A Cross-Disciplinary UK-Wide Integrated Infrastructure for NMR Spectroscopy

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Executive Summary

Following consultation throughout the Physical and Life Sciences NMR communities, it is recommended that:

- A strategic package of investment in NMR is made nationally and regionally, culminating in the establishment of state-of-the-art, flagship ultra high field NMR infrastructure, at a cost of £48.4M over 5 years (of which £34.4M is capital investment);
- The instrumentation should be jointly used and managed by the physical and life sciences communities, with a requirement that synergy and collaboration across the disciplines and with other major research facilities is prioritised;
- There is also an urgent need for additional support for lower field NMR instrumentation at the institutional HEI/Research Centre/Industry level, as a prerequisite for both high-quality and cost-effective research across the UK, and to maximise our training and investment in high field NMR.

Background

Nuclear Magnetic Resonance (NMR) spectroscopy is an extremely powerful and non-invasive spectroscopic technique that provides unparalleled insight into molecular structure, interactions and dynamics. Its versatility enables the characterisation of materials, biomolecules, chemical processes and living organisms, therefore it spans modern physical and life sciences within both academic and industrial settings (Box 1). Hence, NMR spectroscopy is an indispensable tool for use in solving some of the major problems facing humanity over the forthcoming decades. For example, in the physical sciences NMR contributes to the development of sustainable energy supply by the characterisation of new battery and solar cell materials, as well as providing crucial knowledge in the fields of nanotechnology, pharmaceuticals and supra-molecular assemblies. In the life sciences, the technique is an important driving force for chemical and synthetic biology and forms part of the portfolio of modern diagnostics, identifying molecular signatures of disease which constitute the basis of personalised medicine. It also provides fundamental knowledge regarding the molecular mechanisms that underpin the workings of biological macromolecular complexes in both normal and disease states. The NMR technique is widely used to screen for novel compounds that can be developed into medicines, and gives vital information for enhancing crop production and food quality. In the 21st century, NMR will address many new scientific challenges, including, but by no means limited to, the understanding of new materials and their properties and the study of large biological macromolecules, fibrous and amorphous systems, as well as functioning complexes.

BOX 1: Versatility of nuclear magnetic resonance

- Chemistry: For identification and structure determination of molecules and materials in chemical industry and research. No chemistry laboratory can function without NMR spectroscopy.
- Molecular Biosciences: For elucidating the structure, functional dynamics and interactions of small and large biomolecules (proteins, DNA, RNA, sugars), which form the basis of life, health and disease.
- Solid materials: For the characterisation of a range of often novel solid state materials, from use in batteries to food, from plastics to proteins.
- Disease diagnosis: For quantitative analysis of metabolites in disease diagnosis and prevention (metabolomics), and monitoring therapeutic efficacy.
- Biology: For biophysical analysis of fundamental processes underpinning cellular functioning at the genetic and molecular level, in particular the dynamic dimension.
- 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.
- Industry: Supporting industrial biotechnology, fine chemicals, advanced materials and development of pharmaceuticals.

A cross-disciplinary integrated NMR infrastructure

Supported by state-of-art equipment, over the past four decades the UK NMR community has been at the forefront of this research area, as exemplified by its superlative track record. To maintain this world-leading position in NMR it is imperative for the UK to host leading-edge instrumentation with its associated support infrastructure. Underinvestment in NMR instrumentation for over a decade means that the UK has fallen behind its international competition both in capacity and capability (e.g. Germany, France, The Netherlands, Italy, USA) where more readily available access to state-of-the-art solution- and solid-state high-field NMR (with competitive equipment)[1] has become the norm, and funds have already been committed towards the purchase of the next generation of ultra-high field NMR equipment.

Synchronized with enhancements to its instrumentation and infrastructure in line with international competitors, the UK NMR community also proposes a step change in interdisciplinary cooperation, whereby physical and life scientists using related NMR methodology and shared instrumentation will work to develop new synergies that will advance cross-disciplinary science. A step change in NMR infrastructure investment encompassing a comprehensive package of measures needs to be made before 2021. This package comprises the provision of sufficient access for internationally leading physical and life science research to current state-of-the-art NMR equipment, culminating in the establishment of a cross-disciplinary next generation NMR flagship ultra-high field (1.2 GHz[2]) NMR facility served by the next generation NMR spectrometer suitable for both communities and all applications. Collectively, this package of measures will ensure the UK's leading role at the forefront of NMR-based research for the next decade. It is imperative that all these facilities are embedded in state-of-the-art environments and supported by expert technical staff, so as to ensure a maximal return on the capital investment.

The UK NMR community proposes a total investment of £48.4M, consisting of a £34.4M capital investment and £14.0M expenditure over 5 years for infrastructure support, operational costs, and scientific and technical support across all investments. The capital investment comprises £26.0M in narrow bore high- and ultra-high field (including £13.2M in the flagship ultra-high field NMR facility, which is only being developed in narrow-bore) and £8.4M in wide-bore high-field NMR. The community also strongly emphasises an urgent need for additional support for the lower field NMR instrumentation within institutional HEIs/Research Centres/Industry, as a prerequisite for both high-quality and cost-effective research across the UK.

We have identified three strategic priorities for the UK that will be strengthened by funding the above proposed investments: First, acquisition of state-of-the-art NMR equipment will allow the scientific community to remain at the international forefront in terms of scientific discovery, methodological development and training of the next generation of researchers – a source of expertise that underpins key research activities in economically important industrial sectors, such as pharmaceutical, biotechnological and

[1] UK NMR scientists do use some of these facilities (e.g. in the EU Bio-NMR consortium), but access is limited and provision insufficient.

[2] Traditionally, the different NMR spectrometers are characterised by their ^{1}H resonance frequencies (MHz-GHz range), rather than the strength of their magnetic fields, as is the case in Magnetic Resonance Imaging (MRI).

material sciences. Second, funding this proposal would stimulate the scientific synergies, logistical benefits and economies-of-scale that are only realisable from closer cooperation between NMR researchers across the different disciplines nationwide. Third, to tackle the most important future scientific challenges, NMR must be employed as an orthogonal complement to other techniques that have received recent substantial investments, such as synchrotrons, electron microscopy, neutrons, lasers and supporting infrastructure. This will expose those less-expert in NMR to its benefits, as well as increase output through synergies with other major facilities. Additionally, this approach will address the needs of small and medium sized companies that otherwise would not readily employ the technique, thereby increasing UK competitiveness and innovation capacity.

Operational aspects

The NMR community proposes that future provision of high- and ultra-high field NMR in the UK should be through a series of networked, regional NMR centres akin to a "hub and spoke" model, that would encompass existing national NMR centres and geographically distributed HEIs across the UK, with key HEIs in each region acting as the hubs. By incorporating ultra-high field capability into such a network of regional hubs we will, *1)* connect the facility to world-leading research programs, *2)* ensure that the ultra-high field resource is used as effectively as possible, and *3)* enable the transfer of expertise and technology across disciplines and institutions. Importantly, we consider that the restructuring and modernisation of existing NMR equipment throughout the UK would promote efficient sharing of high-field NMR instruments between the life and physical science communities at a national, regional and institutional level. The current proposal is the outcome of a series of discussions between PIs, funding agencies and HEIs that has produced a number of policy and strategy documents (see Appendix 1). Together, it demonstrates that the NMR community is fully engaged in maximising value for money of investments into its scientific equipment and infrastructure.

Solution- and solid state NMR spectroscopy are applied throughout the physical and life sciences. Although there are some infrastructural differences for each approach, e.g. pertaining to bore size, amplifiers or radiofrequency probe technologies, it is now possible to set up systems in a way that can accommodate all implementations. For example, since 2009, the world's current highest field (1 GHz) NMR spectrometer at the Centre for High Field NMR in Lyon, France, has successfully operated on a 3-4 months cycle switching between state-of-the-art solution and solid state NMR applications, a model also proposed for the UK ultra-high field facility.

The community envisions a merit-based access and time allocation model similar to the mechanisms now in place for access to the research facilities at Diamond and current national NMR Facilities, such as the EPSRC/BBSRC funded UK 850 MHz Solid-State NMR Facility hosted at Warwick University. A merit-based access model based founded upon peer-reviewed science will ensure optimal equipment use supported by scientifically sound arguments, thus securing and maximizing scientific and societal benefit.

Conclusions

The investment in a cross-disciplinary integrated NMR infrastructure would support an exciting, cost-effective and coherent strategy for developing a world-class UK NMR infrastructure fit for the 21st Century. This proposal is based upon the joint needs of the physical and life sciences communities and an exploration of effective solutions that maximise value for money. The signatories of this document, representing the NMR community in full, bears witness to the broad support for the proposal.

Through investments in both high- and ultra-high field NMR, limitations that have previously hampered exploration of new scientific avenues will be overcome and the ability to capitalise immediately on new scientific opportunities, will be created. This investments in new NMR infrastructure will maintain the UK at the forefront of international scientific and industrial competitiveness, thus enabling important future scientific discoveries that will underpin human benefits and thus the UK's economic impact world-wide.

Appendix 1: Supporting Documents

(1) Separate linked submissions (July 2014) by the Physical and Life Sciences Communities to the BIS Consultation on Proposals for Long-Term Capital Investment in Science & Research.

(2) CCPN documents on biomolecular NMR infrastructure

"BIOMOLECULAR NMR INFRASTRUCTURE IN THE UK"
(http://www2.ccpn.ac.uk/BISconsultation/UK_NMR_Infrastructure_05032012.pdf)

and

"RCUK Consultation on Capital Investment Roadmap: Biomolecular NMR Infrastructure"
(http://www2.ccpn.ac.uk/BISconsultation/RCUK_NMR_Paper_Final.pdf)

(3) EPSRC documents on Physical Sciences NMR infrastructure

http://www.epsrc.ac.uk/newsevents/pubs/roadmap-to-provide-internationally-leading-nmr-infrastructure-for-uk-physical-sciences/

"Roadmap to provide Internationally Leading NMR Infrastructure for UK Physical Sciences" (2013)

This roadmap was drawn up by EPSRC in consultation with the UK community following publication of

http://www.epsrc.ac.uk/newsevents/pubs/understanding-the-current-portfolio-and-resourcing-implications-of-nmr-infrastructure-underpinning-world-class-physical-sciences/

"Understanding the Current Portfolio and Resourcing Implications of NMR Infrastructure Underpinning World Class Physical Sciences" (2012)