BRUKER

Solid State NMR

- Your Science in HD

Innovation with Integrity

• Meeting New Challenges

Bruker's solutions for solid state NMR are faster, more flexible, more automated and more accessible than ever before. Modern systems offer much higher magnetic fields up to 23.4 T, more efficient shielding, protection from external disturbances, and our fastest MAS probes offer a near tenfold increase in spinning speed compared to the earliest days of solid state NMR. Solid state NMR's reputation for being difficult to master has been superseded by a range of adaptable systems that are welcoming everyone to Solid State NMR.

Solid state NMR spectroscopy is a powerful method in many research areas:

Batteries

In semi-ordered or ordered materials, such as batteries, important transport processes can be measured. Measuring the charge transport in batteries can help understand the reason for its conductivity.

Polymers

For polymers, order, cross-linking and other local connectivity characteristics can be observed and correlated to material properties, enabling improved control for the chemical design process.

Crystallography

Together with mathematical chemistry, solid state NMR has become a key supplementary tool for crystallography.

Pharmaceuticals

In pharmaceutical applications different polymorphic forms of an active pharmaceutical ingredient (API) can be distinguished. This enables quality control of starting materials and monitoring of excipient impact, the production process, as well as its influence on the crystal form of the API.

Proteins

Solid state NMR is becoming one of the most important tools for understanding complex insoluble protein systems, in both structural and dynamic concerns.

Innovative Technology

AVANCE™ III HD

The AVANCE III HD NMR spectrometer range is a fully modular system supported by a large selection of solid state NMR probes. Several families of Magic Angle Spinning (MAS) probes, with sample diameters from 1.3 to 7 mm, provide complete access to a comprehensive range of solid state NMR applications.

While static probes are solely used for special applications, MAS is the routine method of choice, as it introduces resolution into the spectra – unresolved broad lines are history.

High sensitivity and stable sample spinning greatly facilitate daily routine operation and thanks to the highly flexible design of the spectrometer, switching between solids and liquids has never been easier.

Figure 1: AVANCE III HD 600 widebore high performance solid state NMR system.
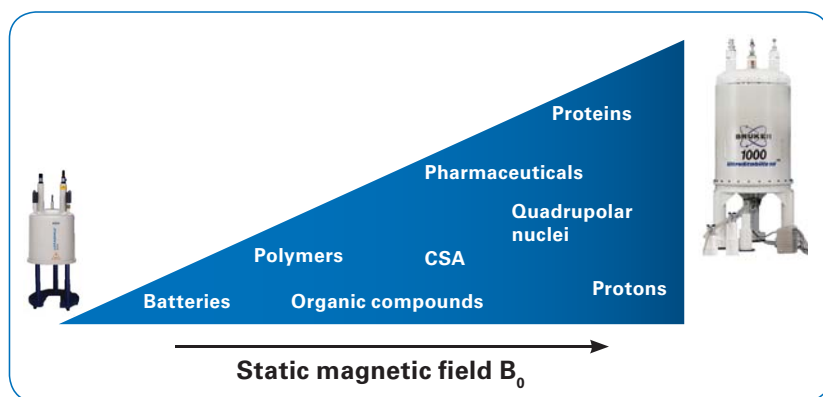
Magnet Technology

The Ascend family of highly compact and stable NMR magnets includes both standard bore and wide bore dimensions. Ascend magnets provide a stable experimental basis for all types of solid state NMR experiments and all rotor diameters.

The new Ascend Aeon magnet family combines the key features of the Ascend magnets (stability, low drift rates, etc) with the latest generation gas liquefaction hardware for either liquid nitrogen or helium re-liquefaction.
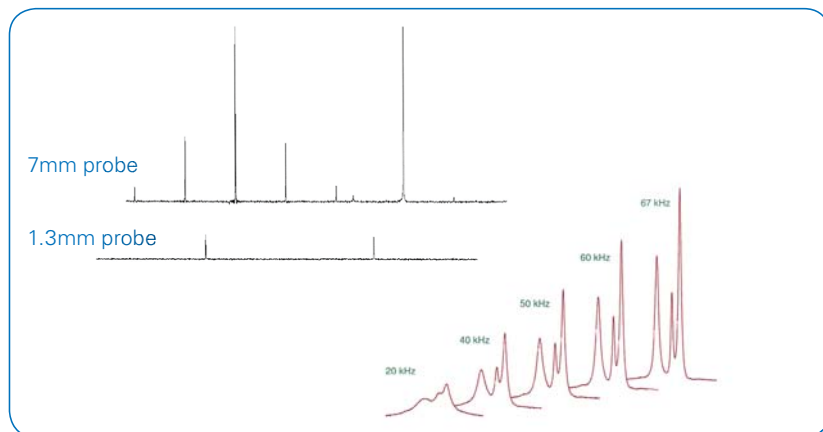

Figure 2: The information achievable through NMR is dependent on the sample properties (couplings/mobility/temperature, etc.) and the chosen magnetic field or MAS probe.

Applications – Life Science

Proteins

Solid state NMR has become a leading method for studying the structure and dynamics of insoluble proteins that either do not, or only poorly, crystallize due to their intrinsic nature. In comparison with solution NMR and X-ray crystallography, solid state NMR has the significant advantage of not having to depend upon tumbling rates or long-range order.

Which Proteins and Systems can be Studied?

- Powders
- Microcrystalline proteins
- Membrane proteins in a lipid environment
- Protein-lipid interactions
- Protein assemblies e.g. amyloid-like protein aggregates
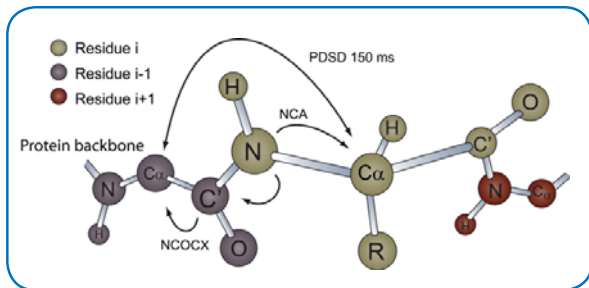- Protein complexes e.g. protein-ligand interactions etc.

Figure 3: Assignment strategy correlating backbone nuclei of consecutive residues in a polypeptide chain, by correlating N and Ca in one residue, then N with CO and Ca in the previous residue to compare the results for sequential assignment.

Structure Elucidation - How to Proceed?

- Intraresidue assignment (amino acid specific information)
- Sequential assignment (protein backbone information)
- Long-range measurements (spatial information)
- Structure calculation
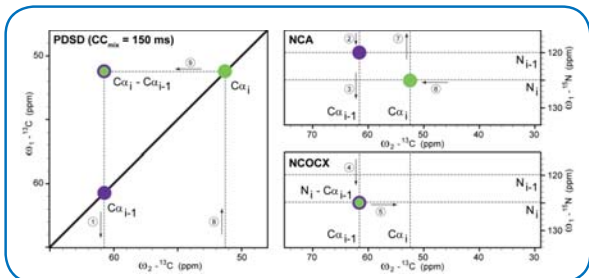- Follow-up studies, e.g. investigating interaction sites, aggregation sites, dynamics, etc.

Figure 4: Sequential correlation.

For an intraresidue assignment, not only homonuclear ^{13}C-^{13}C CP/MAS experiments (e.g. DREAM, DARR, PDSD), but also heteronuclear techniques, such as NCA and NCACX, are commonly recorded. Experiments that involve correlations with preceding residues (NCO and NCOCX) or vicinal amino acids (experiments with long ^{13}C-^{13}C mixing times) are required for a sequential assignment (see Figures 3 and 4). To obtain as many long-range distance restraints as possible, different experimental approaches have been recently developed (e.g. CHHC, PAR, PAIN-CP).

Bruker offers a range of experiments specifically developed for biological samples with different MAS frequencies.

Labeling Schemes

Figure 5: 2D CC correlation of spectra of the type III secretion system PrgI needle proteins, recorded on an AVANCE™ III 850 MHz WB spectrometer at a spinning frequency of 11 kHz. 2D PDSD spectrum (CC-mixing time of 100 ms) recorded for a total experimental time of 20 hours. © Adam Lange. [Loquet A, Lv G, Giller K, Becker S, Lange A. J Am Chem Soc. 2011].
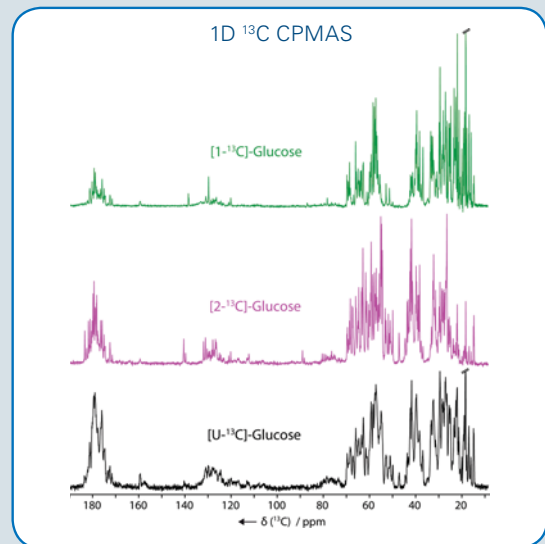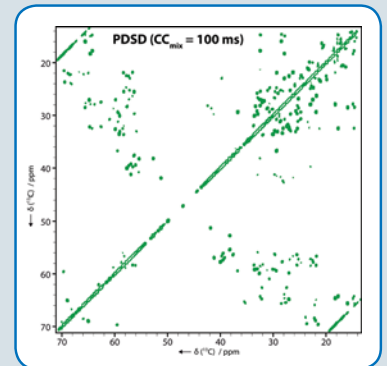

Figure 6: Glucose-based labelling schemes.

Effects of Protein Labeling

In biological solid state NMR, spin-½ nuclei, such as ^1H, ^{13}C, and ^{15}N are mainly detected. Thus, the protein has to be recombinantly expressed. This offers significant potential for manipulating the labeling of either specific amino acids or certain nuclei. Depending on the labeling scheme, the spectral overlap can be reduced and dipolar truncation effects can be minimized, enabling long-range information to be obtained (see glucose labelling, shown in the grey box).

Bruker continuously improves resolution and sensitivity in biological solid state NMR spectroscopy through ongoing hardware developments, such as higher magnetic fields and advanced probes. Master software enables easy access to advanced experiments for producing state of the art analytical results.
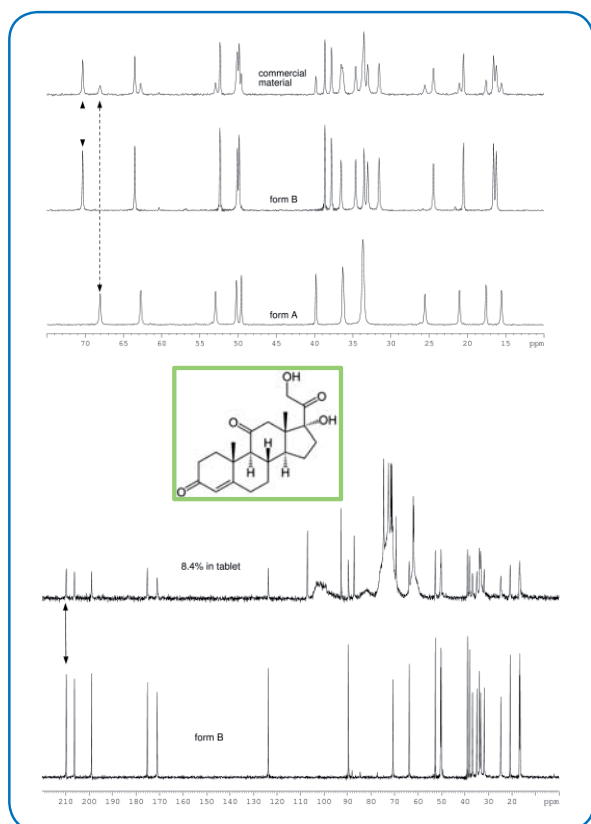

Figure 7: Polymorphism study as an example of process control in the pharmaceutical industry. Top: Commercial cortisone acetate identified as a mixture of two crystal forms (polymorphs) by comparison of its ^{13}C CP/MAS spectrum to its pure crystal forms. Bottom: Polymorphic form of crystalline cortisone acetate in a tablet (8.4% of crystalline API in amorphous excipient) identified by the ^{13}C CP/MAS spectrum of the tablet. All spectra obtained using a 400 MHz instrument and a 4 mm double resonance MAS probe at 15 KHz spinning frequency.

Pharmaceuticals

In addition to protein investigations, organic solids can be analyzed in respect of composition, structure, conformation and dynamics.

Drug Characterization

Solid state NMR is an invaluable tool for pharmaceutical analyses including identification, discrimination, and quantitation of polymorphs of Active Pharmaceutical Ingredients (APIs). This applies to both drug compounds and pharmaceutical formulations, enabling integrity checks of potential changes to crystal structure during tablet production and storage.

Recently developed NMR experiments enable easy access to nuclei that were previously difficult to measure. This extends the scope of solid state NMR to natural abundance samples using inverse detection, fast spinning and strong excitation pulses.

In the field of organic compounds in particular, the highly abundant but low gamma nucleus ^{14}N can now be used as an excellent probe for insights into API's or organic molecules.

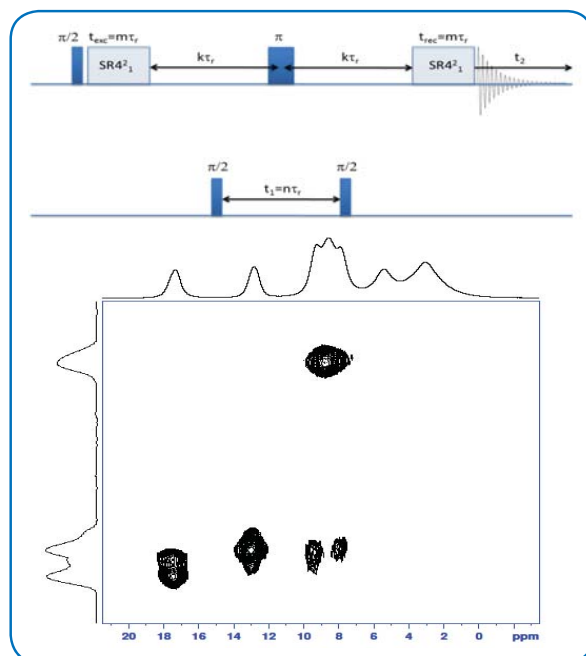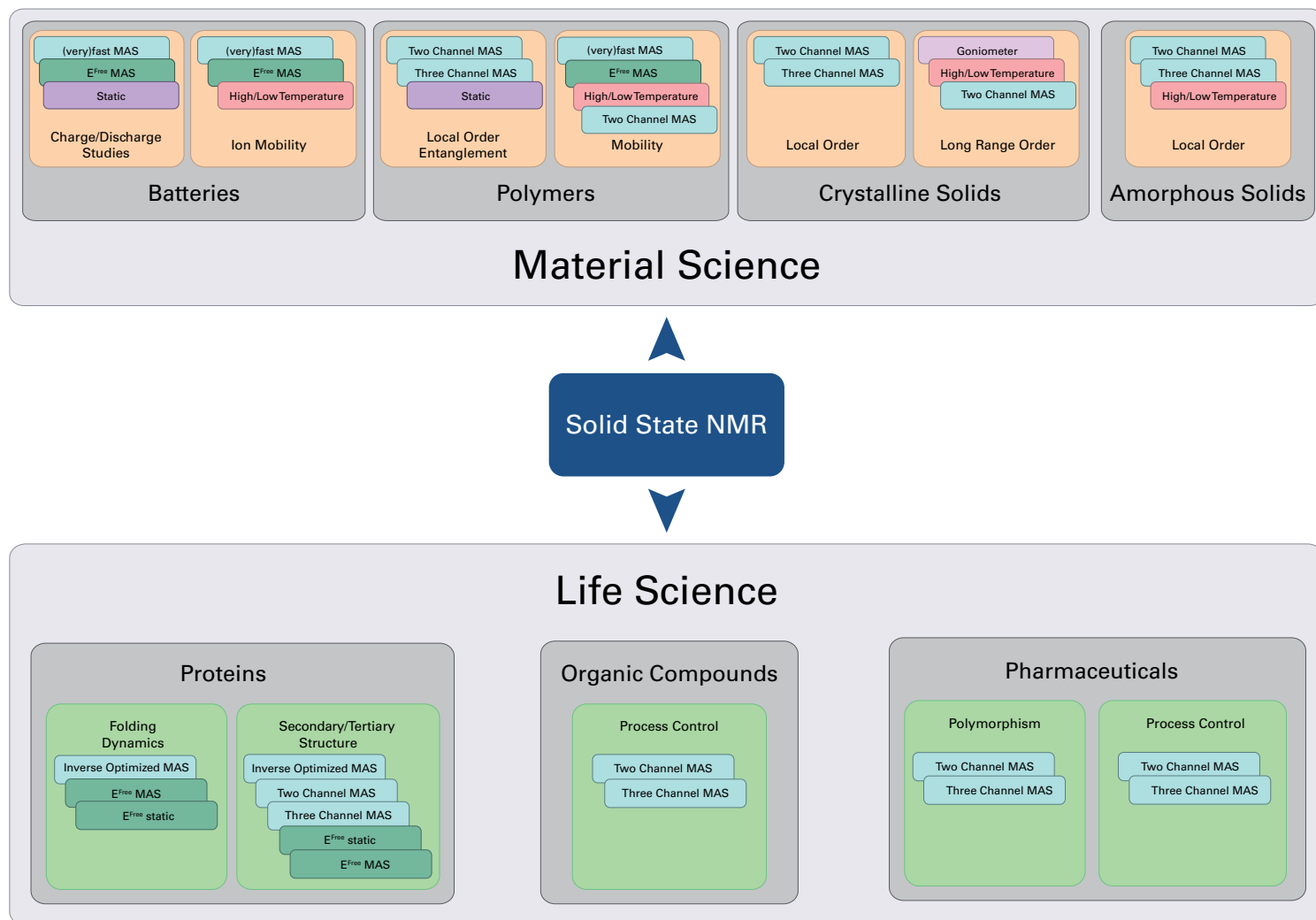Figure 8: Natural abundance ^{14}N correlation experiments are standard for structural studies on active pharmaceutical ingredients (API). Publications - Probing intermolecular interactions and nitrogen protonation in pharmaceuticals by novel ^{15}N-edited and 2D ^{14}N-^1H solid state NMR, Andrew S. Tatton, Tran N. Pham, Frederick G. Vogt, Dinu Iuga, Andrew J Edwards & Steven P. Brown. CrystEngComm Journal Article.

The Right Probe for Your Application

Material Science

Batteries

Charge/Discharge Studies	Ion Mobility
(very)fast MAS	(very)fast MAS
E^{Free} MAS	E^{Free} MAS
Static	High/Low Temperature

Polymers

Local Order Entanglement	Mobility
Two Channel MAS	(very)fast MAS
Three Channel MAS	E^{Free} MAS
Static	High/Low Temperature
	Two Channel MAS

Crystalline Solids

Local Order	Long Range Order
Two Channel MAS	Goniometer
Three Channel MAS	High/Low Temperature
	Two Channel MAS

Amorphous Solids

Local Order
Two Channel MAS
Three Channel MAS
High/Low Temperature

Solid State NMR

Life Science

Proteins

Folding Dynamics	Secondary/Tertiary Structure
Inverse Optimized MAS	Inverse Optimized MAS
E^{Free} MAS	Two Channel MAS
E^{Free} static	Three Channel MAS
	E^{Free} static
	E^{Free} MAS

Organic Compounds

Process Control
Two Channel MAS
Three Channel MAS

Pharmaceuticals

Polymorphism	Process Control
Two Channel MAS	Two Channel MAS
Three Channel MAS	Three Channel MAS

MAS
Magic Angle Spinning solid state NMR. Here, isotropic tumbling of molecules is imitated by spinning the sample around an axis inclined to B_0 with an angle of 54.74° to average out the anisotropic parts of the chemical shift anisotropy, first order quadrupole interaction and dipolar couplings. Combined with both heteronulcear dipolar and J-decoupling, MAS effectively increases spectral resolution.

MQMAS
Multiple Quantum Magic Angle Spinning. A technique for obtaining high resolution spectra of quadrupolar nuclei with half integer spins (e.g. ^{27}Al/^{23}Na/^{11}B/^{87}Rb).

CP
Cross polarization. A method to enhance the excitation of low-abundant and/or low-gamma nuclei (e.g. ^{15}N and ^{13}C) by exciting high-abundant and/or high-gamma nuclei (e.g. ^{1}H and ^{19}F) and transferring the magnetization and a method for correlating heteronuclei in solid state NMR like for example ^{15}N and ^{13}C in structural biology or ^{31}P and ^{13}C or Al in zeolite research.
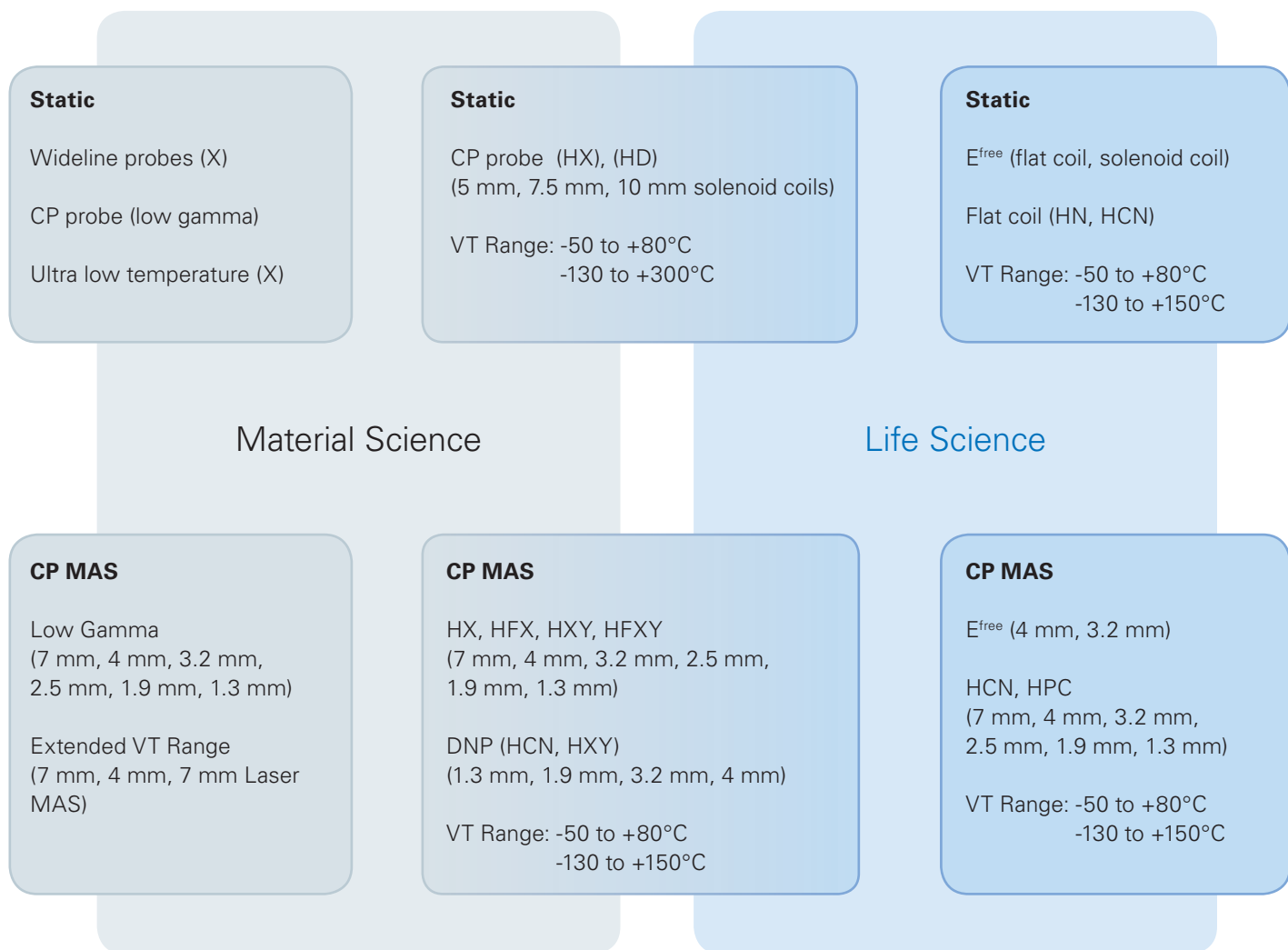
Recoupling Techniques
To reintroduce dipolar interactions in a controlled manner, special recoupling techniques (e.g. PDSD, DREAM, DARR, REDOR and the famous symmetry based C and R sequences) have been designed.

E^{Free}
Probe with special coil geometry to minimize the electric field component of the RF-irradiation at the sample position. Minimizes heating effects in wet and dielectric samples (e.g. proteins in buffer solution)

Flat-/Solenoid-Coil
For different sample geometries we provide optimum coil geometries for optimum experimental conditions. For samples aligned between glass plates we provide the so called flat coil probe, a rectangularly wound rf-coil. The cylindrical solenoid coil is used for bicelle samples.

Static

Wideline probes (X)

CP probe (low gamma)

Ultra low temperature (X)

Static

CP probe (HX), (HD)
(5 mm, 7.5 mm, 10 mm solenoid coils)

VT Range: -50 to +80°C
-130 to +300°C

Static

E^{free} (flat coil, solenoid coil)

Flat coil (HN, HCN)

VT Range: -50 to +80°C
-130 to +150°C

Material Science

Life Science

CP MAS

Low Gamma
(7 mm, 4 mm, 3.2 mm,
2.5 mm, 1.9 mm, 1.3 mm)

Extended VT Range
(7 mm, 4 mm, 7 mm Laser MAS)

CP MAS

HX, HFX, HXY, HFXY
(7 mm, 4 mm, 3.2 mm, 2.5 mm,
1.9 mm, 1.3 mm)

DNP (HCN, HXY)
(1.3 mm, 1.9 mm, 3.2 mm, 4 mm)

VT Range: -50 to +80°C
-130 to +150°C

CP MAS

E^{free} (4 mm, 3.2 mm)

HCN, HPC
(7 mm, 4 mm, 3.2 mm,
2.5 mm, 1.9 mm, 1.3 mm)

VT Range: -50 to +80°C
-130 to +150°C

Enrichment/Labeling Scheme
Enrichment of samples containing low natural abundance nuclei with the NMR active isotope. Very often ^{15}N / ^{29}Si / ^{13}C / ^{2}H / ^{17}O are used for enrichment. In biological solid state NMR the enrichment can be site-specific using a specifically chosen labeling scheme.

VT
Variable Temperature probes can be used to heat or cool the NMR sample during the experiment. The standard ranges are shown in the diagram above.

Decoupling
In cases where MAS alone is not fast enough, e.g. the hetero-nuclear dipolar coupling is not completely averaged, decoupling schemes such as CW, SPINAL or TPPM can be used as well as decoupling of heteronuclear or J-couplings using Waltz, GARP and other well known techniques.

Quadrupole Nuclei
Some NMR active nuclei possess a nuclear spin ½, but an integer spin or integer multiple of ½. e.g. ^{27}Al (I = 5/2) / ^{11}B (I = 3/2) / $^{6/7}Li$ (I = 1 and 3/2) or ^{2}H (I = 1) is a common quadrupole nucleus detectable by solid state NMR.

Low Gamma Nuclei
Nuclei with a low NMR frequency are called low gamma nuclei. By definition all nuclei with frequencies lower than the ^{15}N NMR frequency are referred to as low gamma nuclei.

QCPMG
Quadrupolar Carr-Purcell-Meiboom-Gill pulse sequence. Signal enhancement by use of a multiple spinecho acquisition scheme.

Inverse Probes
Probes optimized for proton detection; X nuclei are detected indirectly.

Applications – Material Science

Structure Elucidation

In recent years, solid state NMR has become the method of choice when approaching structural questions in materials. This is especially true where classical methods fail in providing sufficient insights to enable appropriate structural modeling, e.g. in disordered materials. In the field of battery science and so-called low gamma (low NMR frequency) nuclei, NMR is a powerful contributor in elucidating the inner properties of target samples.

Modern Pulse Program Library

For this purpose a large number of standard sequences are available, enabling the analysis of activation energies, structural motifs or phases in both, crystalline and amorphous sample sets.

Information Where Other Methods Fail

Recoupling methods (e.g. REDOR; Figure 10) can provide distance information and hence structural insights, even in samples where X-ray crystallography does not succeed. This is especially the case in samples of non-crystalline morphology, where solid state NMR can provide precise insights into the sample geometry and structural organization at an atomic distance. scale.

Figure 9: Sensitivity Enhancement.
^{49}Ti NMR spectrum of TiO_2 in rutile modification. Broad lines of nuclei with low gamma/low natural abundance and high C_q values (app. 13 MHz) are easily detected at very high field, as in this case with a 900 MHz AVANCE™ III WB spectrometer. QCPMG is used for signal enhancement. From this spectrum, the anisotropic quadrupole coupling constant can be extracted by using, for example, the TopSpin feature SOLA, to learn more about the electronic/crystal band structure of the material.
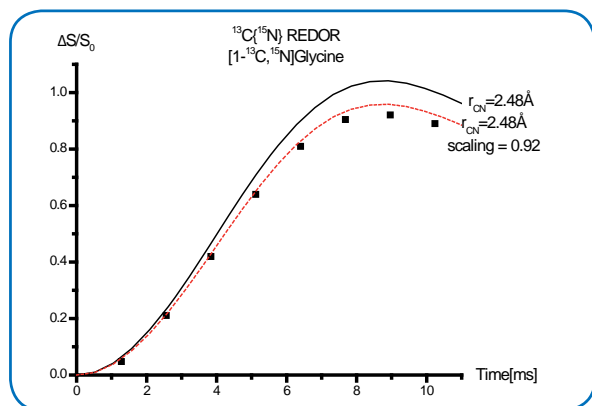

Figure 10: Structural Information.
REDOR experiments can provide insights into the structure of a material. Distances and bond angles can be extracted to produce a detailed view of the atomic structure of a sample.
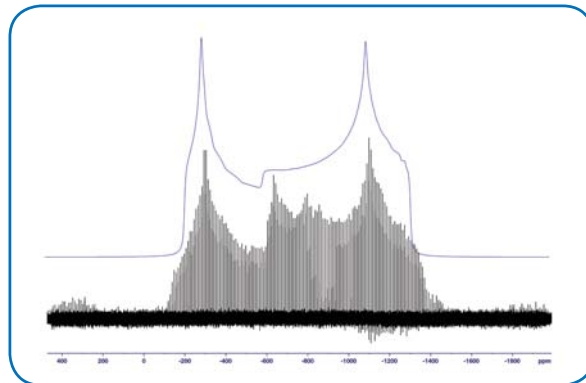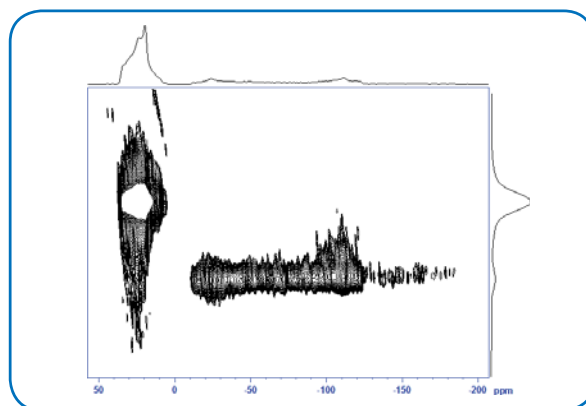

Figure 11: Multi-Quantum NMR.
For quadrupolar nuclei, solid state NMR can reveal the number of structural motifs in your samples, where traditional methods fail. Here, an MQMAS spectrum of Andalusite, detected without any further enhancement methods, is measured with a Bruker 1.9 mm probe. Both, the small coil diameter and the very fast Magic Angle Spinning, enable detection of pure and undistorted spectral features. Measured at 500 MHz/42 kHz MAS.

Polymers and Batteries

Polymer Structure

Polymers owe their desired chemical and mechanical features to a complex combination of chemical and physical properties. Chemical properties, for example, include cross linking and defect structure density; physical properties include phase behavior and phase transitions, heterogeneity and domain sizes, interfaces and interface interactions, as well as local mobility.

Solid state NMR can be applied to materials regardless of their local or long range order. Therefore ordered, as well as disordered, materials can be studied; the same holds true for partially ordered or heterogeneous systems. This makes solid state NMR highly suited to the study of polymers with respect to composition, cross linking, structure, dynamics, and other properties. In the case of heterogeneous or semi-crystalline polymers, structure, domain size, and interfaces can be characterized.

Batteries

Battery materials are subject to intense research due to their importance, for example, in electric powered cars or green energy storage. As with polymers, the desired electrical properties are due to a complex combination of chemical and physical properties. This includes composition and chemical reactions during charging or discharging, phase behavior and heterogeneity, as well as electrical and magnetic properties such as conductivity and paramagnetism. Here solid state NMR can again provide insights into structure, local order, molecular mobility, and chemical processes. Recent developments in high magnetic fields and probes make low gamma nuclei much more accessible with solid state NMR, while recent developments in very fast magic angle sample spinning enable the study of highly anisotropic systems, such as the paramagnetic materials often used in batteries.
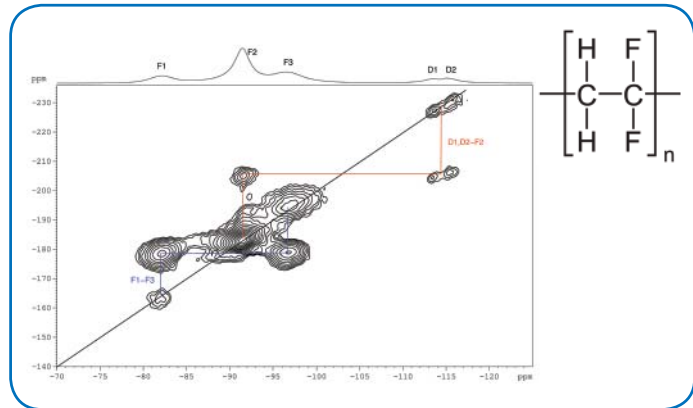

Figure 12: Connectivity.
^{19}F-^{19}F SQ-DQ correlation spectrum with ^{1}H decoupling. Characterisation of domains in semicrystalline poly(vinylidene)difluoride (PVDF) by homonuclear dipolar recoupling. $^{19}F\{^{1}H\}$ MAS experiments: The BaBa (back-to-back pulses) method was employed to achieve through-space dipolar double quantum/single quantum correlation. The experiment reveals two distinct spatially separated phases: (1) a crystalline phase with two inequivalent ^{19}F positions in the unit cell, indicated by the corresponding cross peaks of the F1 and F3 lines (marked in blue); (2) an amorphous phase with a single bulk signal F2 and incorporated defect structures, whose signals D1 and D2 show cross peaks to F2 (marked in red). All spectra were obtained using a 400 MHz instrument and a 2.5 mm H/F/X MAS probe at a spinning frequency of 30 kHz and 130 kHz of proton decoupling.
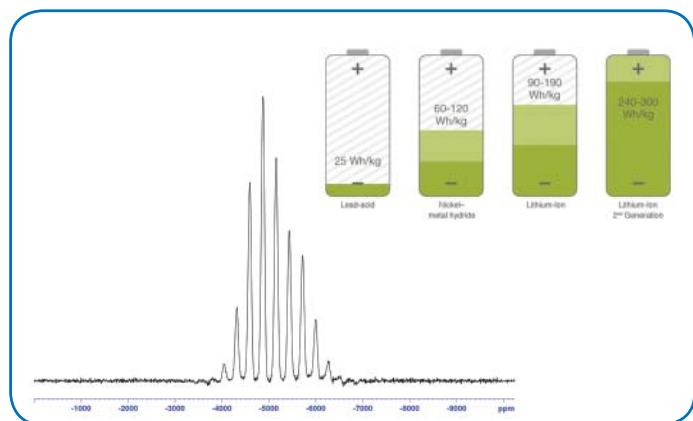

Figure 13: Ionic Materials.
High rotation rate MAS on battery materials. Paramagnetic samples can have a very large CSA contribution. In this case the detection of separated spinning sidebands is only possible at very high MAS rates. Measured at 500 MHz Spectrometer/55 kHz MAS).

● AVANCE III HD Hardware

High Power Solids

The new AVANCE III HD preamplifiers and GaAs FET-based broadband LNA technology increase sensitivity for solid state NMR applications by up to 20% on ^{13}C and other X nuclei. An impedance of 50 Ohms delivers spectra with excellent symmetry, and the built-in, fast, active high power transmit/receive switch guarantees maximum linearity even at low power levels.

Tune and Match

AVANCE III HD has full broadband capacity for solid state NMR, and enhanced electronics to match the sensitivity boosts provided by probes such as the CryoProbe Prodigy™ and SmartProbe™. Everyday routine operation is now much easier, with full automation replacing the need for manual interaction. The HPPR cover module touchscreen display now enables both high definition system tuning and matching and probe status monitoring.
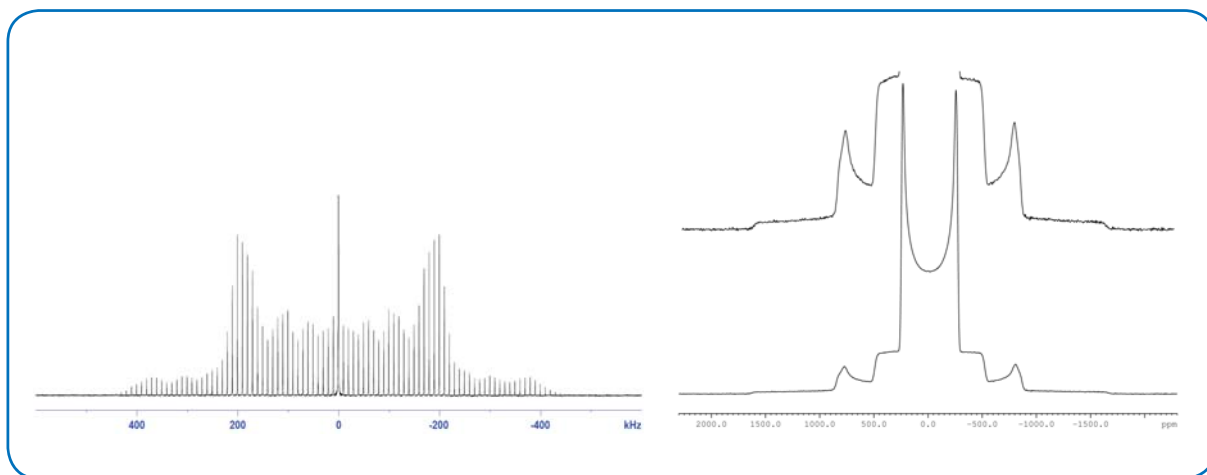

Figure 14: ^{23}Na spectrum of $NaBrO_3$ (left) and ^2H spectrum of D-PMMA (right).

High Dynamic Range NMR

AVANCE III HD's new RF synthesizer delivers significantly increased digital integration, incorporating a lower phase noise local oscillator (LO) and a high speed DA converter running at 960 MHz. This enables extended digital RF power settings up to frequencies of 1.2 GHz. Together with the new high dynamic range and high sensitivity preamplifiers, the AVANCE III HD demonstrates improved immunity to intermodulation artefacts, delivers sensitivity improvements of up to 30% and fully exploits the increased sensitivity of the latest NMR probe technology, for the most demanding applications.

More and more of these applications require excellent spectrometer performance under high dynamic range conditions. Aside from obvious applications such as bio-molecular samples in buffers or detergents, this applies to metabolomics and food & beverage samples. High dynamic range can also be important in trace analyses, such as the detection of impurities in drugs and pharmaceutical compounds.
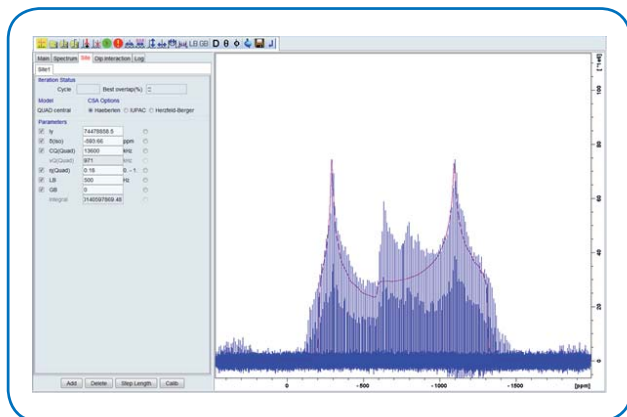
● TopSpin

The Next Generation of NMR Data Acquisition and Processing Software

TopSpin software acquires, processes and analyzes NMR data, all in one convenient, streamlined package. Ideal for those new to spectrometry, as well as routine users, TopSpin's acquisition tools make it easy for both beginner and expert to find their way to an NMR spectrum. TopSpin is designed for Windows®, Linux® and Mac users, and features a highly intuitive interface utilizing the most widespread standards from word processing, graphics and presentation programs, to provide a familar look-and-feel for your NMR applications.

Figure 15: Using the SOLA (Solid Line Shape Analysis) tool of TopSpin to calculate the central lineshape form of ^{49}Ti in Rutile TiO$_2$ (900 MHz / static).

Key Features

- PC-standard user interface offers easy accessibility for Windows® and Linux® users
- Comprehensive functionalities for processing, displaying and analyzing single and multi-dimensional spectra
- Intuitive acquisition
- Non-uniform sampling
- Small molecule characterization
- Dynamics Center
- Method development environment
- Result publishing, predefined and user-defined layouts
- Lineshape analysis for solid state NMR, including dynamic NMR
- Regulatory compliance tools (audit trailing, electronic signature, auto-archiving)
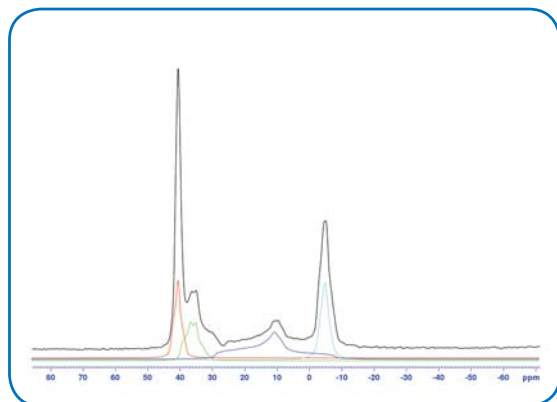- Special licenses for students and universities

Figure 16: Example of using SOLA for fitting several lineshapes; in this example the FIT was conducted on an Aluminiumphosphate sample (500 MHz/ 4mm MAS) and the result was stored as a simulated spectrum.
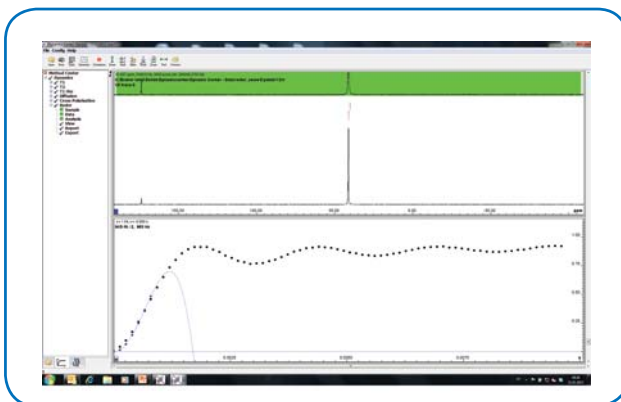

Figure 17: Dynamics Center gives you the tools to analyse your data, providing automatic routine and fitting procedures for T_1/T_2 times, REDOR, CP-Dynamics and Diffusion parameters.