Roadmap to provide Internationally Leading NMR Infrastructure for UK Physical Sciences

1. Introduction

Nuclear Magnetic Resonance (NMR) is a widely used and critically important experimental technique used broadly across the sciences. It thus underpins a broad range of internationally leading research. To understand the requirements and medium term needs for the physical sciences EPSRC recently commissioned a review of NMR infrastructure conducted by Professor Mark E. Smith (Vice-Chancellor of Lancaster University). Pro-Vice Chancellors at the UK's leading research institutions with significant portfolios of EPSRC funding were contacted and asked to complete a proforma to provide information about the current range of NMR equipment, how it had been funded, its current state, its sustainability and the predicted investment necessary over the next few years to allow the continued availability/access for physical sciences researchers of the necessary leading-edge equipment. The report was made available to the whole of the UK community for comment and presented at an open meeting on 22nd March. The report was widely accepted as providing an accurate representation of the current status of this NMR infrastructure and the likely requirements for upgrade and new capability over the next few years. EPSRC has followed this up by speaking directly to academics with research interests in the area of NMR as well as NMR facility managers through the UK NMR Managers group (UKMRM).

This document summarises the capital investments that will be required between now and 2020 in order for the UK's NMR infrastructure to be sufficient to continue to support world leading research. In order to maximise the value of this capital investment it is crucial that funding for experimental officers is maintained. We estimate this cost to be of the order of **£200k per year, per site**.

Two distinct types of NMR spectroscopy will be considered separately: solid- state and solution phase NMR. The new technique, DNP MAS NMR is used for solid state but has been considered in a separate section. NMR instruments vary in the size of the magnetic field used – the higher field instruments generally enabling better resolution and more sensitive measurements to be taken. The field is normally referred to in terms of the corresponding frequency in MHz of protons.

2. Consultation

The following People have been consulted directly during the preparation of this Roadmap.

Professor Mark E. Smith (Lancaster)

Dr Tim Claridge (Oxford)

Professor Sharon Ashbrook (St Andrews)

Professor Simon Duckett (York)

Dr Walter Kockenberger (Nottingham)

Professor Steven Brown (Warwick)

Dr Paul Hodgkinson (Durham)

Dr Dusan Uhrin (Edinburgh)

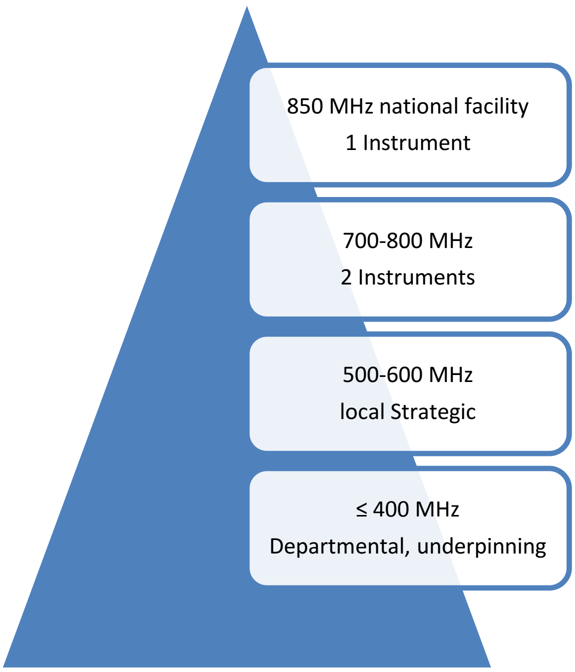
NMR managers at Bath, Bristol, Cambridge, Durham, Edinburgh, Heriot Watt, Nottingham, Oxford, St. Andrews, Strathclyde, Sussex, UCL, Warwick and York have also provided input.

3. Solid State NMR

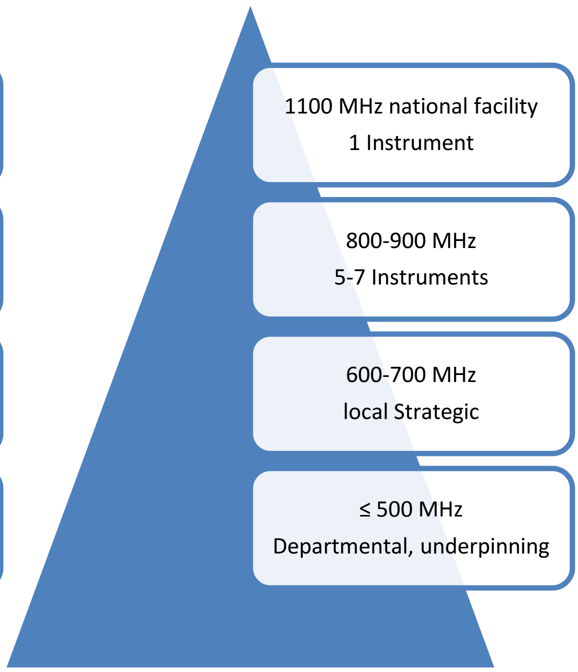
The review conducted by Smith concluded that most NMR instruments at 400 MHz and below are departmental or university facilities that underpin a large range of projects and are part of the general laboratory infrastructure that should be funded by HEIs rather than being a strategic investment through EPSRC funds (it should be noted that there are exceptions such as specialist low field instruments configured for specialised and not general use). Not all universities have solid state NMR infrastructure and the 400MHz solid state NMR service at Durham University currently serves the needs of researchers at these universities. The highest field instrument currently available in the UK is an 850MHz machine situated at Warwick University, which is available as a national facility to the whole community. Currently, this is jointly funded with BBSRC who contributed 10% towards the project. Joint access to the higher field machines for the life and physical sciences will form part of the solution to get the best value from NMR infrastructure. The UK also has an 800 MHz machine used for life sciences at Oxford and a 700 MHz machine at Cambridge used for energy materials research, but is dedicated to a specific research group.

By 2020 we envisage the highest field machine being a 1100 MHz machine, an investment of around £11 M. This will be supported by 5-7 regionally distributed 800-900 MHz machines with investment spread over the next 7 years as indicated in the table below. At a “local strategic” level investment is required at the 600-700 MHz level to maintain international competitiveness (£5 M before 2017 and an estimated further £10 M by 2020). A continued investment in upgrading and maintaining instruments by replacing the RF consoles and probes will cost an estimated £6 M. This represents a total of **£44 M over the next 7 years**.

Current Landscape



Projected Landscape 2020



Projected Investments in Solid State NMR Infrastructure

	By 2015	By 2017	By 2020
Low field ≤600 MHz	Review 400 MHz service (Durham)	5 x 600 MHz **£4 M**	10 x 600 MHz **£8M**
Medium field 700-900 MHz	3 machines **£6 M**	2 machines **£4 M**	2 machines **£5 M**
High Field > 900 MHz	1 x 1100 MHz **£11 M**		
Upgrades	Consoles/Probes **£6 M**		

4. Dynamic Nuclear Polarisation (DNP) Magic Angle Spinning (MAS) NMR

DNP MAS NMR is a novel strategy to increase the sensitivity of NMR experiments by 10 to 100 times. The technique requires specialist hardware that has now been commercialised. The availability of stable and robust hardware to the solid state NMR community has opened up the field for application-driven research with many leading solid state NMR groups across Europe now entering the field to develop new applications in materials and biomolecular research. There will be 15 DNP MAS NMR instruments operational by early 2014 in mainland Europe. The UK currently participates in the field of hardware development through a Basic Technology- funded project at Warwick, however there is no commercial system available for users who want to use the novel technology for their own applications. EPSRC's Consultation concluded the following

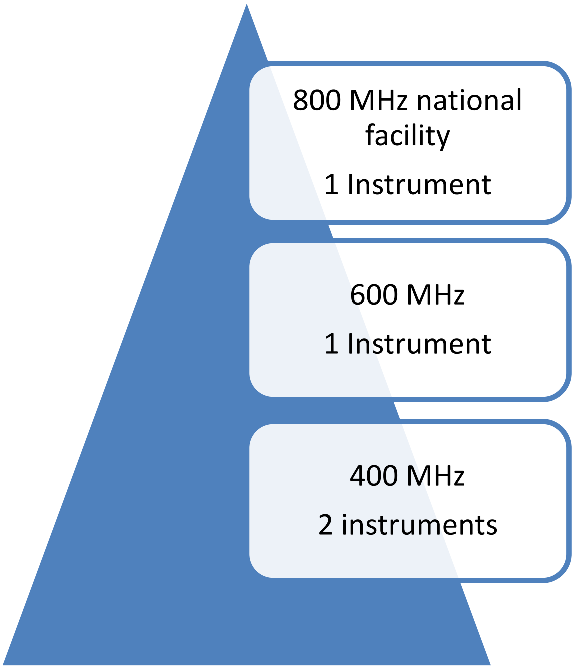
(A) The UK has currently clearly fallen behind the rapid DNP NMR spectroscopy developments that have taken place in other European countries, in particular in terms of developing applications. A facility should be established immediately that enables UK users to develop their own application portfolio tailored to the specific requirements of DNP NMR. A **600 MHz DNP MAS NMR facility** is proposed. The instrument costs ~£2.1M.

(B) Based on the usage of the first facility by the UK user group, additional DNP instruments should be set-up across the UK in medium term. Extrapolating from the rapid development in mainland Europe it is proposed to plan for at least **two additional instruments** to cover the needs of the UK NMR community (costs of 400 MHz DNP MAS NMR instrument: ~£1.5M). After reviewing the experience obtained from the available high field (800MHz) DNP MAS NMR instruments (Lyon/Utrecht/Jülich) it should be considered to establish such a facility also in the UK once commercial hardware was delivered and working reliably in the field (**800 MHz DNP MAS NMR** instrument costs: ~£3.5M)

(C) Although the commercial instruments provide already a high sensitivity gain in DNP NMR experiments, research efforts continue to improve the hardware and experimental strategies to reach even higher signal enhancements and resolution. It is proposed to plan for future upgrades of microwave sources (a gyrotron microwave source costs ~£1M). In particular, on-going research may lead to **novel microwaves sources** that have superior performance (amplitude modulation, frequency modulation, pulsed mode) in comparison to the currently used constant-wave microwave gyrotrons.

DNP MAS NMR finds applications across the Physical and life sciences. There is thus an urgent need to coordinate activities between research councils as well as other funders to cover the capital costs.

DNP MAS NMR projected Landscape 2020



Short Term (by 2015) 600 MHz instrument **£2.1 M** and one 400MHz, **£1.5M**

Medium Term (by 2017) An additional 400 MHz instruments **£1.5 M**

After reviewing experience of European high field DNP MAS NMR instruments 1 x 800 MHz **£3.5 M**

Longer term (by 2020) Upgrades of microwave sources 4 x £1 M = **£4 M**

Total £12.6 M

5. Solution Phase NMR

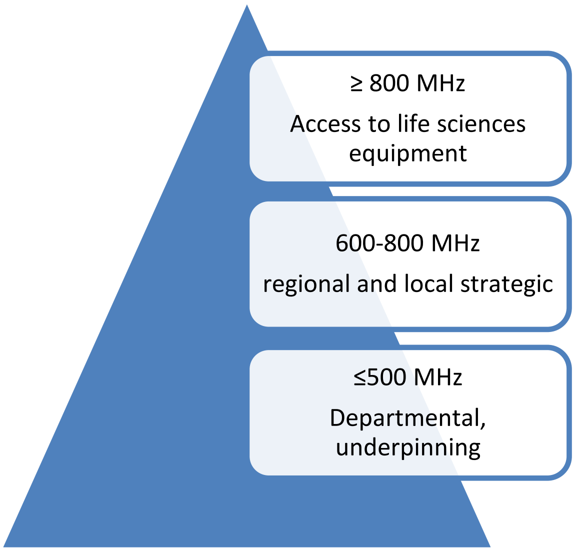
Solution Phase NMR is an underpinning technique for all chemistry departments. EPSRC's consultation has identified 500 MHz and below as the level at which departmental or institutional support is required. There is, nonetheless, recognition that certain hardware investments (for instance cryo-probes) can boost the capability of these instruments to make them a strategic investment that can lead to a step-change in the type of research that is possible. In 2012-13 EPSRC invested around £5.3 M in NMR equipment through the "Core Chemistry" call for proposals and a further £0.7 M through the Strategic Equipment Scheme. This investment covered primarily machines at 500 MHz and below.

Continued investment will be required to ensure that these lower field instruments can maximise their capability through upgrades and to maintain and enhance capability currently provided largely by infrastructure that has become outdated or obsolete. An on-going issue for all stakeholders (higher education institutions, the research councils and HEFCE) is to identify where these funds ought to come from. An estimated **£12 M** in addition to the recent £6 M investment is recorded in two tranches in the table below.

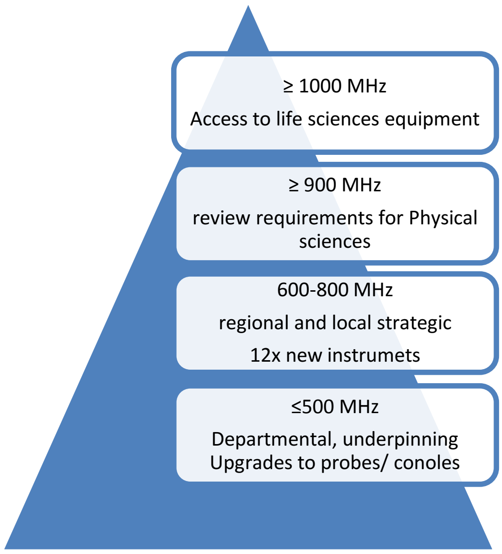
At the mid-field range (600-700 MHz) there is also a demand for modern probes and RF consoles to upgrade these instruments and increase capability. There is also likely to be a requirement for up to 10 new instruments before 2020. This will require around **£16 M** by 2020. There is some demand from physical scientists to access 800 MHz instruments for solution phase experiments and, while these needs are currently largely met by accessing instruments used primarily by life science researchers, investment in one or two instruments dedicated to the physical sciences will be required before 2020, an estimated investment of **£4 M.**

Although there is some demand for access to 900 MHz facilities for solution state NMR, the primary concern here was that the high cost of investment should not compromise the pressing need for investment in mid-field instrumentation. At present the requirements for high field in the physical sciences are met by accessing instruments primarily used for the life sciences. In the short to medium term this access needs to be secured and in the longer term we should review the need for physical sciences access to high field instruments.

Current Landscape



Projected Landscape 2020



Projected Investments in Solution Phase NMR Infrastructure

	By 2015	By 2017	By 2020
Low field ≤500 MHz probe & console upgrades	(£6 M)*	**£6M**	**£6M**
Medium field 600-800 MHz	10 x 600/700 **£16 M;** 2 x 800 MHz **£4 M**		
High Field > 900 MHz	Access to life sciences facilities		Review requirements

*This investment has already been made through EPSRC's "Core Chemistry" initiative and Strategic Equipment Scheme in 2012-13. The source of funding for this type of underpinning

6. Working with the Life Sciences

NMR techniques (solid and solution state, as well as DNP) are crucial for the life sciences as well as the physical sciences. At the lower field, underpinning, departmental level, instrumentation tends to be dedicated to one or the other area, whereas for higher field instrumentation, potentially operating as regional centres, sharing between the life and physical sciences becomes a cost efficient option as shown by the 850 MHz facility at Warwick. Especially for solution phase NMR, the current requirements for physical scientists to access the highest field instruments can potentially be met by sharing infrastructure with colleagues in the life sciences. The potential for shared use instruments needs to be reflected by the Research Councils working together on joint funding of high field NMR facilities where requirements overlap and EPSRC has initiated a dialogue with BBSRC and MRC to address this.

Daniel Emmerson, EPSRC, August 2013