200 nm as depicted from HRTEM analysis. Detailed magnetic study of the nanospheres has been carried out at varying temperatures. A dose dependent transverse relaxation time and contrast property study of the nanosystem reveals the potential of the nanosystem for its use as a MRI T_2 contrast agent.

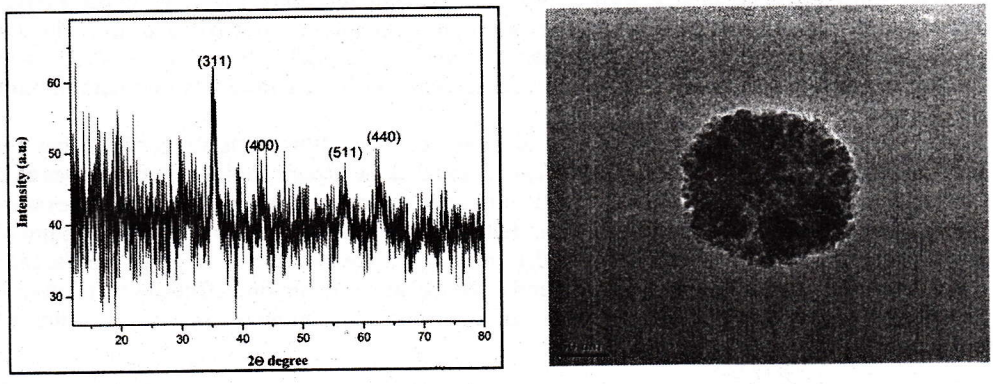

Figure (a) X-ray diffraction pattern of the iron oxide nanospheres (b) HRTEM micrographs revealing the spherical nature of the iron oxide nanosystems.

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HAMLET and related alternatively-folded proteins with novel functions

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HAMLET (**H**uman α-lactalbumin **M**ade **L**ethal to **T**umour cells) and its related partially unfolded protein–fatty acid complexes are novel biomolecular nanoparticles that possess relatively selective cytotoxic activities towards tumour cells [1,2]. Spearheaded by C. Svanborg and her associates - through the utilization of a full arsenal of techniques in cell biology, transcriptomics, proteomics, imaging, and *in vivo* studies - significant progress has been made to deduce the underlying mechanism(s) of cell death brought about by HAMLET and other related complexes such as BAMLET [3,4]. From a protein biophysical chemists' / structural biologists' point of view, during the past few years, we have chosen to ask what would be the 'minimal cytotoxic unit' to give rise to this remarkable property. It is now well known that one of the key characteristics is the that the protein is partially unfolded - also resulting in endowing native proteins with additional functions in the alternatively folded states – but how important is this property in terms of the cytotoxic activity? The dynamic properties of conformational exchange on the NMR time scale make residue-specific studies challenging, however diffusion NMR and other techniques have allowed us to obtain initial useful information.

In relation to this, significant results have confirmed previous suggestions that the fatty acid moiety may be the ultimate cytotoxic agent, and that the protein moiety simply serves as carrier (or 'mule') by increasing its effective critical micelle concentration [5]. Through the examples of other cases, we show that the partially unfolded property of the protein as well as the nature of fatty acid binding is as much as important in determining the cytotoxicity – in other words, there is a delicate balance of structural malleability and related changes in binding affinities that determine the tumoricidal properties. Any efforts to design small-molecule mimics appear to require a better understanding of these structural aspects.

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Sharpless asymmetric dihydroxylation in the synthesis of unit-B of cryptophycin-24

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The cryptophycins are familiar as selective tumour cytotoxins, found in blue green algae. Sharpless asymmetric dihydroxylation is introduced for the synthesis of unit-B of cryptophycin-24 (Figure 1). Conversion of α-hydroxy acid ester into the corresponding α-amino acid ester via bromocompound was examined with partial racemization of the product during bromination and direct azidation. Result shows direct azidation of α-hydroxy acid ester using diphenylphosphoryl azide is promoting the asymmetric synthesis of α-amino acid without the loss of chirality during the transformation. Proposed synthetic pathway is also attempted for the tyrosine-unit of other cryptophycins bearing a chloro-substituent on the aromatic ring and found ineffective. ^{1}H-, ^{13}C-NMR spectroscopy is used as the characterization tool for all synthesized compounds.

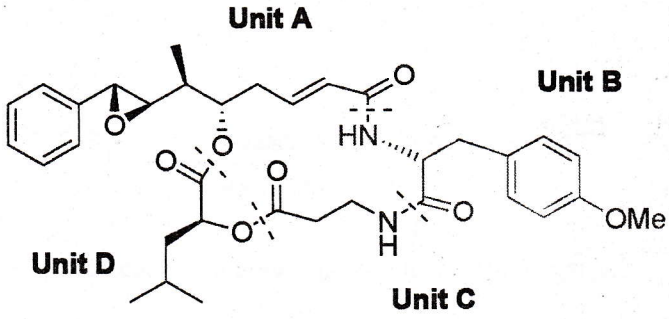

Figure 1: Structure of cryptophycin-24. Unit B is highlighted.

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Efficient synthesis of β-amino carbonyl derivatives using solid acid catalyst

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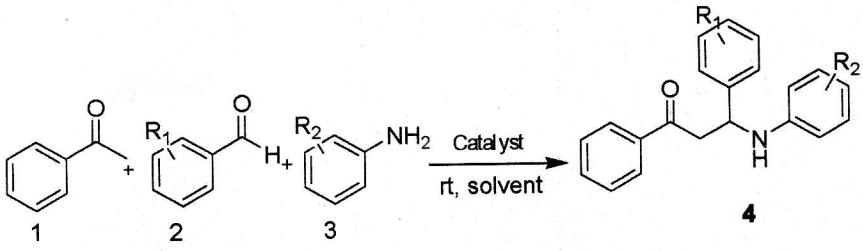
β-Amino carbonyl compounds (**4**) are important synthetic intermediates for various pharmaceuticals and natural products which include the synthesis of amino alcohols, peptides, lactams and as precursors to optically active amino acids[1-2]. In this presentation, we describe an efficient environmentally benign three component Mannich reaction of aldehyde, amine and ketone for the synthesis of β-amino carbonyl compounds (Scheme-1) at room temperature using silica-supported acid catalysts. The significant features of this procedure are the use of recyclable solid acid catalyst, simple product separation, short reaction time and good product selectivity. The entire synthesized β-amino carbonyl compounds are characterized by NMR and other analytical techniques



R_1, R_2 = Electron donating and withdrawing substituent

Scheme-1 Three component Mannich reaction

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Synthesis and characterization of *anti*- 2,3-dihydro-1, 2, 3-trisubstituted-1*H*-naphth[1,2-e][1,3] oxazine derivatives

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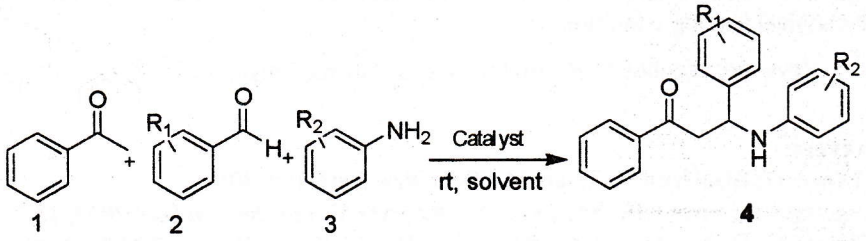
This one pot approach produces a new series of *anti* 2, 3-dihydro-1, 2, 3-trisubstituted-1*H*-naphth [1,2-e][1,3]oxazine derivatives (1) with good yields from the three component reactions of 2-napthol(1 mmol), aromatic aldehydes (2 mmol) and various electron rich aromatic or aliphatic primary amine(1 mmol) (Scheme-1) in presence of trichloroacetic acid (0.5 mmol) as catalyst. The reactions are carried out in ethanol at room temperature and under solvent free condition at 100 °C. The products are characterized by various NMR techniques such as HETCOR, DEPT, COSY, NOESY ,^{1}H NMR and ^{13}C NMR and along with other analytical techniques.. The *anti* -stereochemistry of two hydrogen atoms on carbon atom 1 and 3 of the oxazine ring is also confirmed with COSY, NOESY, and single crystal XRD studies.



R_1, R_2 = Electron donating and withdrawing substituent

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Preperation of Cu (II) modified zeolite catalysts for C-N coupling reaction between aryl halide and N- heterocycles

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Cu-catalyzed C-N coupling reaction between aryl halides and N-heterocycles or amines has received wide attention due to their applications in pharmaceuticals, natural products, biological and material sciences [1]. Development of ligand-free Cu-catalyzed coupling and use of microwave irradiation in presence of water are important strategies for efficient C-N coupling reaction now a days [2]. Herein, Cu(II) modified zeolite beta, ZSM-5 and NaX catalysts with different amount of Cu(II) have been prepared by both wet impregnation method and ion-exchange method from an aqueous solution of Copper acetate [3]. The catalysts have been characterized by X-ray powder diffraction (XRD), scanning electron microscopy (SEM), infra-red spectroscopy (FTIR), differential scanning calorimetry (DSC), TGA (thermogravimetry), Hammett indicator (measurement of base strengths) and N_2 adsorption-desorption techniques. The catalysts thus prepared have been utilized for C-N coupling reaction between aryl halides and N-heterocycles. Both impregnated and ion-exchaged zeolites are found to catalyze the reaction effectively at elevated temperatures (100-150 °C) under classical heating condition.

Keywords: zeolite, C-N coupling, Cu-acetate monohydrate

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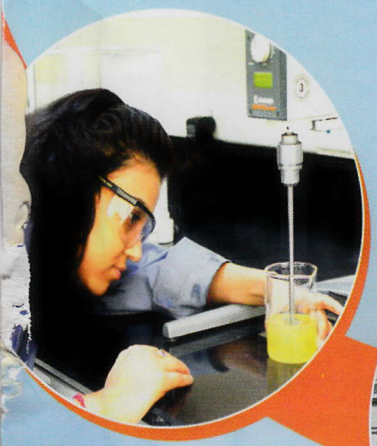

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