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Norwegian Society for Magnetic Resonance

The 13th National MR Meeting

Tuesday, January 14th and Wednesday the 15th, 2014

in Trondheim,

Thon Hotel Prinsen

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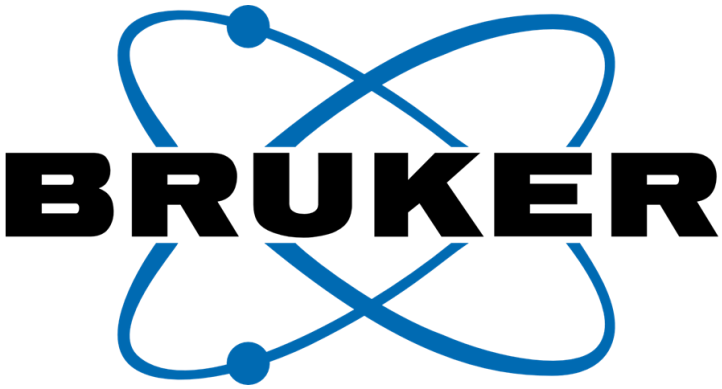

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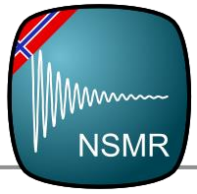


Norsk selskap for magnetisk resonans

Norwegian Society for Magnetic Resonance

The 13th National MR Meeting
Tuesday, January 14th and Wednesday the 15th, 2014 in Trondheim
at Thon Hotel Prinsen

08:00 – 09:00	Registration and coffee
09:00 – 09:10	Welcome by Prof. Olav Haraldseth

Session: Clinical and Preclinical MRI and MRS studies
(Chair: Øystein Risa PhD)

09:10 – 09:50	Memorial Lecture for Ingrid Gribbestad (By: Prof. Arend Heerschap, Radboud University Nijmegen Medical Centre)
09:50 – 10:05	News on the 9.4T animal scanner in Oslo (By: Lili Zhang PhD, UiO)
10:05 – 10:20	News on 7T animal scanner in Bergen (By: Tina Pavlin PhD, UiB)
10:20 – 10:35	News on 7T animal scanner in Trondheim (By: Marius Widerøe PhD, NTNU)
10:35 – 10:50	**Coffee Break**
10:50 – 11:05	New PET MR scanner at NTNU/St Olav, plans for the future (By: Live Eikenes PhD, NTNU)
11:05 – 11:20	An introduction to hyperpolarised 13C MR by Dynamic Nuclear Polarisation, and applications in cancer research (By: Deborah K. Hill PhD, NTNU)
11:20 – 11:35	The effect of melatonin on brain development after hypoxic-ischemic brain injury in neonatal rats. (By: Hester R. Berger)
11:35 – 12:30	**Lunch break**

Session : NMR in Metabolomics
(Chair: Prof. Tone Bathen)

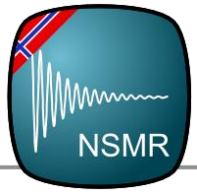
12:30 - 13:00	NMR based clinical research and result validation (By: Claire Cannet)
13:00 – 13:30	Craft: A new way to process your NMR spectra and to extract frequency and amplitude information (By: Dimitris Argyropoulos PhD, Agilent)
13:30 – 13:50	**Coffee Break**
13:50 – 14:05	Metabolomics and cancer (By: Guro F. Giskeødegård PhD, NTNU)
14:05 – 14:20	Environmental Metabolomics (By: Trond Størseth PhD, SINTEF)
14:20 – 14:35	NMR Metabolomics in Pregnancy and Infancy (By: Daniel Sachse, UiO)
14:35 – 14:50	Targeting choline phospholipid metabolism: GDPD5 and GDPD6 silencing decreases breast cancer cell proliferation and invasion (By: Maria Dung Cao, NTNU)
14:50 – 15:15	**Coffee Break and preparing for Speed Updates and Poster Session**

Session: Speed Updates
(Organiser: Torill Sjøbakk PhD)
Five stands; four presentations at the same time on four different stands, the fifth is a stand with coffee break. We divide the attendance into 5 groups.

15:15 – 16:15	**Speed Updates**

Session: Poster
(Organiser: Dirk Petersen)

16:15 – 17:00	Refreshments and drinks will be served during the poster session.
17:15 – 18:00	**Årsmøte for NSMR 2014 (Budsjett, aktivitet, valg)**
19:00	**Conference Dinner**



Norsk selskap for magnetisk resonans

Norwegian Society for Magnetic Resonance

Wednesday, January 15th 2014

08:30 – 09:00	Registration and coffee

Session: NMR on Macromolecules
(Chair: Finn Aachmann PhD)

09:00 – 09:40	Protein Dynamics and Flexibility by NMR (Malene R. Jensen, Institute de Biologie Structurale, Grenoble, France)
09:40 – 09:55	*Educational lecture:* Why "big fields" for "big molecules" (By: Øyvind Halskau PhD, UiB)
09:55 – 10:10	Highlighting the Protein for NMR Spectroscopy (By: Edith Buchinger, NTNU)
10:10 – 10:30	**Coffee Break**
10:30 – 10:45	Influenza A virus PB1-F2 proteins -distinct structural signatures and highly pathogenic influenza viruses (By: Prof. Torgils Fossen, UiB)
10:45 – 11:00	Structure and properties of wild-type and the R555W mutant of transforming growth factor beta induced protein (By: Jarl Underhaug PhD, UiB)
11:00 – 11:30	Poster session
11:30- 12:30	**Lunch Break**

Session : NMR in Natural and Synthetic Products
(Chair: Prof. Nebojsa Simic)

12:30 - 13:00	*Educational lecture:* NMR as a tool in elucidating compound structure in organic chemistry (By: Assoc Prof. Nebojsa Simic, NTNU)
13:00 – 13:15	Structure elucidation of Breitfussins A-H Isolated from the Arctic Hydrozoan Thuiaria breitfussi (By: Johan Isaksson PhD, Ui Tromsø)
13:15 – 13:30	Sclerochloa dura: A new source of anti-inflammatory compounds (By: Majid Bukhari PhD, NTNU)
13:30 – 13:45	Compound identification by 13C HSQC correlation plots (By: Trygve Andreassen PhD, NTNU)
13:45 – 14:00	**Coffee break**

Session: NMR on Solids and Porous Material
(Chair: Prof. John Georg Seland)

14:00 – 14:30	Diffusion: Home brewed pulse sequences for efficient researchers (By: Geir Sørland PhD, AnTek, Trondheim)
14:30 – 14:45	Water structure near a solid surface as investigated by NMR spectroscopy (By: Prof. Willy Nerdal, UiB)
14:45 – 15:00	Spatial redistribution of water in meat during Drip LOSS as Probed by low field 1H-NMR (By: Han Zhu, UiO)
15:00 – 15:15	Correlations between inhomogeneous magnetic fields, internal gradients, and transverse relaxation, as a probe for pore geometry and heterogeneity (By: Prof. John Georg Seland, UiB)
15:15 – 15:30	Poster results and closing remarks

NSMR 2014

Printed on Fri 10 January 14 at 10:42:03

Name	Organisation
AACHMANN, Finn L.	NTNU
ANDERSSON, Fredrik	JEOL Skandinaviska AB
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ARGYROPOULOS, Dimitris	Agilent Technologies
ARSTAD, Bjørnar	SINTEF
AUSTDAL, Marie	NTNU
BATHEN, Tone Frost	NTNU
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HALSKAU, Øyvind	University of Bergen
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	WIDERØE, Hege Christin	Statoil
	WIDERØE, Marius	NTNU
	ZHANG, Lili	IEMF, Oslo University Hospital
	ZHU, Han	University of Oslo
Total	62	

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Prof. Arend Heerschap, Radboud University Nijmegen Medical Centre

Memorial Lecture for our colleague and previous board member:

Professor Ingrid Susann Gribbestad

01.12.1961 - 20.04.2013

Ingrid S. Gribbestad actively contributed for over 25 years to bring basal, MR technology and clinical research environments together for a common goal to improve cancer diagnostics. She started her research career in 1987 in SINTEF initially as research scientist and later on as research manager. Ingrid was among the first to establish dynamic contrast enhanced MR imaging for breast cancer diagnostics. She was also among the first to show how MR spectroscopy could be used to differentiate types of breast cancer, and for this work she received the Bill Negendank Award in 1998.

In 2005 she became professor at the Department for Circulation and Medical Imaging at the Norwegian University of Science and Technology (NTNU). The MR Cancer group was established by Ingrid in close collaboration with the clinicians at the St. Olav's hospital; the main emphasis being the use of MR technology for cancer diagnostics and treatment. Ingrid was central in the establishment of the Metabolomics lab at the Faculty of Medicine, NTNU and she was also eager to introduce the use of relevant animal models for translational research. Through her scientific skills and results, and also her enthusiasm, Ingrid established international networks and tight collaborations throughout the world.

NEWS ON THE 9.4T ANIMAL SCANNER IN OSLO: CARDIAC MRI IN RODENTS

Lili Zhang[1*], Kristine Skårdal[1], Emil K. Espe[1], Ivar Sjaastad[1]

[1]*Institute for Experimental Medical Research, Oslo University Hospital, Ullevål, Kirkeveien 166, NO-0407 Oslo, Norway*
[*]*Corresponding author (lili.zhang@medisin.uio.no)*

Abstract
Magnetic resonance imaging (MRI) has emerged as a powerful and reliable tool to noninvasively study the cardiovascular system in clinical practice.

Rodents,especially transgenetic mice have become a key tool in experimental animal research because of technical and economic considerations.

Technological advances in MRI over the last decade have provided critical insights into cardiac and vascular morphology, function, and physiology/pathophysiology in many murine models of heart disease.

Besides the standard quantitative evaluation for cardiac function, masses and infarct size from MRI, phase-contrast MRI (PC-MRI) has allowed to quantify myocardial wall motion and blood flow as well. T1-mapping of the myocardium visualizes the percentage of fibrosis, an important clinial parameter associated with worsening cardiac function and adverse remodeling. Furthermore, molecular cardiac MRI detects biomarkers for atherosclerosis in vivo and magnetic resonance spectroscopy (MRS) allows the nondestructive study of myocardial metabolism in both isolated hearts and in intact mice.

This presentation reviews the current research interests and techniques including examples of applications of MRI/MRS technology to murine models of cardiovascular disease at the Institute for Experimental Medical Research in Oslo.

SMALL-ANIMAL MRI FACILITY AT UNIVERSITY OF BERGEN

Tina Pavlin[1]

[1] *Department of Biomedicine, University of Bergen, Jonas Lies vei 91, 5009 Bergen, Norway*
[*] *Corresponding author: Tina Pavlin (tina.pavlin@biomed.uib.no)*

Abstract
The Molecular Imaging Center at the University of Bergen owns a wide range of imaging equipment spanning from nanometer to sub-millimeter imaging resolution. Live-animal imaging systems include a recently installed PET/CT system, a small-animal Ultrasound, several optical imagers and a small-animal MRI scanner.

The 7.0 Tesla MRI scanner was installed in December 2004 and was upgraded with new hardware in December 2012. The upgraded system can deliver state-of-the-art MR images of rat and mouse anatomy, as well as pathology and physiology. It has a 2nd-order shim and a stronger gradient system (760 mT/m) which means that our users are finally able to use advance imaging protocols that rely on fast imaging techniques, such as diffusion tensor imaging (DTI), arterial spin-labeling, and fMRI. The multi-channel receive technology enables the use of phased-array coils that give a superior signal-to-noise ratio and enable accelerated imaging, thus minimizing ghosting artifacts in echo-planar imaging (EPI).

In my presentation I will give a brief overview of recent and current projects performed on our MRI system, such as:

- Anatomical and functional imaging of tumors (glioma, glioblastoma) in rats and mice
- Studies of melanoma brain metastasis
- Multi-modal imaging of prostate cancer in mice
- Longitudinal studies of demyelination in mice models of multiple sclerosis
- Imaging of salivary glands in mice using dedicated hardware
- Imaging of fat-distribution in fish, mice and rats

Figure 1: 7T small-animal MRI facility at Vivarium, University of Bergen.

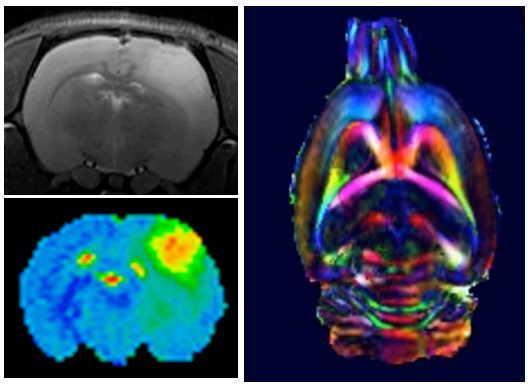


Figure 2: MR images of rat head: T_2-weighted image of glioma (top left), ADC map of glioma (bottom left) and DTI of healthy rat brain (right).

7 Tesla small animal MRI at MR Core Facility in Trondheim

Marius Widerøe
MR Core Facility, Department of circulation and medical imaging, NTNU, Trondheim

Abstract
Preclinical research with MRI of small animals has been conducted at the MR Center in Trondheim since the late 1980'ies. In 2005 a new state-of-the-art 7 Tesla Bruker Biospec small animal MRI system was installed as part of the then newly established NFR appointed FUGE Molecular Imaging Center. In 2012, at the end of the FUGE period, the small animal MRI lab was included in the newly established MR Core Facility at NTNU and went through a major upgrade of all electronic hardware, including several new coils, thus bringing the system back to a state-of-the-art technology. The upgraded system has more powerful gradients (660mT/m), improved field homogeneity with 1^{st}, 2^{nd} and 3^{rd} order shim and multi-channel receive possibilities for 1H enabling use of phased array coils. In consequence, users now experience better SNR, faster image acquisitions and especially improved image quality in diffusion weighted imaging.

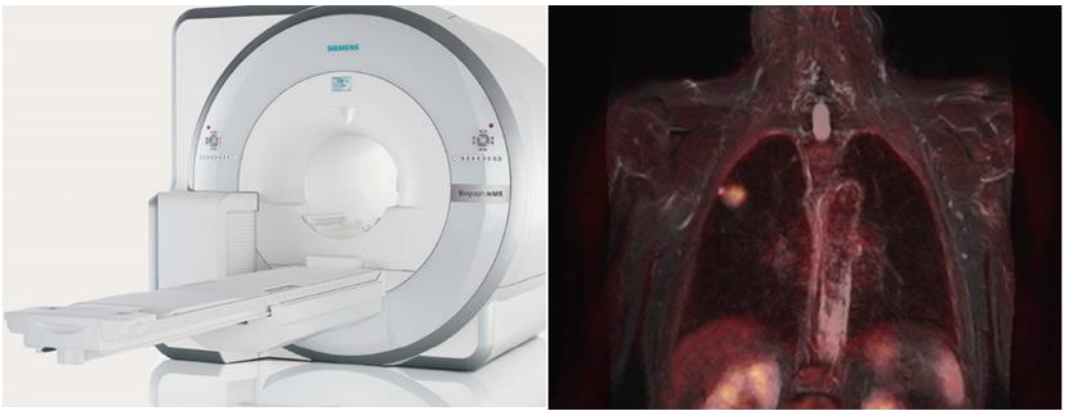
In this presentation I will give a short presentation of the small animal MRI lab and look into the prospects of high-field MRI in pre-clinical animal research using examples from previous and ongoing research in Trondheim.

Live Eikenes

New PET/MR scanner at St. Olavs Hospital/NTNU

Autumn 2013, a new hybrid simultaneous positron emission tomography/magnetic resonance imaging (PET/MR) scanner was installed at St. Olavs Hospital in Trondheim. This is the first PET/MR scanner to be installed in Norway. The scanner consists of a 3 T state of the art MR scanner, which acquires anatomical images of the body, and a PET scanner, producing physiological images of functional processes in the body. In the same way that PET/CT has been shown to be a powerful multimodality imaging tool, there are compelling reasons for combining PET and MRI. The benefits of combined PET/MR over PET/CT includes improved soft-tissue contrast, reduced ionizing radiation, the possibility of MR-based motion correction, and the acquisition of truly simultaneous multiparametric images. Applications in neurology, psychiatry, and oncology from diagnosis to treatment planning and therapy control will probably benefit from multimodality PET/MR measurements.

Although the new simultaneous PET/MR system has shown great potential, there are many technical and methodological issues not resolved for the system to be used in a daily clinical setting. One of the most important issues is photon attenuation correction, which is a prerequisite for both qualitative and quantitative PET imaging. The first research projects that will be conducted at St. Olavs Hospital and NTNU are studies of lung cancer and lymphoma pasients that will be acquired with both PET/CT and PET/MR. The main aim of these first studies is to investigate whether PET/MR will improve the accuracy when assessing the extent of disease compared to today's method of choice, PET/CT, and to solve some of the technical and methodological challenges in the acquisition and analysis of simultaneous PET/MR examinations, with the main focus on attenuation correction.



An Introduction to Hyperpolarised ^{13}C MR by Dynamic Nuclear Polarisation, and Applications in Cancer Research

Deborah K. Hill[1,2,3*]

[1]*Department of Circulation and Medical Imaging, NTNU, Trondheim, Norway,* [2]*St. Olavs University Hospital, Trondheim, Norway,* [3]*CR-UK and EPSRC Cancer Imaging Centre, The Institute of Cancer Research and Royal Marsden NHS Trust, United Kingdom*

[*]*Deborah Hill (deborah.hill@ntnu.no)*

Abstract

Signal enhancement by Dynamic Nuclear Polarisation (DNP, Fig. 1) is revolutionising ^{13}C MRS applications, allowing acquisition of real-time metabolic information both *in vitro* and *in vivo* [1]. The most widely studied molecule to date is [1-^{13}C]pyruvate, which is used to determine the apparent rate (k) of pyruvate-lactate exchange (Fig. 2). This apparent exchange rate has been linked with lactate dehydrogenase activity (LDH) [2], a key metabolic enzyme that is commonly upregulated in cancer cells. Modelling of DNP data allows a quantitative assessment of the cellular metabolic status, offering potential as an early biomarker of treatment response.

Recently, a phase I clinical trial was completed at UCSF, San Francisco in prostate cancer. The encouraging results of the trial have demonstrated the great potential of DNP for applications in the clinic (Fig. 3), and a dedicated clinical polariser system is now available from GE Healthcare. Current clinical trials are being carried out in cancer and cardiac research, and initial studies have shown promise in other areas such as hepatic function, where clinical trials are expected to begin soon.

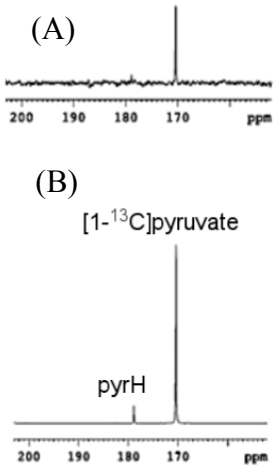


Fig. 1: ^{13}C spectra of [1-^{13}C]pyruvate. (A) thermal equilibrium, 64 scans (5 min). (B) hyperpolarised, 1 scan (<1 s).

This presentation includes a description of the DNP technique, as well as a summary of some key findings from *in vitro* and preclinical *in vivo* studies, and the UCSF clinical trial.

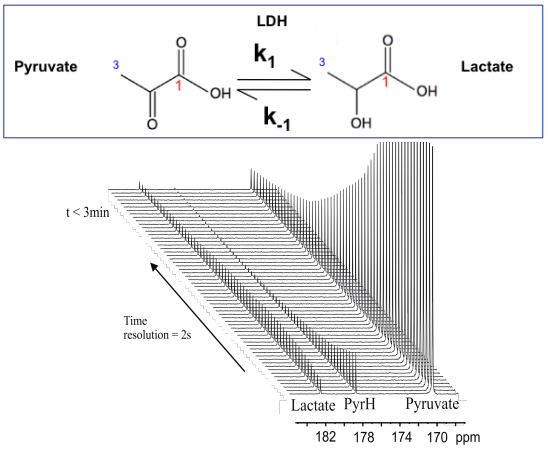


Fig. 2: Pyruvate-lactate exchange reaction, with ^{13}C labels indicated. Representative *in vitro* spectra acquired at 500 MHz.

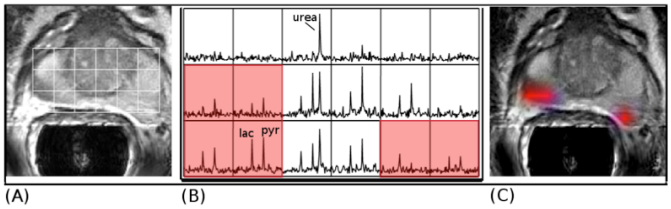


Fig. 3: Figure adapted from [3]. MRSI of a prostate cancer patient following hyperpolarised [1-^{13}C]pyruvate injection. (A) Abnormality on left side of T_2 weighted image (dark region) but not on right. (B) Red voxels have elevated lactate/pyruvate signal. (C) Overlay of elevated regions of lactate/pyruvate in red on T_2 weighted image highlights the presence of abnormal signal on both sides of the prostate.

References

[1] Ardenkjaer-Larsen, J.H., *et al*. Proc Natl Acad Sci (2003). [2] Day, S.E., *et al*. Nat Med (2007). [3] Nelson, S.J., *et al.* Sci Transl Med 5 (2013).

The effect of melatonin on brain development after hypoxic-ischemic brain injury in neonatal rats.

Hester R. Berger[1], Tora Sund Morken[1], Axel K.G. Nyman[2], Ann-Mari Brubakk[1], Marius Widerøe[2].

[1] *Department of Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology (NTNU), Trondheim, Norway.*
[2] *Department of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim, Norway.*
**Hester R. Berger (hester.berger@ntnu.no)*

Background: Treatment options for neonatal hypoxic-ischemic brain injury (HI) are limited. Melatonin is an endogenously produced hormone that has shown potential neuroprotective capabilities, but its influence on long-term brain development following HI has not earlier been investigated. The aim of the study was to assess the effects of melatonin following neonatal HI on short and long-term brain tissue destruction.
Methods: In seven-days-old rats the right carotid artery was severed followed by exposure of the pups to 8% oxygen for 105 min, resulting in HI to the right hemisphere. Littermate controls were sham-operated. An intraperitoneal injection of either melatonin 10 mg/kg dissolved in DMSO 5% and PBS (HI+MEL), DMSO 5% dissolved in PBS (HI+DMSO) or only PBS (HI+PBS) was given at 0, 6 and 25 hours after hypoxia. One day after HI, *in vivo* MR imaging (apparent diffusion coefficient maps (ADC)) and spectroscopy (single voxel ^{1}H) was performed. MRI (T_2-w images and diffusion tensor imaging (DTI)) was repeated at postnatal day (P) 14, 27 and 50. On P 50 animals were euthanized and the brains prepared for histological examination.
Results: Preliminary data show similar ADC values 1 day after HI in the ipsilateral cortex, hippocampus and caudate putamen in the HI+MEL and sham groups, whereas the ADC values of the HI+PBS and HI+DMSO groups were significantly lower in these areas indicating cytotoxic edema. The early ADC values in all ipsilateral areas were positively correlated with right cerebral tissue volume on P 50. The HI+MEL group had less brain tissue loss, smaller cysts and a lower percentage of injured cortex than the HI+DMSO and HI+PBS groups. As in the shams, the right cerebral tissue volume increased over time in the HI+MEL group (figure1). In contrast, in the HI+DMSO and HI+PBS groups the right cerebral tissue volume was unchanged over time while the cyst volume and percentage injured cortex increased between P 14 and P 50. Analysis of MR spectroscopy and DTI data are pending.
Conclusions: Melatonin reduced short and long-term brain tissue destruction and improved the trajectory of brain growth after HI in the developing brain. This study supports the further investigation of melatonin as a potential therapeutic candidate in the treatment of neonatal HI.

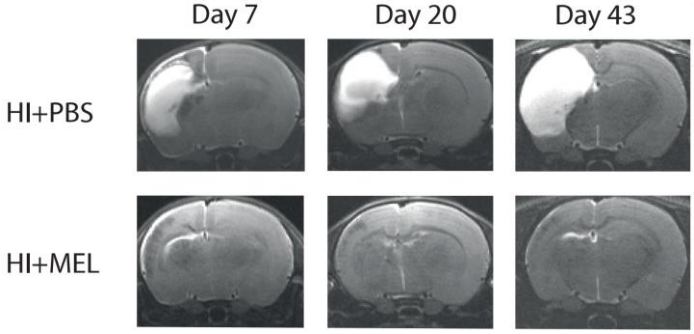


Figure 1: T2-w images of the brain after neonatal HI. Typical animal treated with PBS (upper level) and one typical treated with melatonin (lower level).

Abstract:

NMR based clinical research and result validation

M.Spraul, H.Schäfer, B.Schütz, C.Cannet, D.Krings, F.Fang

Bruker BioSpin GmbH Germany

NMR is one of the 2 major tools in Metabonomics. Its advantages in the investigation of biological fluids are well known, ranging from straightforward sample preparation, unmatched reproducibility to push button operation. Transferring Metabonomics routines to clinical questions opens a way to more efficient diagnosis and treatment monitoring. In order to save money in the future in the health care system, clinical research has to be operated under strict standard operation procedures (SOPs), which can be reproduced in clinical diagnosis later. Since statistical analysis on bodyfluids needs many samples due to high variability in the human system, it is necessary, that multiple systems deliver the results to build meaningful statistical tools. In order to get perfect quantification results, it is also mandatory to strictly follow the established SOPs. In clinical setting it is mandatory to run strict validation procedures. In this contribution, the requirements for clinical NMR are discussed, examples given and the validation explained.

CRAFT: A NEW WAY TO PROCESS YOUR NMR SPECTRA AND TO EXTRACT FREQUENCY AND AMPLITUDE INFORMATION.

Dimitris Argyropoulos[1],
[1] *Agilent Technologies UK, 10 Mead Road, Oxford OX5 1QU, U.K.*

Abstract
The intrinsic quantitative nature of NMR had been largely ignored so far but it is increasingly exploited in areas ranging from complex mixture analysis (as in metabolomics and reaction monitoring) to quality assurance/control. NMR spectra are usually complex and most real-life samples are mixtures of components, therefore extraction of quantitative information generally involves significant prior knowledge and/or operator interaction to characterize resonances of interest. Moreover, in most NMR-based metabolomic experiments, the signals from metabolites are normally present as a mixture of overlapping resonances, making quantification difficult. Time-domain analysis approaches have been reported to be better than conventional frequency-domain analysis at identifying small changes in signal amplitude. We discuss a time-domain analysis method that can achieve a complete reduction to amplitude frequency table (CRAFT) in an automated and time-efficient fashion – thus converting the time-domain FID to a frequency-amplitude table. CRAFT tables can be used for further data mining of quantitative information using fingerprint chemical shifts of compounds of interest and/or statistical analysis of modulation of chemical quantity in a biological study (metabolomics) or process study (reaction monitoring) or quality assurance/control. The basic principles behind this approach as well as results to evaluate the effectiveness of this approach in mixture analysis will be presented together with examples from complex food samples.

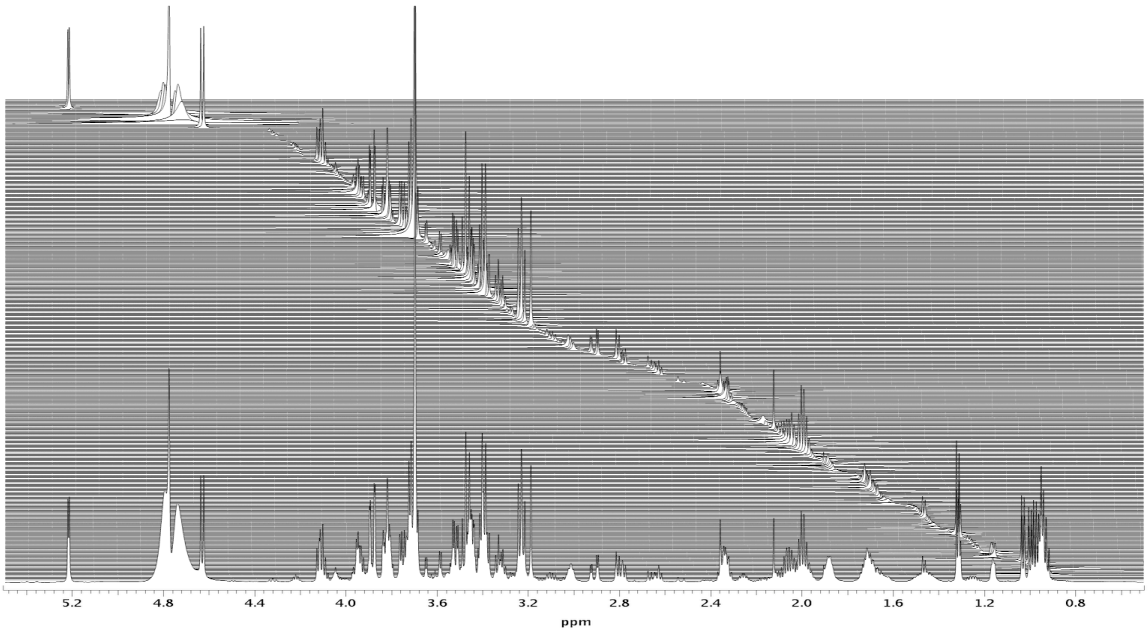


Figure 1: Example of CRAFT analysis result from a fermentation broth sample.

References

1. Krishnamurthy, K., *Magn. Reson. Chem.,* 51: 821–829 (2013).

Metabolomics and Cancer

Guro F. Giskeødegård
Dept. of Circulation and Medical Imaging, NTNU, Trondheim, Norway

MR metabolomics can be used for studying metabolic changes related to cancer development and progression in tissues and biofluids. Metabolic changes in cancers may arise from abnormal proliferation rates, with changes in glycolosis, choline and fatty acid metabolism. Using *ex vivo* high resolution magic angle spinning (HR MAS) MRS, highly resolved spectra can be obtained from tissue samples with minimal sample pretreatment. Several studies have shown metabolic changes in cancer tissue compared to normal tissue in different types of cancers such as breast, prostate, and brain cancers, and specific metabolic patterns have been related to prognostic markers and tumor grade. Biofluids such as urine and blood can be easily acquired, and MR metabolomics of biofluids have a great potential both for detection and monitoring of cancer. In this presentation, I will give some examples of how MR metabolomics is being used for examining metabolic changes related to cancers using both tissues and biofluids, and some main results from cancer detection, diagnosis and treatment monitoring will be presented.

Environmental Metabolomics

Trond R. Størseth, PhD

SINTEF Materials and Chemistry, Environmental Technology

7465 Trondheim

Environmental Metabolomics is the application of metabolomics within the environmental sciences to study interactions between organisms and their environment at the molecular level. Nuclear magnetic resonance spectroscopy has been an important part of the development of environmental metabolomics and several contributions to NMR metabolomics methodology has come from methods development in conjunction with environmental studies. This includes extraction and sample preparation as well as data processing and NMR protocols. A short review of the development of environmental metabolomics during the last decade will be given in this presentation with examples from the literature and in addition some local examples of studies.

NMR METABOLOMICS IN PREGNANCY AND INFANCY

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Abstract
NMR Metabolomics was utilized in two studies exploring the junction of pregnancy and early infancy. The first, STORK Groruddalen, was a prospective cohort study of ~800 women from Oslo who were followed during and after pregnancy. NMR spectra of urine were analyzed in order to characterize the development of metabolite excretion over time, as well as to identify markers for gestational diabetes [1]. Correlations with the women's individual breastfeeding habits were also investigated. The second study, the PRENU RCT of an enhanced nutrition protocol, analyzed urine samples from ~50 premature, very-low-birthweight infants with respect to growth and development.

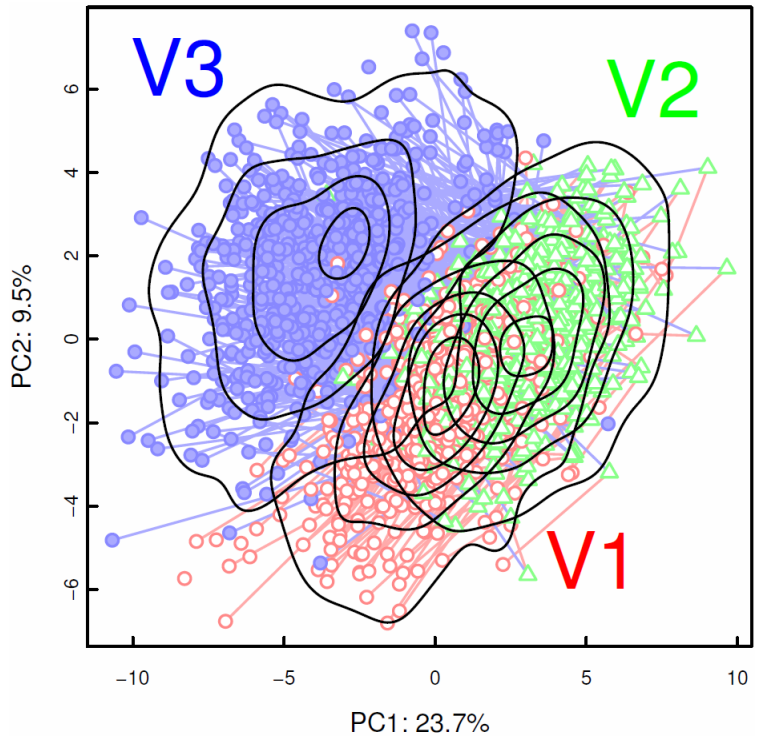

Figure 1: PCA scores plot of metabolite profiles of urine samples taken in the STORK Groruddalen study at mid- (V1) and late pregnancy (V2) as well as three months after delivery (V3).

References

1. Sachse D, Sletner L, Mørkrid K, Jenum AK, Birkeland KI, Rise F, Piehler AP, Berg JP: Metabolic Changes in Urine during and after Pregnancy in a Large, Multiethnic Population-Based Cohort Study of Gestational Diabetes. *PLoS One* 2012, 7(12): e52399.

"Targeting choline phospholipid metabolism: GDPD5 and GDPD6 silencing decreases breast cancer cell proliferation and invasion"

Maria Dung Cao[1,2,*], Menglin Cheng[2], Lu Jiang[2], Tiffany R Greenwood[2], Balaji Krishnamachary[2], Zaver M Bhujwalla[2], Tone F Bathen[1], and Kristine Glunde[2,3]

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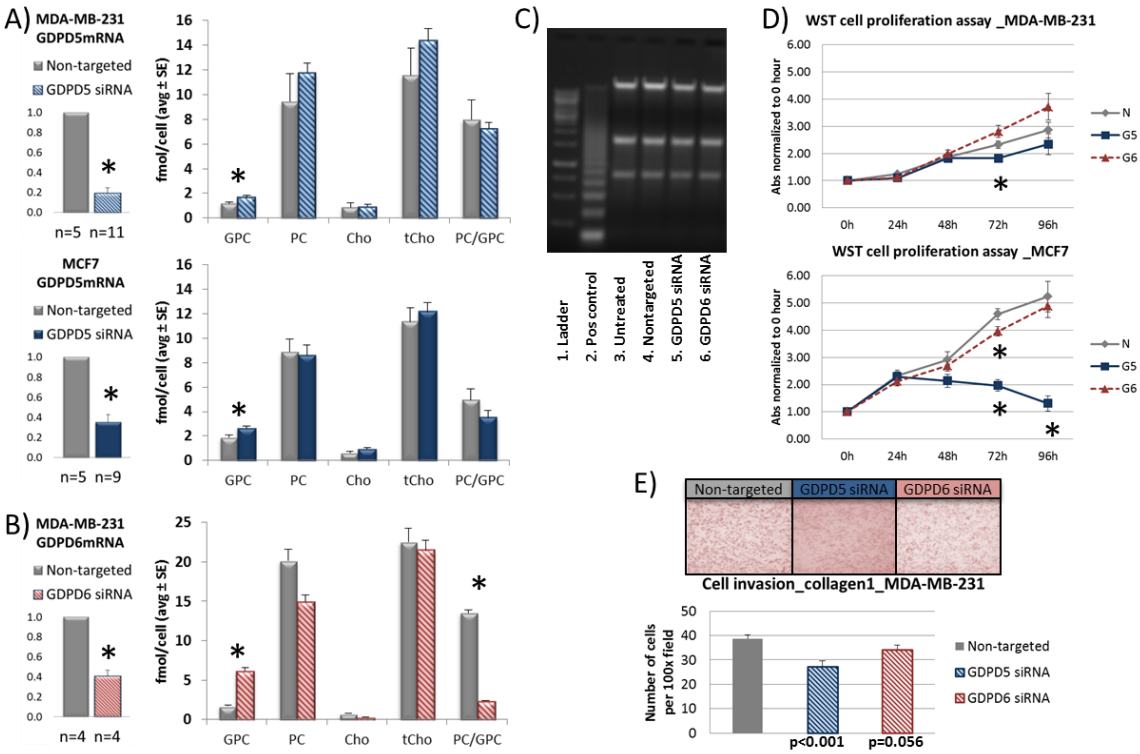
INTRODUCTION: As choline phospholipid metabolism has been shown to be associated with tumor malignancy and treatment response, the genes and enzymes regulating this pathway are interesting potential targets for treatment of breast cancer. We have demonstrated that the glycerophosphodiester phosphodiesterase GDPD5 is partially responsible for the relatively low glycerophosphocholine (GPC) levels in human breast cancer cells and human breast tumors [1]. In a recent study, GDPD6 has been shown to be involved in cell migration and metastasis [2]. Our purpose was to investigate the biological effects of targeting GDPD5 and GDPD6 for treatment of breast cancer using small interfering RNA (siRNA) in weakly malignant human MCF-7 and highly malignant human MDA-MB-231 breast cancer cells.



RESULTS:

A) GDPD5 siRNA qRT-PCR and ^{1}H MRS. GDPD5 was successfully down-regulated by 80% and 65% in MDA-MB-231 and MCF7 cells, respectively. Significant increase in GPC (∗=p<0.05) was observed in GDPD5 siRNA treated cells compared to control.

B) GDPD6 siRNA qRT-PCR and ^{1}H MRS. GDPD6 was successfully down-regulated by 60% for both MDA-MB-231 and MCF7 (data not shown) cells. GPC was increased in MDA-MB-231 cells compared to control. (MCF7 data in progress).

C) Apoptosis assay. DNA laddering was negative for both cell lines treated with GDPD5 and GDPD6 siRNA (n=2).

D) Cell proliferation. In GDPD5 siRNA treated cells, both cell lines experienced a decrease in cell proliferation compared to control at 72h. MCF7 cells treated with GDPD6 siRNA displayed a decrease in cell proliferation compared to control at 72h (n=6 per time point).

E) Cell invasion. GDPD5 and GDPD6 treated MDA-MB-231 showed a significant decrease in cell invasion compared to control. However, lower cell invasion was observed in GDPD5 compared to GDPD6 siRNA treated cells (p=0.024, n=3, MCF7 data in progress).

DISCUSSION and CONCLUSIONS: Here we investigated the effects of targeting choline phospholipid metabolism using GDPD5 and GDPD6 siRNA in two breast cancer cell lines, MCF7 and MDA-MB-231. Our study shows that GDPD5 and GDPD6 siRNA treatment increases GPC levels identified by high resolution MRS, decreases proliferation and invasion, but did not cause apoptosis. The effect of GDPD5 siRNA on cell proliferation was more severe in the less malignant breast cancer cell line. Decreased cell invasion was observed in GDPD5 compared to GDPD6 siRNA treated cells. Our results suggest that GDPD5 and GDPD6 silencing alone/combined can have a potential role as new molecular targets for treatment of breast cancer.

REFERENCES [1] Cao M.D. et al, NMR in Biomed 2012. [2] Stewart JD, Proc Natl Acad Sci U S A. 2012. Acknowledgements: This work was supported by NIH R01 CA134695.

Speed updates; 15:15 – 16:15

Five stands; four presentations at the same time on four different stands, the fifth is a stand with coffee break. We divide the attendance into 5 groups. Everyone give marks to the presentation they think is the best of the four given by

1. **Jana Cebulla**
2. **Morteza Esmaeili**
3. **Øyvind Halskau**
4. **John Georg Seland/Siri Aaserud**

Diffusion Weighted and Contrast Enhanced MRI Reveal Response to PI3-Kinase/mTor Inhibition in Ovarian Xenograft Models

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[1]*Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway*

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Purpose: The PI3-kinase (PI3K) pathway is frequently upregulated in cancer and is a promising target for anti-cancer therapies [1]. The aim of this study was to evaluate the predictive value of diffusion weighted (DW)-MRI and dynamic contrast enhanced (DCE)-MRI for tumor response to PI3-kinase/mTOR inhibition in ovarian cancer xenografts.

Methods: Xenografts of the human ovarian cancer cell lines TOV-21G (n=12) and TOV-112D (n=12) were grown on the hind leg of athymic mice. Eight mice per group were treated with 65mg/kg BEZ-235 (PI3K/mTor inhibitor) on days 1, 2, and 3. MRI was performed on day 0 and 3 on a 7T Bruker Biospec. Five sagittal slices were acquired with FOV=23x23mm^2, matrix size=64x64 and slice thickness=0.7mm using (i) DW EPI: 4 segments, NEX=4, b-values =100, 300, 600, 1000 s/mm^2, three orthogonal gradients; (ii) DCE-MRI: 200 T1w images at a temporal resolution of 4.8s (TE= 7.2ms, TR=300ms, RARE factor=4). An i.v. bolus of Omniscan (0.3mmol/kg) was administered during the 11th repetition. Apparent diffusion coefficient (ADC) maps were calculated from the DW data. Maps of the extravascular extracellular space per unit volume (v_e) were calculated from the DCE data assuming a two-compartment model [2] and a biexponential vascular input function [3]. Non-enhancing voxels were excluded [4].

Results: Significant tumor volume decrease after treatment indicates a strong treatment response for the TOV-21G tumors while the TOV-112D only showed slower growth (**Fig.1a).** The median v_e values increased significantly for treated TOV-21G and slightly for TOV-112D tumors while ctrl tumors experienced a decrease (**Fig.1b**). ADC increased only for treated TOV-21G tumors (**Fig.1c**). **Fig.2** shows increases in both v_e and ADC throughout the tumor after treatment.

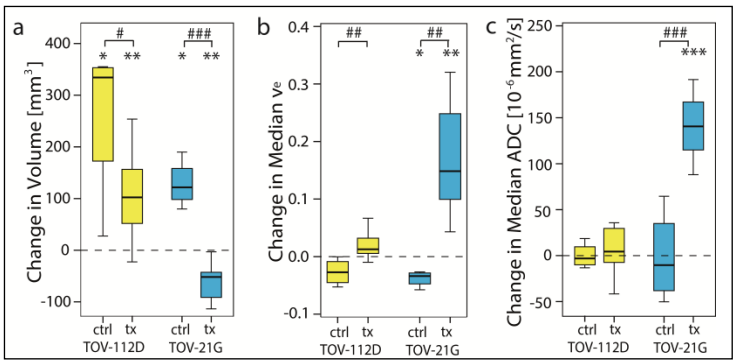

*Fig. 1: Box plots of change in (a) tumor volume (b) median Ve and (c) median ADC. * p<0.05, ** p< 0.01, *** p< 0.001 paired sample t-test pre vs post treatment. # p< 0.05, ## p<0.01, ### p<0.001 two sample t-test of change in ctrl vs treated.*

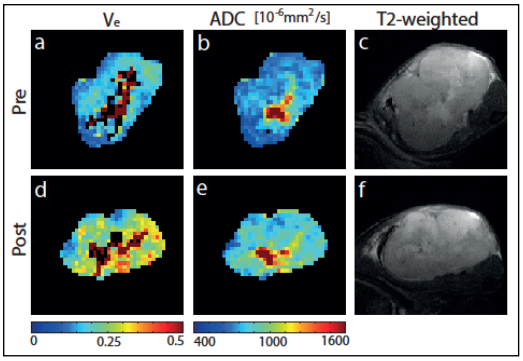

Fig.2: Ve maps (a,d), ADC maps (b,e) and T2w images (c,f) of one representative TOV-21G xenograft pre-treatment (a,b,c) and the corresponding slice post-treatment (d,e,f).

Discussion: Previous studies of protein levels indicated a high PI3K signalling activity in TOV-21G cells and low activity in TOV-112D cells. This is in accordance with our data which showed stronger response in form of decreased volume, higher ADC and v_e in treated TOV-21G compared to TOV-112D tumors. Our results indicate that both median ADC and median v_e are promising candidates for biomarkers of response to PI3-kinase/mTOR inhibition.

References: [1] Chalhoub N *et al.* Annu Rev Pathol. 2009;4:127-50. **[2]** Tofts PS *et al.* J Magn Reson Imaging 1997; 7(1): 91-101. **[3]** Jensen LR *et al.* Cancer Biol Ther. 2007; 6(11): 1810-1816. **[4]** Huuse EM *et al.* J Magn Reson Imaging 2012; 35: 1098-1107.

High resolution ^{31}P MR spectroscopy reveals post-exercise impacts on energy metabolism of heart failure rats

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INTRODUCTION: Exercise training increases maximal oxygen uptake (VO_{2max}) and cardiac function after myocardial infarction (MI) but the relative effect of moderate vs. high intensity training on myocardial energy metabolism is uncertain. Phosphorus (^{31}P) magnetic resonance spectroscopy (MRS) allows detection of high energy phosphate in the heart muscles; adenosine triphosphate (ATP) and phosphocreatine (PCr)[1]. Reduced myocardial PCr/ATP ratio in heart failure patients correlates with the New York Heart Association (NYHA) classes[2]. A clinical study showed that PCr/ATP ratio might be a stronger predictor for cardiovascular mortality than functional or clinical indexes[3]. The purpose of the present study was to investigate myocardial phosphate energy reservoir in the left ventricle from rats with MI after exposure to moderate intensity (Mod) and high intensity (High) aerobic interval training regimens.

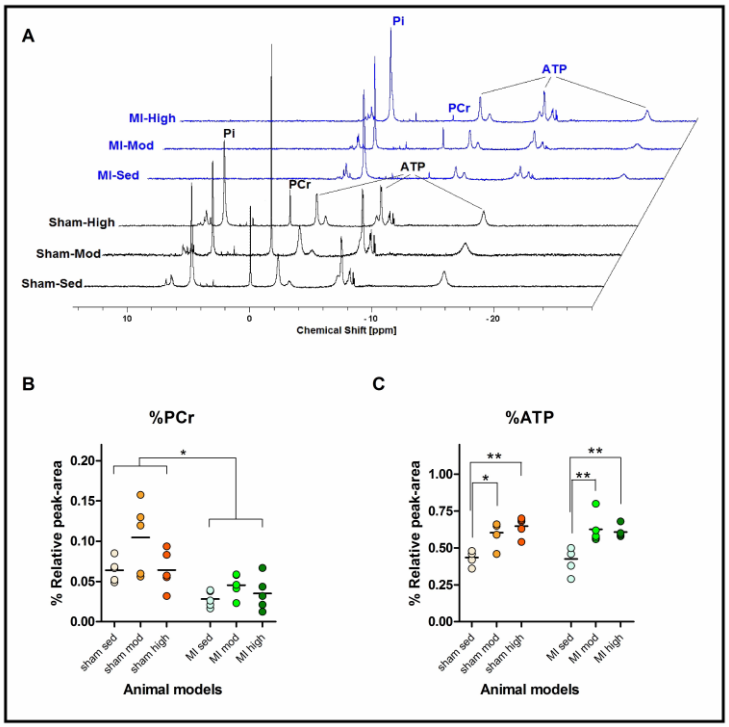

*Figure 1: (A) Examples of high resolution ^{31}P NMR spectra of heart muscle tissue extracts obtained from MI and healthy rat models; sedate, moderate- and high-intensive trained. (B) MI caused significant decrease in PCr levels compared with the sham control group. Dots indicate the normalized PCr levels measured from individual MR spectra. The mean values were compared using the non-parametric Mann-Whitney test (GraphPad Software, Inc. V 4.03, CA, USA). (C) ATP production increased post-training. Symbols * and ** denote $P < 0.05$ and $P < 0.01$ respectively.*

METHODS: Animal models: Rats were randomized to either sham or MI operations. MI was induced by ligation of the descending artery, as previously described[3]. After 4 weeks, rats with MI operation were examined by echocardiography to determine the extent of MI. Only rats with MI between 40-50% of the left ventricle were included to this study. High- and Mod-intensity training was performed as described in detail previously[3]. The experiments were performed according to the Guide for the Care and Use of Laboratory Animals. Tissue extraction: The rats were anesthetized and the hearts were removed and placed in ice-cold saline for dissection. To avoid fibrotic and ischemic parts, tissue from the septum towards the apex was cut out from every heart and immediately frozen and later extracted using perchloric acid as described previously[4]. Time from removal of the heart to snap freeze was approximately 1 min and did not differ between groups. MR experiments: NMR experiments were performed on a 14.1 T spectrometer equipped with a multinuclear QCI CryoProbe (Bruker Avance III 600 MHz/54 mm US-Plus, Ettlingen, Germany). ^{31}P NMR spectra were obtained with ^{1}H-decoupling, a 30˚ flip angle, 8192 scans, TR=3.62 s, spectral width of 14577 Hz into 47104 data points. MR spectra were analyzed using jMRUI software[5]. Metabolites were normalized to the area under the peaks of total metabolites; inorganic (Pi), ATP, and PCr. In situ mitochondrial respiration: Mitochondrial function was assessed using high-resolution respirometry (using oxygraph-2k, Oroboros instruments, Austria) in chemically permeabilized heart muscle fibers. Saturating concentrations of combined malate, glutamate (supplying electrons to complex I) and succinate (supplying electrons to complex II) results in maximal oxidative phosphorylation, expressed as pmol O2·s-1·mg-1 wet weight.

RESULTS: High intensity training increased the oxygen consumption by 40% while the moderate intensity training increased the maximal oxygen consumption by 20%. Both modes of exercise training increased ATP concentration in sham and MI groups (Fig. 1). PCr levels in MI group were depleted significantly compared with sham control ($P < 0.05$), although a trend toward increased PCr storage was observed in the post-exercise MI group. Maximal oxidative phosphorylation of mitochondria was reduced in MI heart compared to sham (162 vs. 243 [pmol/s.mg], respectively). Exercise did not increase the maximal respiration (176 and 181 [pmol/s.mg], respectively in moderate- and high intensity training).

CONCLUSION: The results demonstrate the potential of ^{31}P MRS to investigate the efficacy of different exercise regimens to improve cardiac performance. When translated to the clinic, this technique may benefit patients with MI heart by determining the effect of training by monitoring the high energy metabolism in vivo.

REFERENCES: 1. Neubauer S et al., *N Engl J Med.*, 2007 **2.** Loennechen JP et al., *Am J Physiol Heart Circ Physiol.*, 2001 **3.** Wisloff U et al., *American journal of physiology*, 2001 **4.** Gribbestad IS et al., *NMR Biomed.* 1994 **5.** Naressi A et al., *Magma*, 2001.

INITIAL BINDING OF TWO ANNULAR OLIGOMER-FORMING PEPTIDES TO LIPID MEMBRANES

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Abstract
Breakdown of the plasma membrane integrity or of the carefully regulated processes taking place at it will usually lead to cell death, cell proliferation or cell aberration. The membrane-perturbing annular oligomers (AOs) have been found to be much more toxic than the inert and insoluble amyloid plaques which they may eventually turn into. AOs are thus examples of debilitating protein misfolding events, hypothesized to be catalysed by specific membrane constituents, such as cholesterol. Why and how some protein/polypeptides convert readily to AOs, and the role of lipids and the membrane in this conversion is not well understood. Such transitions require large changes in conformation, aggregation state and solubility state, and neither the transitions involved nor the final conformational states are understood well. We have embarked on an investigation of the underexplored links between AOs, loosely folded membrane-associated proteins and the composition of the lipid membrane. We have developed an attractive model system for studying AOs. These are two 56 AA polypeptides, based on parts of the α-Lactalbumin sequence involved in membrane binding, AO-formation and, it turns out, oleat-binding in AO-inducing, cytotoxic fatty-acid complexes. They are prolific AO-formers, in particular the A-Lnk-C. We present preliminary results on which part of the protein backbone is involved in protein-membrane binding. We hope to be able to catch differences in how different peptide sequences respond to different lipid compositions.

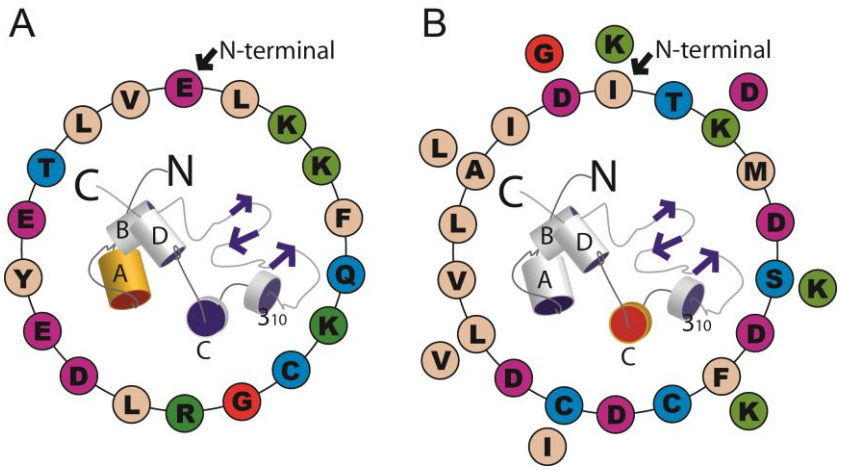

Figure 1: Two membrane- and AO-forming segments and their location in the α-Lactalbumin fold. The peptides consist of these segments linked by a flexible chain and a mini-fold.

References

1. Baumann, A., Gjerde, A. U., Ying, M., Svanborg, C., Holmsen, H., Glomm, W. R., Martinez, A. & Halskau, Ø. (2012). HAMLET forms annular oligomers when deposited with phospholipid monolayers. Journal of molecular biology. 418, 90-102.

ABSTRACT TEMPLATE FOR THE 13TH NATIONAL MR MEETING

CHARACTATIZATION OF APPLE JUICES BY USE OF DIFFUSION-ORDERED NMR SPECTROSCOPY

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Abstract

Diffusion-ordered NMR spectroscopy (DOSY) has become a powerful technique for characterizing complex chemical mixtures [1]. In a DOSY experiment, magnetic gradient techniques are applied [2], making the measurement sensitive to the translational movement of the molecules within the mixture. The result is a series of NMR spectra, where each frequency-dependent signal decays exponentially according to the self-diffusion rate of the molecule from where the signal originates. The simplest implementation of DOSY results in a 2D NMR data set, where one dimension gives spectral (chemical shift) information, and the other dimension distinguishes molecules based on their self-diffusion coefficient. By adding more spectral dimensions to the experiment, the DOSY technique can also be further extended [3] (3D-DOSY).

In this study we have applied 2D- and 3D-DOSY techniques to characterize different types of apple juices. Experiments were obtained using both ^{1}H and ^{13}C as the detected nucleus. An example of a typical DOSY spectrum is shown in Figure 1. The obtained results show that DOSY is a promising technique for characterizing these samples.

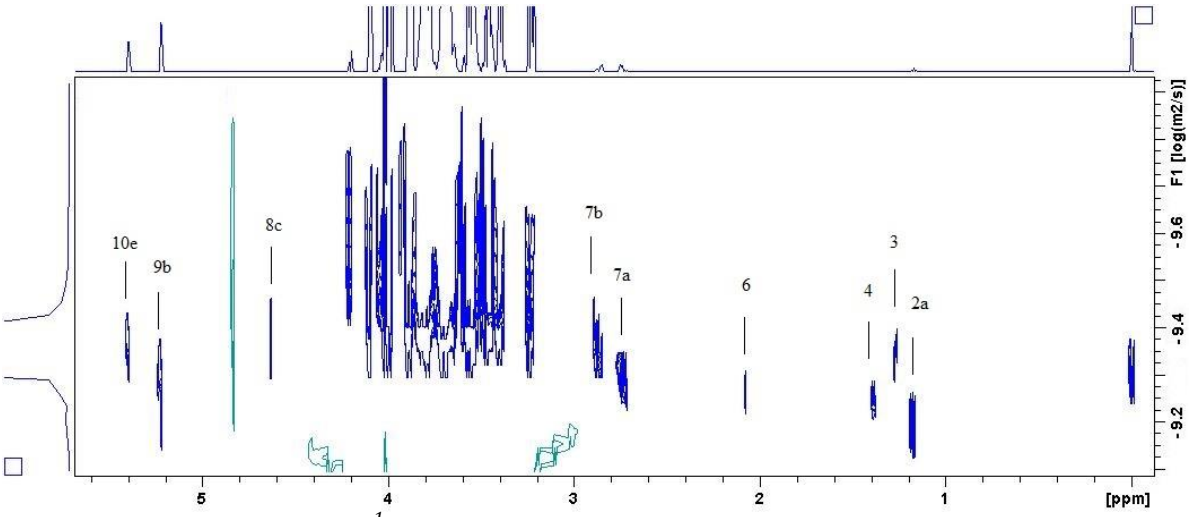

Figure 1: ^{1}H DOSY of commercial Eldorado apple juice.

References

[1] Antalek, B., Concepts Magn. Reson., 2007. **30A**: p. 219-235.
[2] Price, W., Concepts Magn. Reson., 1997. **9**: p. 299-336.
[3] Vermillion, K., N.P.J. Price, J. Magn. Reson., 2009. **198**: p. 209-214.

Poster presentations; 16:15 – 17:00

INSIGHTS INTO THE STRUCTURE AND FUNCTION OF A LYTIC POLYSACCHARIDE MONOOXYGENASE BY NMR SPECTROSCOPY

Finn L. Aachmann[1], Morten Sørlie[2], Gudmund Skjåk-Bræk[1], Vincent G.H. Eijsink[2] and Gustav Vaaje-Kolstad[2]

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Abstract: Lytic polysaccharide monooxygenases (LPMO) previously classified as carbohydrate binding module family 33 (CBM33) and glycoside hydrolase family 61 (GH61) and currently classified as Accessory Activities AA9 and AA10 [1], are likely to play central roles in future biorefining [2]. Still, the molecular basis of their unprecedented metal-dependent catalytic activity remains largely unknown. Here we have used NMR and ITC to study chitin binding protein 21 (CBP21), a chitin-active CBM33/AA10 [3]. NMR dynamic data showed that CBP21 is a compact and rigid molecule, the only exception being the catalytic site. NMR data further showed that H28 and H114 in the catalytic site bind a variety of divalent metal ions with a clear preference for Cu^{2+} (Kd = 55 nM; from ITC) and even better Cu^{1+} (Kd ≈ 1 nM; from an experimentally determined redox potential for CBP21-Cu2+ of 275 mV using a thermodynamic cycle). The higher affinity for Cu^{1+} was also reflected in a reduction in the pK_a values of the histidines by ~3.6 and ~2.2 pH units, respectively. Cyanide, a mimic of molecular oxygen, was found to bind to the metal ion only. These data support a model where copper is reduced on the enzyme by an externally provided electron, followed by oxygen binding and activation by internal electron transfer. Interactions of CBP21 with a crystalline substrate were mapped in a $^{2}H/^{1}H$ exchange experiment, which showed that substrate binding involves an extended planar binding surface, including the metal binding site. Such a planar catalytic surface seems well-suited to interact with crystalline substrates.

References:

[1] Levasseur A et al. (2013) Biotechnol Biofuels 6;41.
[2] Horn SJ et al. (2012) Biotechnol Biofuels 5;45.
[3] Aachmann FL et al. (2012) PNAS 109;p18779.

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Feasibility of MR metabolomics for immediate analysis of resection margins during breast cancer surgery

Tone F. Bathen[1, 2], Brigitte Geurts[3], Beathe Sitter[4], Hans Fjøsne[5], Steinar Lundgren[6], Lutgarde Buydens[3], Geert Postma[3], Ingrid S. Gribbestad[1, 2], Guro F. Giskeødegård[1, 2]

Purpose/Introduction

In order to minimize the risk of local recurrence after breast cancer surgery, it is important that infiltrating tumors are completely removed with free resection margins. Currently, resection margins are evaluated by a pathologist after surgery, and a significant number of patients must be scheduled for re-surgery. Providing information to distinguish between tumor and non-involved adjacent tissue during breast cancer surgery can help surgeons identify the tumor borders more accurately, thereby reducing the number of re-resections. The aim of this study was to evaluate the accuracy of high resolution magic angle spinning (HR MAS) MRS derived classifiers distinguishing malignant and non-involved adjacent tissue, in order to examine the feasibility of future on-line analyses in the surgical theater.

Subjects and Methods

Tumor samples obtained during breast cancer surgery (n=228 patients, 328 samples) were analyzed by HR MAS MRS on a Bruker Avance III 600MHz/54 mm US. Samples were spun at 5 kHz at a temperature of 4 ^{o}C. CPMG spectra were acquired with an effective echo time of 285 ms. The spectral data were analysed using partial least squares discriminant analysis (PLSDA), and the classification results were validated by robust double cross-validation and permutation testing. Alternative ways of PLS-DA model making were investigated by handling samples with very low tumor content in different ways; either by defining samples with a low tumor content (between 0-4%) as adjacent non-involved tissue, or by defining all samples with tumor content > 0% as tumor tissue. Models were also made by removing samples with low tumor content from the training data and including them only in the test set. As an additional approach, classification was performed using only the spectral region containing the choline-containing metabolites (3.252 - 3.196 ppm) as input for the classification model. This approach is relevant for the ongoing discussion concerning choline metabolism in cancer.

Results

Tumor and non-involved tissue were discriminated by removing tumor samples with very low cancer content (< 5% tumor cells) from the training set used to build the multivariate model. The classification accuracy was 90 % (sensitivity: 88%, specificity: 92%; obtained using the complete data set). The results were highly significant ($p < 0.001$). The cancer samples were characterized by higher levels of choline, taurine, and glycine and lower levels of glucose compared to the non-involved samples.

Discussion/Conclusion

HR MAS MRS can be used for accurate discrimination of tumor and non-involved adjacent tissue. The complete analysis can be performed on-line during surgery.

Preliminary metabolic subgrouping of breast cancer using HR MAS MRS and hierarchical cluster analysis

Tonje H. Haukaas*, Guro F. Giskeødegård*, Ingrid S. Gribbestad*, Rolf Kåresen (1,2), Kristine Kleivi (3), Anne-Lise Børresen-Dale(2,3), Tone F. Bathen*

** Department of Circulation and Medical Imaging, Faculty of medicine, NTNU, Trondheim, Norway (1) Department of Surgery, Oslo University Hospital, Ullevål, Oslo, Norway (2) Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway (3) Department of Genetics, Institute for Cancer Research Oslo University Hospital, The Norwegian Radium Hospital, Norway*

Purpose: Worldwide, breast cancer is the most frequently diagnosed cancer type and the leading cause of cancer deaths among women [1]. The heterogeneous tumor biology of breast cancer has led to the need for detection of clinically relevant subgroups. Based on microarray analysis and hierarchical clustering the molecular subgroups Claudin Low, Basal Like, Her2 enriched, Normal Breast Like, Luminal A and Luminal B have been identified [2]. Here we show the resulting metabolic subgroups using hierarchical clustering on MR metabolic profiles from 281 breast cancer patients. The main aim is to combine this preliminary result with information of gene expression results from the same patients and relate these to their clinical information.

Methods: High resolution magic angle spinning magnetic resonance spectroscopy (HR MAS MRS) is a method that can be used to determine the metabolic composition of tumor biopsies. By using this method it has been shown that breast cancer tumors have altered concentration of the metabolites such as choline, phosphocholine (PCho), glycerophosphocholine (GPC), lactate and glycine when compared to normal tissue [3]. In this study we have examined the metabolic profiles of a large cohort of breast cancer patients (N=281) using HR MAS MRS. Further, the multivariate method Principal Component Analysis (PCA) was used to extract the metabolically important principal components (PCs) before hierarchical cluster analysis using Ward's method was performed.

Results: Four clusters based on metabolic differences (see **Error! Reference source not found.**) were evaluated. Comparing the mean spectra for each of these clusters to the total mean spectra revealed the main differences to be the levels of lactate, taurine, PCho, GPC, choline and glycine (see Table 1). The breast cancer biopsies in cluster 1 has lower levels of lactate, PCho, GPC and glycine, while cluster 2 contains samples with low levels of taurine, choline and glycine, but higher levels of PCho. Samples in cluster 3 have high levels of lactate, taurine and glycine relative to the mean spectra, while samples in cluster 4 are characterized by higher levels of GPC and lower levels of glycine.

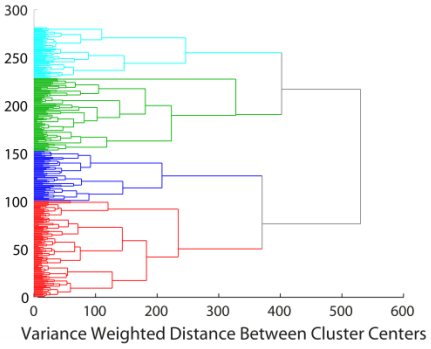

Figure 1: Dendrogram of breast cancer samples using Ward's Method. The four clusters were evaluated for metabolic differences and clinical relevance.

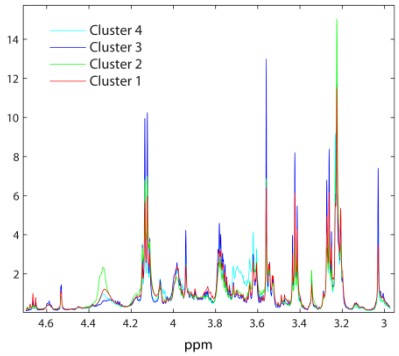

Figure 2: Comparison of mean spectra for the four clusters

Table 1: Main differences in metabolite levels between mean spectra from the four clusters. Arrow pointing up represents cluster where the metabolite level is higher when compared to the mean quantity from all samples. Arrow pointing down indicates lower level.

	Cluster			
Metabolite	**1 (=100)**	**2 (n=76)**	**3 (n=52)**	**4 (n=53)**
Lactate	↓		↑	
Taurine		↓	↑	
PCho	↓	↑	↓	
GPC	↓			↑
Choline		↓		
Glycine	↓	↓	↑	↓

Discussion: The molecular subgrouping of breast cancer with microarray based gene expression analysis has shown to have prognostic value where the basal-like/triple-negative subtype has the shortest survival. The current abstract focuses on the detection of metabolic subgroups, rather than the genetic, in a large cohort of samples. These subgroups show differences in metabolites that previously have been found important in breast cancer. Lactate and glycine for example have been evaluated as potential markers for prognosis in estrogen receptor-positive breast cancers [3] and GPC/PCho ratio is higher when comparing basal like breast cancer to luminal like [4]. The metabolic subgroups will be further characterized by looking into the gene expression patterns. Furthermore, clinical data is available for the whole cohort, and this will be used to detect frequencies of traditional prognostic and predictive factors within the clusters.

Conclusion: Finding the relation between the molecular, metabolic and clinical profiles may improve the understanding of breast cancer heterogeneity, leading to more patient specific treatment. Also, this study may prove MR metabolomics to be a potential diagnostic tool for clinical use.

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GOLD(III) COMPLEXES: SYNTHESIS AND CHARACTERIZATION

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The interest in organo-gold compounds continues to grow. Gold(III) complexes are being investigated as catalysts for organic transformations including the coupling of alkenes and alkynes to other organic fragments.[1,2] A key step in the catalytic reactions involving gold(III) is assumed to be the coordination of a C-C multiple bond to the gold center. However, gold(III) alkene, alkyne, allene, or arene complexes have until recently not been conclusively detected and characterized.[3]

We have developed a microwave synthesis to efficiently prepare a cyclometalated gold(III) complex, $Au(OCOCF_3)_2(tpy)$ (**1**) in high yields.[4] Complex **1** reacts reversibly with ethylene. ^1H NMR has been used to investigate the reversible ethylene insertion depicted in Figure 1.

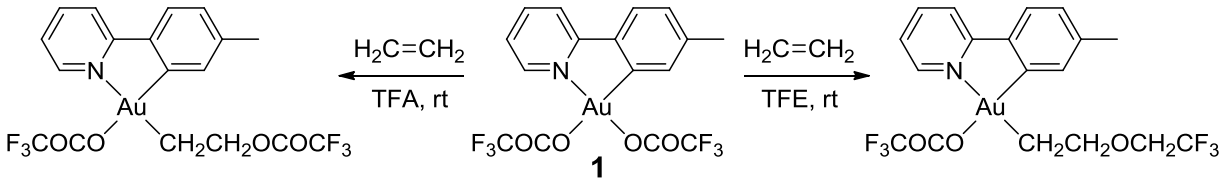

Figure 1: Ethylene insertion into a gold(III)-oxygen bond.

We also use $Au(OCOCF_3)_2(tpy)$ (**1**) to prepare several other interesting gold(III) complexes, amongst them the first crystallographically characterized gold(III) alkene complex $[(cod)AuMe_2^+][X^-]$ (cod = 1,5-cyclooctadiene, Figure 2).[3] This unambiguous demonstration of the existence of gold(III) alkene complexes validates their inclusion in mechanistic proposals and allows further work to increase the understanding of mechanisms that potentially involve gold(III) alkene complexes.

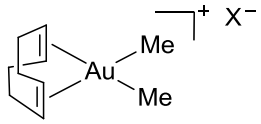

Figure 2: The gold(III) alkene complex $[(cod)AuMe_2^+][X^-]$ (X = OTf, NTf_2 or BArF).

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Extraction, Isolation and Structure Elucidation of Saponins from *Herniaria incana*

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Species of the *Herniaria* genus have been reported to have several medicinal uses.[1,2] Two of the species from this genus, *Herniaria glabra* and *Herniaria hirsuta*, have both been documented to contain saponins.[3,4] This can explain the health beneficial use of these plant species, since saponins are known for their various biological properties.[5i] However, the lack of information on one of their relatives, *Herniaria incana*, makes this species a target for further investigation. The aim of this project was to determine the total saponin content of *H. incana*, as well as to extract, isolate and closely investigate saponin compounds in this species.

The total saponin content was determined colorimetric[6], using ginsenoside Rb1 as standard. Measurements were carried out at 550 nm, and the results gave a total saponin content of 114 μg ginsenoside equivalent saponin content per milligram of the plant extract.

A saponin (Figure 1) was isolated from *H. incana* by means of TLC and column chromatography. The structure was elucidated by the use of a combination of 1D (^{1}H, ^{13}C) and 2D NMR techniques (COSY-45, edited HSQC, HMBC, H2BC, HSQC-TOCSY, NOESY and ^{1}H,^{1}H *J*-resolved experiment) as *O*-α-L-rhamnopyranosyl-(1→4)-*O*-β-D- glucopyranosyl-(1→6)-*O*-[β-D-6-*O*-acetylglucopyranosyl-(1→2)]-β-D-glucopyranosyl Medicagen-28-ate. The monosaccharide sequence was also confirmed by ESI-CID.

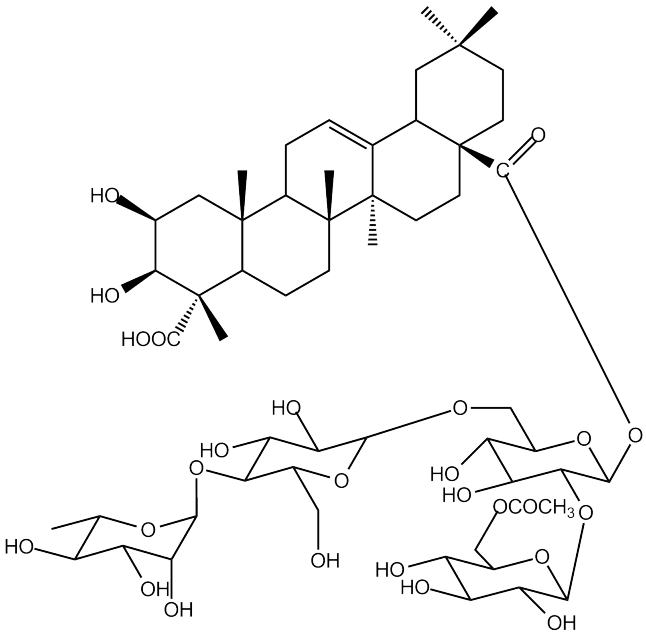

Figure 1 Structure of the isolated saponin from *H. incana*

References

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Thermal Stability of α-Halodiazoacetates

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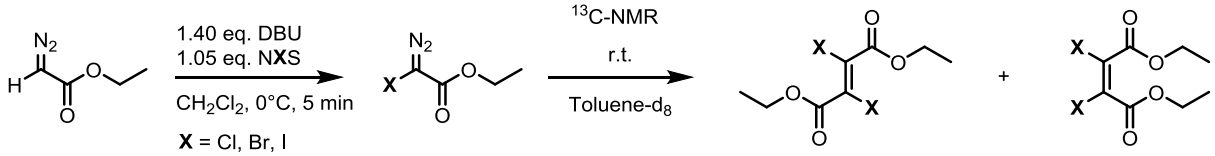
Diazo compounds are known to undergo a variety of metal-catalyzed reactions, including cyclopropanation, C-H insertion and ylide transformations,[1] making diazo compounds a valuable moiety for the synthetic organic chemist. Examples of thermal reactions of diazo compounds on the other hand are few, and to the best of our knowledge systematic studies of thermal decomposition/stability of diazo compounds are scarce.

We have developed a method for comparing stability and selectivity of the thermal dimerization of α-halodiazoacetates, previously prepared in our group[2]. By monitoring the reaction by ^{13}C-NMR with the relevant NMR-parameters optimized, we have obtained quantitative trends for the decomposition of the halodiazoacetates and the influence of the α-halo substituent.



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ABSTRACT TEMPLATE FOR THE 13TH NATIONAL MR MEETING

INVESTIGATING EFFECTS FROM RESTRICTED DIFFUSION IN MULTI-COMPONENT DIFFUSION DATA

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Abstract

Heterogeneous systems are encountered both in petro physical NMR and in biomedical MRI. In such systems multiple diffusion coefficients can be detected, which potentially can be assigned to different diffusion domains. However, when high values of the gradient strength are applied, this may introduce contributions from restricted (non-Gaussian) diffusion to the experimental diffusion attenuated signal, leading to erroneous results [1]. Therefore, multi-exponential diffusion models may contain contributions from non-Gaussian restricted diffusion as well as multiple diffusion compartments. In this study we have investigated model systems where we can separate the effects of restricted diffusion from effects caused by multi-component diffusion.

The experiments were performed at 25 °C on a Bruker Avance 500 MHz instrument, using a commercial probe (DIFF30). We used a combined diffusion-T_2 (D-T_2) measurement and analysis technique [2,3]. Water saturated close packing of mono-sized (100 μm) beads represented diffusion domains with potentially non-Gaussian, time-dependent behavior. One of the samples contained polystyrene (PS) beads (T_2=1800 ms), and another contained glass beads (T_2=60 ms). This gives the same diffusion behavior, but different relaxation properties in these two samples. Two white oils (ExxonMobil), Marcol 52 ($D\approx 1\times10^{-10}$ m^2s^{-1}, T_2=315 ms) and Marcol 152 ($D\approx 2\times10^{-11}$ m^2s^{-1}, T_2=120 ms) represented domains with Gaussian behavior, but with lower diffusion, and with different relaxation properties. These 4 samples were prepared in small separate containers (MAS rotors). The containers were stacked inside an ordinary 5 mm NMR tube, allowing measurements on a single sample or on two samples together. Series of experiments with diffusion times varying between 5 and 100 ms were performed.

The results show that an analysis based on multiexponential models (biexponential diffusion model or 2D-ILT) is not able to correctly account for effects caused by restricted diffusion in a system with multicomponent diffusion. However, an analysis based on separating components due to differences in dynamic behavior prior to the diffusion analysis [2] (T_2-filter or D-filter), combined with the second cumulant approximation [3] is more robust, and is more accurate when it comes to taking into account effects from restricted diffusion in a situation with multicomponent diffusion.

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ABSTRACT TEMPLATE FOR THE 13TH NATIONAL MR MEETING

HIGH FREQUENCY MODULATED GRADIENT SPIN ECHO DIFFUSION MEASUREMENTS WITH CHEMICAL SHIFT RESOLUTION

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Abstract

The use of the Modulated Gradient Spin-Echo (MGSE) technique [1] enables self-diffusion measurements at very short displacements. The oscillating phase factor produced by the modulated gradients results in a signal decay that depends on the Velocity Auto-correlation Function of the molecules. The diffusion dependent signal attenuation can then be accumulated over several rapidly oscillating cycles of the modulated gradients, making the measurement sensitive shorter time scales than what is achieved in the Pulsed Gradient Spin Echo experiment. The motion is described in the form of a Displacement Power Spectrum or a diffusion spectrum. We present a new MGSE pulse sequence based on CPMG-refocusing in a constant gradient, that enables diffusion measurements with chemical shift resolution in the obtained spectra, and with higher modulation frequencies than previously obtained [2]. To avoid effects from gradient-slicing and unwanted coherences [1], while maintaining high chemical shift resolution, the samples were prepared in a shigemi tube (0.5 mm sample hight). Figure 1, left shows the obtained diffusion coefficients as a function of the modulation frequency (diffusion spectrum) in a water sample. The measurements are stable up to 1.6 KHz. The diffusion spectrum obtained in a sample of a Winsor's I type microemulsion (Fig. 1, right) is flat for both oil and water. The average value of $D(\nu)$ obtained in the range 600-1600 Hz is $1.6 \cdot 10^{-9}$ and $8.0 \cdot 10^{-10}$ m^2/s, respectively for water and oil (heptane). Thus, neither for water or oil we were able to observe any short-time diffusion behaviour. The results are as expected in this type of microemulsion, with nano-sized and closely packed droplets [3].

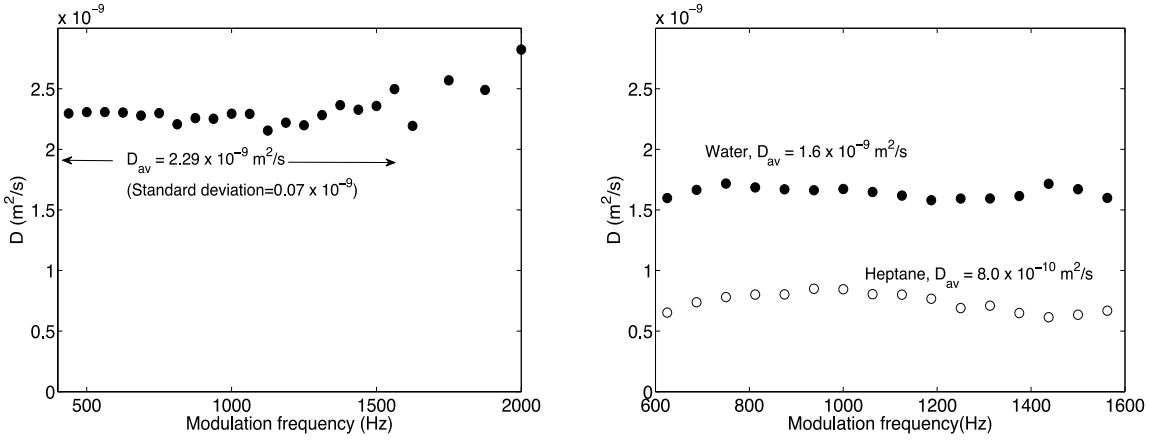

Figure 1: D(ν) in water (left) and in a Winsor's I type microemulsion (right).

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ABSTRACT TEMPLATE FOR THE 13TH NATIONAL MR MEETING

MEASURING WETTABILITY ALTERATION IN ROCK CORES USING CORRELATIONS BETWEEN DIFFUSION, SUSCEPTIBILITY GRADIENTS AND T_2.

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Abstract

We performed an NMR study of wettability alteration [1] in rock cores using G_0-T_2 and D-G_0 (where G_0 is the susceptibility gradient) correlations [3-5], enabling an investigation with a broader range of dynamic correlations compared to previous studies. The measurements were performed at 35°C on a Maran DRX 12 MHz spectrometer. Four Berea sandstone rock cores (strongly water wet) were aged in a heating cabinet for nine weeks. All cores reached a state of intermediate wettability (Amott).

In the G_0-T_2 correlations no significant changes was observed during aging. The average T_2 of oil decreased after forced water imbibition, indicating a more oil wet surface [2].

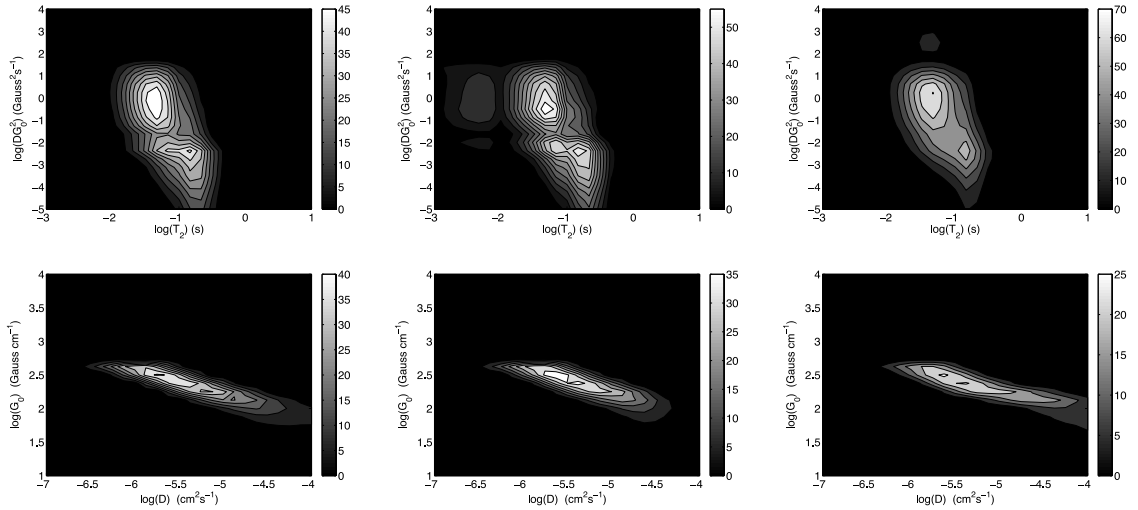

Fig. 1: Correlations between G_0-T_2 (upper row) and D-G_0 (lower row), before aging (left column), after aging (middle column), and after forced water imbibition (right column)

Inspection of the D-G_0 data showed that the average diffusivity of oil increased from $3.0 \cdot 10^{-6}$ to $3.4 \cdot 10^{-6}$ cm^2s^{-1} during the aging process, while the corresponding average value of G_0 decreased from 410 to 360 G/cm. These effects need to be investigated further. Overall, G_0-T_2 and D-G_0 measurements are promising techniques for characterization of wettability alteration in rock cores.

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Årsmøte for NSMR 2014

Tirsdag 14.januar 2014. Thon Hotel Prinsen. Kl. 17.15 – 18.00.

Sakspapirer – se sendt i egen innkalling.

Flavours of functional protein disorder

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Over the last decade, classical structural biology has experienced a shift towards a more dynamic paradigm with the realization that a protein can be fully functional even in the absence of a stable, folded structure. It is estimated that up to 40% of the proteins encoded by the human genome are intrinsically disordered or contain disordered regions of significant length (> 50 amino acids)[1]. These so-called intrinsically disordered proteins (IDPs) are inherently dynamic and ensemble descriptions have emerged as the preferred tool for representing the structural and dynamic properties of IDPs. NMR spectroscopy is uniquely suited to characterize disordered proteins at atomic resolution from parameters such as chemical shifts and residual dipolar couplings that report on all conformations sampled in solution up to the millisecond time scale[2].

I will present our recently developed sample-and-select approach to obtain representative ensemble descriptions of IDPs on the basis of experimental NMR data providing detailed insight into the conformational sampling of the IDPs at amino acid resolution[3–5]. Examples will be given of the characterization of functional protein disorder in important biological systems such as human viruses and cell signalling cascades[6].

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Why big fields for big molecules

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Highlighting the Protein for NMR Spectroscopy

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Abstract

Nuclear magnetic resonance (NMR) is a powerful method to determine protein dynamics and protein-ligand interactions. New NMR techniques have extended the size limit for the observation of NMR signals to over 100kDa, but signal overlap in large proteins can hinder spectral analysis.

New techniques enable labeling of a segment or single amino acids of the whole protein. Both techniques can be used for structural studies as well as for interaction studies. The reduced spectral complexity results in less overlap and faster analysis.

One method of segmental isotopic labeling relies on the protein splicing activity of split inteins. Protein splicing needs no cofactors or reagents to excise an intervening sequence and ligate two flanking N-and C-terminal segments via a peptide bound. As example of segmental isotopic labeling AlgE4 belongs to a family of structurally related alginate epimerases called AlgE1-7 produced by *Azotobacter vinelandii*. All these epimerases consist of only two modules, designated A-and R-module, which are present in varying numbers. The A-modules are catalytic active; the R-modules strongly enhance this activity although they don't possess any catalytic activity. AlgE4, has one N-terminal A-module and one R-module (A-R) and is the smallest member of the family. The A-modules consist of approximately 385 amino acids, whereas the R-modules consist of approximately 150 amino acids. The structure of the A-module of AlgE4 has been solved by X-ray crystallography and the structure of the R-module was recently solved by NMR spectroscopy. To investigate the role of the R-domains in the AlgE-family we obtained an active segmentally labeled AlgE4 (^{14}N-A-^{15}N-R) for alginate binding studies to the R-module by NMR [1].

Membrane proteins are challenging for structural biology. Many membrane proteins cannot be expressed in *Escherichia coli* system and 60% of the trans-membrane segment consists of the following 6 amino acid: Ala, Leu, Ile, Phe, Gly and Val. The recent development in cell-free expression system allows now to obtain high yield of active membrane proteins for NMR studies. An additional advantage of the cell-free system is the possibility of selective amino acid labeling. Proteorhodopsin (PR) is found in uncultivated marine bacteria. Over 4000 putative PRs have been reported. PRs are found in bacteria were heavily investigated due their anticipated role in ocean carbon cycling and energy flux. The NMR structure of the monomeric PR in the short-chain lipid diheptanoyl-phosphocholine (DHPC) was solved recently. This PR was expressed in an *E.coli* based cell-free expression system in present of Digitonin and DHPC. Combinatorial labeling allowed assigning 96% of the backbone resonances. The structure was solved by a combination of NOEs, distance restraints derived from paramagnetic relaxation enhancement and residual dipolar couplings [2, 3].

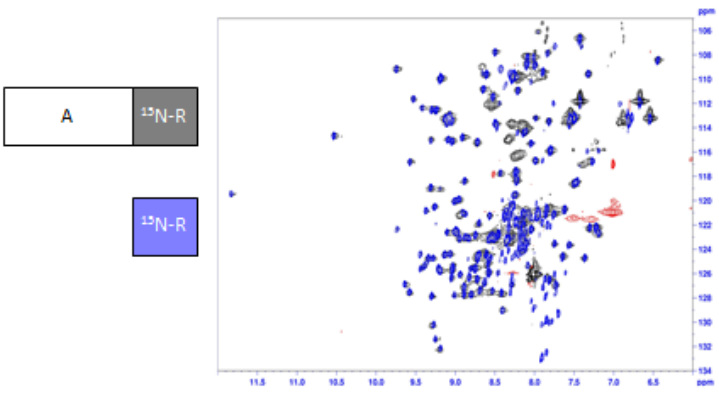

Figure 1: *Comparison of ^{15}N HSQC spectra of segmentally labeled AlgE4 (A-[^{15}N]-R) in black with the R-module alone (blue). Few amino acids at the splicing site were exchange to enhance the ligation. Except these signals the two spectra overlap perfectly.*

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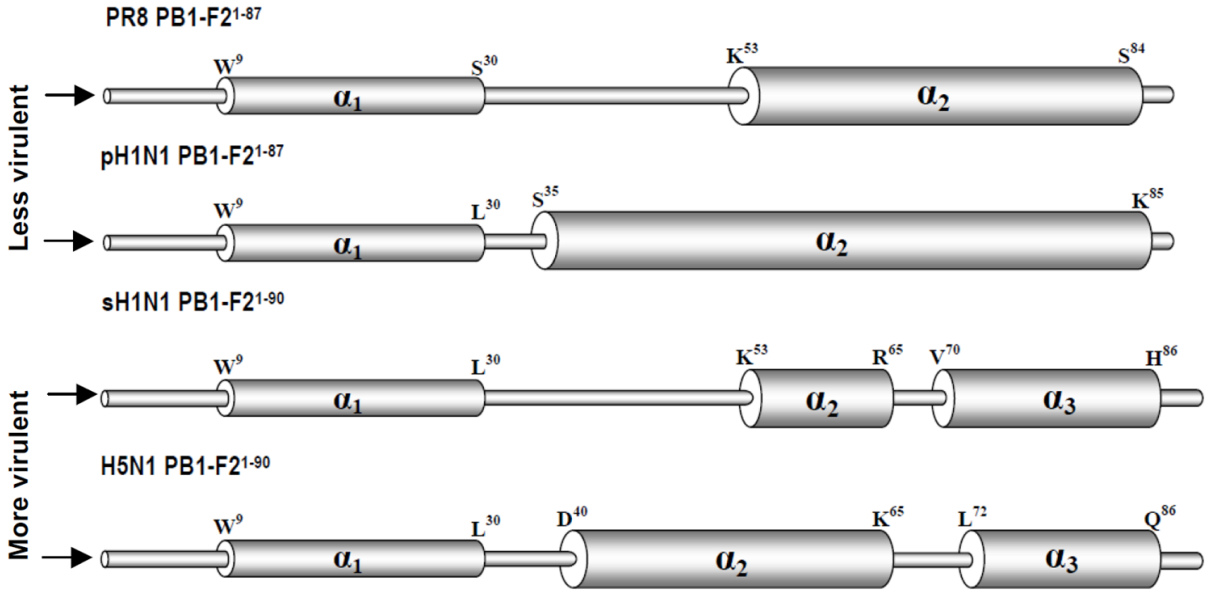
Influenza A virus PB1-F2 proteins –distinct structural signatures and highly pathogenic influenza viruses

Sara M.Ø. Solbak, Alok Sharma, Karsten Bruns, René Röder, David Mitzner, Friedrich Hahn, Rebekka Niebert, Anni Vedeler, Petra Henklein, Peter Henklein, Ulrich Schubert, Victor Wray, Torgils Fossen

The proapoptotic influenza A virus PB1-F2 protein contributes to viral pathogenicity and is present in most human and avian influenza isolates. The structures of full-length PB1-F2 of the influenza strains Pandemic flu 2009 H1N1, 1918 Spanish fluH1N1, Bird flu H5N1 and H1N1 PR8, have been characterized by NMR and CD spectroscopy. The study was conducted using chemically synthesized full-length PB1-F2 protein and fragments thereof. The amino acid residues 30–70 of PR8 PB1-F2 were found to be responsible for amyloid formation of the protein, which could be assigned to formation of β-sheet structures, although α-helices were the only structural features detected under conditions that mimic a membranous environment. At membranous conditions, in which the proteins are found in their most structured state, significant differences become apparent between the PB1-F2 variants investigated. In contrast to Pandemic flu 2009 H1N1 and PR8 PB1-F2, which exhibit a continuous extensive C-terminal α-helix, both Spanish flu H1N1 and Bird flu H5N1 PB1-F2 contain a loop region with residues 66–71 that divides the C-terminus into two shorter helices. The observed structural differences are located to the C-terminal ends of the proteins to which most of the known functions of these proteins have been assigned. A C-terminal helix–loop–helix motif might be a structural signature for PB1-F2 of the highly pathogenic influenza viruses as observed for 1918 Spanish fluH1N1 and Bird flu H5N1 PB1-F2. This signature could indicate the pathological nature of viruses emerging in the future and thus aid in the recognition of these viruses.



Structure and properties of wild-type and the R555W mutant of transforming growth factor beta induced protein

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Abstract
Hereditary mutations in the transforming growth factor beta induced (TGFBI) gene cause phenotypically distinct corneal dystrophies characterized by protein deposition in cornea. We show here that the R555W mutant of the fourth fasciclin 1 (FAS1-4) domain of the protein (TGFBIp/keratoepithelin/βig-h3), associated with granular corneal dystrophy type 1, is significantly less susceptible to proteolysis by thermolysin and trypsin than the WT domain. High-resolution liquid-state NMR of the WT and R555W mutant FAS1-4 domains revealed very similar structures except for the region around position 555. The R555W substitution causes W555 to be buried in an otherwise empty hydrophobic cavity of the FAS1-4 domain. The first thermolysin cleavage in the core of the FAS1-4 domain occurs on the N-terminal side of L558 adjacent to the R555 mutation. MD simulations indicated that the C-terminal end of helix α3′ containing this cleavage site is less flexible in the mutant domain, explaining the observed proteolytic resistance. This structural change also alters the electrostatic properties, which may explain increased propensity of the mutant to aggregate *in vitro* with TFE. Based on our results we propose that the R555W mutation disrupts the normal degradation/turnover of corneal TGFBIp, leading to accumulation and increased propensity to aggregate through electrostatic interactions.

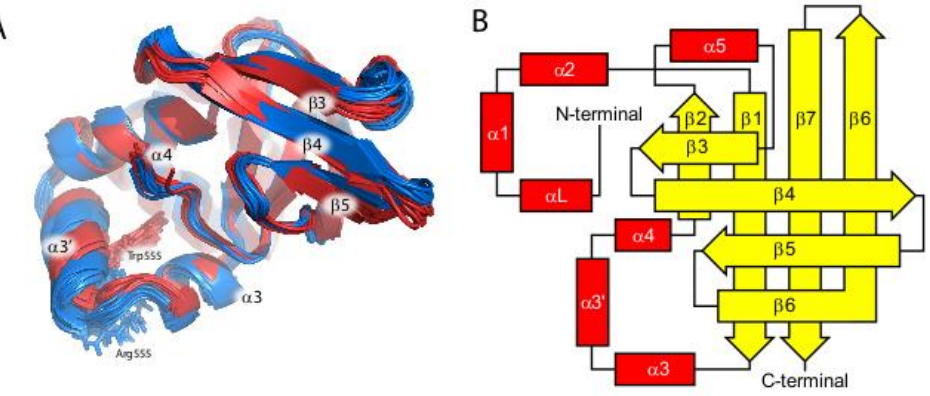

Figure 1: (A) Structure of WT FAS1-4 (blue) and R555W (red). (B) Schematic structure.

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J. Underhaug, H. Koldsø, K. Runager, J. T. Nielsen, C. S. Sørensen, T. Kristensen, D. E. Otzen, H. Karring, A. Malmendal, B. Schiøtt, J. J. Enghild, N. C. Nielsen, *BBA - Proteins. Proteom.* (2013).

NMR AS A TOOL IN ELUCIDATING COMPOUND STRUCTURE IN ORGANIC CHEMISTRY

Nebojša Simić

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Abstract

Almost 70 years after discovery of NMR phenomenon and broad application of NMR in various fields, its use in structure elucidation of organic compounds is still among the most important applications. A variety of experiments have been designed with the aim to extract information about a molecule, which could help in its identification. Certain experiments have been developed to provide specific information about the molecule: while some of them give information about connectivity, the others reveal stereochemistry, contributing to better understanding of compound's reactivity or biological function. The development of 2D and multi-D experiments represented a breakthrough in the NMR field and revolutionated NMR methods for structure elucidation. In ever growing number of new methods and applications, newbeginners in the NMR world are often faced with a challenging task to select the most appropriate experiments for their assignments. The aim of this lecture is to facilitate that task by giving a short overview on the standard NMR experiments (1D: proton-, ^{13}C- BB decoupled and DEPT; 2D: HSQC, HMQC, COSY, HMBC, HSQC-TOCSY, H2BC and NOESY) and strategies used for structure elucidation of organic compounds. Choice of experiments is discussed in light of their advantages and limitations. The applications are illustrated by practical examples.

Structure elucidation of Breitfussins A-H Isolated from the Arctic Hydrozoan *Thuiaria breitfussi*

Kine Østnes Hanssen[1], Bruno Schuler[2], Antony Williams[3], Taye Demissie[4], Espen Hansen[5], Johan Svenson[6], Jeanette H. Andersen[5], Marcel Jaspars[7], **Johan Isaksson[6*]**

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Abstract

Atomic force microscopy (AFM) with atomic resolution has for the first time been used to aid in the elucidation of unknown natural products.[1] AFM shows great potential for the structural characterization of planar, proton-poor compounds, as these compounds are difficult to elucidate with spectroscopic methods. We show here the combined use of spectroscopic methods, AFM, computer assisted structure elucidation (CASE) and electronic structure calculations (DFT) to solve the structures of breitfussins A and B, isolated from the Arctic hydrozoan *Thuiaria breitfussi*.
Six additional novel halogenated compounds, breitfussin C - H, were isolated along with two previously reported analogues, breitfussin A and B. The structures of the new compounds were elucidated by NMR and MS.
This study presents the first compounds from the hydrozoan *Thuiria breitfussi*, revealing uniquely modified dipeptides, with a framework containing a combination of indole-, oxazole- and pyrrole rings.

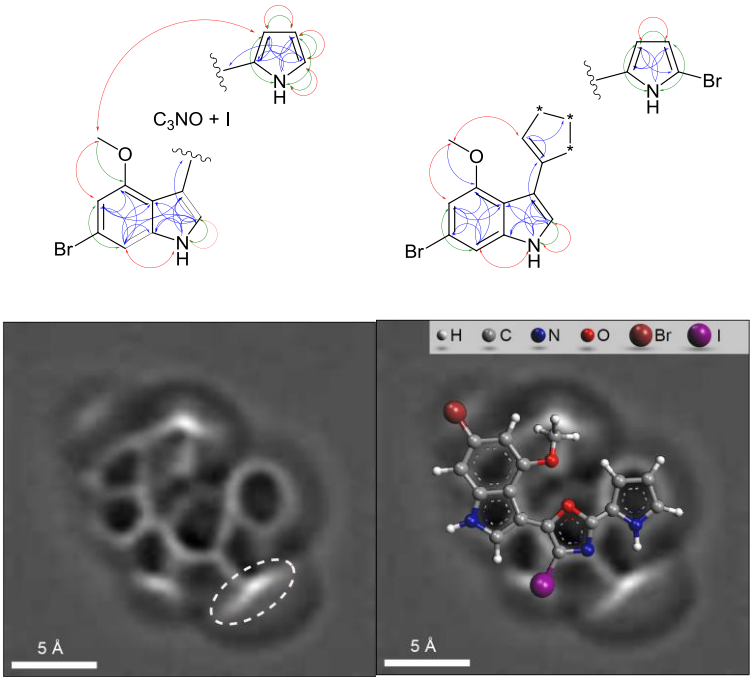

Figure 1: Figure captions are entered below the figures.

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Sclerochloa dura: A new source of anti-inflammatory compounds

Syed Majid Bukhari[1], Astrid Jullumstrø Feuerherm[2], Hanna Maja Tunset[2], Stian Moe Isaksen[1], Mari Sæther[2], Thor Håkon Krane Thvedt[1], Susana Villa Gonzalez[1], Rudolf Schmid[1], Erik Fuglseth[3], Bojan Zlatkovic[4], Berit Johansen[2], Nebojsa Simic[1].

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Abstract

Sclerochloa dura plant is traditionally used in small communities in South-Western parts of Balkan Peninsula for treatment of menstrual disorders characterized by pain and excessive bleeding. The focus of this investigation was to identify the compounds present in the plant extract which show inhibitory effects on the release of arachidonic acid (AA) in an AA release assay. This assay was chosen as the AA metabolites are known to propagate both pain and cramping [1-3]. The methanol extract of the plant was subjected to a multistage fractionation approach by liquid chromatography to isolate bioactive fractions. The structure elucidation of enriched compounds in the bioactive fractions was done by using NMR operating at a proton frequency of 600.18 MHz, with a 5 mm triple-resonance cryo probe, equipped with a z-gradient. A set of 1D and 2D experiments including ^{1}H NMR, ^{13}C NMR, H,H-COSY, HSQC, HMBC, HSQC-TOCSY and NOESY enabled to get necessary information about the structures of molecules. An NMR software Top Spin 3.1 was used to process all the experimental data. Accurate mass determination was performed by ESI-TOF-MS. By using AA release assay as a guide for biological and anti-inflammatory activity, the novel compound 1-*O*-(3-*O*-linolenoyl-6-deoxy-6-sulfo-*α*-D-glucopyranosyl)-glycerol was identified in methanol extract from aerial parts of *Sclerochloa dura*. This glycerol derivative compound was found to be an effective inhibitor of AA release with an IC_{50} value of 114.1 ± 31.1 µM. Further, five additional compounds were identified in the methanolic extract of *S. dura* with strong anti-inflammatory activity in the AA release assay. These five compounds include a glycerol derivative [1-*O*-feruloyl glycerol], three flavonoids [isovitexin, tricin 4′-*O*-(erythro-*β*-guaiacylglyceryl) ether 7-*O*-*β*-glucopyranoside and tricin 7-glucoside] and a glucoside [byzantionoside B].

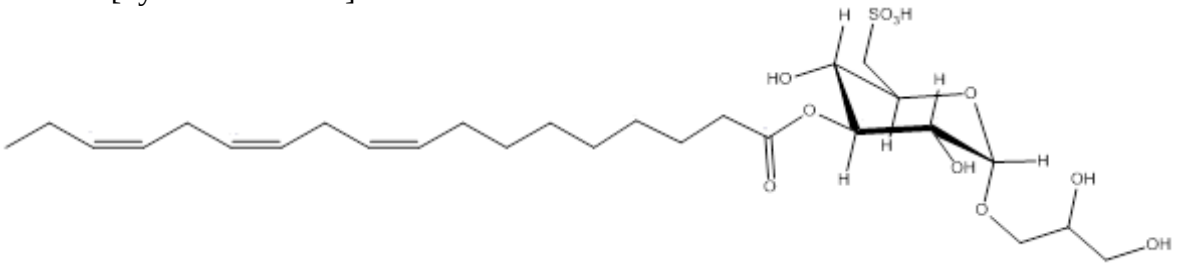

Figure:1-O-(3-O-linolenoyl-6-deoxy-6-sulfo-α-D-glucopyranosyl)-glycerol

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COMPOUND IDENTIFICATION BY ^{13}C HSQC CORRELATION PLOTS

Tommy Öman[1], May-Britt Tessem[2,3], Tone F. Bathen[2,3], Helena Bertilsson[4], Anders Angelsen[4,5], Henrik Antti[1], Mattias Hedenström[1], **Trygve Andreassen***[,6]

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Abstract
2D NMR experiments are excellent tools for elucidating the structures of novel organic compounds. For complex mixtures, structure elucidation becomes much more challenging, since it is often unclear which signals belong to which compound. When analyzing multiple spectra of similar (non-identical) mixtures, such as in metabolomic studies, signals from the same compound will be strongly correlated. This has been extensively used on ^{1}H data (STOCSY [1]) and very recently demonstrated on ^{13}C HSQC data (2). In this work we have used ^{13}C HSQC correlation plots to unambiguously identify known metabolites from post-prostatic palpation urine (Figure 1). The method shows promise as a useful aid for identifying novel compounds from mixtures, especially for compounds containing isolated spin systems which cannot be connected by conventional NMR experiments.

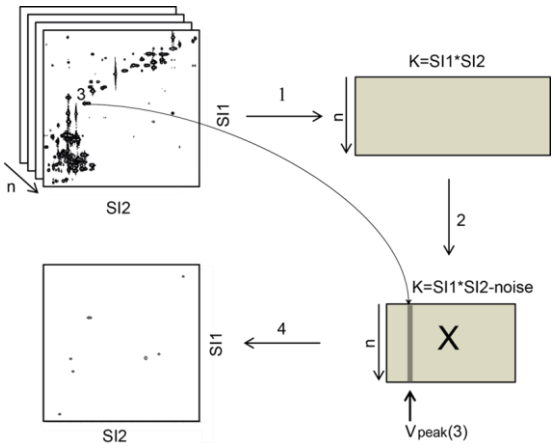

Figure 1: Generating HSQC correlation plots from multiple HSQC spectra.

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The pulsed field gradient (PFG) NMR method is a well-established technique for studying molecular motion without disturbing the system under investigation, the non-invasive approach. A large variety of sequences or techniques have been proposed that are optimized for different tasks, such as diffusion measurements in the presence of internal magnetic field gradients, convection, or large eddy current field transients. This variety of PFG sequences not only reflects the increasing interest in using the NMR technique in diffusion studies, but also shows that it is not necessarily a trivial task to extract the true diffusion coefficient from a PFG NMR experiment.

In the following some home brewed PFG-NMR sequences that bypass the requirement of 5 times T1 will be presented, accompanied with examples of application.

ABSTRACT TEMPLATE FOR THE 13TH NATIONAL MR MEETING

WATER STRUCTURE NEAR A SOLID SURFACE AS INVESTIGATED BY NMR SPECTROSCOPY.

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Abstract

The properties of water in different environments have been the focus of numerous studies since the early 20th century. The behavior of water molecules in the vicinity of solid surfaces is not clarified, for instance the range of ordering of water molecules due to presence of a silica surface is not fully understood. Furthermore, in samples containing both adsorbed and bulk water it is difficult to distinguish between water in the two states experimentally; hence, most previous studies have been conducted either by molecular modelling and/or with only few monolayers to sub-monolayer water surface coverage. Here we employ NMR spectroscopy[1,2] to investigate the extent of water ordering at a silica surface.

A reason for the large interest concerning the properties of adsorbed water is that most surface science focus on aqueous environments where the surface induced water structures play an important role in the surface behavior of other molecules.[3] For example, in medicinal and biological research, knowledge about molecular interaction with the cell membrane or macromolecules is important in order to understand biological mechanisms and the effects of drugs.[4] Furthermore, surface chemistry is important in the petroleum industry due to the significance of liquid transport properties in porous media and enhanced oil recovery (EOR) processes.[5]

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SPATIAL REDISTRIBUTION OF WATER IN MEAT DURING DRIP LOSS AS PROBED BY LOW FIELD ^{1}H-NMR

Eddy W. Hansen[1], Han Zhu[2]

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Abstract

In accordance with previous NMR spin-spin relaxation rate measurements three distinct water components in meat/muscle are identified [1] of which one component reveals neither a change in intensity nor a change in relaxation rate with (drip) time (t_d). The two remaining water components are assigned to intra- and extra cellular water, respectively. By introducing a first order reaction model, the redistribution of water between the two regions during drip loss can be modeled, and enables the corresponding rate constants to be derived. As a consequence, the time behavior of both the intensity and the spin-spin relaxation rate within the two spatial domains can be calculated, as exemplified in Figure 1.

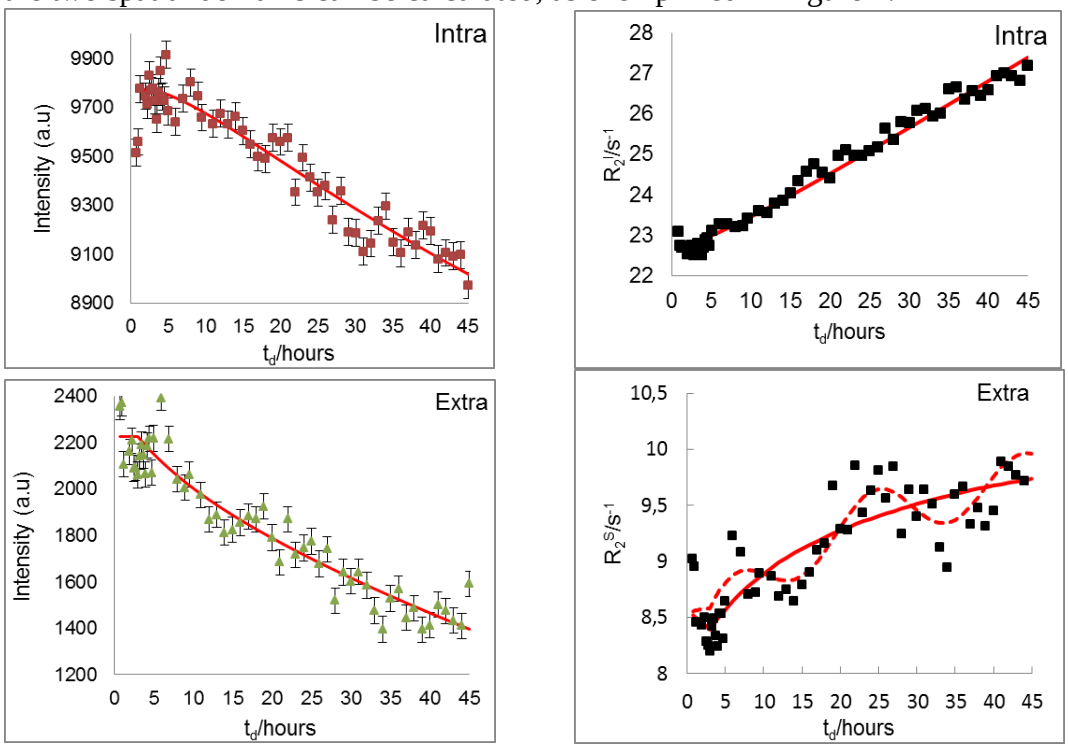

Figure 1: Left) The intensity and Right) corresponding spin-spin relaxation rate of intra- and extra cellular water during (drip) time. The red curves represent model fits. The apparent oscillation of the extra cellular water spin-spin relaxation rate during 'drip is illustrated by the dotted curve.

In the presentation, the first-order reaction model will be discussed with the objective to rationalize the observations shown in Figure 1. Also, the apparent oscillating behavior of the extra cellular water relaxation rate during drip will be considered.

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ABSTRACT TEMPLATE FOR THE 13TH NATIONAL MR MEETING

CORRELATIONS BETWEEN INHOMOGENEOUS MAGNETIC FIELDS, INTERNAL GRADIENTS, AND TRANSVERSE RELAXATION, AS A PROBE FOR PORE GEOMETRY AND HETEROGENEITY.

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Abstract

When a porous media is placed in a static magnetic field, a spatial inhomogeneous magnetic field (ΔB_0), which depends on the geometry of the porous network and on the differences in magnetic susceptibilities, is generated within the media [1]. This spatial inhomogeneity of the magnetic field causes inhomogeneous line broadening in the NMR spectrum of a confined liquid, and leads to creation of internal gradients within the sample. It is well known that the distribution of relaxation times and internal gradients within the porous media both can be related to the geometry of the system. In addition, it has been shown that different values of the spatial inhomogeneous magnetic field (i.e. different parts of the NMR spectrum) also represent water in different parts of the porous network [2,3].

We have applied 2D NMR experiments where the spatial inhomogeneous magnetic field, ΔB_0 is correlated to both the internal magnetic field gradients (G_0) and the transverse relaxation time (T_2). This enables us to obtain more localized information about the geometry of the porous network. The experiments were performed on different types of close packing of glass beads, all saturated with water. The obtained results show that the distribution of G_0 and T_2 obtained for different values of the spatial inhomogeneous magnetic field can be related to the local geometry of the different samples. An example is shown in Figure 1.

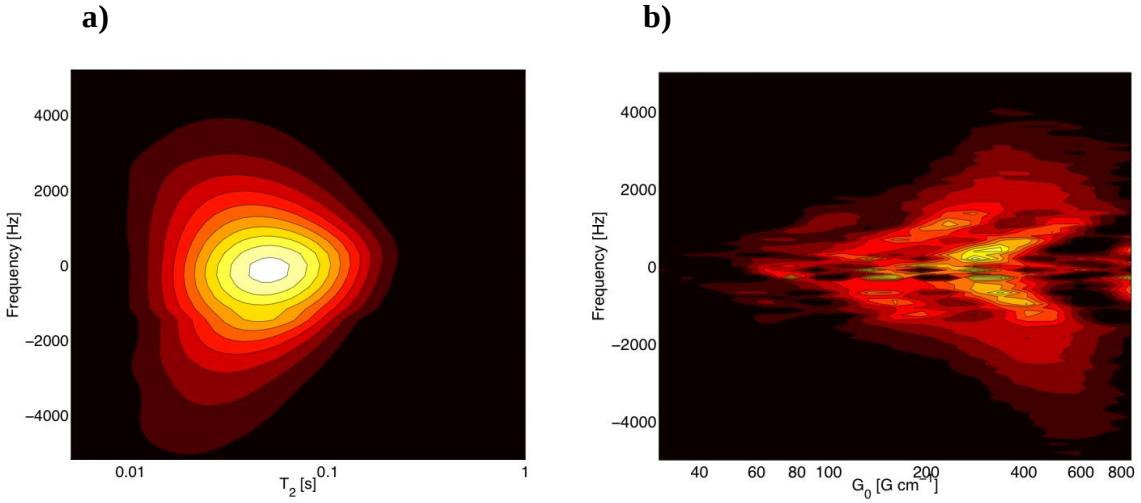

Figure 1: Dynamic correlations: a) ΔB_0-T_2 and b) ΔB_0-G_0. Water in 100 μm glass beads.

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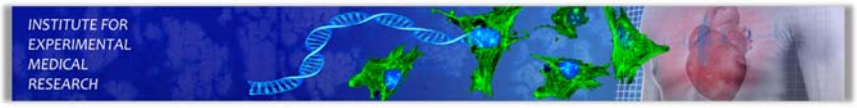

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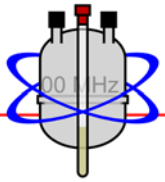
University of Oslo  NMR Center

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