

The EU-NMR project, spanning Networking, the provision of Transnational Access, and Joint Research Activities for the Bio-NMR community in Europe, has recently finished its second year. At this, the project's halfway point, the current edition of the EU-NMR newsletter takes stock of the project's progress until now, as we look toward the future of the NMR infrastructure research system.

### SCIENTIFIC HIGHLIGHTS FROM THE EU-NMR PROJECT

#### *13C DIRECT DETECTION*

Tremendous improvements in instrumental sensitivity (high magnetic fields, cryo-probes, etc.) have recently been used for the direct detection of low gamma nuclei. A series of exclusively heteronuclear NMR experiments (protonless NMR), based on <sup>13</sup>C direct detection, have been developed that enable the complete sequence specific assignment of a protein without actively exploiting protons. These can be used as a complementary tool to proton detected NMR experiments for biomolecular applications, providing independent information on complex systems or for automation purposes. Protonless NMR experiments are geared to the study of specific systems where <sup>1</sup>H is bound to fail, such as paramagnetic systems, very large systems, and unfolded systems. Experiments based on <sup>13</sup>C direct detection may also benefit from the use of proton polarization as a starting point (<sup>1</sup>H-start) in all cases in which transverse <sup>1</sup>H relaxation is not the limiting factor.

#### *SENSITIVITY ENHANCEMENT OF METABOLOMICS APPLICATIONS: DNP-NMR*

Dynamic Nuclear Polarization (DNP) is a technique for the enhancement of NMR signal intensity that has recently received significant attention. An innovative application of DNP to the field of metabolomics, the characterization of the levels of all metabolites within a tissue or body fluid, and how these are affected by factors such as disease, drug treatment, diet, and aging, has recently been developed within EU-NMR. DNP can be used to boost the signal to noise ratio in the analysis of metabolomics samples; this enhancement can be obtained using automated sample handling, crucial in the processing of tens to hundreds of samples per day. DNP can open the way for the application of 2D NMR spectroscopy to metabolomics, which has been limited by time requirements and the difficulty of isotopically enriching samples.

#### *TOWARDS CRYO-PROBES FOR SOLID STATE NMR*

Solution NMR spectroscopy has benefitted tremendously from the availability of so-called cryo-probes, i.e. probes whose electronic parts are maintained at very low temperature while the sample is kept at around room temperature, affording an unprecedented increase in signal to noise ratio. An analogous improvement has recently been achieved within EU-NMR for solid-state studies, through the development of cold probe prototypes. In these probes, the entire system is maintained at a low temperature, including the sample. While there are currently limitations in terms of the loss of resolution / line broadening, limiting the impact for the study of biomacromolecules, this is a key step towards bringing one of the most important technological breakthroughs that has been achieved in solution NMR in the last decade to solid-state NMR.

### TRANSNATIONAL ACCESS

#### *STATISTICS*

One of the fundamental goals of the EU-NMR project is the provision of transnational access to the five Research Infrastructures for Life Sciences researchers throughout Europe. The table below summarizes the current statistics reflecting the project's performance in this endeavor, and reveals that EU-NMR is not only meeting its contractual obligations, but exceeding them.

	Access provided (number of days)	Number of users	Number of user groups
Stipulated per year	791	81	59
1 <sup>st</sup> year	1023	121	66
2 <sup>nd</sup> year	1143	131	82

#### *FEEDBACK FROM THE USERS*

A questionnaire prepared by Prof. Henriette Molinari was circulated among the users in January 2008 to assess all steps in their interactions with the RIs. A very positive picture of RI access emerged from the responses, including the following highlights:

- Evaluation phase: 50% of the users declared that they received useful suggestions from the evaluation panel that improved their experiments
- Access to wet lab: the overall quality of access was very highly judged (all marks 9/10 or 10/10)
- Access to instrumentation and quality of support: 90% of users needed technical support for experimental set-up and data analysis, and this was of excellent quality (all marks 9/10 or 10/10); 84% said that their knowledge level increased and that they modified their experiments as a result of interactions with supporting scientists

## RESEARCH INFRASTRUCTURES IN STRUCTURAL PROTEOMICS: ASSESSMENT OF BIO-NMR REQUIREMENTS

The availability of state-of-the-art NMR Research Infrastructures is strategically necessary to maintain Europe's leadership position in Structural Biology. To this end, the European Commission (EC) sponsored an assessment of the present and future needs of NMR Research Infrastructures from the users' perspective, carried out by the Forum for European Structural Proteomics (FESP), a Specific Support Action that addresses large-scale infrastructures within Structural Proteomics (including NMR spectroscopy, electron microscopy, protein production, bioinformatics, and synchrotrons). FESP circulated a questionnaire among the users of bio-NMR Research Infrastructures and to NMR research scientists throughout Europe and summarized the findings in a report to the EC. The report addresses the current status of European biological research utilizing NMR infrastructures, and is intended to contribute to the formulation of policies concerning infrastructure requirements for Structural Genomics / Structural Proteomics (SG/SP) and Structural Biology (SB) over the next 5-10 years.

In summary, FESP strongly recommended the continued funding of access to Bio-NMR facilities, including support for user travel, sample shipment, technical staff, and running costs. The report found that existing research infrastructures providing transnational access are adequate to meet current needs. However, it is foreseen that demand will significantly increase in the near future, with a wide range of emerging applications, increasing interest in solid-state NMR, and users from new EU member states. FESP believes that procedures for the generation of automated NMR data acquisition routes should be enforced in order to ramp up throughput, and remote access procedures should be implemented to reduce user expenses and time-consuming user travel to the NMR Research Infrastructures. Finally, the development of NMR methods should be strengthened, as the design and implementation of new technologies for macromolecular characterization and preliminary analysis by NMR in solutions and solids are essential for maintaining the competitiveness of European SG/SP and SB in both academia and industry, and require close collaborations between NMR manufacturers and the NMR community. Such developments include higher magnetic fields, improved sensitivity, further exploitation of cryogenic probe technology for solution and solid-state NMR, dynamic nuclear polarization (DNP), fast data acquisition, very high speed magic-angle spinning (MAS) and probes optimized for proton detection in solid-state NMR, and automation software and hardware. Methodological aspects to be addressed include NMR techniques to obtain structural restraints for high molecular weight systems (residual dipolar couplings, paramagnetic tags) and the combination of NMR with complementary techniques (e.g. X-ray crystallography, Small Angle X-ray Scattering, EM, etc.).

### THE IMPORTANCE OF NETWORKING

A meeting entitled "Networking in Bio-NMR" was held on January 5, 2008 in Florence, Italy for representatives of regional bio-NMR facilities as they address their modes of interaction in the face of the new challenges posed to NMR by their users. This meeting was sponsored by the EC-funded Coordination Action NMR-Life and involved 35 representatives from European NMR infrastructures, who were invited to share their suggestions on how to improve the network among them. The first session addressed the EU-NMR project, under which part of this network is currently active. One point of discussion was related to new forms of integration between the national and transnational facilities. It was suggested that networking funds be used to advertise the potentialities of each laboratory to the others, and that seed money be provided to encourage the implementation and exchange of new and advanced experimental methods. It was foreseen that future developments in I3 projects will be in such directions as offering sample preparation and labeling schemes, networking with regional/national infrastructures to broaden the user base and provide pre-screening of users' needs, and expanding the offer of service to Life Science projects in agriculture and food science. The idea that the I3 should continue to focus on encouraging users in emerging applications at the forefront of Systems Biology was stressed, and ideas for future applications were presented.

### THE FUNCTION OF THE INTERNATIONAL EVALUATION PANEL

At the recent joint EU-NMR – CA NMR-Life annual meeting, Prof. Katalin Kövér presented her comments on the function of the project's International Evaluation Panel. The general sentiment was that the panel was pleased with the function of the application/evaluation process, along with the high quality of the applications received. Prof. Kover also presented some suggestions for the improvement of the process on an administrative level, including the need for improved communication among different evaluators working on individual applications to avoid lost opportunities for evaluation and overlap.

Further information can be found online at the EU-NMR website:

<http://www.eu-nmr.eu>

