

Understanding the Current Portfolio and Resourcing Implications of NMR Infrastructure Underpinning World Class Science in the UK

1. Context

In winter 2012/13 the EPSRC undertook a survey of the NMR equipment base serving the physical sciences community in the UK. The impetus for undertaking the 2012 survey was several-fold. First, there is an undoubted link between the availability of modern state of the art experimental infrastructure and the ability to carry out world-leading research. Hence to maintain the UK's position as one of the world leaders in research in this area, the future availability of state of the art NMR research infrastructure is critical. Second, following the 2008 banking crisis and the reshaping of the Government finances by the 2010 Coalition Government, Research Councils became much more capital constrained¹. This occurred in parallel with the 2010 Wakeham Review on full economic costing (FEC)² which added to our understanding of the sustainability of equipment infrastructure. The RCUK response in the context of both of these drivers was captured in the report 'Efficiency 2011-15: Ensuring Excellence with Impact'.³ The EPSRC responded to this by adopting a radically different approach to funding equipment, removing larger equipment (>£50k in 2012) from responsive mode grants, and the introduction of the Strategic Equipment Panel. To improve the basis of decision making at the Strategic Equipment Panel, understanding how a particular bid for NMR hardware fitted not only into the individual university context, but also the wider regional and national landscape was important.

NMR instrumentation was a good starting point to adopt this approach as it is a very widely used strategic experimental technique within the physical sciences, thereby acting as a good exemplar for the challenges facing the provision of infrastructure for key experimental techniques. Additional drive was provided when in response to the 2012 call for Core Capability for Chemistry Research there were 20 bids from 22 universities requesting NMR in the immediate future of £8.2M (part A) and near future of £19M (part B), making up a sizeable fraction of the total funding requested under that call. Under part A approximately 40% of the approved funding went to NMR instrumentation. This was strong evidence that there was significant demand and indicated a backlog of outdated infrastructure at the time of the study. Such an observation spoke to the issues the sector (which is taken here as a combination of higher education institutions (HEIs), research institutes, the research and funding bodies and indirectly Government) faced concerning the sustainability of such high-end research capital infrastructure.

A further element to the changing capital infrastructure was a consultation by RCUK. The life sciences community responded by a forward look at its NMR infrastructure needs⁴ and a direct response to the consultation.⁵ The resulting RCUK report was launched by the then Chancellor in November 2012.⁶ To position EPSRC's thinking around NMR infrastructure in physical sciences its original report⁷ which arose from a consultation in November 2012, was published in January 2013

¹ It turned out that looking at capital spend the initial heavy cuts were reversed, but did not go back as a straight replacement for the reduced capital lines, but as a mixture of some replacement and large one-off announcements.

² 2010, Financial Sustainability and Efficiency in Full Economic Costing of Research in UK Higher Education Institutions.

³ <http://www.rcuk.ac.uk/research/efficiency/efficiency2011/>

⁴ BIOMOLECULAR NMR INFRASTRUCTURE IN THE UK.

http://www2.ccpn.ac.uk/BISconsultation/UK_NMR_Infrastructure_05032012.pdf

⁵ http://www2.ccpn.ac.uk/BISconsultation/RCUK_NMR_Paper_Final.pdf

⁶ <http://www.rcuk.ac.uk/Publications/policy/CapitalInvestment/>

⁷ 'Understanding the Current Portfolio and Resourcing Implications of NMR Infrastructure Underpinning World Class Physical Sciences', M.E. Smith on behalf of EPSRC

and discussed at a town hall meeting (21/03/13). The methodology used at that time involved writing directly to the 25 heaviest HEI users of NMR infrastructure in the physical sciences community. This then led the physical sciences community, in partnership with the EPSRC, to develop an NMR infrastructure roadmap⁸. Four years further on it was felt timely to refresh these reports giving an up to date overview of the NMR infrastructure currently available to the community.

The timing of the present report has been driven by several factors:

- (a) from an EPSRC perspective the Strategic Equipment Panel has been operating for around 5 years now,
- (b) there have been a further four years of the bedding in of the Wakeham recommendations that encouraged more effective and efficient utilisation of existing and new assets across the research base through, for example, equipment sharing, such that changes in operation and behaviour to these drivers can be more fully ascertained,
- (c) following separate, but linked consultations there was a joint submission⁹ to the 2014 BIS capital consultation. The resulting BIS capital roadmap of December 2014¹⁰ flagged NMR for potentially £22M of new investment, which translated into a letter of intent from BEIS in August 2016.

The increasing sophistication of the state of the art has driven up the cost of providing leading-edge facilities, especially instruments equipped with the very highest magnetic fields available. The roadmaps^{5,8} presented a pyramidal representation of NMR infrastructure, with Tier 1 as the apex. The instruments just below the uppermost 'Tier 1' level have also seen improvements in the associated technology (e.g. probes, electronics, etc.) such that upgrade of such existing instruments is also desirable. There are the additional factors of increasing demand for access to Tier 1 and 2 instrumentation at a time when the available budget to meet their running costs has not increased at the same rate; impacting on sustainability. As the criteria for the new investment are developed, understanding the current landscape for NMR infrastructure would be very timely to provide the best possible background information for decision making.

2. Methodology used in this Review of the UK's Current NMR Infrastructure

The UK has a first class reputation in leading the development and application of NMR techniques, and there are groups across both physical and life science disciplines using NMR in this way. In the physical sciences, NMR as an experimental technique touches almost all areas including materials science, engineering (e.g. chemical, civil), physics and chemical biology. However, it is as an analytical technique underpinning chemical research where NMR facilities are regarded as absolutely essential to sustain an internationally competitive chemistry environment. With the £22M allocation for ultrahigh/high field spectroscopic capability covering all science areas it was necessary to expand the remit of the survey to include the life sciences. Hence, although the EPSRC coordinated the survey, all the Research Councils contributed. Rather than just target the biggest users directly, an open call was made on the EPSRC website¹¹ and communications were sent out via various Research Councils and the user lists of various facilities

⁸<https://www.epsrc.ac.uk/newsevents/pubs/roadmap-to-provide-internationally-leading-nmr-infrastructure-for-uk-physical-sciences/>

⁹ http://www2.ccpn.ac.uk/BISconsultation/A_UK_wide_cross_discipline_NMR_infrastructure_v3.4.pdf

¹⁰ https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/383439/14-1248-science-capital-consultation-response.pdf

¹¹ <https://www.epsrc.ac.uk/research/ourportfolio/themes/researchinfrastructure/strategy/equipmentroadmaps/nmrallforevidence/>

(e.g. the EPSRC 850 MHz mid-range facility). There was also more ambition in the range of information sought than in 2012. Questions were asked to ascertain whether an instrument was largely used for physical sciences/life sciences/both and was primarily configured for solution/solids/both. There were questions about the field, range of frequencies covered, probes, specialist capability (e.g. extended temperature range, unusual frequency combinations, ultrafast MAS, double angle rotation, etc.) and age. There was a more subjective question about whether an instrument configuration was core or world-leading capability. It is clear that similar instruments might be classified in either of these categories. For example a 500 MHz instrument might be considered to be core capability if it has a standard probe configuration, whereas examples of configurations that would classify it as 'world-leading' might be if it had a four channel capability (that could operate e.g. in $^1\text{H}/^{19}\text{F}/\text{X}$ mode) or was equipped with a full MAS gradient set. Information was sought whether an instrument was largely used for analysis/characterisation or was primarily used for technique/instrument development.

In addition to better understand sustainability the different sources of capital funding were identified. The sustainability question was further probed by asking for a range of background information such as an estimate of actual level of usage, what personnel support there was, and whether an instrument was used by a single department or across the institution. There was also a question about the model for charging for use of the equipment and then an estimate of the current state of the infrastructure. Thirty three universities and research institutes replied to the survey which included all of the major NMR-using universities. From our knowledge of the sector, further high-level data from websites was also included (e.g. field, physical/life, solution/solid) for a further 10 universities. Hence data from 43 universities have been included in the data presented herein. Note that there are variations between totals in different parts of the survey as the same level of information was not available for every instrument. For example, for all instruments we had the main field and frequency of operation, but not necessarily the age of each instrument. It should be noted this survey excluded NMR instruments used for imaging in a clinical setting.

3. Overview of the Current Portfolio of NMR Instrumentation

There were 362 NMR instruments declared in this survey. In the majority of the analysis below only instruments with proton frequencies ≥ 100 MHz have been included. Fields below this have been excluded since there are so many different instruments and the types of application are very varied at lower fields such that it is difficult to have a common view about this group. Some instruments are also very old 60 MHz ^{13}C solution instruments used for straight chemical characterisation which are generally not competitive as research instruments, whereas some low field benchtops are being developed for high impact, relatively low cost process/quality control applications, e.g. the GARField imaging systems which provide some very interesting 'in the field' imaging studies in the physical sciences. There were also some interesting very low field fundamental physics studies using magnetic resonance reported. Hence, the 23 instruments that fall into this category at <100 MHz have been excluded from the analysis (and hence figures) below. It should be stressed that this makes no comment or judgement on the importance or excellence of some of the science being conducted on this type of instrumentation.

The survey indicates that the field distribution is still sharply peaked at 400 MHz (Fig. 1), but rapidly falls off at lower field. Higher field instruments extend to 800 MHz and beyond, with 950 MHz being the highest field currently available in the UK. It was noted in the 2013 report that given how long magnetic fields much higher than 9.4 T had been routinely available, it is surprising that 9.4 T remains the most commonly available field with the UK NMR community. This is

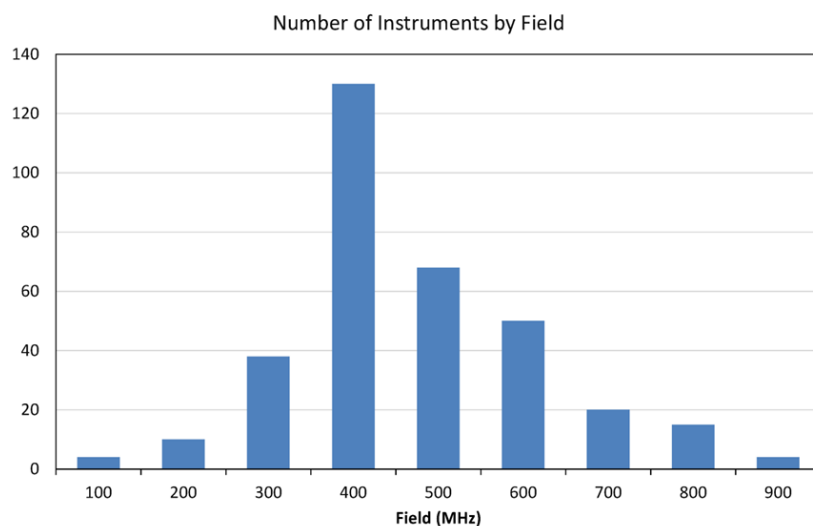


Figure 1. The distribution of the main magnetic field (expressed as the ^1H frequency) of NMR spectrometers in the UK

probably an indication of a combination of underinvestment and an element of legacy as magnets have a long lifetime. The distributions between solution state and solid state NMR activity undertaken, and its application to life and physical sciences are shown in Fig. 2.

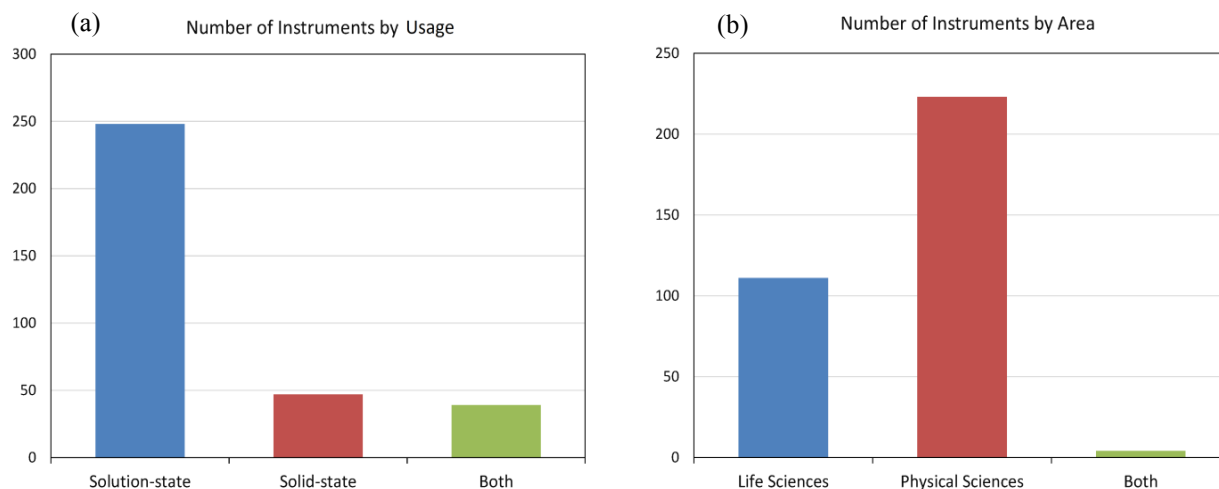


Figure 2. Distribution of UK NMR instrumentation by, (a) mode of use (solution vs solid), and (b) predominant area of application (life sciences vs physical sciences)

Unsurprisingly, solution state instrumentation dominates this analysis comprising 74% of the portfolio, whereas 14% were dedicated to solid state NMR studies and 12% of the portfolio is intended to be switched between these two configurations. By far the majority of instruments have been configured to operate in either solution-only or solid-only modes. This is quite interesting as many commercial instruments can be set up in both modes. However ready switching requires up to date hardware, which is often not available, and of course the technical expertise to be able to operate in both modes. *This observation may have implications for the purchase of an ultrahigh instrument with the new funding available.* A question for the upcoming Town Hall meeting will be can the most modern instruments be readily switched between

operating modes or is there still an apparent compromise to be made, meaning that any 'Tier 1' instrument should still be optimised for solution or solids operation?

The life sciences make up roughly a third of the instrumentation. Hence, there are significantly more NMR spectrometers in the physical sciences. This present study also further reinforces the conclusion drawn from the 2012 survey that within the physical sciences NMR is clearly concentrated within Chemistry departments where NMR is regarded as an essential underpinning experimental technology that has widespread use across its sub-disciplines. Based on the number of instruments reported here, it is clear that while NMR is still a very important technique in the life sciences there is generally a different perspective on NMR infrastructure. In Chemistry, NMR is an all pervasive, underpinning technique, whereas in life sciences departments it is more targeted to specific uses such as studies of the structure and dynamics of macromolecules as well as metabolomics, both of which cross the life sciences/biological chemistry interface.

The field distribution from the overall summary in Fig. 1 can be recast in terms of the differential field distribution for solution vs solid (Fig. 3) and physical vs life (Fig. 4). While the distributions for both solid and solution state NMR instrumentation peak markedly at 400 MHz, it is the more strongly favoured field for solid state NMR spectrometers, making up 40% of the available instruments compared to 32% for the solution counterparts. Away from the most common field there are some interesting differences. For solid state instruments 500 and 600 MHz instruments each only make up 8% of the portfolio, whereas they make up 20% and 14%, respectively, of the solution state portfolio. A factor here must be the relative cost of wide bore compared to standard bore magnets. For both solution and solid state NMR, the UK still possesses a very limited availability of 700 MHz instruments and above thus comprising only 10% of the portfolio. For the very highest fields of ≥ 900 MHz there is only solution capability. The availability of ultrahigh/very high field NMR instrumentation is limited when compared to many rival national science systems, especially in Europe. This is particularly true when one considers the size of the science systems, especially in Europe. This is particularly true when one considers the size of the science community and the scale of the science portfolio that needs to be underpinned in the UK.

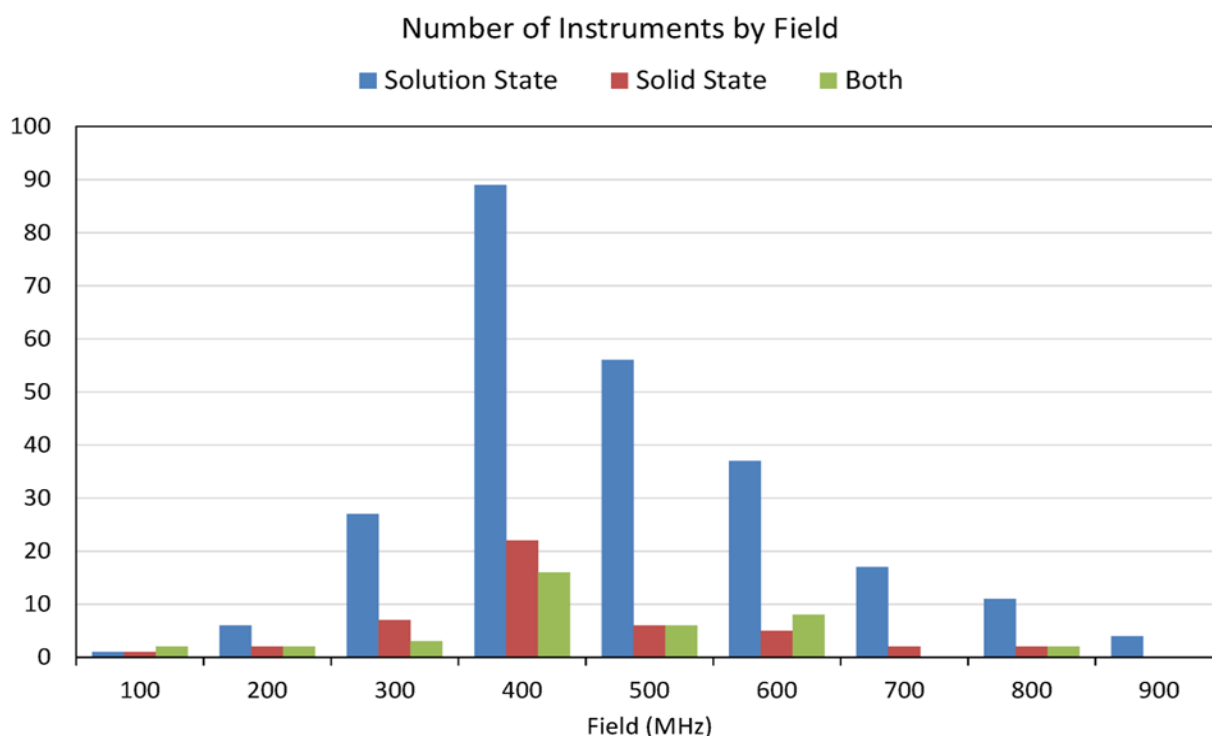


Figure 3. Distribution of NMR spectrometers by main magnetic field split by the major mode of operation

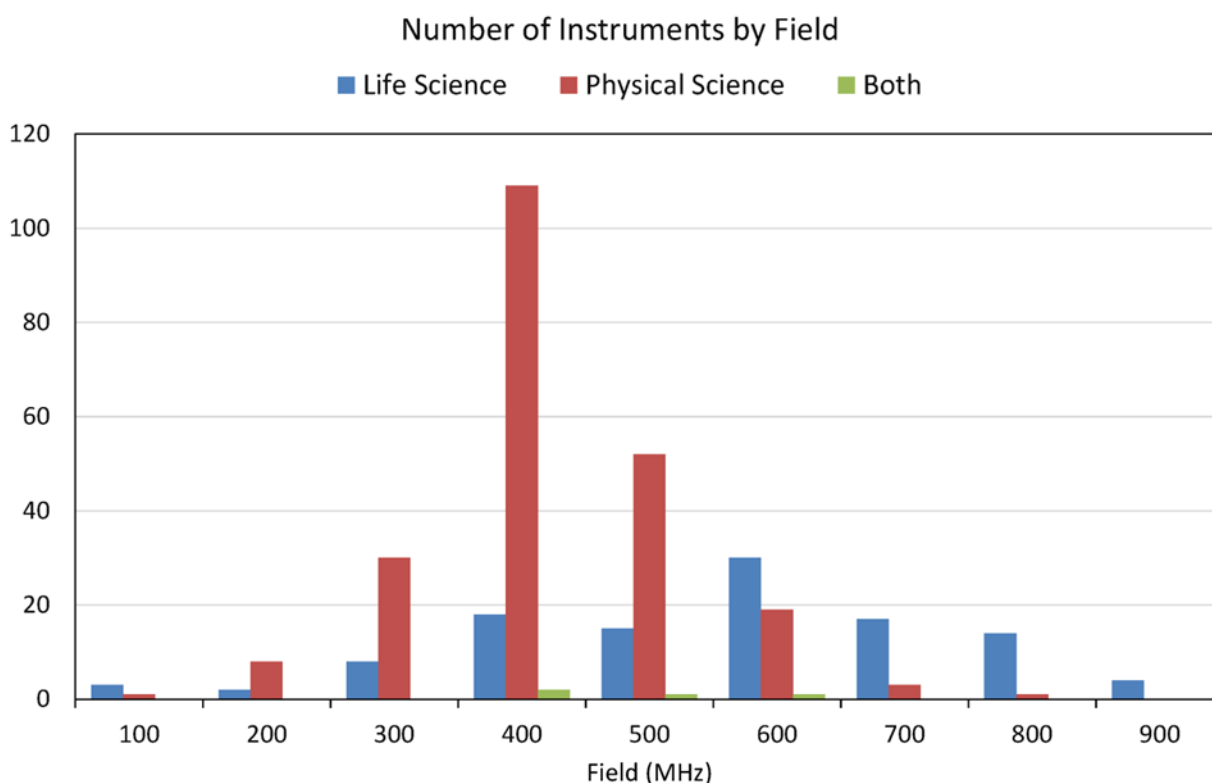


Figure 4. Distribution of NMR spectrometers by main magnetic field split by the main area of application (life vs physical sciences)

Comparison of the field distributions between the life and physical sciences (Fig. 4) shows that the fields for the life sciences peak at 600 MHz (28%) whereas for the physical sciences it is at 400 MHz (48%). This distribution is driven by the need in the life sciences community to study larger molecules where the higher resolution and sensitivity of higher field instruments is critical. For the physical sciences there are only four (2%) instruments available at ≥ 700 MHz, whereas the corresponding number for the life sciences is 30% of its dedicated instrumentation. This can be explained to some extent by the fact that many biological macromolecules simply cannot be studied at fields lower than 800 MHz. However, there are also very significant advantages to many physical science problems (e.g. quadrupolar nuclei with large quadrupolar interactions) so it is somewhat surprising that this discrepancy in the availability of high magnetic fields is so great. Some of the key observations made in the 2013 EPSRC report remain valid four years further on and extend into the life sciences as well. The number of instruments at ≤ 300 MHz is 16% of the overall portfolio, but this is more prevalent for physical sciences instruments at 18% compared to life sciences where it is only 11%. This observation may be a result of the development of the portfolio by upgrading and adding to existing instruments, rather than active replacement, which is perhaps a natural tendency, particularly when key pressures relate to capacity and funding issues. The significant gains in sensitivity in solution NMR that cryoprobes provide has seen an increased availability of such probes, with the survey revealing at least 40 spread across the UK.

4. Age Profile of NMR Infrastructure in the UK

The survey also explicitly probed the age of all existing equipment. One complication is that the three main components of an NMR spectrometer age at different rates. Magnets can last for a very considerable time, e.g. well beyond 30 years, whereas a console (the amplifiers, receiver, etc.) become obsolete much more rapidly, becoming last generation technology on the 5-10 year

timescale and completely worn out around 10-15 years. Probes have very variable lifetimes, but again this is typically around 7 years. As equipment ages it becomes physically worn out leading to more down time, along with lower inherent sensitivity than latest generation instruments leading to both lower capability and efficiency. A point where there has been some progress, but where there certainly needs to be more is around magnets and the sustainability of running them. The number of shielded magnets has increased, which has the benefit that the estates footprint is considerably reduced, especially for the very highest field magnets. There are more helium-

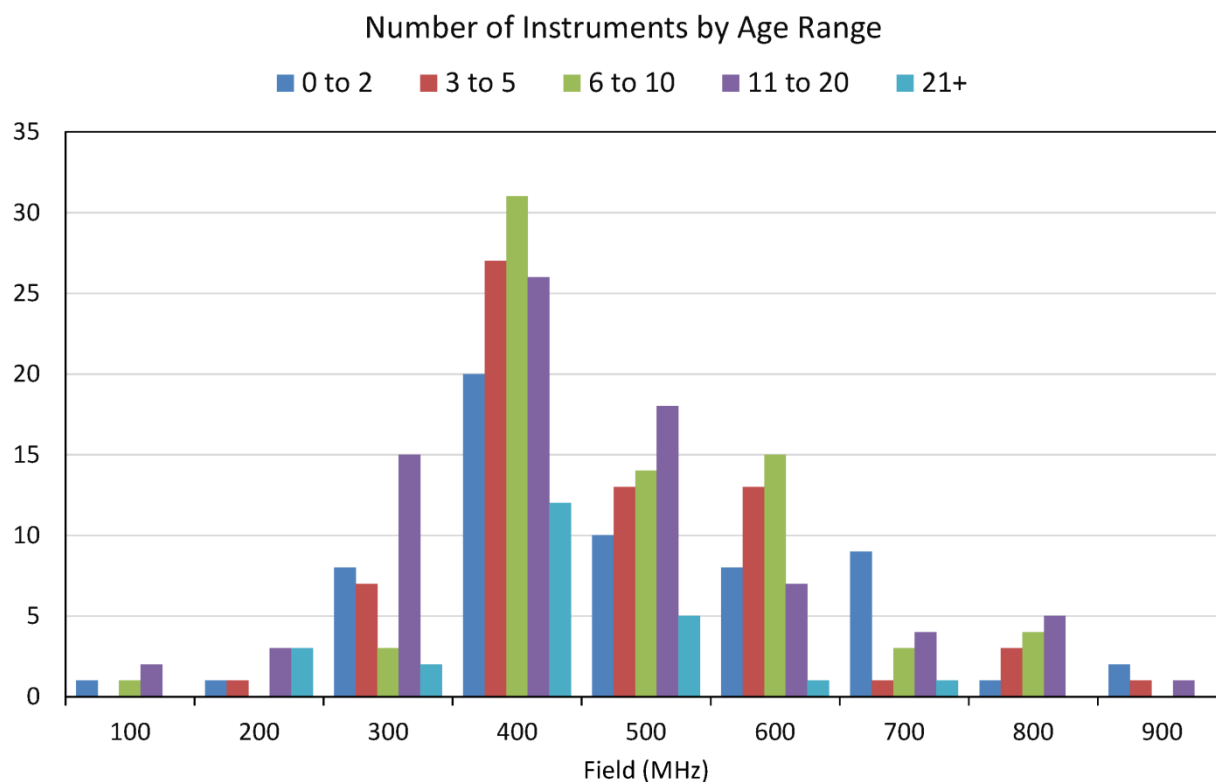


Figure 5. The age profile of NMR spectrometers divided between the main magnetic field

recycling schemes in place, which has an upfront capital outlay, but then benefits from lower helium recurrent costs and helps with the environmental sustainability of a finite resource. There has also been the development of closed cryogen cycle systems and of competitive pumped magnets even to quite high field that are cryogen-free. However, there is a distinct lack of access to more recent and sophisticated experiments that can be performed on newer instruments. Examples of this include the enhanced sensitivity of cryoprobes and, in particular, ultrafast magic angle spinning (MAS) (i.e. > 100 kHz). Increasing digital capability has led to complex and sophisticated pulse sequences and also allowed different approaches for detection, not possible on previous generation instruments. The age profile of spectrometers taken largely on the basis of the console's age is shown in Fig. 5 split into the different main fields. It can be seen that for the lower fields, although there are some new instruments the majority are quite old i.e. > 10 years. There is quite a considerable fraction in this age range also for the 300, 400 and 500 MHz systems, although for the 400 and 500 MHz instruments there has also been some considerable recent (< 2 year) investment. However, although there has been investment in solution state 700 MHz instruments which aligns with the investment strategy outlined in the 2013 roadmap⁵, it can be seen that there are now a considerable fraction of the > 600 MHz instrument population that is not state of the art.

The age information is converted into an overall distribution in Fig. 6. This provides an interesting comparison to the distribution determined in the 2013 report for the instruments then concentrated in the physical sciences. Although there is an increase in the very oldest instruments at >20 years (remembering this now covers a different range of instruments as life sciences are now included) from 3% to 8% there has been a decrease in number of instruments > 10 years down from 48% to 35%; i.e. overall it can be observed that there has been a modernisation of the portfolio. The number of instruments installed in the last two years is 20%, such that the fraction of the portfolio less than five and less than 10 years has increased between 2012 and 2016 from 31% to 42% and 52% to 65% respectively, indicating the significant investment in NMR infrastructure that has taken place.

Percentage of Instruments by Age Range

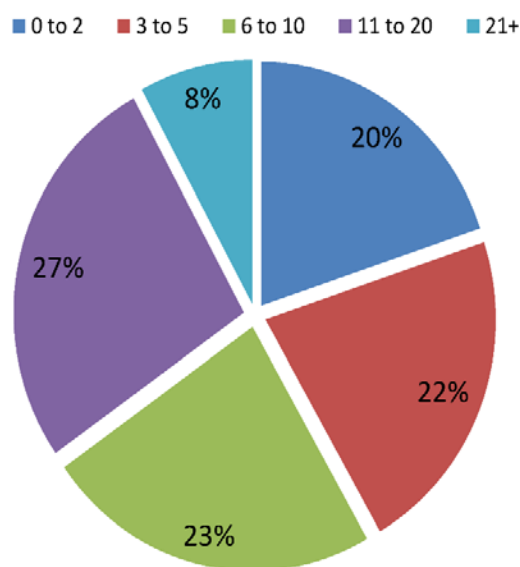


Figure 6. The age distribution of NMR spectrometers in the UK across all areas of application

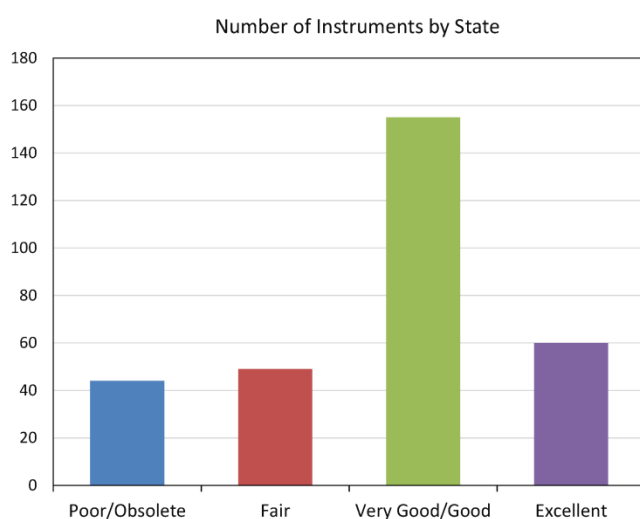


Figure 7. Estimated condition of NMR spectrometers in the UK

In the present survey the state of the instrument was also more explicitly asked about. Again although this requires a somewhat subjective judgement by the person filling in the form it does provide some useful information. The 'state' of the equipment is shown in Fig. 7. To a certain extent there is a fair correlation to the age of the equipment, with 70% of the portfolio in good or better condition, nevertheless 14% was described in poor or obsolete condition. With an instrument in this state there is a severe impact on the quality of the research that can be performed, and there are the added costs of the repairs for such equipment and the time that has to

be devoted to troubleshooting these problems. There is additionally the problem that in some cases spare parts are difficult to source. With certain manufacturers having moved away from providing NMR, dwindling support, especially from some manufacturers, makes it more difficult to keep older instruments working. The reduction in manufacturers also means that instruments supplied in the last couple of years have been dominated by one supplier, especially at higher magnetic fields.

5. Funding of NMR Equipment and its Support in the UK

The rich patchwork of funding that has been brought together to fund the UK's NMR infrastructure was clearly revealed in the survey. Funding from the Research Councils is very

significant with EPSRC, BBSRC and MRC making sizeable investments. The impact of specific calls is very evident such as the Core Chemistry Capability, JREI and Equipment Refresh, with a significant number of instruments being funded from such sources. Some of the instruments funded in the last two years in physical sciences can be directly correlated to actions identified on the NMR Roadmap developed in 2013.⁸ It is also interesting to note that for the EPSRC the equipment funding attached to Centres for Doctoral Training (CDTs) has also been used, especially for upgrading (as opposed to purchasing complete new instruments) of NMR facilities. When the HE funding councils had significant capital funding for scientific equipment, schemes such as JIF, CIF and SRIF were also very important. Across the landscape there are other contributors such as the Royal Society and the Wolfson Foundation. For the life sciences charities play an important role in the overall mix for capital funding with the Wellcome Trust a very important sponsor of such research. Cancer Research UK and the British Heart Foundation also contribute to NMR equipment.

European funding plays an important role, with universities exploiting structural funds (e.g. ERDF, ESIF, etc.) which has augmented UK funding for NMR equipment. With structural funds there is the additional dimension that there is often the need to couple the science more directly with business users and make the facility open to others as a condition of the grant. The European Research Council (ERC) is making some significant investments in NMR infrastructure with at least two instruments already funded from this source in the UK. While it is welcome that all of these sources have been used to fund NMR infrastructure, the range of sources make it a little difficult to plan the sustainability of such equipment in a coherent manner.

It was argued in the previous 2013 report⁷ that responses to specific calls was to either fix a short term urgent problem or expand capacity, with sustainability somewhat a secondary consideration. With Equipment Panels now more explicitly asking for business plans and evidence of a university's approach to sustainability, as well as a more explicit discussion of what should be directly funded from grants, and what should be regarded as part of a well-founded laboratory and should be part of a university's capital replacement strategy, this has raised the profile of sustainability issues. There is now further evidence that more universities are already drawing a clear distinction between 'workhorse' underpinning facilities that are vital to the more general health of the discipline and the really leading-edge instrumentation that facilitates really novel research in a related area, or for development of the technique/application itself.

Within the medium-term capital planning of universities there is increasing provision of funding for scientific equipment, both new and replacement. Universities are also becoming more used to being directly responsible for funding capital from their own cash resources. The survey here clearly shows that universities and research institutes are big funders of NMR equipment from 'own' funds (although the exact definition of 'own' funds in each case is not clear), both new systems and upgrades, especially in the part of the field distribution where an NMR instrument is part of the 'well found' laboratory expected to underpin research. Of the approximately 330 instruments (≥ 100 MHz) examined in this review and where funding information was provided, the Research Councils were the largest funder with around 140 'instrument equivalents' funded, with 70% solely funded by the Research Councils (although the records of the different Research Councils vary widely), thus leaving 30% as jointly-funded, with universities typically contributing between 33 and 50%. Universities contributed 90 instrument equivalents, with 75 fully funded by the universities themselves. It is thus clear that the provision of this equipment portfolio is a genuine partnership, suggesting there should be a more coherent forum for Research Councils, other funders and universities to discuss the responsibilities and contributions each should make to equipment provision. It should also be noted that universities are at different states of developing their thinking over what they should provide.

6. Sustainability and the Efficient Usage of NMR Equipment

As in the 2012 survey many contributions indicated that providing the information requested for this present survey was, for the most part straightforward. The push in recent years to create university-wide equipment, searchable databases helped with this survey in a number of institutions. HEIs having this information readily available helps them to better understand the scale of the financial liability associated with the sustainability of the equipment base. In dipstick testing the information provided to the survey, a number of universities websites were checked directly. Some were easy to find and were very informative, where the available NMR equipment was clearly and completely described. Others were somewhat confusing and could not really be interpreted by the interested non-expert user, and one or two websites were completely impenetrable. Given much of this resource is publically funded it should be clearer to the outside

Percentage of Instruments by Capacity Usage

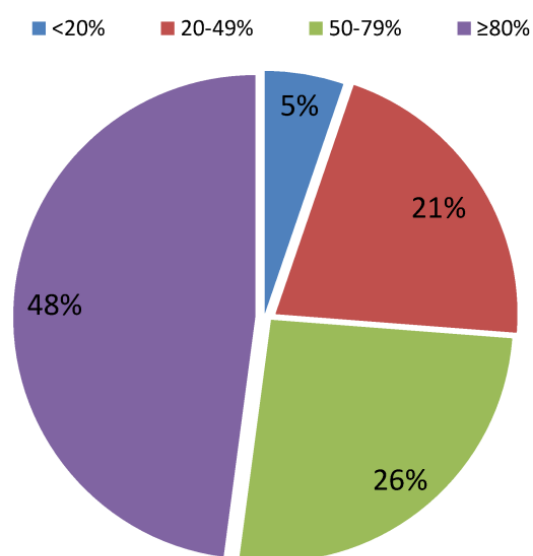


Figure 8. The distribution of estimated capacity used of NMR spectrometers across the UK

world what is available. Also given the frequent need to generate external resources to make the equipment more sustainable some of these sites will encourage usage and others will certainly not help. It has been known for some time that to get the most out of such facilities, skilled specialist personnel are necessary. The typical model is to have an academic member of staff acting as the lead, with support from an experimental officer/technical support. Although it is expected that these support personnel costs will be significantly recovered from funded research, most universities seem to have underwritten these positions with indefinite contracts. There are some universities where the academic still effectively tries to do everything themselves with relatively limited support. There is some correlation between the usage data and the quality of support.

There has been relatively little progress in the last couple of years of institution's creating single integrated facilities between the physical and life sciences, largely based on different philosophical approaches/equipment configurations and geographical locations of these different activities. In a given Faculty, equipment can often be concentrated in a Department, usually Chemistry for the physical sciences. It is clear that centralisation of NMR facilities can be achieved providing that there is a will within senior management of a department/faculty/university for this to occur. However, this is not to suggest that there should be a single monolithic model for equipment location, as the specialised equipment associated with a research group can be in a separate location. For the specialist research group there still appears to be some resistance to mixed models of operation (i.e. core research, alongside more collaborative work with perhaps an element of service work).

Overall usage figures shown in Fig. 8 show that approximately half of all NMR spectrometers exhibit full usage (> 80% on a 24/7 basis). Subsequently, it has to be acknowledged that there is some potential for increased efficiency as roughly a quarter are used less than 50% of the time. In particular, some are used < 20% of the time and these institutions would need to be convinced that such equipment is really necessary as it is very unlikely on this basis that it could ever be made sustainable. The survey explicitly asked for likely plans for NMR equipment upgrades

that would be necessary in the next five years. An idea of the scale of the liability is that roughly 30% of the consoles would need upgrading in this period. It is clear that different universities saw their responsibilities for funding this quite differently. Some recognised that funding would need to be in partnership with the Research Councils, with some seeing only lower field open access instruments as their responsibility. The conclusion had already been reached in 2012 for the physical sciences that the greater sensitivity and throughput with increased magnetic fields meant that the underpinning university facility specific solution NMR equipment should be 400/500 MHz, with significant cryoprobe availability at 500 MHz and above. It had also been noted then that access to 500-600 MHz solution state NMR was regarded as essential for competitive research within Chemistry Departments, as a lack of on-site access can significantly impact on productivity and potential for world-leading status of such research. In the current survey there was also a good number that saw upgrading of core 400 MHz facilities as the responsibility of the university. The discussion of the boundary (although it is undoubtedly blurred) where this university responsibility lies for the life sciences, given the shifts in the distributions between life and physical sciences (Fig. 4) suggests this should be at higher field. However, given the significantly increased costs, one could argue that this differential expectation would be unfair. It is clear that a balance has to be struck between upgrading, complete replacement and increase in the overall capacity. There is an indication that approaching 20 new systems (as opposed to upgrades) in the next five years will be sought, i.e. an expansion of capacity. The point noted in 2012 about improving access to 600 MHz is now extended to particularly 700 MHz solution facilities, as well as to a lesser extent 800 MHz. In keeping with the sustainability discussion most of the new 600 and 700 MHz instruments proposed were seen as direct replacements for existing 500 MHz spectrometers. The trend noted in 2012 on solid state NMR migrating from a specialist technique to a role increasingly more akin to some core departmental/faculty is also seen here.

Instrument Distribution by Organisation

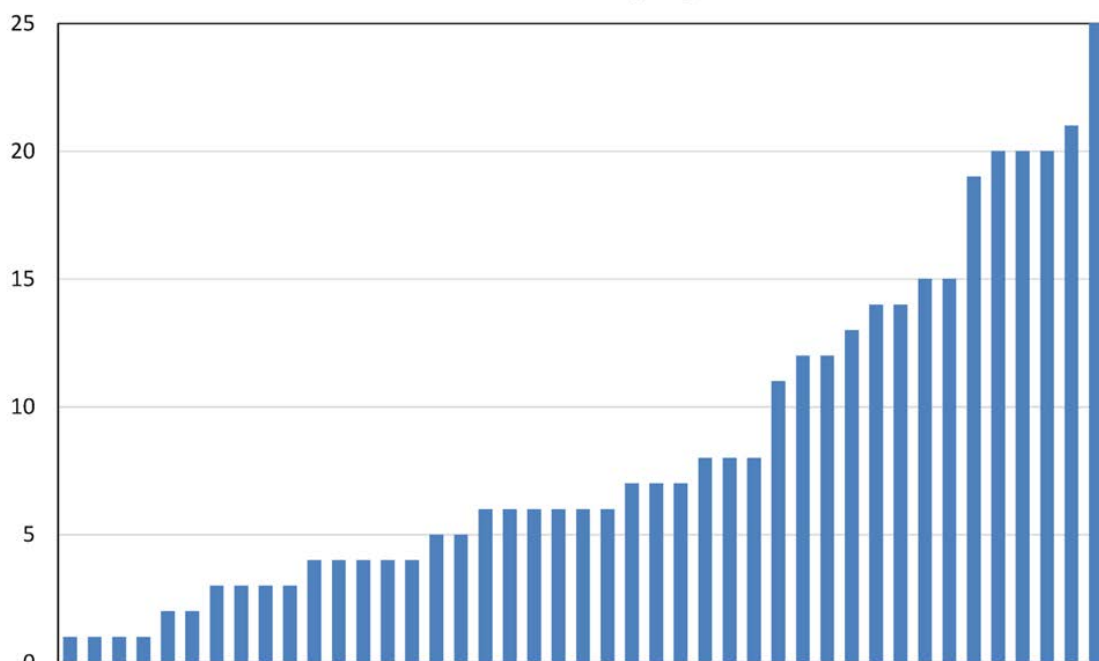


Figure 9. Distribution of instruments in each institution across the UK

The scale of the equipment sustainability challenge can be seen by the distribution diagram for different institutions (Fig. 9), where it can be observed that five universities have 20 or more NMR instruments in their portfolio. The survey did not explore if equipment was used as a specialist research facility. If it can be charged across a broad portfolio of activities it can be

designated as either a Major (MRF) or Small Research Facility (SRF). The number of NMR facilities that are charged as MRFs is still very small, although quite a few more are charged as SRFs. The survey did look at the different internal mechanisms as to whether they charge directly or operate as free at the point of access. The latter of course means that the cost is passed on elsewhere in the system. The replies indicated 56% had a direct charging mechanism. There is no doubt that in looking at the sustainability the instruments with high usage fall into two categories. Those supporting a specialist NMR team that do their measurements directly and those run as a service. Such services can be effective when they have the specialist dedicated support and those that are open access running with automatic sample changers.

It was interesting to note for open access cases how important the state and efficiency of the sample changer is in the overall effectiveness and efficiency of such instruments. There is still work needed to understand how under full economic costing (FEC) a sustainable situation can be achieved and whether or not any modification of the model is required. Tangled up with the sustainability question is the use of such infrastructure by PhD students. It is well known that PhD students funded from Doctoral Training Accounts receive less funding than in Centres for Doctoral Training, and as noted above some CDTs include an equipment element. It is also increasingly true that universities themselves are big funders of PhD students, when much of this additional cost is *not* built into that funding. There is still much work to do to provide a better understanding as to how the various funding streams (e.g. indirect and estates research costs, QR-related elements, direct project funds, etc.) come together to fund work on equipment. As noted earlier, Chemistry Departments are big users of NMR and often have departmental facilities. The different approaches used by universities to this is interesting, with one example showing in some respects a fairly standard facility approach, but with some nationally leading aspects to it in being split between departmental users (59%), other institutional users (27%), regional academics (7%), regional industrial users (5%) and national academic users (2%). It would be very interesting to know how variable the split is between different universities and different groups, and how much of an effect this has on instrument sustainability. Referring to the usage figures above there is apparently significant unused NMR instrument capacity in the UK, but unfortunately largely not at magnetic fields where there is the highest demand.

7. Equipment Sharing, Efficiency of Use and Strategy Development for NMR Infrastructure

Another area where an explicit question was asked was over equipment sharing. Several submissions recognised that for routine instruments local access on a day-to-day basis is essential. Hence genuine equipment sharing is only likely to be considered when the equipment is regarded as beyond the reach of a single institution, but there was an acknowledgement that this did depend on the institutional perspective. Some of the groupings mentioned in the previous report have strengthened such as GW4 (Bath, Bristol, Cardiff, Exeter), N8 (Durham, Lancaster, Leeds, Liverpool, Manchester, Newcastle, Sheffield, York), SES (Cambridge, Imperial, Oxford, Southampton, UCL), with M5 (Birmingham, Leicester, Loughborough, Nottingham, Warwick – now adding Aston to become Midlands Innovation), with a new all Scottish consortium of universities forming the ScotChem grouping. It was also interesting to see that linked to several of these consortia were further relationships to either smaller or less research-intensive institutions to provide on a more formal footing access to key infrastructure that it would be unlikely less research-intensive HEIs could individually provide. There was explicit mention of the support for smaller research institutions in several submissions.

In the 2012 EPSRC-funded report 'Sharing for Excellence and Growth'¹² it was clearly noted there needed to be a balance as to what was locally available and that which could really be shared. Although sharing of highly specialised equipment is always possible, an estimate was made that there was likely to be a financial threshold in the window £200-500k where such sharing becomes more likely, although this value is probably now higher. For these groupings, or even wider groups, coordinated procurement certainly enables more efficient use of resources. This is often greatly in the interests of HEIs, provided that any geographically distributed processes can ensure that individual researchers have their particular specification needs catered for in detail. Such processes do not work well with very short procurement times related to requirements of rapidly needing to spend specific funding streams, which can only reduce the value for money it is possible to achieve. There still remains the question as to whether the Research Councils via UK SBS should play a more active role in procurement, and with the formation of UKRI this should be revisited. To encourage sharing, ensuring that full costs of sharing (e.g. coordinating access) are met from funders was suggested, at least initially.

There was also clear further development of, and use being made of equipment databases. There were more examples of developed databases at individual universities. This then feeds through to good examples of regional databases (e.g. N8, Midlands Innovation (MI)) and hence into national databases. In the case of MI there is an overarching research efficiency committee where the use of shared facilities is considered and the shared database is used to ensure that potential duplication and overlaps with existing resource are considered before any application. This information feeds through to submissions on equipment sharing and indicated the extent to which regional groupings are shaping the thinking and adding to the efficiency of procuring high-end equipment i.e. when a specialist high value facility is required that can be readily shared there are now much better developed links allowing more straightforward discussions of these situations and there was evidence that such processes are taking place. The N8 equipment sharing database (<http://www.n8equipment.org.uk/>) allows researchers to locate and request access to NMR equipment across the N8 Group of universities. Research Council proposals from the N8 for capital equipment are vetted against this database to avoid duplication of resource. The group has agreed an equipment sharing protocol, as part of the Core Capability in Chemistry initiative, that also ensures cross-institution access in the event of spectrometer breakdown. In addition the N8 shares training courses for biomolecular NMR, and N8 NMR facility support staff share technical expertise as appropriate. Facility managers of the high field NMR installations across the N8 pool expertise and knowledge via the Reson8 project.

In Scotland equipment sharing has progressed via the establishment of the Scottish NMR User Group (SNUG), which although having a broad remit across the range of areas NMR impacts has a particularly strong interface with ScotChem. It was also clear that in many individual institution's processes for considering strategic investments in equipment have become more sophisticated. There is evidence that smaller institutions (with consequently limited equipment resource) can benefit from interfacing with research-intensive regional groupings, through some access to a wider range of instruments and providing some insurance against single point of failure. Although regional networks are strengthening there was a perception that by comparison with the main European competitors (e.g. France, the Netherlands, Germany) there has been less of a nationally-led systematic development of nationwide networks of higher field instruments (≥ 700 MHz) for both solution and solid state NMR.

The returns argued quite strongly that there needs to be a careful balance between local availability, when local demand can sustain an instrument, especially when transport of samples to

¹² N8 Report 'Sharing Excellence for Growth' July 2012, www.n8research.org.uk

a central facility can be problematic or that significant specialist peripheral infrastructure is necessary for handling samples. There was a sense that classification of instruments into three categories might be helpful:

- (1) regular and routine access with high throughput;
- (2) specialist capability where local expertise is necessary, e.g. difficult sample handling, instrument/technique development; and
- (3) where leading-edge capability was necessary for short, but concentrated periods of time.

Cases (1) and (2) are best served by local needs, whereas (3) is best served by a regional or national facility. This thinking maps somewhat onto the three-tier classification of infrastructure that has been advanced for NMR equipment as in the 2012 and 2013 Roadmaps^{5,8}, by the life sciences and physical sciences communities. Given the relatively limited geographical scale of the UK, with the UK's distributed NMR capability the question was raised as to whether a nationally coordinated and centralised system for cataloguing both the NMR capability, as well as for collecting and shipping samples might bring significant system efficiencies and might be worth exploring. It is clear that the NMR community has bought into the use of national facilities, which in the life sciences are provided in a more distributed sense and for the physical sciences in solid state NMR (with some life sciences use) through the mid-range 850 MHz facility at Warwick. The 850 MHz facility was cited as a model for how the provision of such facilities should be run having supported researchers from 23 different UK universities since 2010. The advantage of concentrating resource at the very highest magnetic fields to ensure equipment can be maintained at the state of the art, together with very high quality experimental officer/research support is seen as vital. In a post-Brexit world one consideration is whether the considerable number of NMR groups in the UK who are involved in European networks will continue to benefit from equipment sharing with Europe which provides the UK with extended access to capability.

8. Implications for Leading-Edge Investments in NMR Infrastructure

This survey has reinforced the message that NMR is a key technique in life and physical sciences. The UK has a lot of capacity, having been modernised in the last few years, but there is still a very significant legacy requiring investment which challenges the whole community (Research Councils, university and institute senior administrations and NMR researchers) to think about how it can be brought up to date and sustained in the future. Surveying life and physical sciences at the same time a more complete overview of the technique has been obtained. It was noted in the 2012 report that for solution NMR in the physical sciences there are surprisingly few instruments at > 700 MHz. In the life sciences, however, where high fields are perhaps even more critical for both sensitivity and resolution considerations there is indeed a much higher proportion of instruments at ≥ 700 MHz. The previous reports indicated that a key discussion point for the community in the near to medium term (up to 2020) was the provision in the UK of an ultrahigh field NMR (> 1 GHz) instrument which fed through to the NMR roadmaps. This was driven by the fact that several important experiments only really become feasible at these higher field strengths. Four years further on it is known that orders for around 10 such instruments have been placed from France, Germany, Italy, Switzerland and the Netherlands. The Netherlands included ultrahigh field NMR as a priority of their large facilities roadmap released in May 2012. It is not clear whether the UK will have any access to these European facilities in the future. Looking at future equipment needs however, the very significant cost of a single > 1 GHz instrument needs to be *carefully rationalised against the potential for more widespread provision of instruments* just below this level given the capacity issues. Consideration should also include the potential for

ensuring that all ≥ 800 MHz systems are in a leading-edge state. This is perhaps of particular relevance to the life sciences community. In the last 5-10 years great progress has been made in the use of solid-state NMR for structural studies of biological macromolecules, but hardly any of UK's 800 MHz instruments are equipped with suitable hardware.

More broadly to make the equipment base as efficient and leading-edge as possible, and more sustainable, a discussion between the Research Councils and the NMR community around 'upgrades', but on basis of discarding redundant or poorly used capacity could be carried out – perhaps an 'NMR scrapping' scheme. This could be incentivised through upgrading instruments with better, more efficient cryoprobes for better sensitivity and for the more wide spread use of modern open access instruments with automatic sample changers. As part of the sustainability discussions the Research Councils in partnership with probably regional groupings of universities should ensure that the Tier 1 and 2 instruments that are run as facilities should have a planned maintenance and upgrade schedule to keep this vital national capability as state of the art. There could be an agreed future funding profile, provided that certain key performance indicators were being met, forming the funders' contribution to a more sustainable future. Dynamic Nuclear Polarisation (DNP) was just making a more widespread impact in 2012. This survey showed that there are now 10 DNP systems, most configured for solution type work and three with broader capacity, including solid state MAS capability. The EPSRC responded to a recommendation in the 2012/2013 reports which advocated developing a DNP facility based on a commercial 9.4 or 14.1 T instrument. A 14.1 T national facility is now operational at the University of Nottingham. One of the questions for the next strategic investment is whether there should perhaps be an 800 MHz instrument with the capability of performing DNP. An eye should also be kept on DNP instrument development around pulsed, tuneable microwave sources that would potentially increase DNP spectrometer flexibility. In looking at the potential leading-edge high field investments it should be stressed this should not be seen to underplay the importance of other leading-edge NMR work that the UK undertakes, has a world class reputation in, and which also requires investment – for example, HRMAS, low field imaging and diffusion measurements, ultrahigh and ultralow temperature measurements, hyperpolarisation schemes via other routes, etc.

9. Key Observations and Recommendations

- 9.1 There is a continuing recognition of the direct connection between the provision of world-leading NMR equipment and the maintenance of the UK's position in producing world class research in both the life and physical sciences, both in technique development and in the science underpinned by access to NMR.
- 9.2 Compared to 2012 the portfolio of NMR instrumentation is much newer, with the stock less than 5 years old rising from 31% to 42% and that less than 10 years rising from 52% to 65%. However much still needs to be done to further improve this situation and ensure true sustainability.
- 9.3 There is still a legacy issue with older, unreliable equipment remaining in the field and a more systematic upgrading/retirement of such equipment needs to be developed. Schemes for accelerating such activity should be considered. Upgrading/retirement of instrumentation should be intrinsically coupled with national replenishment schemes so that the full research capability of the institutions *and* the UK NMR community is enhanced, but with improved sustainability.
- 9.4 Utilisation shows a mixed picture, with a significant fraction having very high utilisation rates, but too much that is used at far too a low capacity. However this is often due to

a combination of the lack of funding to upgrade equipment and a reluctance to discard old equipment when replacement equipment is funded (see 9.3).

- 9.5 Comprehensive searchable databases and groupings of universities sharing strategies for the joint provision of leading-edge equipment have developed more strongly in the last four years. However, the visibility and accessibility of information about NMR equipment available is very variable between different databases and university websites.
- 9.6 Given the highly competitive nature of the UK HE funding system there are fewer 'larger scale facilities' at the disposal of the system, in contrast to other more centrally planned EU countries (e.g. France, Germany, Scandinavia, etc.). However access can often be difficult and instrument time allocations limited in centralised networks, especially those with more limited infrastructure, so that proper programmatic research is often not readily possible. A national debate that looks more holistically at a network of Tier1/2 NMR infrastructure and thus defines the way business/access is conducted in the future would be very useful.
- 9.7 There has been development of a clear partnership, if somewhat implicitly, between the funding bodies and HEIs in their respective responsibilities for funding of NMR equipment.
- 9.8 Real progress has been made in meeting some of the needs identified in the 2013 roadmap for NMR in the physical sciences, although there is still more to do.
- 9.9 The UK still has a deficit in the availability to both life and physical sciences of very high magnetic field instruments in comparison with our leading overseas competitors. There is an opportunity with the injection of capital available to both make some direct investments to move the situation forward, but also to catalyse a discussion over the operation of facilities in the system and their sustainability.

10. Conclusions

An extensive survey and collection of data concerning the NMR infrastructure underpinning research in UK Higher Education and closely related institutes has been carried out. This is believed to be the most comprehensive and complete survey of any extensively used research technique in any large scale research system to date anywhere in the world. The survey has provided real insight into the current portfolio, the state and extent to usage of that portfolio and the likely challenges for funding of this over the next few years. Since 2012 demonstrable progress in refreshing the portfolio has been made, but a significant legacy issue remains. Many of the priorities identified in the previous reports and roadmaps have been implemented and good progress has been made, with for example a small, but definite increase in the availability of ≥ 700 MHz instrumentation and the creation of an open access 600 MHz national DNP facility.

Databases of equipment, regional consortia and equipment sharing have further developed. These have allowed more joined up and systematic approaches to capital infrastructure provision and procurement between groups of institutions, although more can be done here. It should also be noted that such an approach does not preclude local provision where this is the most sensible and efficient way to do things. It is clear that the Research Councils, HEIs and the Wellcome Trust are the major funders of NMR infrastructure, and developing a forum to discuss and clarify the responsibilities and partnership over funding such provision would be helpful. This survey did not really reveal how well FEC recovery is working and making facilities sustainable, but the previous life sciences survey and report made it clear that many NMR facilities struggle to recover their costs and more thought needs to be given to how to make them genuinely sustainable. In the context of mid-range experimental equipment more generally the

outcomes of a recently commissioned piece of work by the Financial Sustainability Strategy Group should provide some more commentary on this.

This report also provides the backdrop for consultation over the BEIS investment of £22M in ultrahigh/high field NMR infrastructure. The work done leading up to 2012/13 and subsequently by the both the life sciences and physical sciences communities has pointed to this being a > 1 GHz national facility plus other (2-3) > 800 MHz instruments for life and physical sciences, to ensure that both solution state and solid state capability is enhanced. Whilst it is clear that UK needs access to state of the art equipment, > 1 GHz instruments are very expensive and one should examine whether this is still the optimum strategy at this point in time? Many of the existing \geq 800 MHz instruments are certainly no longer currently latest generation, and the UK particularly lags in the provision of such instruments for solid-state studies of biological macromolecules at the interface of Chemistry and Biology, as well as for core materials research. Research groups need straightforward access to both solution and solid-state capabilities at these field strengths. It is clear that mixed use (solution and solid) while entirely possible is not currently a common mode of operation, and the extent to which this has become more straightforward with current instrumentation needs to be understood. These considerations argue that the upgrade and refurbishment of existing equipment in these categories should also be a priority component of the investment. In the DNP space there needs to be consideration of the facilities for > 600 MHz DNP. A detailed discussion concerning the optimum use of the £22M needs to be carried out with the community.

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