NMR Spectroscopy is Quantitative. No Adjectives Required

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Why is that more than half a century has passed since the commercialization of NMR spectrometers, and this still needs to be stated? Well, perhaps the field is a victim of its own successes. The emphasis of NMR research and development has focused on deciphering intricate structural information – an important function, no question. This has been supported by the increased magnetic field strength (up to 1.3 GHz at the time of this writing!), enhanced sensitivity (cryoprobes, hyperpolarization) and sophisticated pulse sequences (ultrafast, anisotropy, nD) that help eke out fundamental structural information for increasingly complex molecules at ever decreasing concentrations. These efforts have expanded the boundaries of NMR spectroscopy in an undoubtedly elegant manner – ***for research***. While certainly solidifying the reputation of NMR as being the most information-rich spectroscopic technique, it has also inadvertently hindered its wider adoption by the end user, by application, and by sector. It just may be that expanding the structural elucidation toolbox has come at the expense of the other unique aspect of NMR – its inherently quantitative nature. In fact, when this facet is discussed, it is dubbed 'qNMR' as though it is not intrinsic to the technique itself.

So, what are the obstacles hindering the widespread adoption of 'qNMR'? As we see it, the answer is three-fold: (i) accessibility, (ii) the lack of NMR-based quality control methods, and (iii) public perception.

The first two obstacles have either already been addressed or are currently being addressed. The reemergence of permanent magnet-based NMR spectrometers in the early 2010s was aimed at providing the underserved users with easier access to this powerful technique and to help proliferate the incorporation of NMR spectroscopy into new applications and sectors. With no need for cryogens or weekly maintenance, the so-called 'benchtop' NMR is equipped with a modern interface focused on supporting automation, aligning with GxP data integrity requirements, and reducing expertise needed to acquire and process NMR data. By providing an accessible and affordable platform, the benchtop NMR opens the doors to expanding the use of routine NMR spectroscopy in quality control and at process lines. However, these 'industry-grade' NMR methods must still be developed, validated, and (re)certified for both emerging and established materials and/or products. Thought leaders have begun this work and examples, with corresponding value propositions, have been circulating within the community as internal institutional protocols (with a published example provided in reference[1]) as well as guidance issued by regulatory body assays.[2,3] While internal methods can be adopted more rapidly at the institutional level, it is a long process for new consensus based methods to be verified and/or (re)validated by the appropriate standards development organization or regulatory bodies. While select assays have been successfully updated to feature lower magnetic field strength requirements, such as the modernization of the *Hydroxypropyl Betadex* monograph, in which the magnetic field strength requirement was lowered from 6 Tesla to 1.4 Tesla (^{1}H operating frequency reduced from 250 MHz to 60 MHz)[4], the pathways to method modernization remain frequently convoluted, due to regulatory uncertainty, analytical non-equivalence and even the resulting end-user hesitation.

This final hurdle to qNMR adoption – public perception – remains the hardest to address. It requires a mindset switch not only from within the greater analytical community, but also amongst many NMR spectroscopists. When is the last time you attended an NMR conference and were presented a basic, well-acquired 1D NMR experiment simply aimed at quantifying an important analyte metric? Possibly never. This may be considered borderline banal. The elegance of structural elucidation methods and high-end advancements have left many with the same mentality. Community discussion panels that perhaps should focus on democratizing benchtop NMR and identifying the barriers hindering its widespread adoption, e.g.: "how do we develop a suitable NMR-based assay?", "what degree of (re)validation is required?", "what strategy can replace mainstay analytical techniques?", or "what is the minimum viable tool required?" often turn to "what is the highest magnetic field strength possible?", "how many nuclei can I observe?", or "can I do triple resonance experiments?" While this mindset has al-

lowed qualitative NMR to flourish, it may be time to refactor our thinking to now foster the propagation of qNMR.

While modifiers of NMR – q, benchtop, for example – are certainly helpful for differentiation and even branding, NMR spectroscopists need to unify on the fact that they are just not necessary scientifically. Why must we say qNMR? Why must we call it benchtop NMR? All these adjectives unintentionally provide the misnomer that these are distinct or unique, when they simply are not. How do we turn NMR spectroscopy into NMR spectrometry? To proliferate NMR and facilitate widespread industrial adoption we need the community to rally behind NMR – ***the technique***. We must define clear standards, guidelines and best practices to develop and validate assays that are specific to NMR as an analytical method. We must then educate and champion NMR methods until the inherent quantitative properties of NMR become synonymous with its name, unified under the term NMR. No additional qualification required.

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