**EMAR- Science meeting 2334**

# Scientific report

*Dynamic Nuclear Polarization: New Techniques, Methods and Applications*

*Monastery Eberbach, Eltville, Germany*
*4- 5 September 2009.*

Organised by JW Goethe University, Frankfurt am Main

http://www.bio-dnp.org/

*Local organizer:*

**Prof. Dr. Thomas Prisner,**
**BMRZ, JW Goethe University, Frankfurt**
**Tel: (49) 69 798 29406**
**prisner@chemie.uni-frankfurt.de**

**CONTENT of this document**

## Summary of the Meeting

The meeting brought together major European groups working on new technical and methodological aspects of DNP. The discussion of major recent developments and achievements of DNP at high magnetic fields led to many new insides and ideas.

## Scientific Content and Discussion

The concept of this workshop was rather different from usual scientific meetings and conferences. Instead of oral presentations of the participants, it focused on an open discussion of perspectives and general possibilities of the method, on the comparison of the different instrumental approaches, developments in microwave technology and novel ideas for effective polarization transfer methods. The discussion was structured by different topics (see program below) where two participants just encouraged the discussion by their own personal statements on perspective, potential applications (but also limitations) of their respective method. The discussion was critical but fair, and immediately stimulated all participants to an open and very constructive exchange of ideas, hints and remarks.

This concept worked extremely well; already the first discussion about **Dissolution-DNP**, conducted by Walter Köckenberger and Rolf Grütter went extremely lively (and much longer than expected):

Dissolution-DNP experiments are currently operating at 95 and 140 GHz using Gunn and Impatt diodes to generate the microwaves for the polarization process. This method utilizes DNP in the solid state at very low temperatures (1.2 K) at magnetic fields of 3-5 T. The polarization step is followed by rapid dissolution with a suitable solvent, and finally transfer of the sample to either a higher magnetic field, high resolution NMR spectrometer or MR imager. Very high polarizations for $^{13}C$ can be retained within the dissolution and transfer process. Limitations of the approach are the fact that the polarization times are hours, that the sample is diluted by a factor of

~70 in the dissolution process, that the dissolution is irreversibility, and that the sample must be shuttled between magnets.

Some of these problems are partially circumvented by integrating single scan 2D-NMR methods into the technique and by a new type of integrated magnet system with two centers, developed by Oxford and installed in Nottingham. The DNP enhancement obtained in the experiment is roughly identical to that observed in gyrotron based experiment, but an additional signal gain is obtained by the temperature jump, resulting in an additional Boltzmann enhancement factor of ~250. The experiment has been used to boost sensitivity, time resolution and contrast for applications in spectroscopy and imaging, and will undoubtedly be developed further in the future.

The second discussion session about **High-Field Solid State DNP** was moderated by Frank Engelke and Robert Griffin.

MAS DNP experiments are currently operating between 140 and 400 GHz microwave frequency at MIT; plans to move the experiments up to 600 GHz exist. Bruker is offering a commercial Solid-State MAS DNP spectrometer at 400 MHz NMR / 258 GHz EPR frequency (9.8 T). Biradicals have been shown to give larger signal enhancements compared to the solid-effect or thermal mixing at high magnetic fields by the cross-effect. At present the enhancements achieved in the experiment range from 40-400 at 90 K. Details of the polarization transfer mechanism as well as applications of the method are subject of current research. The high microwave excitation field used for this method can only be delivered by fixed frequency gyrotrons adapted for DNP requirements. Higher frequency tunable CW sources are under development and might interface to existing solid state NMR spectrometers. This approach has already been successfully applied to enhance MAS spectra of biological samples, as membrane and amyloid proteins. Because the instrumentation for MAS DNP experiments is now commercially available the application of this method, especially to membrane protein samples is expected to increase in the future and to solve resisting problems with the optimal preparation and conditions of such protein samples for DNP experiments.

In the last discussion session of the day Hans-Martin Vieth and Christian Griesinger introduced state-of-the-art and potential of the **Shuttle-DNP** method.

Shuttle-DNP combines well-established low-field EPR and high-field, high-resolution liquid NMR knowledge in a straightforward manner. The shuttle process is the most critical technological part and must be optimized with respect to shuttle speed and field profile. One big advantage of this approach is that the final NMR experiment can be performed in the usual way without any sacrifice with respect to spectral resolution, sensitivity and repetition of the experiment. The reduced polarization enhancement because of the polarization/detection field ratio might be compensated by more sophisticated polarization transfer pathways, as for example pulsed microwave excitations, which can be rather easily implemented at low microwave frequencies. Additionally, it might be possible to use higher polarized electron spin systems (as optical excited triplet states or radical pairs) in such systems. The field profile within the shuttle is very critical to avoid polarization losses by level crossings or by fast relaxation processes.

The second day started with a discussion on **High-field liquid DNP** moderated by Arno Kentgens and Thomas Prisner.

High-Field Liquid DNP polarizes the liquid solution *in-situ* at the magnetic field of the NMR detection and therefore without altering the sample parameters within the polarization-detection cycle. Promising high enhancements of 70 (at 3.4 T) and 30 (at 9.8 T) have been observed. Thus, if technical problems related to sample size, electric field heating and field homogeneity can be solved, this method could be very useful for extended NMR measurements typically encountered in structural studies on biological macromolecules. This observed enhancements cannot be explained by the force-free model used at magnetic fields below 1 T; new models including more realistic dynamics of the DNP agent and target molecules and more sophisticated quantum mechanical treatment of the DNP process are currently investigated and necessary for the prediction of enhancements at higher magnetic fields. Also the integrated double resonant EPR/NMR structures might become rather impractical at field values above 10 T and be substituted by separated structures. On the other hand, the possibility of exciting electron and nuclear spins simultaneously offers versatile prospects for coherent spin manipulations which might lead to improved polarization transfer pathways and new type of experiments.

It followed by a discussion on the necessary **high frequency microwave technology** for such DNP experiments with contribution from Daniella Goldfarb, Graham Smith and Vladimir Bradman.

Semiconductor microwave technology (Gunn and IMPATT diodes) reaches its limit at frequencies of ~100 GHz, corresponding to a magnetic field of 3.5 T (150 MHz $^1$H NMR). Higher frequencies can be attained most conveniently by generating higher harmonics, but with significant losses in power. Alternatives are vacuum electron devices, where an accelerated electron beam is modulated by suitable slow wave structures or magnetic fields. A number of different designs exist for continuous wave or pulsed operation, variable or fixed frequency. Devices such as backward wave oscillators, orotrons, and carcinotrons are used at high frequencies. Because of the presence of a slow wave structure, which has a size comparable to the microwave wavelength, the electron beam density close to this structure is limited, and leads to maximum deliverable microwave powers in the 0.1-1 W range. Gyrotrons, referred to as fast wave devices, circumvent this problem by replacing the slow wave structure with a cavity immersed in a magnetic field. In this configuration CW output powers in the watt range are achieved in devices designed specifically for DNP at MIT and more recently at Fukui University. Such devices are meanwile also available commercially from Bruker/ CPI and Gycom. To date the gyrotrons used for DNP experiments are fixed frequency oscillators, but tuneable sources and gyroamplifiers for time domain experiments would offer new opportunities for implementation of optimized polarization transfer schemes. Transmitting the microwaves to the sample in the probe with minimal losses can be accomplished by corrugated overmoded or metallo-dielectric waveguides. Quasi-optical microwave technology can be used for the detection of the EPR signal.

The final discussion on new **methods for spin manipulation** for DNP applications was headed by Steffen Glaser and Geoffrey Bodenhausen.

Here new methodological approaches for DNP were discussed. Long-lived singlet states can potentially be used to store the polarization over long time periods. This could be extremely important for all DNP methods were the sample has to be moved to the final target, as for example in MRI application of DNP. Pulse sequences to make such states useful for NMR experiments were discussed and proposed. Optimum-control theory and numerical methods can be used to optimize pulse sequences for polarization transfer from electron spins to nuclear spins or between nuclear spins. Additionally effort has to be spent to investigate the effect of spin diffusion on the final global DNP effect. A thorough theoretical understanding of the DNP mechanism at high magnetic fields will help to optimize the experiments and the DNP agent/target systems for specific applications.

A general discussion on potential common projects or initiatives on a European level was initiated by Thomas Prisner. DNP as an interdisciplinary new and emerging field has a very high scientific competence and manpower within Europe, but at the moment most of the funding and initiatives are on a national and local level. The EU COST program could be helpful to support further symposia and exchange between the research groups. Marie Curie Training Initial Training Network could help to advance the knowledge and skills of young researchers working in the field and bring them in contact with different applications and industry. An EU Framework 7 Design Study Project could place the foundations for DNP Research Infrastructures, which would support a broader community with this new method and bolster up new applications.

## Assessment of the results and impact of the event on the future direction of the field

The result of the workshop was rather on sharing of visions and ideas, unpublished results, trials and failures of the experts in the specific DNP techniques and methods, than presentation of published experimental results. In such a new and emerging field, with many open questions and obstacles, such an exchange of ideas and expertise’s is crucial for a fast and efficient development and a win-win situation for all participants. It will be important for the further advancement of the field to find efficient and good ways to establish such a cross-exchange between the active research groups. Potentially that could be established by integrated projects on a European level which could foster synergistic activities and joint developments.

**Programme**

Instead of conference talks and presentations the workshop consisted of discussion panels on several aspects of DNP. The two discussion leaders for each panel mainly stimulated the very lively discussions

***Friday, 4th September 2009***

| | |
|---|---|
| 14:00 - 15:00 | *Registration & coffee / tea* |
| 15:00- 15.30 | Introduction by Thomas Prisner |
| 15.30- 16.30 | Dissolution DNP (Discussion leaders W. Köckenberger/ R. Grütter) |
| 16.30- 17.00 | *Coffee Break* |
| 17.00- 18.00 | High-Field Solid State DNP (Discussion Leaders: R. Griffin/ F. Engelke) |
| 18.00- 19.00 | Shuttle DNP (Discussion leaders: C. Griesinger/ H.-M. Vieth) |
| 19.30-20.30 | *Guided tour Monastery Eberbach with wine tasting* |
| 20.30 | *Dinner* |

***Saturday 5th September 2009***

| | |
|---|---|
| 9:00-9:40 | Liquid State DNP (Discussion leaders: A. Kentgens / T. Prisner) |
| 9:40 – 10:20 | Microwave Technology (Discussion leaders: D. Goldfarb/ M. Smith) |
| 10:20-11:00 | *Coffee break* |
| 11:00 – 11:40 | Manipulation of Spins (Discussion leaders: G. Bodenhausen/ S. Glaser) |
| 11:40 – 12:30 | Summary and prospective Initiatives: Thomas Prisner |
| 12:30 | *Lunch/ Departure* |

**List of Participants:**

1. Marina Bennati (MPI Biophysical Chemistry,  Göttingen, Germany)
2. Geoffrey Bodenhausen (Ecole Normale Supérieure, Paris, France)
3. Vladimir Bratman (Gycom, Nizhny Novgorod, Russia)
4. Frank Engelke (Bruker,Karsruhe, Germany)
5. Steffen Glaser (Technical University, Munich, Germany)
6. Christian Griesinger (MPI Biophysical Chemistry Göttingen, Germany)
7. Daniella Goldfarb (Weizmann Institute, Rehovot, Israel)
8. Robert Griffin (MIT, Cambridge, USA)
9. Rolf Grütter (Ècole Polytechnique Lausanne, Switzerland)
10. Ulrich Günther (University Birmingham, UK)
11. Arno Kentgens (University Nijmegen, Netherlands)
12. Walter Köckenberger (University Nottingham, UK)
13. Claudio Luchinat (University Florence, Italy)
14. Kerstin Münnemann (MPI Polymer Research Mainz, Germany)
15. Thomas Prisner (JW Goethe University Frankfurt, Germany)
16. Miquel Pons (University Barcelona, Spain)
17. Graham Smith (University St. Andrews, UK)
18. Mark Smith (University Warwick, UK)
19. Hans-Martin Vieth (Free University Berlin, UK)
20. Vasyl Denysenkov (JW Goethe University Frankfurt, Germany)
21. Mark Prandolini  (JW Goethe University Frankfurt, Germany)