NMR in the Netherlands

A strong past and present - a versatile and promising future

Strategic Investment Plan 2012-2021

Contents

List of abbreviations

NMR	Nuclear Magnetic Resonance
NWO	Netherlands Organisation for Scientific Research
MRI	Magnetic Resonance Imaging
T	Tesla

1. Summary

A roadmap is presented for the investments in Nuclear Magnetic Resonance (NMR) Spectroscopy in the Netherlands. NMR spectroscopy is a versatile technique that is employed in diverse scientific areas, including life science, material science and medicine. The technique also has a wide range of medical and industrial applications, for example as medical diagnostic tool, in the food industry and in industrial quality control.
NMR spectroscopy traditionally has been a scientific stronghold in the Netherlands, with well-recognized, excellent research groups active in all the above-mentioned research areas. This position was bolstered in the past by the long tradition of support for the Dutch NMR infrastructure, both for NMR spectrometers and support staff. New technical developments enable a next step in NMR technology, promising exciting new applications. In the Netherlands investments in the NMR infrastructure are required to remain at the international forefront.
The proposal calls for an investment of close to 90 million euros over the next decade. This investment will maintain the Dutch NMR infrastructure at the highest level and allow the traditionally strong Dutch NMR community to keep its renowned position and continue to develop and apply the technique for innovative solutions benefitting society. Therefore, the proposed investment will stimulate the development of a Dutch knowledge-based economy, and contribute to addressing major outstanding challenges in areas such as health & life science, chemistry and sustainability.

Nederlandse samenvatting

In dit document wordt een investeringsplan gepresenteerd voor een verbeterde infrastructuur voor kernspinresonantie (nuclear magnetic resonance, NMR) spectroscopie in Nederland. NMR-spectroscopie is een veelomvattende techniek die wordt toegepast op talrijke wetenschappelijke terreinen, zoals de levenswetenschappen, materiaalwetenschappen en geneeskunde. De techniek heeft ook allerlei medische en industriële toepassingen, bijvoorbeeld in medische diagnostiek, de voedingsindustrie en industriële kwaliteitscontrole.
NMR-spectroscopie is al lang één van de pijlers van de Nederlandse wetenschap met excellente en beroemde onderzoeksgroepen die werken op bovengenoemde terreinen. Aan de basis van dit succes ligt een uitstekende, structurele financiële steun voor de Nederlandse NMR-infrastructuur, zowel voor apparatuur (NMR-spectrometers) als personeel. Nieuwe technische ontwikkelingen maken een volgende stap in NMR technologie mogelijk, met de belofte van spannende nieuwe toepassingen. Investeringen in de Nederlandse NMR-infrastructuur zijn noodzakelijk om aan het internationale front van de wetenschap te kunnen blijven.
Er wordt voorgesteld om circa 90 miljoen euro te investeren in het volgende decennium. Deze investering zal de Nederlandse NMR-infrastructuur op het hoogste internationale niveau houden en zo de traditioneel sterke Nederlandse NMR-gemeenschap de kans geven om zijn internationale positie te behouden en uit te bouwen, en door te gaan met de ontwikkeling en toepassing van deze techniek ten dienste van de maatschappij. Daarmee draagt deze investering direct bij aan de Nederlandse kenniseconomie en in het bijzonder aan de aanpak van uitdagingen op belangrijke gebieden betreffende gezondheid & levenswetenschappen, chemie en duurzaamheid.

2. Preamble

The development of molecular sciences for materials, food and health critically depends on comprehensive and non-invasive product characterization. Nuclear magnetic resonance (NMR) spectroscopy is probably the most widely applied analytical method and has now found widespread application in biology, medicine and materials research (Box 1). The versatility of the technique to characterize equally well all kinds of materials, biomolecules, processes and living organisms makes NMR spectroscopy an indispensable tool in the search for solutions for major problems that face our society. To give some examples, NMR spectroscopy contributes to the development of sustainable energy supply by characterisation of new battery and solar cell materials. It is applied to obtain fundamental knowledge of the causes of disease and to screen for new compounds that can be developed into medicines, and NMR spectroscopy is used to improve crop production and food quality.

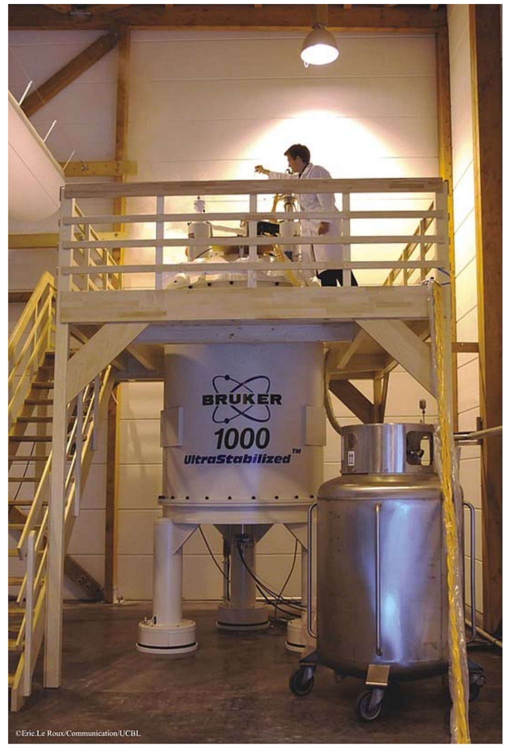
NMR can be considered special because *fundamentally* novel scientific discoveries in NMR have consistently emerged with the development of science. This has resulted in six Nobel prizes awarded across disciplines and over several decades, the most recent one in 2003. The versatility of NMR is rooted in the sensitivity of nuclei towards their environment, in combination with the ability to manipulate nuclei in many different ways, for both spectroscopy and imaging, virtually without perturbing the object of investigation.

The Netherlands has a strong position in NMR, which is underpinned by a long scientific and educational tradition. The Dutch NMR community has demonstrated a trendsetting role in shaping European NMR research across disciplines. NMR scientists from the Netherlands are internationally recognized and receive international respect in the form of scientific awards and memberships of international conferences and editorial boards. In recent years, a new generation of scientists, supported by PIONIER and VICI grants, has started reshaping the Dutch NMR research, ahead of the international competition. Benefitting from the historically strong infrastructure, they were able to exploit and expand the breakthroughs in NMR for structural biology, materials science and imaging from the 80s and the 90s.

BOX 1: Versatility of nuclear magnetic resonance

- Chemistry: For identification and structure determination of molecules and materials in chemical industry and research. No chemistry lab can do without NMR spectroscopy.
- Life Science: For elucidating the structure, functional dynamics and interactions of large biomolecules (proteins, DNA, RNA, sugars) that are the basis of life, health and disease.
- Solid materials: For the characterisation of a range of solid state materials, from batteries to food, from plastics to proteins.
- Imaging: For the visualisation and functional analysis of tissues and organs of human beings (e.g. for diagnosis of patients) as well as animals, plants, food and materials.
- Disease diagnosis: For quantitative analysis of metabolites in disease diagnosis and prevention (metabolomics).
- Transport processes: for characterization of flow in (bio)porous materials with applications in diverse fields like chemical engineering, medicine, food technology, geophysics, biology and ecology.

However, the Dutch infrastructure in NMR is in danger of falling behind[1] compared to those in other Western European countries and already a new generation of NMR instrumentation and hardware is on the horizon. Exciting developments include ultrahigh field magnets, based on new materials for superconducting magnets, as well as portable, low field NMR/MRI with many industrial applications. Such improvement and diversification of equipment offer great prospects for forcing further breakthroughs.



The 1 GHz NMR spectrometer in Lyon.

Image taken from www.bruker-biospin.com/av1000-gallery.html

The magnet is at the heart of any NMR spectrometer and it is the quest for stronger and higher magnetic fields that has always been the main driving force in the fast growth and diversification of the NMR technique. Increased field strength enhances the sensitivity, allowing to measure on smaller or more dilute samples, and it also improves the resolution of the NMR spectrum, enabling more complex samples to be analyzed. For example, the ultrahigh fields will make it possible to perform high-resolution NMR experiments on living cells, and they will extend greatly the fundamental understanding of the biomolecular interactions that underlay healthy and diseased biochemical processes. Another application will be in the characterisation of thin films, for example for battery materials. The enhanced sensitivity at high fields is critical to obtain sufficient signal from these thin layers.
Such high-field instrumentation is not yet available within the Netherlands and planning of national budgets in balance with international developments is therefore required. The current plan focuses on advanced NMR and imaging (MRI) research facilities. Clinical MRI centres are not included.

In contrast with the past, when the scientific field was split into the subdomains of structural biology, (bio)materials science and imaging, each with its own scientific culture and accompanying values, recent scientific cross-fertilization has led to a unification in methodology development among the new generation of NMR

[1] "The current national resources for infrastructure have been highly insufficient for a number of years now. As a result the pressure on the limited resources that NWO has available for infrastructure, has been very high, in particular for medium and large-scale facilities. This situation represents a serious threat for the development and innovation of research in The Netherlands, which partly for this reason threatens to fall behind internationally."

Translated into English from *Startmotor NWO-strategie, Gespreksnotitie voor externe consultatie over de NWO-strategie 2011-2014*, p.8

spectroscopists in the Netherlands. This generation has set out on a course to forge a versatile and unified NMR infrastructure for the Netherlands that follows the national strategies in the life sciences and materials sciences and will keep the Netherlands at the forefront in NMR spectroscopy.

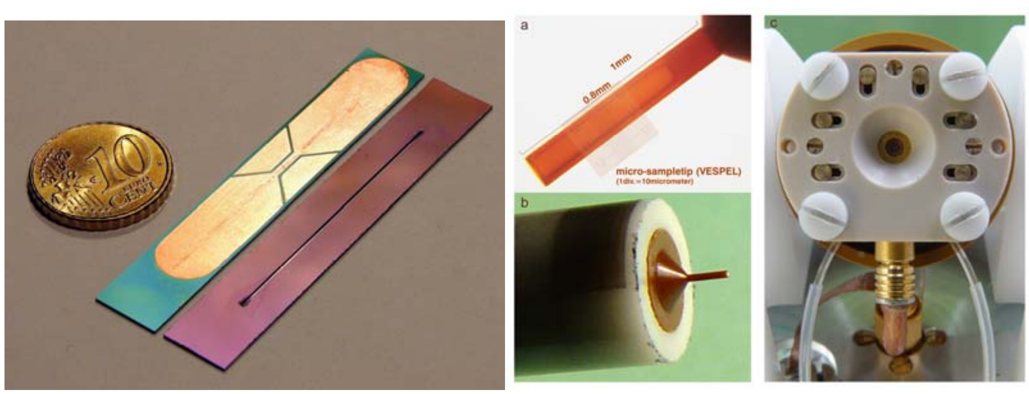
The purpose of this document is to present, at a high scientific ambition level, main focal points and a roadmap for the continuous development of a national NMR infrastructure. This roadmap builds on major investments and strengthens the national strategies focused on maintaining global economic competitiveness, improvement of public health, protection of the environment, efficient use of energy and other resources, security of food supply, and mitigation of the threat of climate change.

In chapter 3 the importance of NMR spectroscopy in three application areas is illustrated and in chapter 4, the roadmap for investments in NMR infrastructure is laid out.

3. Focus Points

3.1 The Role of NMR in Energy & Materials

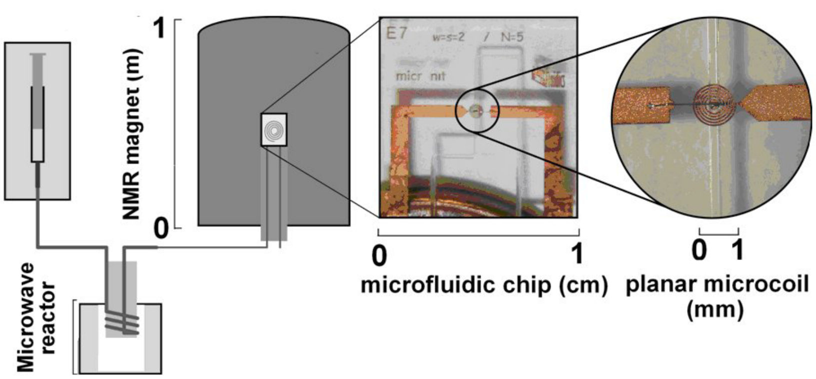
The analytical power of NMR will be key to the great technological challenges that face mankind concerning the sustainable energy supply for the future. Research in this area is rapidly gaining interest, as evidenced by the commitment of the European Union (EU) to realize a European Research Area in the field of energy. In this context, the European Commission (EC) is developing a Sustainable Energy Systems policy. Creating a sustainable energy supply is also high on the agenda of the Dutch government. The Netherlands Organization for Scientific Research, NWO, has recently launched an initiative for funding multidisciplinary energy research, covering the whole spectrum of energy conversion and storage. The Foundation for Fundamental Research on Matter (FOM) is expanding and relocating the Rijnhuizen Institute to the FOM Institute for Energy Research, which should be the pivot of a national and international collaboration of research groups focusing on fundamental energy research.
Discoveries and breakthroughs in sustainable energy technologies depend strongly on progress of materials research to yield insight in the structure-function relations of new materials. NMR has developed into the most versatile tool to study both ordered and disordered materials. Ongoing research programs comprise photovoltaic conversion, hydrogen storage and production, nuclear fusion and clean combustion and new ones are proposed for hybrid conversion of biomass, solar fuels, distribution of electricity and energy storage. Examples of the application of NMR technology in energy research are highlighted below.



New miniaturized NMR detector technologies open the way for detection of nanoliter volumes. In the liquid-state the stripline detector (left) allows in-situ reaction monitoring in microfluidic devices, whereas the piggy-back magic angle spinning device (right) opens the way for high-resolution solid-state NMR of micro crystals.
Ongoing research at the Radboud University Nijmegen.

Solar cells. Solar energy is one of the most attractive supplies of sustainable energy, because enough solar radiation reaches the Earth's surface every *hour* to meet the world's *annual* energy needs. The problem lies in harnessing this resource. A major challenge is finding an optimal balance between efficiency and durability. This is approached from different sides, either by mimicking the processes taking place in nature to create solar fuels (see below). Alternatively, an important supply in the near future is based on inorganic materials that convert light into electricity. Understanding the structure and functional properties of these materials at the nanometer scale, solid-state NMR techniques are indispensable. This calls for high-field implementations and novel NMR probes with microcoils to improve sensitivity to the level that single layers of the photovoltaic material can be analyzed.

Batteries. The introduction of sustainable energy supplies is accompanied by the need for more efficient energy storage media. Such developments require a fundamental understanding of the relation between the substance that contains the energy and the storage medium. For example, to design materials optimized for hydrogen storage and release (e. g. for cars) we need knowledge of the interactions at the atomic scale between the components of these complex materials. Thus, analytical methods will play a vital role in the production of successful battery materials.
Recent work on battery materials has shown that modern, high field NMR can characterize disordered materials, and in particular the crucial small and mobile atoms, such as hydrogen and lithium. It can also be used to analyze batteries during operation, helping to understand the charging/discharging process, the performance and the aging. A range of NMR techniques, like pulsed field gradient techniques and imaging approaches, can also be applied to study transport phenomena within the novel materials, both in bulk and thin films.



Nanoliter NMR spectroscopy in a hyphenated microwave-NMR-on-a-Chip set-up.
Ongoing research at the Technical University Twente

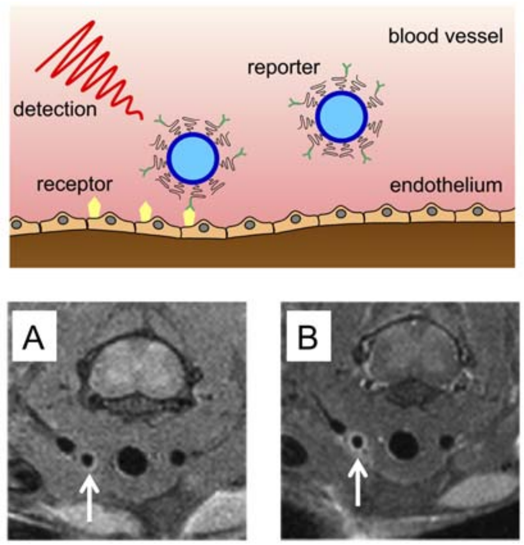
Biofuels and other biomaterials. In a sustainable economy, plant products are used for the so-called **4F**-products, not only for **F**ood and **F**eed (animal foods), but also as an alternative source of raw materials (**F**ibers/chemicals) and **F**uel, to replace fossil fuels. The development of a bio-economy requires improvement of the knowledge of the plants and microbes providing the renewable resources, in soils that need to be properly managed for sustainable bio-production as well as in bio-product processing. For example, economical catalytic routes have to be developed to break down biomaterials, such as cellulose, into compounds for chemical industry. Many NMR methods, like flow NMR, imaging and high resolution solution and solid state NMR, can contribute to this development, for example in the following areas:

- Analysis of key plant functions, like distribution of water, carbon and nutrients, and structures.
- Determination of water and substance transport in soils.
- Composition and structure analysis of plant-based products.
- Control of the processing of biological materials to measure quality and conversion efficiency.

3.2 The Role of NMR in the Life Sciences and Health

NMR spectroscopy is used for understanding the foundations of life and causes of illness but also for very practical applications in drug development and diagnosis of disease. Developing applications offer great promise, like NMR as a tool in personalized medicine.

New health-related applications. Over recent years NMR has found new applications as an analytical tool in health care. At the micro-millimeter scale, the NMR variant magnetic resonance imaging (MRI) has provided insight into anatomy and tissue function under a variety of clinical conditions. Rapid advances in molecular medicine and nano-technology provide unique opportunities for the development of MRI-guided therapies of human diseases. Magnetic Resonance Spectroscopy represents a powerful analytical tool for metabolic profiling with applications ranging from biological fluids and isolated cells to the human brain. Furthermore, NMR is combined with other analytical techniques (e.g. MS, HLPC) and also has become a leading technology as a screening method, for instance in drug-development.

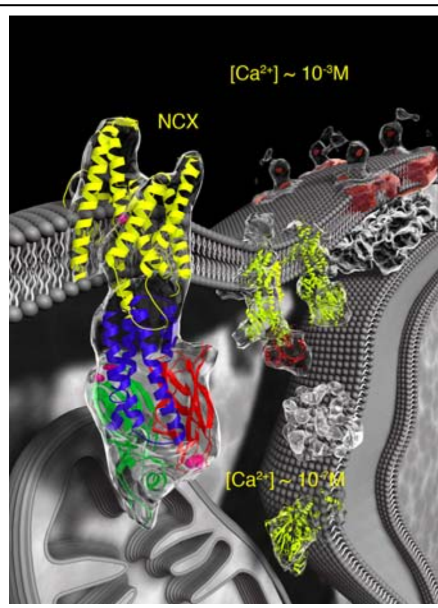


Imaging of molecular markers of disease with MRI. (*top*) Schematic of a targeted contrast agent that binds to a blood vessel wall. (*bottom*) MR images of the neck region of a mouse with atherosclerosis taken before (A) and after injection of the contrast agent (B), lighting up specifically a diseased blood vessel wall. Work from the Technical University Eindhoven.

NMR for structure and dynamics. In the classical application of NMR spectroscopy to infer molecular structure and dynamics at atomic scale many exciting developments are taking place. The size barrier that hampered NMR studies on large biomolecules and their complexes for a long time has been overcome, now enabling atomic-level information to be extracted from large molecular machines.
Recent progress in solution-state and solid-state NMR reveals that under cellular-like conditions and even in living cells, the examination of 3D molecular structure and its variation through functional processes has become possible.
Rapid developments of solid-state NMR methods result in exiting synergies in the technologies and approaches used by the researchers in this field and those of the solution NMR field. Integrated studies have provided crucial insight into the structural aspects of molecular misfolding in a variety of neurodegenerative diseases and these approaches are readily applicable in health-related research areas such as drug quality control, regenerative medicine or the design of biomaterials.

Understanding the processes of life & disease. NMR spectroscopy offers approaches to achieve a central goal in life sciences, i.e. the comprehension of the processes of Life, responsible for the function or malfunction of cells and tissues. To understand how biological processes, such as DNA replication and protein folding, are carried out, pictures and action movies in atomic detail are needed. A merger of crystal diffraction, electron microscopy and NMR spectroscopy is ongoing with each technique providing pieces of the puzzle. NMR spectroscopy is capable of providing structural 3D details as well as valuable information about dynamical processes regarding the interacting biomolecules. For example, it is the only technique that yields information about transient interactions at the atomic level and recent NMR studies on such systems have revolutionized our thinking about biomolecular interactions and proven the previously postulated concept of the 'encounter complex'.
NMR-derived interaction data can be used to model interaction networks within the cell. Such models enable identification of suitable drug targets for treating common human diseases, ultimately leading to a more effective approach in the form of personalized therapeutic interventions.

All these developments demonstrate that NMR applications are rapidly expanding into entirely new fields with numerous unforeseen possibilities and benefits. NMR research in the Netherlands is at the forefront of many of these developments. Given the appropriate support Dutch researchers can contribute to the establishment of NMR as the leading technology to examine processes in the living cell in a comprehensive manner from the test tube to the clinical setting.

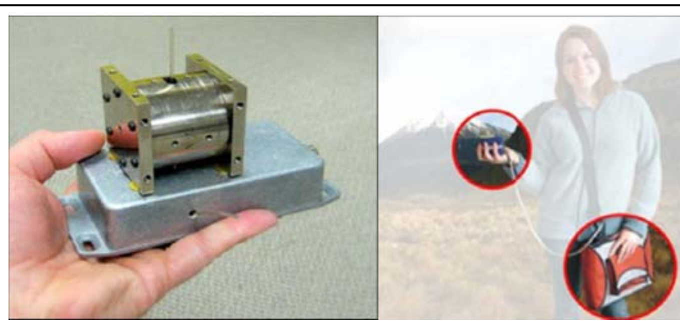


The sodium-calcium exchanger protein maintains the correct calcium levels in de cell. The regulation of this essential process has been elucidated with NMR spectroscopy by researchers at the Radboud University Nijmegen.

3.3 The Role of NMR in Food

Various NMR and MRI methods are important for food product innovations, like new food with proven health promoting components. The development of healthier food with less fat, salt and sugars is not trivial, because the ingredients define the texture, consumer appreciation and stability. For many questions about composition and (micro-)structure high-field, frequency-domain NMR instruments are crucial. In addition, time-domain (TD) instruments operating at relatively low-fields have also found wide spread use. This is primarily due to their relatively low cost, ease of operation and ability to quickly provide quantitative information on product structure and composition. TD-NMR instrumentation can be found throughout all areas of food science and technology, including industry.
Future challenges are the development of advanced NMR/MRI methods to study structure-function relations during processing of healthy and functional foods (including bio-nanotechnology) and to demonstrate health effects.

Food structures under shear-stress: processing, cooking, chewing. Structures at different length-scales are common in foods and determine many properties such as texture and controlled delivery of healthy components. Product innovations in this area are often hampered by the lack of understanding of the relations between food processing, resulting structures and the properties relevant for the consumer. The assessment of food structures over the entire range from nanometer to centimeter is a major bottleneck, which is addressed by new developments in MRI techniques. These new approaches will add to the understanding of food structure formation and degradation during food processing, as well as during consumption, offering food scientists and technologists opportunities to design superior food materials such as structured gels/emulsions (e.g. Unilever), composite products and ingredients (e.g. FrieslandCampina and Unilever) and meat/fish alternatives (e.g. Vion).



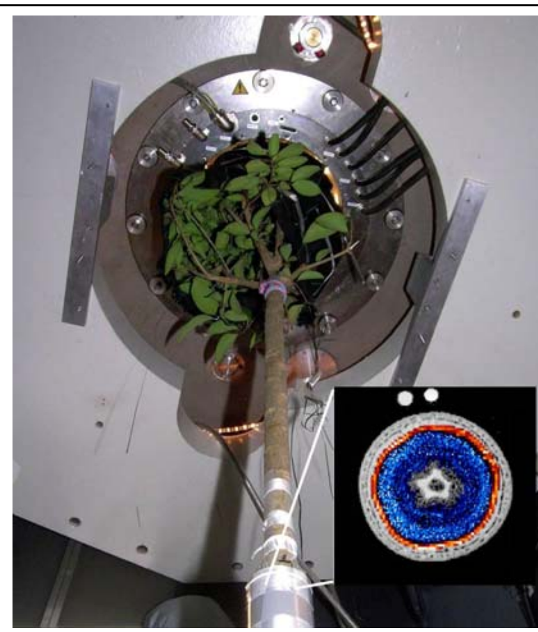
Portable NMR/MRI:
There is a strong development in downsizing NMR and MRI sensors for various specific research applications and in-line quality assessment. Such research is ongoing at Wageningen University

Pictures taken from B. Blumich, J. Perlo, F. Casanova, Prog. NMR Spectroscopy 52 (2008), 197-269.

Healthy food. Food can also contain health promoting components. Demonstrating the beneficial effects is, however, not straightforward. NMR is a quantitative, universal detector for organic compounds, a property exploited in metabolomics (see Box 1 on page 4). This technique can help to analyze health promoting effects by body fluid analysis. The potential for diverse applications like pre-patient diagnostics, healthy aging, personalized medicine, dietary correction of the onset of diseases, are enormous. The success of such applications strongly depends on high-throughput methods, well-developed databases, automated data interpretation and increased NMR sensitivity and specificity.
The growing concerns on the increase of diet and lifestyle related diseases will increase funding for disease prevention and health maintenance research initiatives. Within large scale intervention trials and cross-sectional cohort studies NMR distinguishes itself as a tool for rapid acquisition of metabolic signatures for impact of diet and lifestyle on health status. Without adequate NMR infrastructure the Netherlands will not be able to benefit from national and European funding opportunities.

Food, health and consumer interaction:
An example.

Consumers have a high appreciation for Fruits and Vegetables (F&V) as essential ingredients of attractive and good tasting products. Furthermore, F&V are our major dietary source of vitamins and several other essential food components. Thus, the intake of F&V has been associated with a wide range of beneficial health effects. Nevertheless, the Dutch take only half of their daily recommended consumption of F&V, which leads to app. 120.000 deaths, and a 3% increase in national health care cost.
A main hurdle for consumers to raise their daily intake is the lack of convenience in preparing foods. The food industry has addressed this by offering the consumer dried F&V that are rehydrated shortly before consumption ('just add water'). There is a major market for such products, but their lowered quality is a bottleneck for further growth.
Time-Domain NMR, MRI and NMR based metabolomics methods on plant extracts and body fluids offer new and exciting approaches to unravel the relation between food structure, water behaviour during de- and rehydration, chemical (nutritional) composition and health stimulating effects.



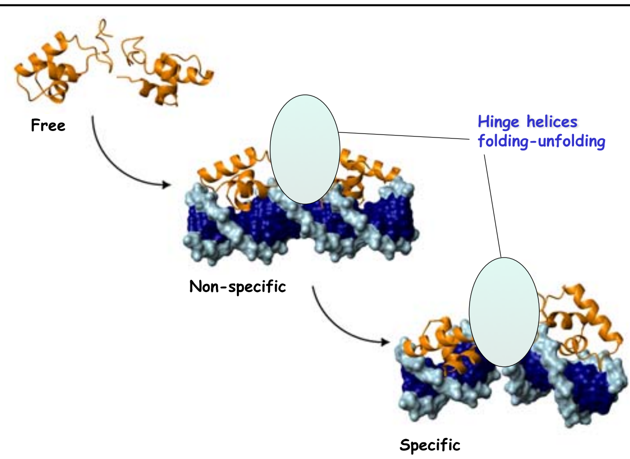
With MRI on intact plants the transport of water in the stem can be monitored directly and non-invasively. The inset shows a slice trough the stem, coloured according to flow properties.
Such studies are essential for improvement of crop production, especially in green houses. This research is ongoing at Wageningen University

4. Roadmap for the Future of NMR in the Netherlands

4.1 Investments in infrastructure

The NMR magnet presents the most relevant and decisive aspect of any NMR spectrometer. For most NMR methods a very strong magnetic field is a necessity and new application areas have become accessible with each increase in available magnetic strength. Both the resolution, i.e. the discriminative power, and the sensitivity of NMR spectroscopy improves with the increase of the strength of the applied magnetic field. It should be noted though that high magnetic fields are not required for all applications and interesting developments are forthcoming in the design of portable NMR machines with small magnets for specific applications in the field of food technology and quality control.

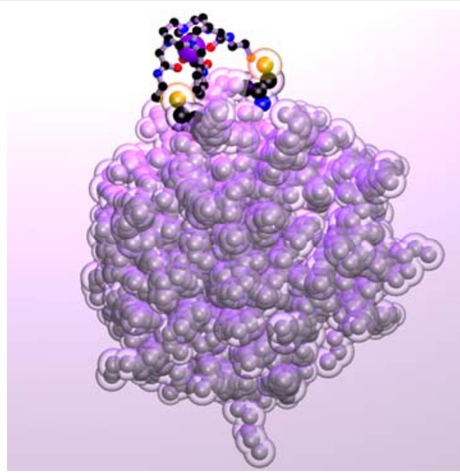
Not only the field strength, also its homogeneity and stability are essential for the generation of high quality results. Over the last few decades enormous progress has been made in producing homogeneous, highly-stable and ever increasing fields. This development was propelled in particular by the introduction of superconducting magnets. In these magnets a strong current runs permanently through a long, coiled superconducting wire that is cooled to very low temperature with liquid helium. The highest magnetic field achieved for a NMR spectrometer with this technique is 23 Tesla (T) or ~1 GHz proton resonance frequency. For comparison, the earth magnetic field is 460,000 times smaller (0.00005 T).
The first 23 T spectrometer was installed in Lyon, France, in the summer of 2009, whereas three 22.3 T spectrometers have been installed recently in Europe (Oxford, Frankfurt, Paris), and a similar number will soon come in North America (Kannapolis, Maryland, Toronto). With the materials currently used for the wire, significant further increases in the field strength are deemed not possible, but new superconducting materials, with properties even better suited for creating strong fields, are available. For a long time it was not feasible to create a long wire from these brittle materials, but this problem has recently been overcome by technological innovations. Thus, in the NMR community it is expected that in coming 5 years 25.7 T and 28 T magnets will become available. It is important to note that within the Netherlands currently only a single 21 T spectrometer is available. Thus



With NMR spectroscopy it was demonstrated how a protein binds to DNA to regulate gene expression. This research was performed at Utrecht University.

the Netherlands has lost possibilities for NMR research at the highest available field. Hence most of the NMR experiments are inescapably performed under non-optimal conditions on 9 – 14 T spectrometers. Similar reasoning applies to the so-called horizontal-bore magnets for life science and biomedical research: 11.7 Tesla currently is the highest field available in the Netherlands, whereas 16.4 T systems have recently been installed elsewhere.

An assessment of the improvements obtained from previous increases in field strength shows great significance for the quality of NMR spectra as well as the resolving power in imaging applications. Higher sensitivity will again make it possible to pursue new applications, such as high resolution NMR within living cells or characterization of thin films, e.g. for batteries (see sections 3.1 and 3.2). Clearly, if our country intends to maintain its leading role in NMR research, we should empower our research groups with competitive equipment and hence investments in NMR infrastructure will be absolutely necessary.



A metal-containing molecule attached to a protein. The molecule is a probe specifically developed for advanced NMR studies of proteins at Leiden University

Below, we outline a two-phase investment strategy[2] (see Table 1) that first provides the NMR infrastructure a position at the international front (phase 1) and then guarantees to maintain that for the coming 10 years (phase 2).
We designed the investment strategy considering the diverse needs of the different applications of NMR technologies. As magnets become increasingly expensive with increasing field strength, it is imperative to use them for as wide a range of applications as possible. An important property in this respect is the bore size of the magnet, i.e. the inner diameter that determines the type of samples that can be measured. Standard bore (SB) can be used for all high-resolution NMR on liquid samples (e.g. structural biology, metabolomics). Solid state NMR and imaging require more space in the magnet and use wide bore (WB) magnets. Thus, the best solution is to have several top field spectrometers, both SB and WB, in the main NMR centers in the Netherlands, supported by lower field magnets in those centers as well as other NMR groups (see section 4.2).

Phase one of the investment strategy, "Reaching the forefront", covers the period 2012-2016 and will bring the infrastructure back to an internationally competitive level, supporting a new generation of NMR spectroscopists in Eindhoven, Leiden, Nijmegen, Utrecht and Wageningen. In addition, upgrades and improvements to currently available NMR magnets across the Netherlands are also budgeted. Investments in the past have ensured that lower field NMR spectrometers are available in the Netherlands (see site descriptions in Appendix I). As the lifetime of their magnets is long (up to 20 years) and in most cases not expired, replacement of their now outdated electronic equipment (the "console", maximum lifetime 7-9 years) re-establishes full-scale operational capabilities. In Phase one, already resources should be allocated for actively engaging in the aforementioned new superconducting technology that is currently emerging. Germany, Switzerland, France and Italy have already planned investments in vertical-bore 28 T spectrometers as soon as they will come available on the market. In order to be among the first sites installing this next round of NMR spectrometers, options for purchasing from the developing manufactures (Bruker/Agilent) need to be negotiated now, in the early stages of their development. It is expected that the first spectrometer at this field can then be operational toward the end of Phase one.

Phase two, "remaining at the forefront, 2017-2021", investments in two additional 28 T spectrometer are foreseen to expand the possibilities of such high fields to all the applications that need the increased bore size. In phase two, resources should also be allocated for the installation of a 18.7 T horizontal-bore system for life-science and biomedical research and a wide-bore flow system for plant research.
In the Netherlands we have one of the few high-field magnet laboratories in the world. The magnets in these labs are either resistive or hybrids of superconducting and resistive magnets. Although in principle not suitable for NMR, pilot experiments have shown that these magnets can be adapted to play a role in development of the technology leading to ultra high field NMR spectrometers and can support specific solid-state NMR experiments of functional materials. Following up on the developments in the Nijmegen HFML we like to take on the challenge to create unique opportunities for NMR at fields of 30, 38 and 45 T.

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[2] Our plans only relate to research NMR spectrometers and not to medical MRI scanners. Several high field MRI scanners (7 T) dedicated for patient care have recently been installed in hospitals in the Netherlands.

The roadmap for the NMR infrastructure proposes to invest an average 9 million Euros per year for the coming ten years, in an essential part of Dutch research infrastructure. This investment will re-establish the level of NMR infrastructure at the international competitive level and assure its position at the forefront for the coming decade. NMR spectroscopy and imaging have proven records of innovative contributions to society and the ongoing developments described in the section above show that more can be expected from such an investment. It will allow the traditionally strong Dutch NMR community to maintain its renowned position and continue to develop and apply the technique for innovative solutions, with benefits for science, society and commerce.

Table 1.

Roadmap for investments in NMR infrastructure for the coming decade.

(SB = standard bore, WB = wide bore)

	Phase I	Phase II	
Year	2012 - 2016	2017 - 2021	Total
Eindhoven	Imaging (WB, horizontal) M€ 5		5
Leiden	paramagnetic bioNMR (SB) M€ 4	Ultrahigh field NMR (28T WB) M€ 18	22
Nijmegen		Ultrahigh field NMR (28T WB) M€ 18	18
Utrecht	Ultrahigh field NMR (28T SB) M€ 18		18
Wageningen	850 MHz metabolic profiler (SB) M€ 3	2nd generation Intact Plant MRI (WB) M€ 4	7
Nationwide: upgrade & maintenance	M€ 10	M€ 10	20
Investment (M€)	35	55	**90**

4.2 National and international embedding of Dutch NMR groups

The nationwide infrastructure will form a grid of complementary facilities. Each of the major NMR centers has specific expertise areas and are embedded in the focus areas of the 'sectorplan Chemie'. Most Dutch NMR groups participate in activities of the European Union, as facilities, in European Networks or with extensive collaborations.

- The NMR groups (Nicolay, Magusin) at Eindhoven University of Technology develop advanced NMR imaging and spectroscopy techniques for materials, life science and biomedical research. The Nicolay group is active in an FP6-Network-of-Excellence, an FP6 Integrated Project, an FP7 Integrated Project and two COST actions (*i.e,* COST action D38, entitled 'Metal-Based Systems for Molecular Imaging Applications', and the recently approved COST Action TD1004, entitled 'Theragnostics Imaging and Therapy'). In the sectorplan Chemistry, Nicolay's group is involved in focus area "Complex Molecular Systems". TU/e also participates in the focus area "Catalysis" of the sectorplan Chemistry.

- Leiden houses two major NMR groups with a focus on high resolution NMR on proteins and protein-drug interactions (Ubbink, Siegal) and MRI and MR spectroscopy in medical context and solid-state NMR (de Groot, Matysik, Alia). The Ubbink/Siegal group participates in the focus area 'Chemical Biology', together with two other groups. This area was supported in the sectorplan by positions for an additional full professor and a tenure track researcher. Ubbink has been coordinator of a European Training Network on Protein Interactions and has many NMR collaborations throughout Europe.
  The group of de Groot is part of the focus area 'Theory and Spectroscopy', supported in the sectorplan with a position for a full professor and has managed an EU facility for high-field solid state NMR. Currently, it participates in a NMR working group for the EU ESFRI project Instruct (An Integrated Structural Biology Infrastructure for Europe).

- Nijmegen functions as a solid-state NMR facility for functional materials research. Locally two groups are active, focusing on the development of new NMR methodology and its application in materials science (Kentgens) and metabolomics and nucleic acids (Wijmenga). The groups are part of the Institute for Molecules and Materials (IMM), focusing on designing and understanding functional molecular constructs and materials. The IMM accommodates a number of advanced spectroscopic facilities such as the High Field Magnet Laboratory, Nanolab, NMR and the Free Electron Laser Facility. The NMR spectroscopy groups participate in the focus areas 'Advanced spectroscopy on molecules and materials' and 'Chemical Biology', which have been supported with several positions in the sectorplan. The Kentgens group has coordinated a European Training Network in the past and is currently involved in the I3 Infrastructures (European Magnet labs) by coordinating a Joint Research Activity for the development of resistive and hybride magnets larger than 30 T (EUROMAGNET I and EUROMAGNET II in the sixth and seventh framework programmes). The Wijmenga group is involved in a EU STREP project.

- Utrecht comprises three NMR groups with a focus on high resolution solution (Boelens), solid state (Baldus) and computational (Bonvin) studies of biomolecules and their interactions. By following a holistic approach integrating computational structural biology methods with information from NMR and various biophysical, biochemical and bioinformatic sources the groups aim at obtaining a comprehensive description of the structural and dynamic landscape of complex biomolecular machines. The Utrecht NMR groups is a prominent member of the Bijvoet centre that received support in the sectorplan focus area 'Structural Biology'. Utrecht has been a NMR Research Infrastructure for Biomolecular NMR since 1994. In the current programs (EastNMR, 1999-2013, and Bio-NMR, 2010-2014) the Utrecht facility provides access on their instruments for both solution- and solid-state NMR on biomolecules. Average access ~280 days per year. In addition Utrecht is an e-Infrastructure in Life Sciences, e-NMR, serving computational needs of biomolecular NMR users from Europe, also beyond the NMR Research Infrastructures. From November 2010 this continues as We-NMR, by including complimentary techniques such as SAXS, and expanding to a worldwide network. In addition Utrecht is involved in the NMR working groups for the EU ESFRI project Instruct (An Integrated Structural Biology Infrastructure for Europe). The Utrecht groups also have been involved in a large number of EU projects and Networks.

- Wageningen focuses on (TD)NMR and MRI development and applications to study intact plants for plant performance and production, food processing and quality (Van As, Van Duynhoven), high-resolution hyphenated NMR for food-health relationship by body fluid analyses (high throughput metabolomics, proteomics and biomarker search; Vervoort, Van Duynhoven) and (ribosome-bound nascent) protein folding (Van Mierlo). Since 1992 Wageningen NMR Centre (WNMRC) has been supported by EU funding to stimulate access to Research Infrastructure WNMRC for NMR in agriculture, food and biology. In the sectorplan Chemistry, the WNMRC is involved in the focus area Biomolecular Sciences, including Colloid Chemistry and Bionanotechnology, and contributes to research in the focus areas Food Chemistry & Technology, Biomedical & life sciences and Physics of Life.

A more extensive description of the research focus points can be found in Appendix I.

4.3 Returns for Society

Generation of knowledge. The investments proposed here will stimulate the application of NMR research in the diverse areas of energy, a sustainable society, food and health. Each of these areas poses major challenges with great societal impact. As detailed in the section above, the ever-increasing ability of the non-invasive analysis tools that NMR spectroscopy and imaging offer, will be pivotal in reaching new solutions to those serious problems facing our society.

Education and training. The proposed infrastructure will reinforce the status of Dutch universities as leading research and educational institutions on an international scale.
Training in frontier research areas by university staff ensures that students of all levels will receive high quality education. Education in NMR in the Netherlands has always been important at universities in the Netherlands, forming many well renowned scientists over the years, like the most-cited chemist, Dr. Ad Bax (NIH). Teaching NMR spectroscopy is embedded in all chemistry departments at both bachelor and master levels because NMR plays an important role in any chemical synthesis lab. The need for well-trained analytical chemists has been recognized by the industry leading to the TI-COAST initiative. Nowadays, NMR spectroscopy and imaging courses are also contributing to the education in an expanding range of other disciplines, like structural biology, biophysics, food and soil sciences, medicine, biomedical engineering and biotechnology.
More advanced courses are offered at the master level, both within universities and at a national level such as the yearly Bijvoet-Nijmegen Research Alliance NMR courses organized for master and PhD students from The Netherlands and for international students. Similar joint initiatives exist for solid-state and in vivo NMR. A yearly course is organized by MRI groups from Wageningen, Eindhoven, Nijmegen and Utrecht. A further expansion of such efforts, forming a truly national NMR training platform, is foreseen in the context of our current initiative.
Finally, all leaders of Dutch NMR groups are involved in teaching at and organization of international PhD schools and workshops (e.g. EMBO summerschools and courses in in vivo NMR organized by ISMRM and ESMRMB) and training courses for industrial partners (e.g. workshops on NMR in Food, and a range of training activities of the international NMR Centers). To maintain NMR education at such a high level it is important to have both active research groups and modern instrumentation.

Industrial activity. Discoveries in NMR research have always been strongly linked to industrial applications. Indeed, NMR has played a leading role in industrial research, development and quality control in health care, food and material science industries. In addition, NMR has fostered the emerging of new companies.
The Netherlands harbors a number of industrial companies that play an important role in the field of NMR. Philips Healthcare, for example, is one of the three major vendors of medical imaging equipment, including MRI scanners for use in patient diagnostics and image-guided therapy. A significant part of the front-end technology developments for medical use of NMR is done at Philips Research. It should be noted that a main part of the NMR scientists working at Philips on improving the clinical utility of NMR, are trained at the centers involved in this initiative.

NMR spectroscopy is also a cornerstone of the analytical sciences, which play a crucial role in innovation in many sectors of our modern society. Therefore, this initiative is supported by TI-COAST, a public-private partnership that aims to reinforce the position of Analytical Sciences in The Netherlands across a wide range of application areas, such as those outlined in 2011 in the proposed "Topsectors" for the Netherlands. NMR contributes to 5 out 9 of these strategic research areas for the Netherlands. The topsector **Chemistry** specifically expressed the need for a nation-wide NMR infrastructure in the Netherlands in their agenda "New Earth, New Chemistry" for use by both academic institutes and industry. In addition, the availability of state-of-the-art NMR equipment will match the plans in the topsectors **Agrofood** ("Healthy Food"), **High Tech & Materials** ("Solar cells"), **Energy** ("Batteries") and **Life Sciences & Health** ("Structural Biology"), as is explained in detail in section 3.

Spin-off company ZoBio: An example

A new approach to drug discovery, called FBDD, holds great promise. Already new medicines that have been derived from FBDD against cancer, thrombosis and many other diseases are in the clinic. Research at Leiden University has led to a patented NMR-based technology for further development of FBDD. In 2004 the company ZoBio was spun out to offer this technology and other NMR services to the pharmaceutical and biotechnology industries on a commercial basis. In the ensuing period ZoBio has worked on cancer, Alzheimer's and anti-viral medicines for a variety of European and American customers. At present ZoBio employs 8 full-time scientists from the technician to Ph.D. level, is profitable and has doubled its income every year of its existence.

Appendix I. NMR Centers in the Netherlands

Amsterdam (UvA, K. Elsevier)

The Amsterdam facilities are centered within the Catalysis and Synthesis groups as a central facility of the Van 't Hoff Institute for Molecular Sciences (HIMS). Other facilities exist at the faculties of medicine and biology and at the v.d. Waals-Zeeman laboratory (physics) and several other, such as the Free University.
The expertise concerns the area of hetero nuclei with low receptivity and detectability, especially transition metal nuclei. This niche is extremely important for research programs in HIMS such as Catalysis and Synthesis. The continuity of research in synthesis and catalysis requires, besides routine NMR for structure elucidation of small molecules (up to 5000 D), access to high field NMR equipment (600-700 MHz) for high-resolution NMR of synthetic materials, diffusion-ordered spectroscopy of supra-molecular entities and aggregates.
Available spectrometers:

4.7	7.0	9.4	11.7
200	300	400	500
1x	2x	1x	1x

Eindhoven (P.C.M.M. Magusin, K. Nicolay)

The Eindhoven Magnetic Resonance Laboratories consist of four groups within the Eindhoven University of Technology. Research and teaching of the BioMedical NMR group (Department of Biomedical Engineering, headed by Nicolay) is aimed at the development and use of in vivo magnetic resonance imaging (MRI) and spectroscopy (MRS) techniques. MRI and MRS are exploited for their unique possibilities to investigate a range of structural, functional and metabolic parameters in living systems. The team plays an important role in the training of *in vivo* NMR experts that go on to take up positions in biomedical NMR research at university medical centers and Philips Healthcare. The group Transport in Permeable Media (Department of Applied Physics) develops and employs NMR scanners to study transport and phase changes in technological porous materials. Typical topics are water and salt transport in building materials, and the curing and durability of coatings. The Solid-State NMR group (Department of Chemistry) investigates materials for heterogeneous catalysis, energy storage and polymer science. A recurrent theme is dynamical processes in nanostructured materials. The group Macro-Organic Chemistry (Departments of Chemistry and Biomedical Engineering) aims at closing the gap between organic chemistry on the one hand and macromolecular chemistry and materials on the other hand. Liquid-state NMR is one of major techniques employed in the group to characterize the molecular structure.
Available spectrometers:

≤ 1.5	4.7	7.0	9.4	11.7
≤ 60	200	300	400	500
8x	3x	1x (horizontal-bore)	3x (1x horizontal-bore)	2x

Leiden (H. J. M. de Groot, M. Ubbink, G. Siegal)

Leiden groups perform fundamental and applied NMR spectroscopy with solid state NMR, for complex systems in solution, in metabolomics and with force detection methods.

The unifying focus of the fundamental research in Leiden is on resolving functional energy landscapes. With NMR spectroscopy we analyze, explain and pave the way for mimicking the functional complexity, static and dynamic, of biomolecular assemblies driving biocatalysis and signal transduction, energy and electron transfer, self-assembly and self-organization, development and evolution. We explore the boundaries in instrumentation with ultrahigh magnetic field, light-induced polarization enhancement, flow-through compound library screening, paramagnetic NMR tools for protein interactions and micro-MRI.

Research aimed at NMR applications focuses on atomic scale MRI, new, faster methods for drug development, translational medicine and pulsed metabolomics. The groups participate in public-private partnerships for in vivo spectroscopy for translational research in medicine, metabolomics, solar fuel research and the development of novel NMR instrumentation. Commercial spin-offs comprise ZOBIO (high throughput ligand screening), PLI (labeling of cells and tissue) and isotope labeling by total synthesis as part of Buchem B.V.

Available spectrometers:

4.7	7.0	9.4	11.7	14.1	17.6
200	300	400	500	600	750
1x	1x	4x	1x	1x	1x
WB	SB	WB, SB	SB	SB,cryo	WB

Nijmegen (A. Kentgens, S. S. Wijmenga)

The three research groups of the Institute for Molecules and Materials (IMM, Radboud University Nijmegen), focusing on Nuclear Magnetic Resonance Spectroscopy, cover a broad range of research topics in the areas of Functional Materials, Sustainability and Health. Their research is structured in three layers. On the highest aggregation level are the applied projects, which are mainly focused on *biomedical applications* (structural biology of biomolecules and their complexes, metabolomics / molecular systems biology) and materials research for *energy storage and conversion,* and *self-assembly* in biomimetic materials. Within these projects the *structure directing forces* and *transport and dynamics* can be identified as fundamental underlying concepts that the groups are exploring to gain an in-depth understanding of the principles that bring a specific functionality to a molecular construct or material. This approach requires appropriate methodology. The groups direct a considerable amount of their research towards *enabling technologies* with the ambition to progress from bulk characterization to an approach that allows unraveling of the inner workings of the smallest functional units in relation to the processes and functionalities under investigation. Here hyperpolarization, microcoil-based probe developments, metabolomic screening approaches and computational strategies are most prominent. Spinnovation has spun-off as a company focusing on metabolic profiling and providing solids and liquids NMR analytical services.

Available spectrometers:

3.5	4.7	7.0	9.4	11.7	14.1	18.8	20.0 T
144	200	300	400	500	600	800	850 MHz
1xWB,DNP	1xSB	1xWB,1xSB	1xWB,1xSB	4xSB	1xWB,1xSB	1xMB	1xWB

Twente (A. Velders)

The University of Twente is internationally renowned in the fields of Supramolecular Chemistry and Nanotechnology and has a strategic focus area in (bio)nanotechnology. New applications of NMR are being developed in three main research lines: (1) Nanoliter NMR using microfluidic chips; (2) Diffusion-Ordered SpectroscopY for investigating self-assembled and/or aggregating supramolecular (bio)nanostructures and nanoparticles; (3) High-resolution/high-sensitivity micro-Imaging of bio-, micro- and nanostructures at 14.1 T.

Available spectrometers:

7.0	9.4	14.1
300	400	600
1x SB	1xWB	1xSB

Utrecht (M. Baldus, R. Boelens, A.M.J.J. Bonvin)

Research at the Utrecht NMR group centers around three focal points:

• Firstly, we are continuously developing NMR-based concepts that permit the structural and dynamical description of biomolecular systems of increasing size and complexity in a solution or solid state.

• Secondly, we apply these methods to characterize elementary biological processes in close relationship to molecular function or pharmacological intervention. Thus far, solution-state NMR methods have been used in target areas such as transcription regulation, DNA repair or protein synthesis. In parallel, solid-state NMR techniques have been designed to examine signal transduction and molecular transport processes across cellular compartments and molecular assemblies at atomic resolution.

• Thirdly, we develop and apply computational structural biology methods that can be readily combined with NMR and/or other biophysical and bioinformatics information sources.

All projects are embedded in a strong local and (inter)national research environment allowing us to describe molecular and cellular structure and organization on different levels of time and spatial resolution.

Available spectrometers:

9.4	11.7	14.1	16.4	17.6	18.8	21.1 T
400	500	600	700	750	800	900 MHz
1	2x	2x	1x	1x	1x	1x
WB	SB	cryo, SB	SB	SB	WB	cryo, SB
On order					On order	

Wageningen (H. Van As, J. van Duynhoven, C. van Mierlo, J. Vervoort)

We aim to characterize (chemically and physically) structure-function relationships of complex mixtures and (bio)systems with applications in life sciences (health, nutrition, ecology, plants, food, biology). A combination of various NMR and MRI spectrometers (low field portable, Time Domain, imaging, solid and liquid state spectroscopy and high field LC-SPE-NMR-MS) is exploited for these purposes.

NMR and MRI hardware and methods development is directed to study intact plants (production, hydraulic conductance, water limitation, product quality), food and fruits ((molecular)composition, processing, structure characterization, functional components, metabolomics, authenticity, safety) and food-health relationship by body fluid analyses (high throughput metabolomics, proteomics and biomarker search). The groups have contributed largely to the development of new methods to unravel transport processes in porous bio-systems and to hyphenated methods for complex mixture analysis.

The 3T intact plant MRI and high field LC-SPE-NMR-MS systems, in combination with available databases and simulation programs for identification, are rather unique. Recently Rheo-MRI for soft matter structure studies under dynamic (stress) conditions has been realized.

The equipment and expertise available within the Wageningen NMR Centre is embedded on local and (inter)national scale, and has been supported by EU funding since 1992 to stimulate access to Research Infrastructure WNMRC for NMR in agriculture, food and biology.

Available spectrometers:

Low Field	<4.7	7.0	9.4	11.7	14.1
1 – 30 (Variable)	30 and 128	300	400	500	600
3x (TD*, incl Portable)	2x MRI (incl Whole Plant)	1x (WB)	1x	1x	1x (LC-NMR/MS)

TD: Time Domain

Appendix II. Short CVs of Leading NMR Spectroscopists in the Netherlands

Henk Van As

Henk Van As (born 12/9/1952) studied physical chemistry at the Free University, Amsterdam, The Netherlands. He completed his Ph.D. (NMR, Water and Plants) in the Lab of Molecular Physics, Wageningen University, in 1982. He continued as a postdoc at the same laboratory, where he developed a portable NMR Bioflowmeter for applications on plants in greenhouses. In 1983 he was appointed assistant professor at the Laboratory of Molecular Physics, Wageningen University, The Netherlands. In 1986 he became associate professor of biophysics at Wageningen University and in 2001 scientific director of the Wageningen NMR Centre.

The research in Van As' group is aimed at unraveling and understanding transport processes and water dynamics at different time and length scales in porous bio-systems. For this, Time Domain NMR and MRI methods are developed and applied. To support interpretation computer simulations are used. Applications are intact plants (cell-to-cell and long distance transport; stress responses), plant-like materials (ripening, storage, processing, moisture migration, drying and rehydration), and foods (composition-processing-structure relationship).

His research has resulted in over 90 peer-reviewed publications. He has been (co-)organizer of a number of international NMR meetings (WNMRC user meetings, 3rd Symposium on NMR Spectroscopy in Soil and Geo Sciences, 9th International Conference on Magnetic Resonance Microscopy and 7th Colloquium on Mobile NMR, bi-annual international PhD student courses *in vivo* NMR, in collaboration with TUE, UU and KUN). He is Treasurer of the Executive Committee of the AMPERE division Spatially Resolved Magnetic Resonance, Member of the Steering Committee of the AMPERE division Magnetic Resonance in Porous Media, and co-founder and CSO of Biqualys B.V. (see www.biqualys.nl)

Selected publications:

1. Mullendore DL, Windt CW, Van As H and Knoblauch M (2010) Sieve plate geometry in relation to phloem flow. Plant Cell 22, 579-593
2. Windt CW, Gerkema E and Van As H (2009) Most water in the tomato truss is imported through the xylem, not the phloem. An NMR flow imaging study. Plant Physiol. 151, 830-842
3. Mohoric A, Vergeldt FJ, Gerkema E, van Dalen G, van den Doel LR, van Vliet LJ, Van As H and van Duynhoven J (2009) The effect of rice kernel microstructure on cooking behaviour: A combined XRT and MRI study. Food Chem. 115, 1491-1499
4. Van As H (2007) Intact plant MRI for the study of cell water relations, membrane permeability, cell-to-cell and long distance water transport. J. Exp. Botany 58, 743 - 756
5. Windt CW, Vergeldt FJ, de Jager PA and Van As H (2006) MRI of long distance water transport: a comparison of the phloem and xylem flow characteristics and dynamics in poplar, castor bean, tomato and tobacco. Plant Cell Environ. 29, 1715-1729

Marc Baldus

Marc Baldus (born 28/11/1967) studied physics at the Technical University of Darmstadt and the University of Florida. After Ph.D. studies at ETH Zurich and KU Nijmegen, he received his doctoral degree in physical Chemistry at ETH Zurich with R.R. Ernst and B.H. Meier in 1996. He continued his research as a postdoc at the MIT/Harvard Center for Magnetic Resonance with R.G. Griffin. From 1999-2000, he worked as University lecturer at Leiden University. From 2000-2008, he directed the solid-state NMR group at the Max-Planck-Institute for Biophysical Chemistry (Gottingen/Germany) as group leader (C3, associate professor). In 2008, he was appointed as full professor for structural Biology at Utrecht University.
The Baldus group is interested in the development of high-resolution solid-state NMR methods and their applications in a biophysical context. Target application areas include molecular assemblies, membrane proteins and (membrane-associated) molecular complexes. Furthermore, research is conducted in the areas of protein folding and aggregation. Studies performed by Baldus et al. resulted in over 100 publications and were awarded with (inter)national prizes in the fields of NMR, Chemistry and Biophysics. MB has been serving in international organizing committees such as the German GdCh subgroup on NMR (2005-2008), the RCSB (PDB-BMRB) Task Group on NMR and is member of the Executive Committee of the Experimental NMR Conference (ENC), USA.

Selected publications:

1. Ader, C, Frey, S, Maas, W, Schmidt, HB, Görlich, D and Baldus, M (2010) Amyloid-like interactions within nucleoporin FG-hydrogels. Proc. Natl. Acad. Sci. USA 107, 6281-6285
2. Etzkorn M, Kneuper H, Dünnwald P, Vijayan V, Krämer J, Griesinger C, Becker S, Unden G and Baldus M (2008) Structural aspects of intracellular, PAS mediated, signal transduction in the histidine-kinase DcuS. Nature Struct. Mol. Biol. 15, 1031-1039
3. Lange A, Giller K, Hornig S, Martin-Eauclaire M-F, Pongs O, Becker S and Baldus M (2006) Toxin-induced conformational changes in a potassium channel revealed by solid-state NMR. Nature 440, 959-962.
4. Ader C, Schneider R, Hornig S, Velisetty P, Wilson EM, Lange A, Giller K, Ohmert I, Martin-Eauclaire M-F, Trauner D, Becker S, Pongs O and Baldus M (2008) A structural link between inactivation and block of a K^+ channel. Nature Struct. Mol. Biol. 15, 605-612
5. Heise H, Hoyer W, Becker S, Andronesi OC, Riedel D and Baldus M (2005) Molecular-level secondary structure, polymorphism, and dynamics of full-length a-synuclein fibrils studied by solid-state NMR. Proc. Natl. Acad. Sci. USA 102, 15871-15876

Rolf Boelens

Rolf Boelens (born 7/10/1951) studied chemistry and physical chemistry at the University of Groningen, The Netherlands. He completed his Ph.D. in the Department of Biochemistry of the University of Amsterdam in 1984. For a postdoc he went to the NMR group of Robert Kaptein. In 1988 he was appointed assistant professor at the Faculty of Chemistry, Utrecht University, The Netherlands. Currently he is professor of biomolecular NMR spectroscopy and director of the high-resolution NMR facility at Utrecht University. He studies protein complexes involved in DNA transcription, DNA repair, and ribosomal proteins and develops methods for biomolecular NMR spectroscopy. Studied systems have been the DNA binding domains of lac and other repressors, several steroid hormone receptors, DNA repair proteins, and enzymes such as phospholipase A2 and subtilisine. A series of computational methods are applied and developed, such as simulated annealing, restrained molecular dynamics and iterative relaxation matrix refinement (IRMA) for structure determination. His research has resulted in ca. 300 publications (h-index 53). He is member the Management Committee of the EU NMR facilities, committee member of the European NMR Association Ampère, board member of the Dutch NMR Discussion-Group and organizer of various international NMR conferences (EUROMAR, NMRLife, Benelux/GERM, LSF Annual User Meetings) and summerschools (BNRA/Bijvoet, EMBO).

Selected publications:

1. Hibbert, Richard G. Hibbert RG, Anding Huang A, Rolf Boelens R and Titia K. Sixma TK (2011) The E3 ligase Rad18 selects for monoubiquitination rather than ubiquitin chain formation by E2 enzyme Rad6. Proc. Natl. Acad. Sci. USA 108, 5590-5595
2. van Ingen H, van Schaik FM, Wienk H, Ballering J, Rehmann H, Dechesne AC, Kruijzer JA, Liskamp RM, Timmers HThM and Boelens R (2008) Structural insight into the recognition of the H3K4me3 mark by the TFIID subunit TAF3. Structure 16, 1245-1256
3. Milon P, Tischenko E, Tomsic J, Caserta E, Folkers GE, La Teana A, Rodnina MV, Pon CL, Boelens R and Gualerzi CO (2006) The nucleotide-binding site of bacterial translation initiation factor 2 (IF2) as a metabolic sensor. Proc. Natl. Acad. Sci. USA 103, 13962-13967
4. Kalodimos CG, Biris N, Bonvin AMJJ, Levandoski MM, Guennuegues M., Boelens R and Kaptein R (2004) Structure and Flexibility Adaptation in Nonspecific and Specific Protein-DNA Complexes. Science 305, 386-389
5. Dominguez C, Bonvin AMJJ, Winkler GS, van Schaik FMA, Timmers HThM and Boelens R (2004). Structural model of the UbcH5B/CNOT4 complex revealed by combining NMR, mutagenesis and docking approaches. Structure 12, 633-644.

Alexandre Bonvin

Alexandre Bonvin (born 07/11/1964) studied Chemistry at Lausanne University, Switzerland. He completed his PhD thesis *cum laude* in 1993 in the department of chemistry at Utrecht University under the supervision of Prof. Boelens and Prof. Kaptein. After two post-doc periods at Yale University (USA) with Prof. Axel Brunger and at the ETHZ (CH) with Prof. Wilfred van Gunsteren, he became assistant professor at Utrecht University in 1998 and was promoted associate professor in 2003. He has been appointed full professor of computational structural biology in 2009 and is also director of education for the Chemistry Department. He received in 2006 a prestigious VICI grant from the Dutch Research Council. He is participating to several EU projects and will be coordinating of the new WeNMR FP7 e-Infrastructure project. His work has resulted in over 100 peer-reviewed publications.

Research within the computational structural biology group focuses on the development of reliable bioinformatic and computational approaches to predict, model and dissect biomolecular interactions at atomic level. For this, bioinformatic data, structural information from NMR and other available biochemical or biophysical experimental data are combined to drive the modelling process. By following a holistic approach integrating various experimental information sources with computational structural biology methods the aim is to obtain a comprehensive description of the structural and dynamic landscape of complex biomolecular machines, adding the structural dimension to interaction networks and opening the route to systematic and genome-wide studies of biomolecular interactions.

Selected publications:

1. Karaca E, Melquiond ASJ, de Vries SJ, Kastritis PL and Bonvin AMJJ (2010) Building Macromolecular Assemblies by Information-driven Docking, Mol. & Cel. Proteom. 9, 1784-1794
2. de Vries SJ, van Dijk M and Bonvin AMJJ (2010) The HADDOCK web server for data-driven biomolecular docking, Nature Prot. 5, 883-897
3. Gelis I, Bonvin AMJJ, Keramisanou D, Economou A and Kalodimos CG (2007). Signal sequence recognition by the translocase motor SecA studied by NMR. Cell 131, 756-769
4. Bonvin AMJJ (2006) Flexible protein-protein docking. Curr. Opin. Struct. Biol. 16, 194-200
5. Dominguez C, Boelens R and Bonvin AMJJ (2003) HADDOCK: A protein-protein docking approach based on biochemical or biophysical information. J. Am. Chem. Soc. 125, 1731-1737

John van Duynhoven

John van Duynhoven (born 19/07/1962) studied chemistry at the University of Nijmegen. He completed his Ph.D. thesis on NMR studies on DNA binding proteins in 1991 at the department of Biophysical Chemistry under the supervision of Prof. C.W. Hilbers. He pursued his career as assistant professor at the University of Twente where he also headed the NMR facility. In Twente his research focussed on NMR applications in supramolecular and polymer chemistry. In 1996 he moved to Unilever Vlaardingen where deployed a wide range of NMR/MRI techniques in food and nutrition research and development programmes. At Unilever he is now heading the spectroscopy and microscopy group. His current research activitiets are in application of NMR in resolving complex food compositions and structure and assessment of the metabolic impact of diet on humans. In these areas he has initiated and led a range of academic-industrial collaborative projects and this has has resulted in over 90 publications in international peer-reviewed journals and books. He has been co-organizer of various national and international NMR meetings, is member of the Executive Committee of the Netherlands Metabolomics Centre and is on the board of the Dutch NMRDG. In november 2010 was appointed as part-time professor at Wageningen University.

Selected Publications:

1. van Duynhoven J, Voda A, Witek M and Van As H (2010) TimeDomain NMR in Foods, Ann. Rep.NMR Spectros. 69, 145-197
2. van Duynhoven J, Vaughan EE, Jacobs D, Kemperman R, van Velzen EJJ, Gross G, Roger L, Possemiers S, Smilde AK, Doré J, Westerhuis JA and Van de Wiele T The metabolic fate of polyphenols in the human superorganism, Proc. Natl. Acad. Sci. USA, in press
3. Mohorič A, Vergeldt F, Gerkema E, van Dalen G, van den Doel LR, van Vliet LJ, Van As H and van Duynhoven J (2009) The effect of rice kernel microstructure on cooking behaviour: A combined XRT and MRI study. Food Chemistry 115(4), 1491-1499
4. van Velzen E, Westerhuis J, van Duynhoven J, van Dorsten F, Jacobs D, Gruen C, Duchateau G, Vis D and Smilde A (2009) Phenotyping tea consumers by nutrikinetic analysis of polyphenolic end-metabolites. J. Prot. Res. *8* (7), 3317–3330
5. Jacobs DM, Deltimple N, van Velzen E, Bingham M, Vaughan E and van Duynhoven J (2008) ^{1}H NMR metabolite profiling of faeces as a tool to assess the impact of nutrition on the human microbiome. NMR in BioMed. 21, 615-626

Huub de Groot

Leiden University, Leiden Institute of Chemistry, The Netherlands Received his PhD in Physics at Leiden University. He was two years at MIT and currently is Professor of Biophysical Organic Chemistry at Leiden University. Has authored ca. 150 papers in functional materials and biophysics research focusing on light-driven reactions in proteins, including natural and artificial light energy conversion processes. He coordinated the EU program that triggered a revolution in the Solid State NMR by the implementation of ultra high field methods. He served as technology coordinator of the CMSB genomics centre of excellence. Recently he initiated the preparation of the ESF science policy brief "Harnessing Solar Energy for the Production of Clean Fuel and the preceding White Paper. Serves on the standing committee for Earth and Life Sciences of the Royal Academy of Sciences. He was the recipient of a Shell prize, the Leiden University Kok Prize, received a Royal Netherlands Academy of Sciences and a NWO PIONIER research career development award. He serves as chairman of the Havinga award committee. De Groot's group uses solid state NMR, prepares biomimetic catalysts and performs multiscale modeling for fundamental research in photosynthesis and the translation to artificial photosynthesis. He serves as scientific director of the Dutch Towards BioSolar Cells consortium and was for three years on the Scientifc Advisory Board of Bruker, chaired by Nobel Prize Winner Richard Ernst.

Selected publications:

1. Ganapathy S, Sengupta S, Wawrzyniak PK, Huber V, Buda F, Baumeister U, Würthner F and de Groot HJM (2009) Zinc chlorins for artificial light-harvesting self-assemble into antiparallel stacks forming a microcrystalline solid-state material. Proc. Natl. Acad. Sci. USA 106, 11472-11477
2. De Groot HJM (2010) Integration of catalysis with storage for the design of multi-electron photochemistry devices for solar fuel. Appl Magn Reson 37, 497-503
3. Ganapathy S, Oostergetel GT, Wawrzyniak PK, Reus M, Gomez Maqueo Chew A, Buda F, Boekema EJ, Bryant DA, Holzwarth AR and de Groot HJM (2009) Alternating *syn-anti* bacteriochlorophylls form concentric helical nanotubes in chlorosomes. Proc. Natl. Acad. Sci. USA 106, 8525-8530
4. Cherepanov AV, Doroshenko EV, Matysik J, de Vries S and de Groot, HJM (2008) The associative nature of adenylyl transfer catalyzed by T4 DNA ligase. Proc. Natl. Acad. Sci. USA 105, 8563–8568
5. Diller A, Roy E, Gast P, van Gorkom HJ, de Groot HJM, Glaubitz C, Jeschke G, Matysik J and Alia A (2007) 15N photochemically induced dynamic nuclear polarization magic-angle spinning NMR analysis of the electron donor of photosystem II. Proc. Natl. Acad. Sci. USA 104, 12767-12771

Arno Kentgens

Arno Kentgens (born 15/08/1959) studied chemistry and physical chemistry at the University of Nijmegen. He completed his Ph.D. thesis on the development of two-dimensional solid-state NMR in 1987 at the department of Molecular Spectroscopy under the supervision of Profs. E. de Boer and W.S. Veeman. This thesis was awarded a prize for Chemistry and Technology of the DSM Chemical Company. From 1987-1988 he was a staff scientist at the Philips Research Laboratories in Eindhoven. From 1988-2000 he was supervisor solid-state NMR of the Dutch National HF-NMR facility. In 2000 he was appointed as full professor for physical chemistry at Radboud University Nijmegen. Recently he also heads the newly formed solid-state NMR facility for advanced materials science. He has been vice-chairman of the subfaculty of chemistry, director of the educational institute for molecular science and was recently appointed as member of the board of the Institute for Molecules and Materials.
The focus of the research program is the development and application of methods that enable the study of local structure and dynamics of functional materials. The requirements to achieve this goal are to attain high resolution to distinguish chemically different sites, establish efficient correlations between nuclei to determine distances and hence geometry, and efficient (and quantitative) excitation of different nuclei in the sample. The research program can be divided in three main lines; 1) NMR Methodology focussing on Sensitivity and Resolution, 2) Development of NMR Techniques for Quadrupolar Nuclei, and 3) Applications of solid-state NMR to functional materials, with an emphasis on materials for energy storage and conversion and catalysts. Furthermore we focus on bio(mimicking) materials such as polyisocyanopeptides which serve as scaffolds for various functionalities. This research has resulted in over 100 papers in international peer-reviewed journals. AK has been co-organizer of various national and international NMR meetings, is member of the editorial board of the journal "solid-state NMR" and is member of the international advisory boards of the Canadian and UK solid-state NMR facilities.

Selected Publications:

1. Bart J, Kolkman AJ, Oosthoek-de Vries AJ, Koch K, Nieuwland PJ, Janssen JWG, van Bentum PJM, Ampt KAM, Rutjes PJT, Wijmenga S, Gardeniers JGE and Kentgens APM (2009) A Microfluidic High-Resolution Stripline Probe. J. Am. Chem. Soc. 131, 5014-5015
2. Kentgens APM, Bart J, van Bentum PJM, Brinkmann A, van Eck ERH, Gardeniers JGE, Janssen JWG, Knijn P, Vasa S and Verkuijlen MHW (2008) Nuclear Magnetic Resonance of Nanoliter Sample Volumes using Microcoil Detectors. J. Chem. Phys. 128, 052202
3. Brinkmann A and Kentgens APM (2006) Proton Selective ^{17}O-^{1}H Distance Measurements in Fast Magic Angle Spinning solid-state NMR for the Determination of Hydrogen Bond Lengths. J. Am. Chem. Soc. 128, 14758-14759
4. Wagemaker M, Kentgens APM and Mulder FMM (2002) Lithium transport for equilibrium between nano-crystalline phases in intercalated TiO_2 anatase. Nature 418, 397-399
5. Kentgens APM and Verhagen R (1999) Advantages of double frequency sweeps in static, MAS and MQMAS NMR of spin I=3/2 nuclei. Chem. Phys. Lett. 300, 435

Pieter Magusin

Pieter C.M.M. Magusin (born 29/03/1963) studied chemistry and physical chemistry at the University of Nijmegen (NL). He completed his Ph.D. thesis on solid-state ^{31}P NMR of nucleic acids inside virus particles in 1995 under supervision of Dr. M.A. Hemminga at the Molecular Physics department of the University of Wageningen (NL). Between 1995 and 1997 he was EU postdoc in the Physical Chemistry group of prof. W.S. Veeman at the University of Duisburg (D), where he investigated the polymer composites using solid-state NMR. Since 1997 Magusin is supervisor (assistant professor since 1998) of the solid-state NMR facility at the Eindhoven University of Technology (NL), His research involves NMR characterization of nanostructure and dynamics in complex materials in the areas of heterogeneous catalysis, energy storage and polymer science in close collaboration with material scientists.
Magusin is board member of the Dutch NMR Discussion-Group and the Section Analytical Chemistry of the Royal Dutch Society for Chemistry (KNCV). He participates in the German-Dutch International Research Training Network "Diffusion in Porous Media" and the Belgian Scientific Network "Advanced Magnetic Resonance". He was co-organizer of various meetings, including the European Magnetic Resonance Conference 2005 in Veldhoven (NL).

Selected Publications:

1. Hensen EJM, Poduval DG, Magusin PCMM, Coumans AE and van Veen JAR (2009) Formation of acid sites in amorphous silica-alumina. J. Catal. 269, 201–218
2. Srinivasan S, Magusin PCMM, Kalisvaart WP, Notten PHL, Cuevas F, Latroche M and van Santen RA (2010) Nanostructure of magnesium-titanium deuteride studied with X-ray diffraction, neutron diffraction and magic-angle-spinning ^{2}H NMR spectroscopy. Phys. Rev. B 81, 054107
3. Orza RA, Magusin PCMM, Litvinov VM, van Duin M and Michels MAJ (2009) Mechanism for Peroxide Cross-Linking of EPDM Rubber from MAS ^{13}C NMR Spectroscopy. Macromolecules 42, 8914-8924
4. Magusin PCMM, Zorin VE, Aerts A, Houssin CJY, Yakovlev AL, Kirschhock CEA, Martens JA and van Santen RA (2005) Template-aluminosilicate structures at the early stages of zeolite ZSM-5 formation. A combined preparative, solid-state NMR and computational study. J. Phys. Chem. B 109, 22767-22774
5. Sun Q, Kooyman PJ, Grossmann JG, Bomans PHH, Frederik PM, Magusin PCMM, Beelen TPM, van Santen RA and Sommerdijk NAJM (2003) The formation of well-defined hollow silica spheres with multilamellar shell structure. Adv. Materials 15, 1097-1100

Carlo van Mierlo

Carlo van Mierlo (1959) obtained his PhD degree with honours at Wageningen University in 1990. His PhD work involved among others the use of multidimensional NMR spectroscopy for the elucidation of the three-dimensional structure of a flavoprotein. Subsequently, he went for a postdoctoral period of two-and a half years to the MRC Laboratory of Molecular Biology, Cambridge, England. During this period he used NMR spectroscopy to unravel the folding of bovine pancreatic trypsin inhibitor. In 1992 he was awarded a five-year Royal Netherlands Academy of Arts and Sciences fellowship to initiate his own research in the Netherlands. Currently, he leads as assistant professor the "Protein Folding and Stability" group at the Laboratory of Biochemistry of Wageningen University. His group uses a variety of spectroscopic techniques to experimentally investigate protein folding. Subjects tackled are: adsorption-induced protein unfolding, conformational features of unfolded proteins, formation of misfolded intermediates, and the characterisation of energy landscapes of protein folding. Five MsC students received their PhD degree under the supervision of van Mierlo, he produced more than 50 articles in international peer-reviewed journals, and his current h-factor is 22.

Selected publications:

1. Nabuurs SM, Westphal AH, aan den Toorn M, Lindhoud S and van Mierlo, CPM (2009) Topological switching between an alpha-beta parallel protein and a remarkably helical molten globule. J. Am. Chem. Soc. 131, 8290-8295
2. Nabuurs SM, Westphal AH and van Mierlo CPM (2009) Noncooperative formation of the off-pathway molten globule during folding of the alpha-beta parallel protein apoflavodoxin. J. Am. Chem. Soc. 131, 2739-2746
3. Nabuurs SM, Westphal AH and van Mierlo CPM (2008) Extensive formation of off-pathway species during folding of an alpha-beta parallel protein is due to docking of (non)native structure elements in unfolded molecules. J. Am. Chem. Soc. 130, 16914-16920
4. Bollen YJM, Kamphuis MB and van Mierlo CPM (2006) The folding energy landscape of apoflavodoxin is rugged: hydrogen exchange reveals non-productive misfolded intermediates. Proc. Natl. Acad. Sci. USA 103, 4095-4100
5. Engel MFM, Visser AJWG and van Mierlo CPM (2004) Conformation and orientation of a protein folding intermediate trapped by adsorption. Proc. Natl. Acad. Sci. USA 101, 11316-11321

Klaas Nicolay

Klaas Nicolay received a MSc in Chemistry of Groningen University in 1979. In 1983, he obtained his PhD at Groningen University. He was a fellow of the Netherlands Cancer Foundation at Utrecht University from 1983-1987. In 1985, he was a visiting scientist at the Biocenter in Basel. In 1987, he received a Huygens fellowship from NWO. In 1991, he became the head of the Netherlands *in vivo* NMR facility at Utrecht University. In 2001, he was appointed as a professor of Biomedical NMR at TU/e. His main research interest is the development of advanced NMR imaging and spectroscopy methods to assess structure, function and metabolism of tissues *in vivo*, in relation to cardiovascular diseases, cancer and metabolic disorders.
Nicolay is member of the editorial boards of Magnetic Resonance in Medicine, Journal of Magnetic Resonance, NMR in Biomedicine and Journal of Cerebral Blood Flow and Metabolism. From 2004-2008, he served on the Board of Trustees of the International Society of Magnetic Resonance in Medicine (ISMRM). He is program director of the Molecular and Cellular Imaging study group, past program director of the Diffusion & Perfusion study group and past chair of the Dynamic NMR Spectroscopy study group of ISMRM. He has delivered many plenary lectures at international meetings, including meetings of the ISMRM, ESMRMB and Gordon Conference *In vivo* NMR. He has organized many educational courses at ISMRM and ESMRMB meetings, including on Molecular and Cellular Imaging, Advanced MRS and Small Animal MRI and MRS. Nicolay is a founding father of the European Society of Molecular Imaging and a member of the council of the (international) Society of Molecular Imaging.

Selected Publications:

1. Mulder WJ, Strijkers GJ, van Tilborg GA, Cormode DP, Fayad ZA and Nicolay K (2009) Nanoparticulate assemblies of amphiphiles and diagnostically active materials for multimodality imaging. Acc. Chem. Res. 42, 904-914
2. Strijkers GJ, Bouts A, Blankesteijn WM, Peeters TH, Vilanova A, van Prooijen MC, Sanders HM, Heijman E and Nicolay K (2009) DTI of left ventricular remodeling in response to myocardial infarction in the mouse. NMR Biomed. 22, 182-190
3. Heemskerk AM, Strijkers GJ, Drost MR, van Bochove GS and Nicolay K (2007) Skeletal muscle degeneration and regeneration after femoral artery ligation in mice: monitoring with diffusion MR imaging. Radiology 243, 413-421
4. Prompers JJ, Jeneson JAL, Drost MR, Oomens CWJ, Strijkers GJ and Nicolay K (2006) Dynamic MRS and MRI of skeletal muscle function and biomechanics. NMR Biomed. 19, 927-953
5. Mulder WJ, Strijkers GJ, Habets JW, Bleeker EJ, van der Schaft DW, Storm G, Koning GA, Griffioen AW and Nicolay K (2005) MR molecular imaging and fluorescence microscopy for identification of activated tumor endothelium using a bimodal lipidic nanoparticle. FASEB J. 19, 2008-2010

Gregg Siegal

Gregg Siegal obtained his Ph.D. on studies of eukaryotic DNA replication at the University of Rochester in the USA under the supervision of Professor Robert Bambara. His PhD thesis was selected as the best in the University of that year. Persuing an interest in structural biology he moved to the laboratory of Professor Kurt Wüthrich at the ETH in Zürich, Switzerland. His work in the Wüthrich group focussed on heteronuclear NMR studies of protein structure and folding. Subsequently he joined the group of Professor Paul Driscoll at the Ludwig Institute of Cancer Research in London, UK where he studied protein structure and small molecule interactions, again using NMR. He moved to Leiden University in 1997 where he received a Dutch Royal Society Fellowship to form his own research group. In 2004 he spun out the company ZoBio to commercialize the TINS ligand screening technology developed in his group and presently serves as the Chief Scientific Officer in addition to his position within the University.
Presently two lines of research are pursued in the laboratory of Dr. Siegal. Biochemical and structural studies of DNA replication and repair processes form a significant part of the research efforts. In particular, recent efforts have focused on understanding the biological role and molecular mechanism of an unusual structure specific DNA binding activity found in two different proteins involved in the replication of the human genome. A new research line has focused on the development of drug discovery technologies and their application to challenging pharmaceutical targets, particularly in the area of oncology. Novel NMR instrumentation has been built to support Target Immobilized NMR Screening (TINS), a patent protected technology that forms the basis of the spinout company ZoBio.

Selected Publications:

1. Kobayashi M, AB E, Bonvin AMJJ and Siegal G (2010) Structure of the DNA bound BRCT region from human Replication Factor C p140 and model of the protein-DNA complex. J. Biol. Chem. 285, 10087-10097
2. Pellecchia M et al. and Siegal G (2008) Perspectives on NMR in drug discovery: a technique comes of age. Nature Rev. Drug Discov. 7, 738-745
3. Röhrig CH, Loch CMP, Guan JY, Siegal G and Overhand M (2007) Fragment-based synthesis and SAR of modified FKBP ligands: Influence of different linking on binding affinity. ChemMedChem 2, 1054-1070
4. Vanwetswinkel S, Heetebrij RJ, van Duynhoven J, Hollander JG, Filippov DV, Hajduk PJ and Siegal G (2005) TINS: Target Immobilized NMR Screening – An efficient and sensitive new method for ligand discovery. Chem. Biol. 12, 207-216
5. Hilge M, Siegal G, Vuister GW, Güntert P Gloor S and Abrahams JP (2003) ATP-induced conformational changes of the nucleotide binding domain of Na,K-ATPase. Nature Struct. Biol. 10, 468-474

Patent: WO/0237309 – Covers the TINS technology.

Marcellus Ubbink

Marcellus Ubbink (26/10/1965) studied Biology at Utrecht University and graduated in 1989 cum laude. He received his PhD in Chemistry cum laude (1994). He worked for several months at the European Molecular Biology Laboratory in Heidelberg and then moved to Cambridge University in the UK to work as a postdoctoral researcher for three years in the Department of Biochemistry. There he was selected for a research fellowship at Darwin College. In 1997 he was appointed as assistant professor on a tenure track at the Leiden Institute of Chemistry. In 2004 he became associate professor and in May 2010 he was appointed as a full professor in Protein Chemistry. From 2000-2004 he was coordinator of a European Network on Transient Protein Interactions in Photosynthesis, leading a consortium of six European research groups. In 2002 he received a VIDI grant from NWO, followed by VICI grant in 2008. He is the secretary of the Dutch Biochemical Society (NVBMB) since 2008.
The research in his group is aimed at understanding protein dynamics and interactions at the atomic level. Several focus points are weak complexes of redox proteins functioning in basic metabolic processes like photosynthesis and respiration, enzyme-substrate and drug-protein interactions, and the development of paramagnetic probes for bioNMR. The work has resulted in about 90 peer-reviewed publications.

Selected publications:

1. Bashir Q, Volkov AN, Ullmann, GM and Ubbink M (2010) Visualisation of the encounter state of the transient electron transfer complex of cytochrome *c* and cytochrome *c* peroxidase. J. Am. Chem. Soc. 132, 241-247
2. Keizers PHJ, Saragliadis A, Hiruma Y, Overhand M and Ubbink M (2008) Design, synthesis and evaluation of a lanthanide chelating protein probe: CLaNP-5 yields predictable paramagnetic effects independent of environment. J. Am. Chem. Soc. 130, 14802-14812
3. Xu X, Reinle W, Hannemann F, Konarev PV, Svergun DI, Bernhardt R and Ubbink M (2008) Dynamics in a pure encounter complex of two proteins studied by solution scattering and paramagnetic NMR spectroscopy. J. Am. Chem. Soc. 130, 6395-6403
4. Vlasie MD, Fernández-Busnadiego R, Prudêncio M and Ubbink M (2008) Conformation of pseudoazurin in the 152 kDa electron transfer complex with nitrite reductase determined by paramagnetic NMR. J. Mol. Biol. 375, 1405-1415
5. Volkov AN, Worrall JAR, Holtzmann E and Ubbink M (2006) Solution structure and dynamics of the complex between cytochrome *c* and cytochrome *c* peroxidase determined by paramagnetic NMR. Proc. Natl. Acad. Sci. USA 103, 18945-18950

Aldrik Velders

Aldrik Velders (12/11/1970) studied chemistry at Utrecht University (NL) and graduated in 1994. He completed his Ph.D. in Coordination and Bioinorganic Chemistry at the University of Leiden (NL) in 2000. He spent three years as post-doc in Italy, first in the Centre of Magnetic Resonance (CERM, Florence) of Ivano Bertini, and consecutively at Molteni (Scandicci), an SME pharmaceutical company. In 2004 he became head of the NMR&MS department at the University of Twente and assistant professor in the Supramolecular Chemistry and Technology group, group leader in 2008 and associate professor in 2009. He studies covalent and non-covalent interactions, in solution and on surfaces, between supramolecular structures, (bio)macromolecules and nanoparticles, and investigates applications of NMR spectroscopy & imaging in micro- and (bio)nanotechnology. His research has resulted in over 50 publications. He is part of several European Research and Training Networks (Carbio, Dynamic Combinatorial Chemistry, Dynamol) and cooperation networks (COST D31/D35).

Selected publications:

1. Gomez MV, Verputten HJJ, Díaz-Ortíz A, Moreno A, de la Hoz A and Velders AH (2010) On-line monitoring of a microwave-assisted chemical reaction by nanoliter NMR-spectroscopy. Chem. Commun. 46, 4514–4516
2. Gomez MV, Guerra J, Myers V, Crooks RM and Velders AH (2009) Nanoparticle size determination by 1H NMR spectroscopy. J. Am. Chem. Soc. 131, 14634-14635
3. Wu CC, Otto C, Reinhoudt DN, Lammertink RGH, Huskens J, Subramaniam V and Velders AH (2009) Porous AFM tips for dip-pen nanolithography of proteins. J. Am. Chem. Soc. 131, 7526-7527
4. Gomez MV, Guerra J, Velders AH and Crooks RM (2009) NMR characterization of fourth-generation PAMAM dendrimers in the presence and absence of palladium dendrimer-encapsulated nanoparticles. J. Am. Chem. Soc., 131, 341-350
5. Gomez MV, Reinhoudt DN and Velders AH (2008) Supramolecular interactions at the picomole level studied by F-19 NMR spectroscopy in a microfluidic chip. Small 4 (9), 1293-1295

Jacques Vervoort

Jacques Vervoort (born 26/10/1954) studied Molecular Sciences at Wageningen University, The Netherlands. After his study he worked at the University of Georgia (Chemistry and Biochemistry departments). He obtained a PhD in Biochemistry in 1986 on protein-ligand interactions using one and two-dimensional NMR methods. In 1986 he was appointed assistant professor at the department of Biochemistry at Wageningen University and became associate professor in 1998. His research is aimed at protein-ligand interaction, ligand biotransformation, high throughput metabolomics, hyphenation (LC-SPE-NMR-MS) and database development for quick and reliable (automated) identification of small biomolecules.

He is the author of over 200 publications.

Selected publications:

1. Moco S, Schneider B and Vervoort J (2009) Plant Micrometabolomics: The analysis of endogenous metabolites present in a plant cell or tissue. J. Proteome Res. 8, 1694–1703
2. Moco S, Forshed J, de Vos RC, Bino R and Vervoort J (2008) Intra- and inter-metabolite correlation spectroscopy of tomato metabolomics data obtained by liquid chromatography-mass spectrometry and nuclear magnetic resonance. Metabolomics 4, 202-215
3. Exarchou V, Krucker M, van Beek TA, Vervoort J, Gerothanassis IP and Albert K (2005) LC-NMR coupling technology: recent advancements and applications in natural products analysis. Magn. Reson. Chem. 43, 681-687
4. van den Burg HA, Spronk CAEM, Boeren S, Kennedy MA, Vissers JPC, Vuister GW, de Wit PJGM and Vervoort J (2004) Binding of the AVR4 elicitor of *Cladosporium fulvum* to chitotriose units is facilitated by positive allosteric protein-protein interactions. J. of Biol. Chem. 279, 16786-16796
5. Exarchou V, Godejohann M, van Beek TA, Gerothanassis IP and Vervoort J (2003) LC-UV-solid-phase extraction-NMR-MS combined with a cryogenic flow probe and its application to the identification of compounds present in Greek oregano. Anal. Chem. 75, 6288-94

Sybren S. Wijmenga

Sybren Wijmenga (born 06/06/1953) studied chemistry at the University of Groningen, The Netherlands. He obtained his Ph.D. at Leiden University in 1984 with Prof.Dr.M.Mandel. From 1984-1987, he was visiting fellow at the National Institutes of Health (Bethesda, USA; Dr.Charney). In 1987, he became supervisor of the Dutch National hf-NMR Facility at the University of Nijmegen. In 1996, he was appointed Professor of Biophysics within the field of NMR Spectroscopic Methods applied to Biomolecules at the Department of Medical Biochemistry and Biophysics in the Medical Faculty of Umea University, Sweden. In 2002, he returned to Nijmegen to become Professor of Biophysical Chemistry at the Radboud University.
His research continues to focus on (NMR) structural studies of (interacting) biomolecules of biomedical interest to understand their functional roles. The main research lines are now: 1. *NMR and AFM of RNA/DNA systems of biomedical importance*, e.g. viral - (HBV, HIV) and regulatory RNAs (riboswitches), and branched DNAs in Huntington's disease. Also, new structure methods are developed, e.g. new isotope labeling approaches and methods to use of chemical shifts as main source of structure information. A major new research is also development of structural methods at the interface of NMR and AFM to better understand dynamics and adaptive recognition (Heus/Wijmenga). 2. *NMR and metabolite/ligand screening (Metabolomics/Proteomics/Molecular Systems Biology).* Three major projects are carried out using NMR and Mass Spectrometry as combined analytical techniques (2 Top Institute Pharma projects and HYPHEN-ID): a) charting the human (and rat/mouse) CSF metabolome and biomarker discovery for molecular diagnosis of multiple scleroses; b) identification/characterization of drug metabolites produced by humanized liver enzymes; c) metabolite identification and quantification in complex protein matrices as plasma. 3. *NMR of proteins of biomedical importance, e.g.* amyloid - and lipid-associated proteins (Wijmenga/Tessari). SW's research has resulted in over 100 papers in international peer-reviewed journals. He has (co)-organized various (inter-) national meetings, coordinated an EU program, is member of the editorial boards of Journal of Biomolecular Structure and Dynamics and of Biomolecular NMR Assignments, has been chairperson of NWO/CW section on Nucleic Acids and member/chair person of various NWO granting juries (VENI, TOP etc).

Selected publications:

1. Gangabadage CS, Zdunek J, Tessari M, Nilsson S, Olivecrona G and Wijmenga SS (2008) Structure and dynamics of human apolipoprotein CIII. J. Biol. Chem. 283, 17416-17427
2. van Buuren BNM, Schleucher J, Wittmann V, Griesinger C, Schwalbe H and Wijmenga SS (2004) NMR spectroscopic determination of the solution structure of a branched nucleic acid from residual dipolar couplings by using isotopically labeled nucleotides. Angew. Chem. Int. Edit. 43, 187-192
3. Ippel JH, Olofsson A, Schleucher J, Lundgren E and Wijmenga SS (2002) Probing solvent accessibility of amyloid fibrils by solution NMR spectroscopy. Proc. Natl. Acad. Sci. USA 99, 8648-8653
4. Cromsigt JAMTC, Hilbers CW and Wijmenga SS (2001) Prediction of proton chemical shifts in RNA - Their use in structure refinement and validation. J. Biomol. NMR 21, 11-29

5. Kolk M, van der Graaf M, Wijmenga SS, Pleij CAW, Heus HA and Hilbers CW (1998) NMR structure of a classical pseudoknot: Interplay of single- and double-stranded RNA. Science 280, 434-438