Center of Nuclear Magnetic Resonance (NMR)

Introduction

The Center of Nuclear Magnetic Resonance (NMR Center), which was incorporated in the Network of Horizontal Laboratory Units and Centers (and from 2010 to the Network of Research Supporting Laboratories) of the University of Ioannina in 1999, has a multi-scientific and technological character and addresses pure and applied research in the Chemistry, Physics and Medicine Departments, the Department of Materials' Science and Technology and the Department of Biological Applications and Technologies, of the University of Ioannina, as well as the Regional University Hospital of Ioannina. Furthermore, the NMR Center is directly linked to the Institute of Biomedicine Research and the technological Park of Epirus (Fig. 1).

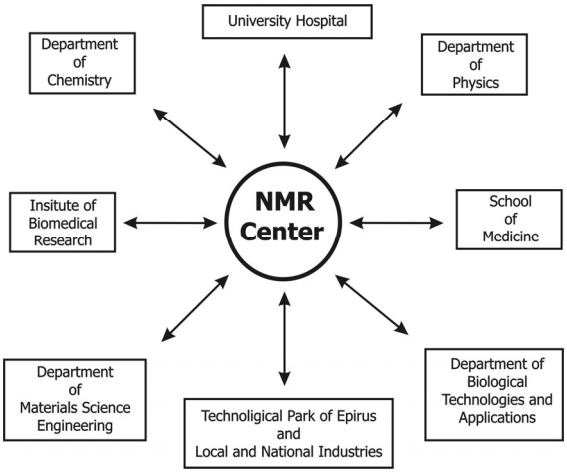


Figure 1: Links between the NMR Center and other Institutions of Epirus.

Nuclear Magnetic Resonance Spectroscopy is based on nuclear magnetic moment transition within a strong static and homogenous magnetic field B_0. These transitions as caused by the application of an electromagnetic irradiation in the region of 1000 – 10 MHz depending on the field strength. The resonance frequency of a particular nucleus, such as ^1H, is not constant but it depends on the electronic environment of the proton (Fig. 2). Based on this property NMR has made a tremendous impact, at a molecular level, in many areas of chemistry, biology and medicine.

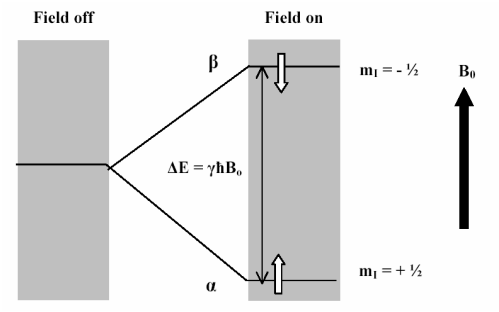


Figure 2: The nuclear spin energy levels of ^1H nucleus in a magnetic field.

Facilities & Infrastructure

Since 1995, the NMR Center is lodged in specially tided up rooms, at the Department of Chemistry of the University of Ioannina. The facility was expanded at 2006. The instrumentation consists of:

- A Brücker AV-250 spectrometer (resonance frequency of ^1H 250 MHz) that has been installed since March 1999 (Fig. 3). It has been bought in the frame of EPEAEK "Bioinorganic Chemistry" and with the subsidy of the deanery of the University of Ioannina. This instrument is suitable for acquiring routine spectra and for teaching purposes. The AV-250 has been recently updated to both hardware and software.
- A Brücker AV-400 spectrometer (resonance frequency of ^1H 400 MHz), with the capabilities of obtaining high-resolution spectra in the liquid and solution state and with the future possibility for NMR spectra in the solid spectra (Fig. 4). This instrument has been supplied with suitable accessories, so it can work in a wide range of temperatures and with almost all the magnetically active nuclei of the Periodic Table. The instrument has been bought through the EEC Stride-Hellas 33 program, in which research groups of the Department of Chemistry and the School of Medicine participate, with further subsidy from the University of Ioannina and public investments of the Department of Chemistry. In 1997, the instrument was further equipped with a field z-gradient probe,

which is appropriate for NMR studies of biological macromolecules in aqueous solution. The AV-400 has been recently updated to both hardware and software. At 2009 a laser unit was supplied that would be hyphenated to the AV400 system.

- A Brücker AV-500 spectrometer (resonance frequency of ^{1}H 500 MHz) hyphenated with LC-SPE system, the latter equipped with a solvent delivery pump, a DAD UV detector and a Prospect 2 solid phase extraction (SPE) unit (Fig. 5). All individual components are connected in line to produce LC-SPE-UV-NMR hyphenation. This modern instrumentation was sponsored by the Greek Community Support Framework III, Regional Operational Program of Epirus 2000 – 2006 (MIS 91629). Moreover the AV500 was equipped with a cryogenic platform and a cryo TXI -probe head (Fig. 6). The latter can be easily "converted" to flow probe and work in flow mode after the necessary modification through the mounting of a flow inlet.

Figure 3: General view of the Brücker AV-250 spectrometer (resonance frequency of ^{1}H 250 MHz).

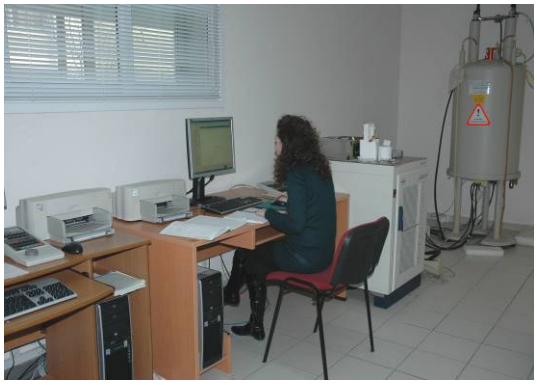


Figure 4: General view of the Brücker AV-400 spectrometer (resonance frequency of ^{1}H 400 MHz).

Figure 5: General view of the Brücker AV-500 spectrometer (resonance frequency of ^{1}H 500 MHz) and the LC-SPE system.

Figure 6: The cryo-unit that is connected to the cryo-probe at the AV500 system.

The running cost of the instruments of the Center is about 16.900 € per year. The payment of the technician or the technicians of the instruments of the NMR Center, the outlet of the fixed consumables (liquid He and liquid N_2) and the repairing of the instruments are covered by the budget of the University of Ioannina.

FUTURE DEVELOPMENT

- Computational Facilities

Three workstations are available to the users for data manipulation. The two of them have the Top-spin suite and the third has additionally the AMIX –Aurelia suite.

Moreover, a computer cluster with several PCs working in the Linux environment will be acquired in the next few months, for facilitating the NMR data acquisition, data retrieval and database integration. Several bioinformatics tools will be installed for protein structure determination, protein structure databases, protein-ligand docking, etc.

- Solid state accessories on the AV-400

With this experimental setting, it would be possible to characterize both the structure and dynamics in the solid state of various systems of interest from the academic and industrial point of view.

- New NMR instrumentation

There will be an increasing demand for NMR equipment in the next few years. The increased need will be both quantitative (number of instruments) and qualitative (higher fields). Furthermore, an exponential increase in number of biological systems to be investigated (quantity) as well as in complexity of these systems (quality) will be expected. The expansion, therefore, of the NMR Center with a high field (greater of equal to 700 MHz) NMR instrument, fully equipped with multinuclear and multidimensional (3D and 4D) capabilities, is of high priority. Moreover, in order to cover all the kind of samples, the purchase of a solid state NMR is of high priority.

Services

The main objective of the NMR Center is to offer the know-how in a cost-effective way and in collaboration with:

- Research groups of the University of Ioannina and other Greek Universities
- Research centers
- Hospitals
- Industries

in the following fields of basic and applied research:

- Synthesis and structural studies of new chemical compounds with emphasis on drug design and biotechnological products.

  Modern NMR techniques contribute significantly in controlling synthetic pathways and in performing conformational studies of a wide range of compounds of biological and pharmaceutical interest. With the recently developed multinuclear and multidimensional NMR techniques, the above studies can be extended to much more complicated biological molecules (such as proteins in complexation with drugs), which can contribute in the field of drug design.

- Materials.

  NMR is a powerful technique (sometimes being the only method of choice) for the study of new materials of technological interest, such as glasses, ceramics, polymers, synthetic membranes etc.

  NMR spectroscopy in the solid phase can be used to investigate reactions taking place in catalytical surfaces, which have important financial and technological benefits. Catalysis includes many important fields of applications such as oxidation, corrosion and formation of hyperfine films of technological interest.

- Food analysis.

  NMR spectroscopy can be used in the verification of the wine aging and authenticity, as well as in the identification of the oil's fatty constituents and the various extracts of natural products. It can also contribute in the investigation of the mechanisms that are responsible for food decomposition, without requiring sample destruction in contrast to the classical chemical analysis techniques.

- Clinical Applications.

  NMR can be used in the location and characterization of metabolites in biological fluids in vivo and ex vivo and thus, can be utilized in the diagnosis of many kinds of diseases.

- Environmental applications.

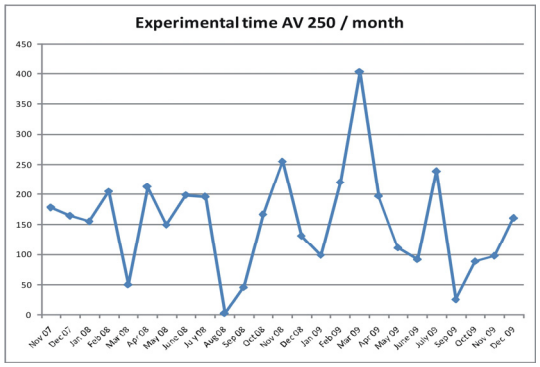
  NMR spectroscopy contributes in the study of environmental issues, concerning air and subsoil pollution (e.g. retention of organotoxic compounds from humic acid).

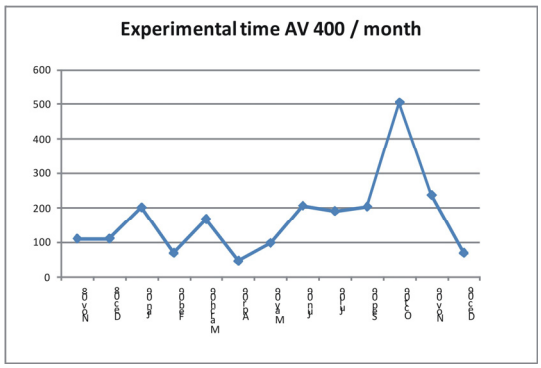
EXPERIMENTAL TIME FOR THE USAGE OF THE NMR CENTER FACILITIES

Figure 6 displays the experimental time occupation of the NMR center facilities. Especially for the AV 500, the cryoprobe resulted in a significant increment of the experimental time occupation.

Staff & Contact Information

An Administrative/Scientific Committee, made up of University of Ioannina staff members, is responsible for the operation of the Center, the improvement of its equipment and the rendering of services. A scientist with a PhD in NMR-related subjects and post-graduate experience abroad is responsible for the instruments. He/she is in charge of obtaining routine and complicated spectra, providing education to researchers and ensuring the normal operation of the instruments.





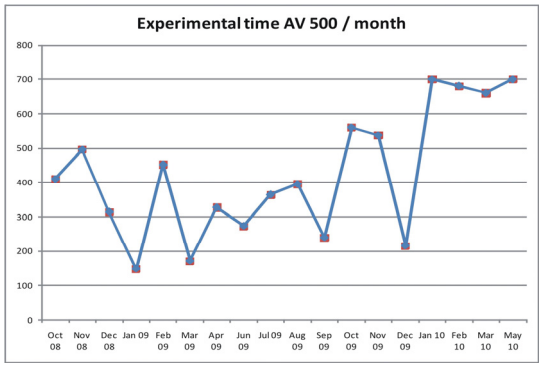


Figure 6. Graphical display of the Experimental time Usage for the three AV units.

Additional information concerning the NMR Center can be obtained from Prof. I. Gerothanassis who is the chairman of the Administrative/Scientific Committee:

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Representative Publications

1. I. P. Gerothanassis, C. Vakka and A. Troganis, "^{17}O NMR Studies of the Solvation State of Cis/Trans Isomers of Amides and Model Protected Peptides", *J.Magn.Reson., (B)*,111, 220-229 (1996).
2. E. Katsarou, A. Troganis and N. Hadjiliadis, "Binary and Ternary Complexes of Platinum (II) with the Dipeptide Esters Gly-GlyOEt, Gly-AlaOMe, Gly-2-AbaOMe, Gly-nValOMe, Gly-nLeuOMe and the Nucleosides Guo (Guanosine) and Cyd (Cytidine)". *Inorg Chim. Acta*, 256, 21-28 (1997).
3. C.G.Kalodimos and I.P.Gerothanassis "Carbon-13 Nuclear Shieldings as a Novel Method in Estimating Porphyrin Ruffling in Hexacoordinated Superstructured Heme Model Compounds in Solution", *J. Am. Chem. Soc.* 120, 6407-6408 (1998).
4. K. D. Soulti, A. Troganis, T. Kabanos, A. Keramidas, Y. Deligiannakis, C.P. Raptopoulou, A. Terzis, "Model Studies of the Interaction of Vanadium(III), IV and V with the Carbonyl Amide Oxygen", *Inorg. Chem*., 37, 6785-6794 (1998).
5. I.P.Gerothanassis, V. Exarchou, V. Lagouri, A. Troganis, M. Tsimidou and D. Boskou, "Methodology for Identification of Phenolic Acids in Complex Phenolic Mixtures by High Resolution One- and Two- Dimensional Nuclear Magnetic Resonance. Application to Methanolic Extracts of two Oregano Species", *J. Agric. Food Chem.* 46, 4185-4192 (1998).
6. T.Tselios, L.Probert, G.Kollias, I.Daliani, E.Matsoukas, A.Troganis, I.P.Gerothanassis, T.Mavromoustakos, G.J.Moore and J.M.Matsoukas, "Design and Synthesis of a Potent Cyclic Analogue of the Myelin Basic Protein Epitope MBP72-85: Importance of the Ala81 Carboxyl Group and of a Cyclic Conformation for Induction of Experimental Allergic Encephalomyelitis (E.A.E)", *J. Med. Chem*. 42, 1170-1177 (1999).
7. A.Troganis, I.P. Gerothanassis, Z. Athanassiou, T. Mavromoustakos, G.E. Hawkes and C. Sakarellos, "Thermodynamic Origin of Cis/Trans Isomers of a Proline-Containing β-turn Model Dipeptide in Aqueous Solution: A Combined Variable Temperature ^{1}H-NMR, Two Dimensional ^{1}H,^{1}H Gradient Enhanced NOESY, One-Dimensional Steady-State Intermoleuclar ^{13}C,^{1}H-NOE and Molecular Dynamics Study", *Biopolymers*, 53, 72 (2000).
8. V. Tsikaris, A. Troganis, V. Moussis, E. Panou-Pomonis, M. Sakarellos-Daitsiotis, C. Sakarellos, " Arg Side Chain-Backbone Interactions Evidenced in Model Peptides by ^{17}O-NMR Spectroscopy", *Biopolymers*, 53, 135-139 (2000).

9. E. Bairaktari, K. Seferiadis, G. Liamis, N. Psihogios, O. Tsolas, M. Elisaf, "Study of the reversible Renal Tubular Damage due to Acute Rhabdo-myolysis by ^{1}H-NMR Spectroscopy of Urine", *Clin. Chem*., 48, 1106-1109, (2002).
10. Y. Georgakilas, G.P. Perdikomatis, A.S. Triantafyllou, M.G. Siskos, A.K. Zarkadis, "Friedel-Crafts Acetylation and Benzoylation of Benzylsilates and Xanthenes', *Tetrahedron*, 58, 2441 (2002).
11. Tatsis, E.C., Exarchou, V., Troganis, A.N., Gerothanassis, I.P., "^{1}H NMR determination of hypericin and pseudohypericin in complex natural mixtures by the use of strongly deshielded OH groups", *Anal. Chim. Acta*, 607, 219-226 (2008).
12. Goulas, V. Exarchou, V., Troganis, A. Psomiadou, E. Fotsis, Th. Briasoulis, E.Gerothanassis, I.P., "Phytochemicals in Olive-Leaf Extracts and their Antiproliferative Activity against Cancer and Endothelial Cells", *Mol. Nutr. Food Res.*, 53, 600-608 (2009).
13. Kontogianni, V.G., Exarchou, V. Troganis, A. and I.P. Gerothanassis, "Rapid and Novel Discrimination and Quantification of Oleanolic and Ursolic Acids Extracts in Complex Plant. Using Two Dimensional Nuclear Magnetic Resonance Spectroscopy-Comparison with HPLC Methods", *Anal.Chim.Acta*, 635,188-195 (2009).
14. Nikolakis, V.A., Stathopoulos, P., Exarchou, V., Gallos, J.K., Kubicki, M., Kabanos, T.A., "Unexpected synthesis of an unsymmetrical μ-oxido divanadium(V) compound through a reductive cleavage of a N-O bond and cleavage-hydrolysis of a C-N bond of an N,N-disubstituted Bis-(hydroxylamino) ligand", *Inorg. Chem.*, 49, 52-61 (2010).
15. Goulas V., Papoti V.T., Exarchou V., Tsimidou M.Z. and Gerothanassis I.P., "Contribution of Flavonoids to the Overall Radical Scavenging Activity of Olive (Olea Europea L.) Leaf Polar Extracts", *J.Agric. Food Chem*. in press (2010).
16. Charisiadis P., Exarchou V., Troganis A.N. and Gerothanassis I.P., "Exploring the "Forgotten"- OH NMR Spectral Region in Natural Products", *Chem.Commun.*, 46, 3589-3591 (2010).
17. I.P. Gerothanassis, "Oxygen-17 NMR spectroscopy: Basic Principles and Applications Part I", *Progr. Nucl. Magn. Reson. Spectrosc.*, 57, 1-110 (2010)

It is noted that more than one hundred (100) articles have been published in international scientific journals, during the first eight years of operation of the NMR Center. Additionally, during the last 5 years (2004-2009), 26 M.Scs and 16 PhDs have been supported by the NMR Center facilities. Furthermore during the above time period, 47 scientific publications in international journals have cited and acknowledged the NMR center facilities.