1.0 General Information

Proposal for the establishment of a network of German Core NMR Centers

1.1 Applicants

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1.2 Topic

Establishing a Network of German NMR Centers

1.3 Research area and field of work

Chemistry, Biophysics, Analytical Sciences, Material Sciences, Structural Biology

1.4 Anticipated total duration

3 years

1.5 Application period

As soon as possible

1.6 Summary

NMR spectroscopy is among the most important analytical methods with unbeaten impact on important areas in Chemistry, Biology, Physics and Medicine. It is an expert technology where quality of both instrumentation and methodological skills are important to ensure best utilization of the technology. NMR spectroscopy is a major analytical and spectroscopic technique with a wide range of applications. There are two major areas of NMR spectroscopy, namely liquid-state NMR and solid-state NMR spectroscopy, with differing levels of technology transfer from the expert level to the user level. The NMR spectroscopic groups in Germany are organized within a group in the GDCh (Fachgruppe Magnetische Resonanz der Gesellschaft Deutscher Chemiker). It is the overall aim of the proposal to establish a network of German NMR centers in Universities and non-University institutes together with representatives from industries and manufacturers and from major German funding bodies to exploit at best the broad application envelope of NMR spectroscopy.

2.0 State of the art and preliminary work

The application intends to establish a network of NMR centers within Germany. The goal is to coordinate, mutually support and promote the application of NMR spectroscopy in all research disciplines. Representatives of the following groups participate in the application:

Group A: Core organizing partners	A1: Ctr for Biomolecular Magnetic Resonance (BMRZ), European RI PI: H. Schwalbe, C. Glaubitz, V. Dötsch, P. Güntert, J. Wöhnert	Structure determination of biological molecules and their macromolecular complexes, structure-function-mechanisms and dynamic assembly of biological macromolecules, methods development. ls cryo-950 MHz, ss 850 MHz, ls cryo-900 MHz NMR, cryo 800 MHz, 800 MHz, cryo-700 MHz and two lasers for time-resolved NMR, ss 600 MHz, ss 2× 400 MHz, ls cryo-600 MHz with fast kinetic device, 600 MHz, 500 MHz, 400 MHz, 400 MHz wide bore
	A2: Bavarian NMR Center (BNMRZ) PI: M. Sattler, B. Reif, S. Glaser, H. Kessler	Structure, molecular recognition and dynamics of biomolecules in solution and solids, methods development (ls, ss NMR), modulation of conformation and/or function of proteins upon binding to RNA and small molecules. ls cryo-900 MHz, ls cryo-800 MHz, ls/ss 750 MHz, ls cryo-600 MHz, ls 600 MHz, ls cryo-500 MHz, ss 500 MHz wide bore, ss 400 MHz wide bore (for service unit refer to group C descriptions below)
Group B: German University NMR Centers	B1: Univ. Halle PI: J. Balbach, K. Saalwächter	Structure determination of proteins, time-resolved NMR, protein folding ls 600 MHz, ls 2× 400 MHz
	B2: Univ. Regensburg, PI: R. Geschwind, H.R. Kalbitzer	Structure determination of biological macromolecules, molecular interactions in metallorganic and bioorganic systems, structure-reactivity-relations, high-pressure NMR. ls cryo-800 MHz, ls cryo-600 MHz, 500 MHz
	B3: Univ. Leipzig, PI: D. Huster	Solid-state NMR studies of membrane proteins. ss cryo-800 MHz
	B4: Univ. Lübeck, PI: T. Peters	NMR studies of oligosaccharide and Glycoproteins. ls 700 MHz with cryoprobe, ls 600 MHz, 500 MHz
	B5: Univ. Darmstadt, PI: M. Reggelin, C. Thiele	NMR spectroscopy of small molecules. ls 600 MHz, 500 MHz
	B6: Univ. Bayreuth, PI: P. Rösch	Structure determination of biological macromolecules and molecular interactions. ls 800 MHz, 700 MHz, 2× 600 MHz, 400 MHz
	B7: Univ. Düsseldorf, PI: D. Willbold	Structure determination of biological macromolecules and molecular interactions. ls 900 MHz ls/ss 800 MHz, 2* ls 600 MHz, 2* ss 600 MHz
Group C: NMR Service units at Universities	B8: Univ. Heidelberg: J. Graf	NMR spectroscopy on small molecules. 600 MHz, 400 MHz, 200 MHz.
	B9: Univ. Frankfurt: C. Richter	refer to group A descriptions above

	B10: Technische Univ. München: W. Eisenreich	200 MHz, 250 MHz, hands-on 250 MHz, 300 MHz, 360 MHz for multinuclear applications, 500 MHz, Cryo-500 MHz ($^{13}C/^{29}Si/^{19}F/^{31}P$-QNP), 500 MHz ($^{19}F$-Lock)
	B11: Univ. Hamburg: T. Hackl	NMR Analysis of glycoconjugates, ligand-receptor interactions, protein-protein interactions. 700 MHz with cryoprobe, ls 500 MHz
Group D: German non-University Centers	C1: MPI Göttingen: C. Griesinger	Methods development, structural biology of biological macromolecules, investigations of dynamics. Signal molecules and membrane proteins 900 MHz, 800 MHz, 700 MHz, 600 MHz cryoprobe, ss 600 MHz, ss 400 MHz, 600 MHz, 400 MHz
	C2: AWI Bremerhaven: M. Köck	NMR studies on marine natural products
	C3: Leibniz-Institut für Polymerforschung Dresden: U. Scheler	NMR methods for the characterization of functionalized polymers and their application to polymers and polyelectrolytes
	C4: Helmholtz-Zentrum Karlsruhe: A. Ulrich	Solid-state NMR on membrane proteins and membrane-active peptides ss: 600 MHz, 2* 500 MHz, 300 MHz ls: 600 MHz.
	C5: Helmholtz-Zentrum München: M. Sattler	refer to group A descriptions above
	C6: Helmholtz-Zentrum Jülich: D. Willbold	refer to group B descriptions above
	C7: Leibniz-Institut für Molekulare Pharmakologie (FMP): H. Oschkinat	ls: 300 MHZ, 3 * 600 MHz, 750 MHz, 900 MHz, ss: 2 * 400 MHz, 600 MHz, 700 MHz
Group E: Industry	E1: NMR manufacturing Companies: Bruker, Agilent	
	E2: NMR units at Industry: BASF, Bayer, Merck, Novartis, Sanofi	
Group F: Fachgruppe Magnetische Resonanz der GDCH	F: Vorsitzender der Fachgruppe Magnetische Resonanz: Dr. E. Haupt	
Group G: Funding bodies	G: DFG, MPG, Helmholtz, Leibniz	

abbreviations: ls → liquid state, ss → solid state

The groups A-F cover the multiple aspects of NMR and are therefore import for the network **G-NMR**.

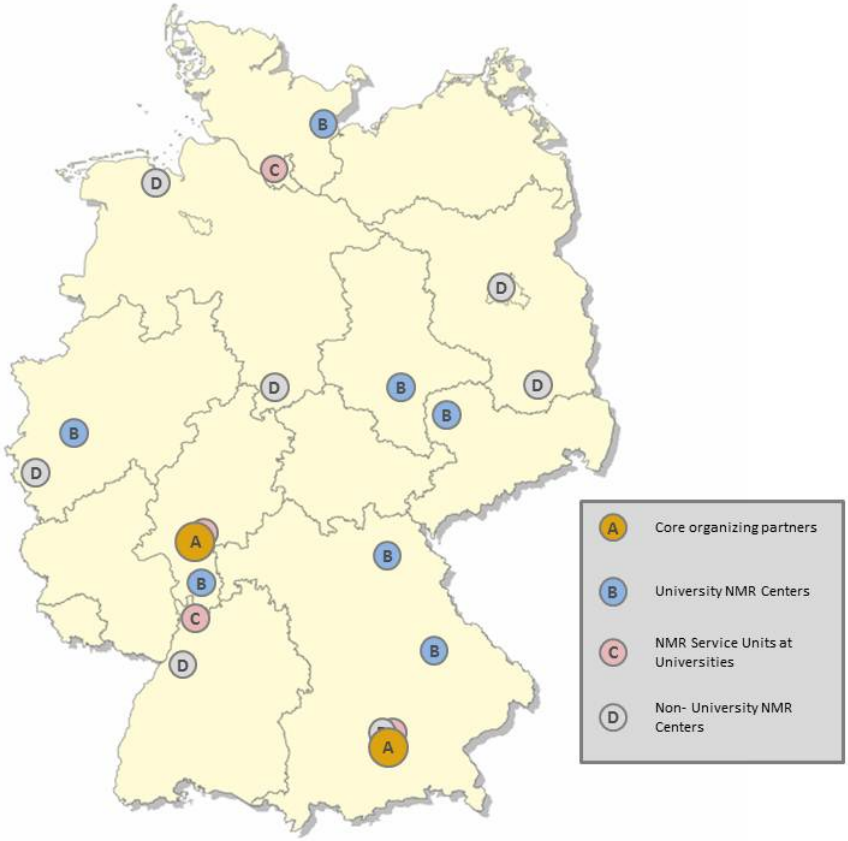
1.) NMR is applied as routine analytical tool in particular in all chemical applications. Every university houses **NMR service units** with several NMR spectrometers, automation hardware etc. Outcomes of research objectives 3.1.1, 3.1.2, 3.1.3, 3.1.5, 3.1.6, and 3.1.8 will have important impact on service units at Universities.
2.) Chemical, biochemical, biophysical, and polymer sciences all benefit from active **NMR research**. Many methods initially developed in a particular field of NMR have an impact for all the other research areas. The development of gradient spectroscopy may serve as a particular important example. The major representatives of German NMR in all these areas are partners in the proposed network. Outcomes of research objectives 3.1.1, 3.1.2, 3.1.3, 3.1.4 will improve the quality of research.
3.) NMR hardware and the required scientific and technological expertise are cost intensive. Major **investments in NMR** in the range between 3 to 10's of millions Euro are required, and both running as well as maintenance costs are significant. DFG and other funding bodies now allow for applying for funds for NMR research provided user concepts have been developed.

The development of common policies in **user concepts in research and in service units** is a major aspect of the proposal. Outcomes of research objectives 3.1.1 and 3.1.7 will have major impact for this topic.

4.) Education on the principles of NMR spectroscopy and its various applications is integral part of the **teaching curricula** in Chemistry, Biochemistry, Bioinformatics and Biophysics. NMR spectroscopy is important for the chemical and pharmaceutical industries for analytical purposes, e.g., in the context of NMR-based drug development. The mutual exchange of the requirements and concepts is important and substantial synergetic effects can be expected within the G-NMR consortium. Outcomes of research objectives 3.1.3 and 3.1.5 will have major impact for this topic.

2.1 Description

G-NMR combines 13 NMR centers and 4 service units that are recognized NMR centers at regional, national as well as international level. The locations of the centers cover all regional areas in Germany, and the participating centers are funded by all major funding institutions (Universities, DFG, MPG, Helmholtz, Leibniz).



In the following, we introduce as representative examples the NMR centers in Frankfurt and Munich.

BMRZ: Center for Biomolecular Magnetic Resonance at Goethe-University Frankfurt

BMRZ is part of the University of Frankfurt and participates as Research Infrastructure in the Access program of the European commission since 1995. H. Schwalbe, PI of this application, has coordinated 5 European projects (EU-NMR, e-NMR, EAST-NMR, UPMAN, Smartscreen) and is speaker of the cluster of excellence: macromolecular complexes and the collaborative research center (SFB 902): molecular principles of RNA-based regulation. In the European framework, BMRZ is offering up to 300 days of transnational access to European users in the fields of liquid- and solid-state NMR and EPR spectroscopy. BMRZ houses in total eleven liquid-state (500-950 MHz) and four solid-state NMR spectrometers (400-850 MHz). High level technical support is provided by Dr. Christian Richter and Dr. Frank Löhr. Both are experts in liquid-state NMR spectroscopy. Management aspects of the facility are organized by Dr. Marco Betz.

NMR service unit at the Institute for Organic Chemistry, Goethe-University Frankfurt

The NMR service unit at Frankfurt university can be considered typical and similar units are in place in all German university in the Chemistry departments. It houses 5 low to medium field NMR spectrometers (250, 300, 300, 400, partial access to 600 MHz). Spectrometers are equipped with sample changers, automation software provided by the manufacturers, gradient probes, low-temperature units, probes for ^{1}H- as well as low-γ-detection. The service unit is supervised by Dr. Christian Richter (with substitutes in place: Dr. Julia Wirmer-Bartoschek) and daily work is carried out by two technical assistants, Reinhard Olbrich and Stefan Bihler.

Figure 1: DFG-funded highest field NMR spectrometers. (left) 850 MHz wide-bore NMR spectrometer with facilities for magic angle spinning (MAS) low-temperature NMR experiments, (middle) worldwide 3rd 900 MHz liquid-state NMR spectrometer, (right) world 1st 950 MHz ultrashielded NMR spectrometer.

BNMRZ: Bavarian NMR Center at Technische Universität München

The Bavarian NMR Center (BNMRZ) http://www.bnmrz.org is located at the Department Chemie of the Technische Universität München (TUM) and is jointly supported by TUM and the Helmholtz Zentrum München (HMGU). It was founded in 2001 by Horst Kessler with support from the State of Bavaria and represents an internationally renowned high-field NMR facility for the development and applications of state-of-the-art NMR of biological macromolecules, Since 2007, Michael Sattler has been appointed as a new Chair in Biomolecular NMR Spectroscopy and Director of the Institute of Structural Biology at the Helmholtz Zentrum München. The PIs at the BNMRZ are key investigators in various national (CiPS-M DFG Cluster of Excellence, Elitenetzwerk Bayern, Graduate Schools), and international research networks (EU projects 3D Repertoire, NIM3, FSG-V-RNA).
The BNMRZ offers a unique infrastructure in the south of Germany with 7 state-of-the-art liquid state (250-900 MHz) and 400 and 500 MHz solid state NMR spectrometers. It provides access for research groups from universities, MPIs and Helmholtz institutes in Bavaria and beyond. Scientific, technical and user support at the BNMRZ is provided by permanent staff PD Dr. Gerd Gemmecker and Dr. Rainer Haessner.

Figure 2: Highfield NMR spectrometers at the BNMRZ (cryo-500 MHz, not shown). From left to right: 500 MHz wide bore (for solid state NMR), 600 MHz, cryo-600 MHz, 750 MHz (liquid & solid state NMR - no. 3 world-wide), cryo-800 MHz, worlds first cryo-900 MHz.

NMR service unit at the Chemistry, TU München

The routine NMR pool at TUM is currently used for by the sections Organic Chemistry, Macromolecular Chemistry and Biochemistry of the department. It currently comprises seven medium field and high field spectrometers (200 – 500 MHz) for general purpose and several dedicated application areas ($^{1}H/^{13}C$ detection; heteronuclear capabilities; cryo-QNP for $^{13}C/^{29}Si/^{19}F/^{31}P$ detection). Most of the spectrometers run in automation mode and are equipped with sample changers. The service unit is supervised by PD Dr. Wolfgang Eisenreich, and a technician is responsible for routine maintenance. The NMR pool is used for both teaching and research purposes, i.e., access to the spectrometers is possible for Bachelor/Master students as well as doctoral students and postdocs. In addition, a "hands-on" 250 MHz spectrometer can be used by the students (after obligatory introduction) in full manual mode (sample change, shimming, pulse calibration, 1D measurements) for educational purposes.

2.2 Project-related list of publications

C. Griesinger, **H. Schwalbe**, J. Schleucher, **M. Sattler** (1994) Proton Detected Heteronuclear NMR. In Two Dimensional NMR Spectroscopy: Applications for Chemists and Biochemists. p. 457-580.

M. Sattler, J. Schleucher, C. Griesinger (1999) Heteronuclear multidimensional NMR experiments for the structure determination of proteins in solution employing pulsed field gradients. Prog. NMR Spectrosc. 34, 93-158

H. Schwalbe, T. Carlomagno, M. Hennig, J. Junker, B. Reif, C. Richter, C. Griesinger (2001) Cross-correlated relaxation measurement of angles between tensorial interactions. Methods Enzymol. **338**, 35-81.

C. Griesinger, M. Hennig, J. Marino, B. Reif, C. Richter, **H. Schwalbe** (2002) Methods for the determination of torsion angle restraints in biomacromolecules. in Modern Techniques in Protein NMR, p. 259-367.

B. Fürtig, C. Richter, J. Wöhnert, **H. Schwalbe** (2003) NMR spectroscopy of RNA. ChemBioChem **4**, 936-962.

H. Schwalbe, H.U. Stilz, H. Kessler (2005) Editorial: NMR spectroscopy of Biomacromolecules in Drug Discovery and Beyond. ChemBioChem **6**, 1475-1478.

B. Simon, T. Madl, C.D. Mackereth, M. Nilges, **M. Sattler** (2010) An efficient protocol for NMR-spectroscopy-based structure determination of protein complexes in solution. Angew Chem Int Ed Engl 49, 1967-70

T. Madl, T. Güttler, D. Görlich, **M. Sattler** (2011) Structural Analysis of Large Protein Complexes Using Solvent Paramagnetic Relaxation Enhancements. Angew Chem Int Ed Engl. 50, 3993-7.

T. Madl, F. Gabel, **M. Sattler** (2011) NMR and small-angle scattering-based structural analysis of protein complexes in solution. J. Struct. Biol. 173, 472-82

3.0 Objectives and work schedule

3.1 Objectives

It is the overall objective of G-NMR to generate a network of German NMR centers for mutual support and exchange of technology, working procedures, educational material and alike. The concept is to involve all partners of the consortium in a bottom-up strategy and to achieve consensus on general aspect on running and maintaining NMR facilities and service units at University in order to best exploit the available resources. Networking of research centers also involves industries that either build and develop NMR spectrometers (Bruker and Agilent) or that heavily rely on the application of NMR spectroscopy. Exchange with these two groups in industry is part of the network application. In addition, discussions with funding bodies on funding requirements and opportunities are an important aim. NMR facilities differ in their size and scope and range from local, regional, national to international centers. The network will monitor developments on the European level to streamline the requirements for national and international funding bodies. Two core centers in Frankfurt and Munich take the responsibility for achieving the goals of the consortium. Actions are intended in eight areas (3.1.1.-3.1.8.) as outlined below.

3.1.1. By-laws for use of NMR facilities and service units (dt. Nutzerordnung) (involved groups: A,B,C,F,G)

Upgrading and maintenance of NMR center and service units is expensive. Often, only insufficient funds are available at the University centers. The DFG now allows researchers to apply for funds to cover the expenses connected with the execution of experiments in the context of a particular research project. One requirement is a clear definition of the costs involved (hourly rates) and the conditions for use of the equipment in form of written by-laws (dt. Nutzerordnung). While there are clear common standards and by-laws in some research fields (e.g. MRI, Cryo-EM), such a consensus does not yet exist on the costs required to operate an NMR facility as well as the additional costs to utilize NMR machines in research. It is the aim of the network center application to develop such a consensus that a.) defines common aspects of NMR requirements and b.) allows for sufficient individual adaptation honoring the different situations within the consortium.
The by-laws will address a number of key points, taking into account previous discussions within the EU FP7 ERA-net instruments project (http://www.era-instruments.eu/, SAB member: M. Sattler): a.) handling of measurement time requests, b.) acknowledgement of funding sources, contributions to the work, handling of co-authorship on publications (what defines collaboration, what defines acknowledgement), c.) ethical conduct of experiments and their interpretation, d.) data ownership (intellectual property) and data handling (access and storage).

The following steps are envisioned:

1.) Writing of a draft by-law for NMR research facilities and for NMR service units by partners A1 and A2. Circulation of this draft among the partners in group B and C at Universities.
2.) Initial discussion of the draft with feedback from the broad NMR community and from DFG
3.) Optimization of the draft by-law. Involvement of individual groups, consensus building within the community.
4.) Final standard by-laws made available on the web-page of the consortium.
5.) Discussion with DFG of accepting the by-laws as draft by-laws for DFG applications.

The exact timelines are outlined under 3.2.

3.1.2. Informatics aspects of G-NMR (involved groups: A,B,C,D,E)

Informatics is a key component for NMR facilities and service units. G-NMR will address some particular important aspects within the context of the network to provide a common platform:

1.) **Measurement time allocation** with automatic referral to reviewers and feedback options. Existing software platforms have been developed by partner A1 in the context of European funding initiatives and have already been implemented in France for measurement time distribution. These platforms will be adapted to the current objectives and disseminated to the distributed NMR infrastructures.

2.) **Workflow** A structured as well as transparent workflow with respect to all aspects of NMR investigations will be supported. Each step from NMR recordings, raw data transformation & analysis to the scientific publication itself will be logged and documented. The spectrometer administration, namely the „spectrometer booking and logging" will be simplified and rules for access will be standardised.
3.) **Remote access** for monitoring NMR experiments and their results in a remote manner via the internet will be discussed and made available.
4.) **Exchange of educational material** will be facilitated by establishing exchange platforms as outlined under 3.1.3. and 3.1.5.

The results of these tasks will be offered as a suggestion to the partners in the consortium, not an obligation. Of course, wide spread use is envisioned and feedback will optimize the informatics resources and help assuring good scientific practice.

3.1.3. Technology transfer and training (involved groups: A-F)

NMR spectroscopy is the standard analytical method for characterizing molecules synthesized in many chemistry labs. Need for NMR technology transfer is covered in 3.1.5 and 3.1.6. NMR is also a major spectroscopic method in biochemical and polymer sciences. Methods are being developed and applied in the laboratories of the partners in the network. From optimized technology transfer, both methods developers and methods appliers benefit for obvious reasons. Therefore, aspects of optimizing technology transfer will be introduced here.

Technology transfer. While solution-state NMR experiments for both applications in Chemistry and Biology are meanwhile well established, different combinations and implementations of experiments are still used at different NMR facilities. We will collect these experiments and approaches and try to **identify a common set of experiments and implementations**, especially for biomolecular solution state NMR applications (which concerns most of the facilities in the network). The goal will be to offer a set of typical and most commonly used experiments with different implementations, for example, regarding the use of water-flip-back, sensitivity enhancement, non-uniform sampling, gradient coherence selection, magnetization transfers etc.. These will represent a standard repertoire of experiments available and usable at the different sites of the NMR network. This pulse sequence library will develop and start from standard experiments provided by the manufacturers (Bruker and Agilent) who will be involved in a working group that performs this task.

Training. While local introductory (or advanced) courses already exists at many NMR facilities, there is currently little exchange between the different centers with respect to subjects covered by the courses, levels of expertise required for advanced courses, teaching techniques and materials in particular. To improve this situation, a network will be set up, involving all people concerned (i.e., staff from larger NMR centers, NMR service units at universities, research institutes and industry). In addition to personal meetings that should take place at least once per year at the meeting of the German Magnetic Resonance group (Fachgruppe MR), further exchange will be organized electronically utilizing internet-based exchange platforms that will be setup for G-NMR under 3.1.2.

Workshops/courses for basic NMR skills will be offered on a regular schedule, depending on the needs of the local users (e.g., once per semester at universities). These courses are intended for master students, doctoral students and Postdoc working in the research groups of the participating principle investigators. Within G-NMR, we will organize the **exchange of teaching material**. Local courses will cover introduction to practical requirements of NMR as needed for successfully applying standard NMR experiments (limited set of NMR experiments, availability of parameters sets, limited number of NMR parameters to be manually set or optimized). Typically these courses will be given locally by local experts, also at smaller NMR centers. In order to ensure highest performance for NMR experiments across sides, **standard samples for the optimization of NMR experiment** will be defined and exchanged between the centers. An important aspect of the basic workshop will be sample preparation.

In addition, specialized **cross-center workshops on complex, advanced and new NMR experiments** will be offered. Such cross-center workshops have been very successfully organized by M. Sattler in the context of EMBO workshops (http://www.bnmrz.org/embo2011/). Similar workshops will be organized by BMRZ for solid-state NMR experiments, where the degree of standardization is

far behind. Other centers will follow and funds are applied for to setup these workshops. As the advanced NMR techniques require a deeper understanding (not only of the experiment, but also of hardware requirements and parameter settings), these courses will be offered in longer intervals or in collaboration with other NMR centers. Such courses may concern topics such as biomolecular NMR, dynamics and relaxation studies by NMR, NMR of "unusual" nuclei/isotopes etc.
The aforementioned software platform (3.1.2.) will facilitate a virtual research infrastructure and thus ease the dissemination of standard operating procedures, exchange of best practices or novel methods, respectively.

3.1.4. Development of solid-state NMR towards broader applicability (involved groups: A,B,D, E)

Solid-state NMR has evolved in the past two decades into a powerful technique for hypothesis-driven biophysical research and it is an emerging technique for structural biology. Its major strength, besides its applicability to microcrystalline proteins or protein fibers, is based on the possibility to study membrane proteins directly within the lipid bilayer. Despite its rapid development and the increasing availability of modern high field instrumentation in core centers, solid-state NMR is still far away from being a broadly applicable routine method such as liquid-state NMR. There are a number of reasons for this:

- High level of involvement of an experienced solid-state NMR spectroscopist is needed to operate the instrumentation, especially when magic angle sample spinning is used, which accounts for 90% of all applications. Often, user interventions are needed at the hardware as well pulse sequence level. The type of intervention varies from experiment to experiment.

- Since solid-state NMR is not (yet) a well-established structural biology method, biomolecular applications are very diverse and involve a very large number of very different methods. The arsenal of required tools includes homo-nuclear and hetero-nuclear recoupling and decoupling experiments (e.g. R2, R3, REDOR, TEDOR, FSLG, C/R type sequences etc.) and their applications to 2-spin and multispin systems for precise distance measurements, correlation experiments or order parameter determinations to name just a few potential uses. Sequential assignment in uniformly labeled samples can be achieved by combining heteronuclear 3D experiments (NCACX, NCOCX, CONCA, CAN(CO)CA). Besides ^{15}N and ^{13}C, also ^{31}P, ^{14}N, ^{19}F or ^{2}H are used often and even the use of quadrupolar nuclei such as ^{51}V has been shown to hold great potential for enzyme studies. For all of these applications, different hardware, different pulse sequences and often different simulation software for data analysis are employed.

Despite of these challenges, broader applications could be envisaged if standard operation procedures would be in place or a set of the most important experiments to lower the access barrier. In order to develop such procedures, standard samples have to be defined first, on which the performance of experiments can be benchmarked and compared between spectrometers. Second, chemical shift standards need to be defined. In most cases referencing is done via an external standard since adding e.g. DSS to the sample is often not possible. The third area to be standardized is a procedure to determine the exact temperature within the MAS rotor during an experiment, a problem, which has not been completely solved yet. Finally, there is still no general pulse sequence library available for solid-state NMR.

Definition and improvements of standard solid-state NMR experiments The NMR centers which are equipped with biomolecular solid-state NMR capabilities (i.e. München, Frankfurt, Göttingen, Karlsruhe, Halle, Leipzig, Jülich) will define and implement a set of standard experiments. Such experiments will, e.g., allow doctoral students to rapidly acquire solid-state assignments and experiments to determination the structure of a uniformly isotopically-enriched biomacromolecule in the solid-state. This set of "standard" experiments will be added to a **common pulse sequence library** that will be shared across centers. Standard experiments could include:

Experiments for protonated protein samples
1) 2D ^{13}C,^{13}C spin diffusion experiments, using PDSD, RFDR, R/C type sequences for mixing.
2) 2D NCO, 2D NCA using TEDOR and CP for ^{15}N,^{13}C polarization transfer
3) 3D NCOCX, 3D NCACX
4) PAIN and PAR

5) Heteronuclear decoupling sequences: TPPM, SPINAL-64
6) Homonuclear decoupling sequences: FSLG, PMLG

Experiments for deuterated samples
1) 2D ^{1}H,^{15}N HSQC/HMQC with MISSISSIPPI / gradients for solvent suppression
2) 2D ^{1}H,^{13}C HSQC/HMQC with MISSISSIPPI / gradients for solvent suppression
3) 3D HNCO, 3D HNCA, 3D HNCOCA, 3D HNCACB for assignment in the solid-state.
4) ^{2}H,^{13}C Optimum Control transfer experiments
4) Dynamics: ^{15}N-T_1, ^{15}N-^{1}H,^{15}N CSA cross correlated relaxation, order parameter measurements via CPPI, REDOR type experiments

Care will be taken to employ a standard pulse program syntax which will facilitate the exchange of pulse programs. Centers which are equipped with spectrometers from different manufacturers (i.e. Jülich / Agilent & Bruker) will perform tests to yield **objective comparisons** with respect to instrument stability and probe performance. Again standardized NMR samples will be prepared and a set of samples will be available at each participating center. N-acetylated amino acids such as Ala or Leu seem to be ideal and can also be prepared as large single crystals for testing static experiments. In particular, tests will include sensitivity tests, achievable line widths (using a limited rf field strength), optimum line width (using the maximum tolerable *rf* field strength), *rf* homogeneity profiles, shimming, accuracy of magic angle adjustment etc.

In the context of the NMR network, the **exchange of measurement time** will be facilitated. Sites which have specialized equipment available, for example, ultrafast MAS capabilities (ν_R > 60 kHz), measurements at low temperature (T = 100 K) or dynamic nuclear polarization (DNP) will offer this within the consortium to provide most efficient use of the available instrumentation across the national network and utilize the specific expertise available at the different NMR facilities. This measure will also promote collaborations between the different centers.

Examples of specialized solid-state NMR equipment:
1) Ultra-high field wide-bore spectrometers:
Göttingen: 850 MHz WB
Frankfurt: 850 MHz WB
München: 750 MHz SB

2) DNP Solid-State NMR
Göttingen: 600 MHz
Frankfurt: 400 MHz
Berlin: 400 MHz

3) Ultrafast probes
Göttingen: 1.3mm (60 kHz +)

3.1.5. Exchange of methods for education (involved groups A,-F)

Research at the cutting-edge can only be performed if students are well prepared to apply NMR spectroscopy. Different to many other spectroscopies, the analytical power of NMR requires in-depth integration into teaching curricula both for graduate and doctoral students that apply and utilize NMR as well as for those that develop new NMR experiments.

Development and exchange of educational material for Bachelor/Master programmes
A particular strength at many of the participating centers is the good integration of teaching NMR spectroscopy in the curricula of Chemistry, Biochemistry, Bioinformatics and Biophysics. A wealth of teaching material is already available in the internet (mostly in English). However, for specific needs it can be very time-consuming to find appropriate material of good quality, or material that is available in a format that allows it to be easily adapted to one's own needs. In addition, problem sets with interesting and challenging NMR quizzes are particularly useful and stimulating for students. A benchmark has been provided by the books of Prof. Berger, Leipzig, in this respect. However, free availability and knowledge on how to use such software for the simulation of, e.g., the effect of pulses can still be improved. Hence it will be useful – in a first step – to collect an overview of such material already available at the different places (scripts, exercises etc.). The material will then be reviewed to

develop a basic, common teaching curriculum, which will be made available within the NMR network. For different reasons (copyright, holding back "solutions" for students' exercises) it will be necessary to partially restrict access to this material (e.g., to registered users only). These resources will be made available to all participating institutions and should be regularly updated to incorporate new developments in the field. We will also identify areas where adequate resources are not yet available (e.g., solid-state NMR) and specifically develop material for that purpose in a shared effort between different institutions.

New web-base teaching initiatives For standard purposes (basic NMR introduction for chemistry/biochemistry students, exercises with 1D spectra etc.) appropriate material will be developed that can be used by students to learn about NMR autonomously. The idea will not be to replace traditional teaching of NMR courses at NMR centers or universities, but to enrich these courses by supplying additional training material (e.g. good quality spectra of substances with various degrees of complexity) where students can further apply and train their skills learned in traditional courses. Of course, such material (scripts and exercises) made publicly available on the internet for self-studies will have to follow a higher quality standard than teaching material intended to be used in traditional NMR courses, where it will be further screened, modified and explained by experienced instructors.

3.1.6. Optimization of the operation of NMR service units (involved groups A-C,E)

NMR service units are part of every German university with curricula in Chemistry. Service units at universities are required to move their operation increasingly into automated data acquisition due to the increasingly difficult (state and federal) funding situation of German universities, with severe budget cuts over the last 10 years. From this monetary point of view, optimization of NMR service units is a constant task. Scientifically, NMR service units face requests from a very diverse set of users. In addition, these requests can quickly change as new faculty members are being appointed at a given university. Expertise in experiments and specific classes of compounds may exist at one university but this knowledge is not broadly disseminated. G-NMR therefore aims at generating platforms for exchange of expertise and will participate in the newsletters (MARS) of the MR group of GDCh. In addition, the following specific aspects will be addressed:

Best practice for user support: scheduling, data access, experimental set-up, automation The current practice in the NMR community concerning the handling of spectrometer access, scheduling, apportionment of costs etc. is quite diverse, ranging from open access, hands-on spectrometers for students up to highly automated departmental facilities with dedicated research equipment. Both management and users of NMR service units will benefit from an exchange of ideas and practice at different sites in order to develop "best practice" standards and recommendations for software (scheduling, billing, data access). This would greatly simplify the set-up and maintenance of such settings and thereby enhance efficiency and transparency. Many of the solutions to these problems have been already implemented in the standard software package of the manufacturers, but exchange of know-how as well as feedback towards specialized needs will be organized with G-NMR.

Transfer of modern technologies into service NMR units The experience of the past decades shows that new NMR methodology is quickly accepted and used in NMR research groups, but much slower to trickle down to (even in-house!) routine NMR units. One reason for this is certainly sometimes the need for new costly hardware components, but also very often knowledge transfer is inefficient about which new techniques have been developed – and which of them promise significant improvements in service NMR units. For such cases, staff at the participating facilities will establish a working group to a) collect and provide knowledge about promising new developments into these units, and b) help implementing these techniques by providing pulse programs, macros and detailed instructions to avoid that every service unit would have to spend considerable spectrometer and human resources in setting up new techniques. In addition, workshops and courses (see above) will help service units to more efficiently introduce new techniques into their repertoire of available methods.

3.1.7. Interfacing with NMR units in Industry (involved groups A-F)

There are two target groups in industry for interfacing with G-NMR: manufacturers of NMR spectrometers (E1) and NMR units at companies (E2).

Interfacing with manufacturer companies Both NMR manufacturers Bruker and Agilent have major research and application laboratories located in Germany, and ties between these companies and groups at German Universities are close. Within G-NMR, we will make contact with the application scientists to discuss aspect of standardization, improvement of hardware, feedback, trouble shooting etc. as discussed in 3.1.3. and 3.1.4. We will also help organizing training workshops for information transfer between the manufacturers and NMR service units, help collecting common requests at different NMR service units and provide hands-on help with installation of new software and computer hardware.

Interfacing with NMR units at companies NMR units are in place in all major chemical and pharmaceutical industries. These units are involved in compound characterization as well as in more in-depth and sophisticated NMR analysis of a large variety of different samples. Increasingly, solid-state characterization on polymers and on crystals and crystal powder need to be performed; solid-state NMR, however, is not yet well established in industry. G-NMR will organize meetings with representatives of companies to obtain feedback on their needs and to inform about research possibilities.

3.1.8. Interfacing with funding bodies (involved groups A,B,D,F,G)

It is the long-term goal of the network of G-NMR to generate consensus within the NMR community on the funding requirements for operating and maintaining the various types of NMR facility. In addition, NMR is a rapidly developing technique that require frequent hardware updates (recent examples in automation, gradient spectroscopy, cryo-probe technology, DNP, large field spectrometers). All of these aspects require exchange between the scientists and the major German funding agencies that will be integral part of G-NMR. Details are also outlined under 3.2.

3.2 Work Schedule

Expected time frame for the work packages defined above The work schedule sets up timelines for specific deliverables. It also identifies the partner (either A1 or A2) that responsible for the integration, communication between the partners in G-NMR and also for reaching the proposed deliverables.

	I/2012	**II/2012**	**I/2013**	**II/2013**	**I/2014**	**II/2014**
3.1.1. By-laws for the use of NMR facilities involved groups: A,B,C,F,G responsible partners: A1 (service) A2 (research)	Preparation of a draft for By-laws for NMR facilities	Discussion of draft By-laws for NMR facilities at Meeting of MR group	Optimization of the By-laws for NMR facilities; individual discussions	Overview of the acceptance of the By-laws for NMR-facilities	Report to DFG on the specific requirements for NMR facilities	Report to community at meeting of MR group
3.1.2. Informatics aspects of G-NMR involved groups: A-E responsible partner: A1	Development of a Net-based application for measurement allocation	Distribution of a Net-based application for measurement allocation to interested users	Development of a Net-based database for raw data storage	Distribution of a Net-based database for raw data storage to interested users	Development of a Net-based database for NMR data processing	Maintenance of the Net-based intranet
3.1.3. Technology transfer and training involved groups: A,B,D responsible partner: A2	Overview of existing local training courses	Discussion of actual and future): basic & advanced training needs (solution NMR)	Discussion of actual and future): basic & advanced training needs (solid state NMR)	Define standards for future basic & advanced NMR training (solution NMR)	Define standards for future basic & advanced NMR training (solid state NMR)	Report to community and discussion at meeting of MR group
3.1.4. Development of solid-state NMR towards broader applicability involved groups: A,B,D,E responsible partner: A1	Definition of standard samples and standard set of experiments	Benchmark experiments performed. Needs for hardware development summarized (draft).	Lists of standard experiments published. Exchange of NMR time organized.	Meeting at MR with experts of participating & other interested units.	Implementation and optimization of standard experiments.	Report to community at meeting of MR group
3.1.5. Exchange of NMR methods for education involved groups: A-F responsible partner: A2	Overview of existing teaching material (include all other units)	Start discussion on actual / future needs for teaching material (include all other units)	Discuss common set of teaching material and tools	Set-up of appropriate web exchange platform (consider access, security)	Make available teaching material available, edit & improve material (input from all units)	Report to community at meeting of MR group
3.1.6. Optimization of NMR service units involved groups: A-C, E responsible partner: A1	Preparation of a draft By-law for NMR service units	Discussion of draft By-law for NMR facilities at Meeting of MR group	Optimization of the By-law for NMR service units; individual discussions	Overview of the acceptance of the By-laws for NMR service units	Report to DFG on the specific requirements for NMR service units	
3.1.7. Interface with NMR units in Industry involved groups: A-C, E responsible partner: A2	Exchange with application scientists at companies	Exchange with application scientists at companies	Workshop with industry representatives at MR group meeting	Compilation of requests from industry for optimal use of NMR in industry	Discussion and summary of requests from industry	Report to community at meeting of MR group
3.1.8. Interface with funding bodies involved groups: A,B,D,F,G responsible partner: A1		Initial feedback from DFG to by-laws		International symposium at meeting of the MR group on the development of NMR spectroscopy	Feedback from DFG to by-laws	

Abbreviation: MR group (Fachgruppe Magnetische Resonanz der Gesellschaft Deutscher Chemiker (GDCH)

3.3 Experiments involving humans or human materials

none

3.4 Experiments with Animals

none

3.5 Experiments with Recombinant DNA

BMRZ (Frankfurt): Permissions to operate S1 (IVMr4653r30.03.UFM85.12.01) and S2 (IV44-53r30.03.UFM53.13.03) laboratories are available.

BNMRZ (München): Permission to operate S1 laboratories (Regierung von Oberbayern, Anlage Nr. 547, Az. Az. 821-8763.13.547/939) is available.

3.6 Research subject to the Convention on Biological Diversity (CBD)

not relevant here

3.7 Data handling

Long-term data storage is secured by the use of a professional RAID hard disk storage area at University Frankfurt. At TUM, data storage and back-up facilities are provided by the Leibniz Rechenzentrum (Garching). Similar installments are available at other participating institutions. Policies on streamlining of raw data handling is part of the topic of G-NMR (see 3.1.2.)

4.0 Funds requested

Cost item	No. of positions	Person-months	Costs
Personel costs:			
P1: BMRZ: PostDoc	1	12	58.000
P2: BNMRZ: PostDoc	1	12	58.000
Other costs:			
A1: Workshops			10.000
A2: Standard Samples (isotope labeled protein/RNA)			5.000
A3: Softw are implementation / licensing			15.000
		total 2012:	146.000
Cost item	**No. Of positions**	**Person-months**	**Costs**
Personel costs:			
P1: BMRZ: PostDoc	1	12	58.000
P2: BNMRZ: PostDoc	1	12	58.000
Other costs:			
A1: Workshops			15.000
A2: Standard Samples (isotope labeled protein/RNA)			5.000
A3: Softw are optimisation / licensing			12.000
		total 2013:	148.000
Cost item	**No. Of positions**	**Person-months**	**Costs**
Personel costs:			
P1: BMRZ: PostDoc	1	12	58.000
P2: BNMRZ: PostDoc	1	12	58.000
Other costs:			
A1: Workshops / Symposium			25.000
A2: Standard Samples (isotope labeled protein/RNA)			5.000
A3: Softw are maintenance / licensing			10.000
		total 2014:	156.000
Total costs for 3 years of project duration:			450.000

Justification of costs:

ad P1: One postdoctoral fellow at BMRZ. His/her main task is to work on the development of Solid-State NMR towards standardization. To achieve this goal, the group of Prof. Glaubitz, BMRZ requires a senior NMR spectroscopist, because maintaining and setting up solid-state experiments and working on their implementation is particularly demanding. Funds from the department of Chemistry are secured to provide the long-term sustainability of this position.

ad P2: One postdoctoral fellow at BNMRZ. His/her main task is to organize technology transfer, in liquid-state and solid-state NMR spectroscopy. The experience in Munich in organizing EMBO workshops is particular important for this task. Funds from the Department of Chemistry are secured to provide the long-term sustainability of this position.

ad A1: The organization of workshops, mostly in combination with the annual meeting of the magnetic resonance group, is an important aspect for network. 10.000, 25.000, and 15.000 have been allocated for this purpose. The higher number in 2013 is due to the organization of an international symposium,

where international scientists will be invited, while the meeting in 2012 and 2014 will support speakers from with the G-NMR consortium. The budget will be allocated by BMRZ.

ad A2: Standard samples will be prepared (ubiquitin by BNMRZ, 14mer tetraloop RNA by BMRZ) and distributed to a low prize for partners interested within the consortium. The budget will be allocated in BMRZ and in BNMRZ (2.500 Euro p.a. each).

ad A3 Software platforms available to the entire consortium will be developed. In 2012, a larger budget (15.000 Euro) is required for the initial installation, while a budget of 10.000 Euro will required in 2013 and 2014, respectively.

5.0 Prerequisites for carrying out the project:

5.1 Members of the applicant's research groups relevant to the project:

BMRZ Frankfurt: Prof. Dr. Harald Schwalbe (NMR methods development for liquid-state NMR), Prof. Dr. Clemens Glaubitz (solid-state NMR), Prof. Dr. V. Dötsch (biomolecular NMR spectroscopy), Prof. Dr. Peter Güntert (NMR-based structure calculations, development of CYANA program), Dr. Marco Betz (Scientific administration), Dr. Christian Richter (NMR expert, methods development), industrial experience with Bruker), Dr. Henry Jonker (NMR-based structure calculation), Dr. Frank Löhr (NMR expert, methods development).

BNMRZ München: Prof. Dr. Michael Sattler (liquid-state NMR: structural biology & methods development), Prof. Dr. Bernd Reif (solid-state NMR: methods development and biomolecular applications), Prof. Dr. S. Glaser (methods development, optimization of NMR experiments), PD Dr. Gerd Gemmecker (NMR expert, biomolecular NMR; scientific administration), Dr. Rainer Haessner (NMR expert, organic chemistry; NMR hardware & software).

5.2 Cooperations with other scientists

defined under 2.0

5.2 Scientific Equipment Available

defined under 2.1

5.4 Running costs for materials

not relevant here

5.5 Conflict of interest with commercial activities

none

5.6 Other requirements

None

6.0 Declarations

We have not requested funding for this project from any other sources. In the event that we submit such a request, We will inform the Deutsche Forschungsgemeinschaft immediately. In submitting a proposal for a research grant to the DFG, we agree to adhere to the DFG's rules of good scientific practice. In preparing our proposal, we have adhered to the guidelines for publication lists (section I.8) and bibliographies (section II.2).

7.0 Signatures

Prof. Dr. Harald Schwalbe

Prof. Dr. Michael Sattler

8.0 List of Attachments

CV Harald Schwalbe

CV Michael Sattler

Support letters from Goethe University Frankfurt for BMRZ

Support letters from Technische Universität München for BNMRZ

Curriculum Vitae – Prof. Dr. Harald Schwalbe

Lab	Institute of Organic Chemistry and Chemical Biology Center for Biomolecular Magnetic Resonance (BMRZ)
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e-mail	schwalbe@nmr.uni-frankfurt.de
homepage	http://schwalbe.org.chemie.uni-frankfurt.de/

Education

1990-1993	Chemistry, University of Frankfurt, Germany, Ph.D. (summa cum laude; Mentor: C. Griesinger)
1985-1990	Chemistry, University of Frankfurt, Germany, Diploma (summa cum laude; Mentor: C. Griesinger)
1993-1995	Postdoctoral fellow at the Oxford Centre for Molecular Sciences, Oxford University (Mentor: C.M. Dobson, FRS)

Professional Career

2011-	Speaker: DFG-SFB 902: “Molecular principles of RNA-based regulation”
2011-	Chairman of the DFG Apparateausschuß
2009-	Speaker: DFG-Cluster of Excellence: Macromolecular Complexes
2009-2010	Member of the DFG Apparateausschuß
2007-2009	Speaker: DFG-SFB 579: “RNA-Ligand-Interactions”
2006-2008	Deputy Director: DFG-Center for Excellence: Macromolecular Complexes
2005-2011	Member of Senate of Goethe-University Frankfurt
2003-	Coordinator of 5 EU funded programmes (STREPs, TOKs, Research Infrastructure for NMR (I3))
2002-2006	Managing Director of the Center for Biomolecular Magnetic Resonance, BMRZ
2003-2008	Head of the Department (Dekan) “Biochemistry, Chemistry and Pharmacy”
2002-	Full Professor (C4), Institute for Organic Chemistry and Chemical Biology, University of Frankfurt
2001	Associate Professor for Biological Chemistry, Massachusetts Institute of Technology
1999-2001	Assistant Professor for Biological Chemistry, Massachusetts Institute of Technology
1995-1999	Work as Habilitand in Chemistry, University of Frankfurt (Mentor: C. Griesinger)

Honors and Awards

2006	1822-Prize for Teaching; University Frankfurt
2002-	Vertrauensdozent of the “Studienstiftung des deutschen Volkes”
2001	Pew Scholar for Biomedical Sciences
2001	Fellow of the Alfred P. Sloan Foundation
2000	Karl Winnacker Preis of Aventis Foundation
1999	Gerhard Hess Preis of DFG
1996	Liebig Stipend of the Fonds der Chemischen Industrie
1993-1995	Human Capital and Mobility Fellow, EU.
1993	Studienabschlusspreis of the Fonds der Chemischen Industrie, Promotion
1989-1993	Member of the Graduate program: “Chemische und Biologische Synthese von Wirkstoffen“, Institut für Organische Chemie, Frankfurt/Main.
1987-1990	Member of the “Studienstiftung des Deutschen Volkes“

Research Interests
Structural Biology of Proteins and RNA studied by NMR spectroscopy
Time-Resolved NMR spectroscopy
RNA Folding
Protein Folding; non-native states of proteins
NMR-based drug design (kinases, phosphatases, GPCRs)
Synthesis of isotope labelled RNA, DNA, peptides and photolabile compounds

Member of Editorial Boards/Scientific Committees
ChemBioChem, Board of ISMAR (2002-2010), Kuratorium des Strüngmann-Forums, Kuratorium der Rolf-Sammet-Stiftung, Kuratorium der Oswalt- und Boris-Rajewski-Stiftung, Preiskommission der GDCH August-Wilhelm-von-Hofmann-Denkmünze, Board of EUROMAR (2010-), Preiskommission des Frankfurter Biophysikpreises der Oswalt-Stiftung.

Organization of Large International Conferences

2002	iLab: G-protein coupled receptors (together with G. Wess, Aventis)
2003	iLab: RNA targeting (together with G. Wess, Aventis, M. Göbel, Uni Frankfurt)
2004	iLab: Systems Biology challenges Chemistry (together with G. Wess, Aventis)
2007	ICMRBS Göttingen (co-organizer)
2009	GDCh Wissenschaftsforum Frankfurt (local organizer)
2011	EUROMAR Frankfurt (co-organizer), GDCh Wissenschaftsforum Bremen (scientific committee), International symposium of the German Society for Biochemistry and Molecular Biology (scientific committee)

Scientific Advisory Boards
Center for Magnetic Resonance Florence
Henry Wellcome Center Birmingham
Frankfurt Institute for Advanced Studies

Reviewing activity
DFG Germany, NWO Netherlands, FWO Austria, CNS France, Wellcome-Trust UK, BBSRC UK, National Science Foundation USA, NIH USA, Science Foundation Belgium, Excellence programme Slovenia, German Israel Foundation, Klaus-Tschira-Preis, Czech Science Foundation, DAAD

Accounts in Chemical Research, Angew. Chem. Int. Ed., Biochemistry, Bioorganic and Medicinal Chemistry, ChemBioChem, ChemComm, Chemistry A European Journal, ChemPhysChem, Febs Lett., J. Am. Chem. Soc., J. Biomol. NMR, J. Chem. Theor. and Computation, J. Magn. Reson., J. Mol. Biol., J. Phys. Chem., Magnetic Resonance in Chemistry, Nature, Nucleic Acids Res., Proc. Natl. Acad. Sci. USA, RNA, Science, Structure.

10 most important publications

NMR method development

M. Sattler, **H. Schwalbe**, C. Griesinger (1992) Stereospecific Assignment of Leucine δ-Methylgroups with ^{13}C in Natural Abundance or Random ^{13}C Labelling. J. Am. Chem. Soc. **114**, 1127-28.

H. Schwalbe, J.P. Marino, S.J. Glaser, C. Griesinger (1995) Measurement of all H,H-Coupling Constants associated with ν_1, ν_2, and ν_3 in uniformly ^{13}C labeled RNA by HCC-TOCSY-CCH-E.COSY. J. Am. Chem. Soc. **117**, 7251-7252.

Protein Folding

H. Schwalbe, K.M. Fiebig, M. Buck, J.A. Jones, S.B. Grimshaw, S.J. Glaser, L.J. Smith, C.M. Dobson (1997) Structural and Dynamical Properties of Lysozyme Denatured in 8M Urea. Heteronuclear 3D NMR Experiments and Theoretical Simulations. Biochemistry **36**, 8977-8991.

T. Kühn, H. **Schwalbe** (2000) Monitoring the Kinetics of Ion Dependent Protein Folding by Time Resolved NMR at Atomic Resolution. J. Am. Chem. Soc. **122**, 6169-6174.

J. Klein-Seetharaman, M. Oikawa, S.B. Grimshaw, J. Wirmer, E. Duchardt, T. Ueda, T. Imoto, L.J. Smith, C.M. Dobson, **H. Schwalbe** (2002) Long-range interactions within a non-native protein Science **295**, 1719-1722.

RNA Folding

J. Noeske, C. Richter, M.A. Grundl, H.R. Nasiri, **H. Schwalbe**, J. Wöhnert (2005) An intermolecular base triple as the basis of ligand specificity and affinity in the guanine and adenine sensing riboswitch RNAs. Proc. Natl. Acad. Sci. USA **102**, 1372-1377.

P. Wenter, B. Fürtig, A. Hainard, **H. Schwalbe**, S. Pitsch (2005) Kinetic investigation of photoinduced RNA refolding by realtime NMR spectroscopy. Angew. Chemie **117**, 2656-2659.

J. Buck, B. Fürtig, J. Noeske, J. Wöhnert, **H. Schwalbe** (2007) Time-resolved NMR methods resolving ligand-induced RNA folding at atomic resolution. Proc. Natl. Acad. Sci. USA **104**, 15699-15704.

J. Rinnenthal, B. Klinkert, F. Narberhaus, **H. Schwalbe** (2010) Direct observation of the temperature induced melting process of the Salmonella fourU RNA thermometer at base-pair resolution. Nucleic Acids Res. **38**, 3834–3847.

NMR-based Drug Design

M. Vogtherr, K. Saxena, S. Hoelder, S. Grimme, M. Betz, U. Schieborr, B. Pescatore, M. Robin, T. Langer, K.U. Wendt, **H. Schwalbe** (2006) NMR-Characterization of kinase p38 dynamics in free and ligand bound form. Angew. Chem. Intl. Ed. Engl. **45**, 993-997.

Curriculum Vitae: Michael Sattler

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Address: Biomolekulare NMR-Spektroskopie, Department Chemie, TU München
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Institute of Structural Biology, Helmholtz Zentrum München,
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Fax: +49 89 3187-193800
Internet: http://www.nmr.ch.tum.de/; http://www.helmholtz-muenchen.de/stb

Education

1986-1991	Study of Chemistry, University of Frankfurt, Germany
Jul 1991	Diploma in chemistry, Universität Frankfurt, Germany
Jan 1995	Dr. phil. nat. Universität Frankfurt, Germany

Professional Experience

1990-1991	Diploma, Inst. for Organic Chemistry, University of Frankfurt, Germany. Advisor: Prof. Dr. Christian Griesinger
1991-1995	Dissertation, Inst. for Organic Chemistry, University of Frankfurt, Germany. Advisor: Prof. Dr. Christian Griesinger
1995-1997	Postdoctoral Associate, Abbott Laboratories, Abbott Park, USA. Advisor: Dr. Stephen W. Fesik
1997-2006	Group Leader *Structural & Computational Biology and Gene Expression Units* EMBL Heidelberg, Germany
2007 -	Professor Biomolecular NMR-Spectroscopy, Department Chemie, TU München
2007 -	Director, Institute of Structural Biology Helmholtz Zentrum München, Neuherberg
2007 -	Director, Bayerisches NMR Zentrum, TU Münche, Garching

Academic Interests

Biomolecular NMR spectroscopy of protein complexes; NMR methods; Structural biology and dynamics in the regulation of gene expression and signal transduction, disease mechanisms;

Professional Activities and Awards

2005	Visiting Professor, Ecole Normale Superieur, Paris, France
2005	Jean-Francois Lefevre Lecturer in Biophysics, Strasbourg, France
2005/2006	Advisory Board, Institute of Toxicology and Genetics, FZK Karlsruhe
2006-2008	Faculty of 1000 Biology
2007 -	Associate Editor - *Biomolecular NMR Assignments*
2008 /2009	Member Working Group NMR, ESFRI - INSTRUCT
2008 -	Scientific Advisory Board, ERAnet Instruments (EU FP7)
2008 -	Editorial Board Member: *J. Biol. Chem.*; *J. Struct. Biol.*
2009 -	Scientific Advisory Board, PDB Europe (PDBe) and IBS Grenoble
2010-	Coordinator DFGCluster of Excellence CiPS^{M}
2011-	Scientific Advisory Board, Biozentrum Basel
2011	"CAS Visiting Professorship for Senior International Scientists" at Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences (TIB, CAS)

Memberships

RNA society, ASBMB (American Society for Biochemistry and Molecular Biology), GDCh (German Chemical Society), GBM (German Biochemical Society)

Selected publications

Mackereth CD, Madl T, Bonnal S, Simon B, Zanier K, Gasch A, Rybin V, Valcarcel J, Sattler M.
Multi-domain conformational selection underlies pre-mRNA splicing regulation by U2AF
(2011) **Nature** *in press* (doi:10.1038/nature10171).

Simon B, Madl T, Mackereth CD, Nilges M, and Sattler M
An efficient protocol for NMR-spectroscopy-based structure determination of protein complexes in solution.
(2010) **Angew Chem Int Ed Engl** *49*, 1967-70

Neufeld C, Filipp FV, Simon B, Neuhaus A, Schüller N, David C, Kooshapur H, Madl T, Erdmann R, Schliebs W, Wilmanns M, Sattler M.
Structural basis for competitive interactions of Pex14 with the import receptors Pex5 and Pex19.
(2009) **EMBO J** 28:745-54 [PubMed]

Corsini L., Bonnal S., Basquin J., Hothorn M., Scheffzek K., Valcarcel J., and Sattler M.
U2AF Homology Motif interactions are required for alternative splicing regulation by SPF45.
(2007) **Nat Struct Mol Biol** 14, 620-9. [PubMed]

Lingel A., Simon B., Izaurralde* E., and Sattler* M.
The structure of the flock house virus B2 protein, a viral suppressor of RNA interference, shows a novel mode of double-stranded RNA recognition.
(2005) **EMBO Rep.** 6, 1149-55. [PubMed]

Markwick* P.R.L., Sprangers R., and Sattler* M.
Local Structure and Anisotropic Backbone Dynamics from Cross-Correlated NMR Relaxation in Proteins.
(2005) **Angew Chem Int Ed Engl 44**, 3232-3237. [PubMed]

Lingel A., Simon B., Izaurralde* E., and Sattler* M.
Nucleic acid 3'-end recognition by the Argonaute2 PAZ domain.
(2004) **Nat Struct Mol Biol** 11, 576-7. [PubMed]

Lingel + A., Simon + B., Izaurralde* E., and Sattler* M.
Structure and nucleic-acid binding of the Drosophila Argonaute 2 PAZ domain.
(2003) **Nature** 426, 465-9. [PubMed]

Selenko P., Gregorovic G., Sprangers R., Stier G., Rhani Z., Kramer A., and Sattler M.
Structural Basis for the Molecular Recognition between Human Splicing Factors U2AF(65) and SF1/mBBP."
(2003) **Mol. Cell** 11, 965-76. [PubMed]

Liu + Z., Luyten + I., Bottomley M.J., Messias A.C., Houngninou-Molango S., Sprangers R., Zanier K., Krämer A., and Sattler M.
Structural basis for recognition of the intron branch site RNA by splicing factor 1.
(2001) **Science** 294, 1098-102. [PubMed]

GOETHE
UNIVERSITÄT
FRANKFURT AM MAIN

Johann Wolfgang Goethe-Universität Frankfurt am Main
Fachbereich Biochemie, Chemie und Pharmazie • Dekanat

An die DFG
Deutsche Forschungsges.
Herrn Dr. Johannes Janssen
Wiss. Geräte und Informationstechnik-
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Datum: 13. Juli 2011

Sehr geehrter Herr Dr. Janssen,

als Dekan des Fachbereichs Biochemie, Chemie und Pharmazie unterstütze ich nachdrücklich den Antrag des BMRZ im Rahmen der Ausschreibung "DFG Geräte-Zentren".

Die beantragte Unterstützung mit Personalmitteln für den Zeitraum von 3+3 Jahren wird dringend benötigt, da das Zentrum mit Hochfeldfestkörper-NMR und insbesondere hinsichtlich DNP erweitert wurde. Eine Nachhaltigkeit wird durch das Weiterführen der anfallenden Aufgaben durch eine unbefristete Landesstelle sichergestellt.

Mit freundlichen Grüßen

Prof. Dr. D. Steinhilber

Johann Wolfgang Goethe-Universität Frankfurt am Main
Fachbereich Biochemie, Chemie und Pharmazie • Dekanat

An die DFG
Deutsche Forschungsges.
Herrn Dr. Johannes Janssen
Wiss. Geräte und Informationstechnik-
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Datum: 13. Juli 2011

Sehr geehrter Herr Dr. Janssen,

das BMRZ ist ein technisches Zentrum der Goethe-Universität und am Fachbereich 14, Biochemie, Chemie und Pharmazie angesiedelt. Dabei spielt es für die zentralen Forschungsinitiativen hier z.B. dem “Cluster of Excellence Macromolecular Complexes”, dem “SFB 807, Membrane Transport”, dem “SFB 902, Molekulare Mechanismen der RNA-basierten Regulation“ sowie für das „Zentrum für angewandte Arzneimittelforschung“ eine wichtige Rolle. Gleichzeitig stellt das BMRZ als European Large Scale Facility die Infrastruktur für Europäische Nutzer zur Verfügung, wofür es internationale Anerkennung erfährt.

Die große Bedeutung des Zentrums wurde auch von der Hessischen Landesregierung anerkannt, die den Erhalt des Zentrums an der Goethe Universität fördert und unterstützt. Das BMRZ erhält daher eine Finanzierung von €500k pro Jahr zur Absicherung der Infrastruktur.

Mit freundlichen Grüßen

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An die DFG
Deutsche Forschungsges.
Herrn Dr. Johannes Janssen
Wiss. Geräte und Informationstechnik-
Chemie und Verfahrenstechnik

D-53170 Bonn

Garching, 14.7.2011

Antragstellung "German network of NMR core facilities"

Sehr geehrter Herr Dr. Janssen,

als Dekan der Fakultät für Chemie unterstütze ich nachdrücklich den Antrag der Arbeitsgruppe von Prof. Dr. Michael Sattler im Rahmen der Ausschreibung "DFG Geräte-Zentren / German network of NMR core facilities ".

Eine Nachhaltigkeit wird durch die Einbindung in das Bayerische NMR-Zentrum sichergestellt.

Mit freundlichen Grüßen

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An die DFG
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Unser Zeichen
NF

München, 13. Juli 2011

Antrag von Prof. Dr. Michael Sattler im Rahmen der Ausschreibung "DFG Geräte-Zentren / German network of NMR core facilities"

Sehr geehrter Herr Dr. Janssen,

die TU München unterstützt den Antrag von Prof. Dr. Michael Sattler für ein DFG Geräte-Zentrum nachdrücklich.

Das Bayerische NMR-Zentrum betreibt den größten NMR-Spektrometerpark an Hochfeldgeräten (500 - 900 MHz) in Bayern und im Süden Deutschlands. Mit den vor Ort beteiligten Forschungsgruppen (1 Lehrstuhl, 2 Extraordinariate, 1 Carl von Linde-Lehrstuhl) sowie zahlreichen Kooperationen unterstützt das NMR Zentrum einen zentraler Forschungsschwerpunkt der Fakultät Chemie. Das Bayerische NMR-Zentrum spielt eine wichtige Rolle im DFG Exzellenzcluster *Center for Integrated Protein Science Munich* (CiPSM) sowie verschiedenen SFBs und EU Verbundprojekten.

Die Geräteausstattung des NMR Zentrums wurde mit DFG Mitteln finanziert und der Unterhalt durch die TUM und den Freistaat Bayern getragen. Im Jahre 2007 wurde eine langfristige Kooperation zwischen der Fakultät Chemie der TUM und dem Institut für Strukturbiologie am HelmholtzZentrum München vereinbart, um den Unterhalt und weiteren Ausbau des Bayerischen NMR-Zentrums zu sichern.

Das Bayerische NMR-Zentrum ist ein wichtiger Bestandteil der langfristigen strategischen Forschungsausrichtung der Fakultät Chemie und der TU München, die das Zentrum auch weiterhin nachhaltig unterstützen werden.

Mit freundlichen Grüßen

Wolfgang A. Herrmann
Präsident