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# Quantum- Chemical Approach to Nuclear Magnetic Resonance of Paramagnetic Systems

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## Abstract

Nuclear magnetic resonance (NMR) is a central method for investigating the microscopic structure and dynamics of molecules and materials, with numerous applications in science, technology, and medicine. Computational modelling is indispensable in NMR research due to the indirect nature of NMR information and the rich physical phenomenology behind its observables. While NMR is conventionally used to study diamagnetic systems, paramagnetic NMR (pNMR) of electronically open-shell systems is rapidly gaining importance. This inaugural article concerns the methodology and application of computational molecular science to the observables pNMR, including current challenges and outlook for the future.

## 1. Introduction

Nuclear magnetic resonance (in short, NMR) is a spectroscopic method of investigating matter in the form of gas, liquid or solid, in which information is drawn from the substance by observing the quantum-mechanical transitions between the states of atomic nuclei (Levitt, 2008). For NMR, the relevant nuclei have a magnetic dipole moment and are characterised by a spin quantum number  $I \geq \frac{1}{2}$ . The states in question correspond to different orientations of such nuclei with respect to the typically quite large magnetic field applied onto the sample by a device called an NMR spectrometer. The different nuclear orientations correspond to different interaction energies of the magnetic dipoles with the field. The orientations can be changed by applying magnetic field pulses on the sample, and the nuclei emit electromagnetic radiation when the spin system subsequently returns to the thermal equilibrium situation in that magnetic field. The excitation pulses are created, and the emitted radiation is detected using radio techniques, at frequencies up to 1 GHz for the most common NMR nucleus,  $^1\text{H}$  (proton), corresponding to the magnetic field of 23.5 Tesla. The distribution of the emitted energy vs. frequency constitutes the NMR spectrum, which is the primary experimental observable containing bountiful information about the microscopic atomic and electronic structure of the sample. The speeds by which the excited spin system returns to the thermal equilibrium, or the relaxation times, are commonly observed and convey details of the dynamics of the substance at the atomic and molecular level.

Since its discovery in the 1940s (Purcell, Torrey & Pound, 1946; Bloch, Hansen & Packard, 1946) NMR has been developed into a primary chemical and materials spectroscopy, with its perhaps best-known application in magnetic resonance imaging of various opaque targets, such as biological tissue (Lauterbur, 1973; Mansfield & Grannell, 1973). The positions and structure of the NMR spectral lines are determined by the electronic structure of the material, *e.g.*, the resonance positions, chemical shifts, of the  $^1\text{H}$  nucleus in different chemical environments are different depending on the atomic composition of the molecule, temperature, motional state of the system, and the intermolecular interactions experienced by the molecule, thereby conveying information of such factors. Computational and theoretical studies are carried out hand-in-hand with experiments in practically all contemporary NMR research. The fact that NMR provides its rich information content indirectly, convoluted into the spectral parameters that are influenced simultaneously by a multitude of competing physical factors, renders NMR theory and computation a fascinating application area of computational molecular science.

The most common target for NMR experiments are electronically closed-shell diamagnetic molecules and materials, where the electrons are arranged in spin-up and spin-down pairs, hence pairwise cancelling the magnetic moments of the electrons, which individually are very large. Also characteristic of the majority of NMR studies is that the magnetic interactions are of sufficiently small magnitude to maintain the investigated systems intact in their ground

electronic state, unlike *e.g.*, the core-level electronic spectroscopies where electronic transitions, even ionisation, are essential, and which cause permanent changes to the investigated substance.

NMR is, however, being increasingly used to investigate also open-shell, paramagnetic molecules and materials, and this subfield is usually called paramagnetic NMR, pNMR (Pell, Pintacuda & Gray, 2019). In such systems, the primary interaction dominating the physics is no longer the interaction between the magnetic field of the NMR spectrometer and the magnetic moments of the NMR nuclei, but the role of the latter is adopted by the moments of one or several unpaired electrons of the system. Indeed, the magnetic moment of an unpaired electron is 658 times larger in magnitude than the largest nuclear moment in a stable nucleus,  $^1\text{H}$ . The NMR nuclei, then, first and foremost interact with the unpaired

electrons and only secondarily with the external field, which causes dramatic changes in the experimental spectra. First, the chemical shift ranges of conventional NMR nuclei are greatly enhanced, meaning that  $^1\text{H}$  signals can appear in the range of hundreds of “part-per-million” (ppm) units, instead of a couple of dozens of ppm seen in conventional diamagnetic systems. The corresponding “magnifying glass” effect for the  $^{13}\text{C}$  nuclei is in thousands of ppm instead of a few hundred. At the same time, NMR relaxation is enhanced by the fluctuating interactions with the unpaired electrons, causing spectral line broadening and even completely disappearing signals from the “blind zone”, the part of the molecule that is very close to the region of the molecule where the unpaired electron density is situated – typically close to the metal ions contained in the system (Figure 1).

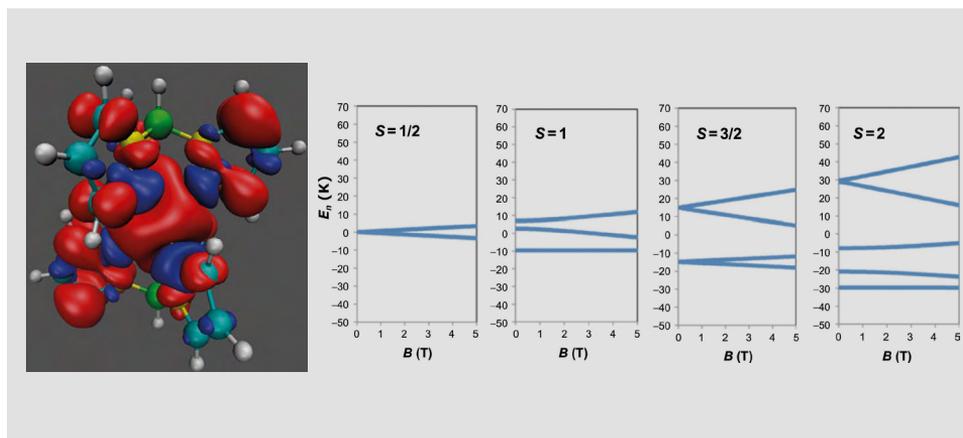


Figure 1. (Left) Calculated unpaired spin density in vanadium pyrazolylborate cation (2 unpaired electrons), with positive (red) and negative (blue) isosurfaces drawn at  $\pm 0.0002$  atomic units (adopted from Pyykkönen, Köhler & Vaara, 2020). (Right) Energy levels (in units of K) of the states belonging to the ground multiplet as functions of the magnetic-field strength (in T) for various spin states. An isotropic  $g$ -value of 2.0023, zero-field splitting parameters  $D = 10 \text{ cm}^{-1}$  and  $E = 3 \text{ cm}^{-1}$  have been assumed (adopted from Vaara, 2013).

From the point of view of theory, an open-shell molecule is no longer characterized by a pure quantum ground state, but a ground *multiplet* consisting of  $2S + 1$  states, where the spin quantum number  $S$  tells the number of unpaired electrons,  $S = 1/2$  (a doublet system) corresponding to a single electron,  $S = 1$  (a triplet) for two,  $S = 3/2$  (a quartet) for three etc. (Figure 1). The states of the ground multiplet are thermally occupied, they are *sc.* Zeeman-split due to the interaction with the external field, and experience, in case there is more than one unpaired electron, also the so-called zero-field splitting (ZFS) interaction primarily on account of the spin-orbit interaction (Harriman, 1978). This situation renders the theory and computation of pNMR parameters, in particular the chemical shift, a much more challenging endeavour than in the conventional closed-shell case. Indeed, first principles-based assignments of spectral lines, detailed analysis of the underlying shift mechanisms, and quantitative predictions of the shift values have started to appear only during the last decade or so for paramagnetic systems.

## 2. Kurland-McGarvey theory of paramagnetic shielding

This article aims at giving an overview of the field of theory and computation of pNMR parameters, in particular its central observable, the nuclear shielding tensor  $\sigma$ . This object is a  $3 \times 3$  matrix that determines how the electron cloud of the

molecule alters the magnitude and direction of the magnetic field experienced by an NMR nucleus, as compared to the externally applied field in an NMR spectrometer. The above-mentioned chemical shift, the position and, in some cases, shape of the spectral line of the investigated nucleus, are determined by  $\sigma$  undergoing averaging over the microscopic molecular dynamics in a given physico-chemical situation, and this provides a fingerprint of the structure and motion. In the simplest case of a liquid solution, an isotropic rotational average of  $\sigma$ ,  $\sigma = (\sigma_{xx} + \sigma_{yy} + \sigma_{zz}) / 3$ , *i.e.*, calculated as the sum of the diagonal elements of the tensor, is left to determine the line positions.

The currently prevailing theoretical formulation of the pNMR shielding tensor is mostly due to the three-step work of Kurland and McGarvey (1970). They started by (1) equating the term appearing in the model NMR spin Hamiltonian that involves  $\sigma$ , with the statistical mechanical expression for the energy arising from the full electronic Hamiltonian, which features both the nuclear magnetic moment and the external magnetic field. (2) They expanded the electronic density matrix in the latter up to linear order in the field and adopted the Hamiltonian terms that are linearly dependent on the nuclear moment, and (3) parameterised the resulting interactions in terms of another model Hamiltonian, that of electron paramagnetic resonance (EPR). This process leads to the expression shown in Figure 2, involving several separately determined molecular property tensors: the EPR tensors  $\mathbf{g}$  and  $\mathbf{A}$ , as well as the orbital NMR shielding tensor  $\sigma^{\text{orb}}$ , which is formally similar to conventional NMR shielding.

Practical shielding expression: 
$$\sigma_{K,\epsilon\tau} = \sigma_{K,\epsilon\tau}^{\text{orb}} - \frac{\mu_B}{\gamma_K \hbar kT} \sum_{ab} g_{\epsilon a} \langle S_a S_b \rangle A_{K,b\tau}$$

- Thermal occupations
- Magnetic couplings

$$\langle S_a S_b \rangle = \frac{\sum_{nm} Q_{nm} \langle n | S_a | m \rangle \langle m | S_b | n \rangle}{\sum_n \exp(-E_n/kT)}$$

Figure 2. (Top) Kurland-McGarvey expression for the Cartesian components  $\sigma_{\epsilon\tau}$  of the pNMR shielding tensor. In a diamagnetic system, only the term  $\sigma^{\text{orb}}$  arising from the orbital motion of the electrons would be present. In the presence of unpaired electrons, the second, explicitly temperature ( $T$ )-dependent term appears, in which the electronic  $g$ -tensor ( $\mathbf{g}$ ) parametrises the interaction of the unpaired electrons with the magnetic field and the hyperfine coupling tensor  $\mathbf{A}$  that of the unpaired electrons with the nuclear magnetic moment. (Bottom) The dyadic of the effective electron spin operator  $\mathbf{S}$  that couples the states  $|m\rangle, |n\rangle$  of the ground multiplet obtained in the absence of the magnetic field and nuclear spin interactions (Vaara, Rouf & Mareš, 2015).

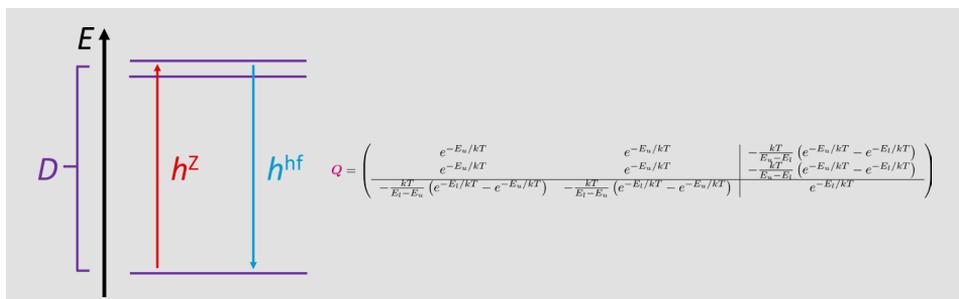


Figure 3. (Left) Structure of the ground multiplet of a cylindrically symmetric  $S = 1$  paramagnetic system with positive  $D$ -parameter of zero-field splitting. The Zeeman ( $h^2$ ) and hyperfine ( $h^{\text{hf}}$ ) interactions couple the ground state (energy  $E_g$ ) to the doubly degenerate upper states ( $E_u$ ) of the ground multiplet. (Right) Matrix  $Q$  appearing in the dyadic  $\langle \mathbf{S}\mathbf{S} \rangle$  of the shielding formula, indicating thermal populations of the lower and upper states, as well as the couplings between them.

One important aspect in the shielding expression deserves particular attention: it contains the dyadic  $\langle \mathbf{S}\mathbf{S} \rangle$  of the effective electron spin operators, stemming from the use of the EPR Hamiltonian in formulating the theory. In the simple case of a single unpaired electron, characteristic of organic radicals or, *e.g.*, copper complexes with  $d^9$  electron configuration (with spin quantum number  $S = 1/2$ , see the energy levels in Figure 1), this dyadic takes on a particularly simple, diagonal form,  $S$

$(S + 1) \mathbf{1} / 3$ . In contrast, for  $S \geq 1$  cases, *i.e.*, when there are more than one unpaired electron and the energy levels of the ground multiplet are affected by ZFS (Figure 1),  $\langle \mathbf{S}\mathbf{S} \rangle$  is a symmetric matrix, the diagonal blocks of which contain the Boltzmann occupation numbers of the states, whereas the off-diagonal blocks represent magnetic couplings between the states (Figure 3).

$$\begin{aligned}
 \mathbf{g} &= \left( \underbrace{g_e}_{\alpha^0} + \underbrace{\Delta g_{\text{iso}}}_{\alpha^2} \right) \mathbf{1} + \underbrace{\Delta \tilde{\mathbf{g}}}_{\alpha^2} \\
 \mathbf{A} &= \left( \underbrace{A_{\text{con}}}_{\alpha^2} + \underbrace{A_{\text{PC}}}_{\alpha^4} \right) \mathbf{1} + \underbrace{\mathbf{A}_{\text{dip}}}_{\alpha^2} + \underbrace{\mathbf{A}_{\text{dip},2}}_{\alpha^4} + \underbrace{\mathbf{A}_{\text{as}}}_{\alpha^4}
 \end{aligned}$$

Figure 4. Term decomposition of the  $g$ - and hyperfine ( $\mathbf{A}$ ) tensors according to their order in the fine structure constant  $\alpha$ .  $\mathbf{1}$  is a 3 x 3 unit matrix, the isotropic free-electron factor  $g_e = 2.002319\dots$  arises from Dirac theory of free electron with quantum electrodynamical corrections, and  $\Delta g_{\text{iso}}$  and  $\Delta \tilde{\mathbf{g}}$  are isotropic and anisotropic, mainly spin-orbit interaction-induced corrections of the Zeeman interaction within matter, respectively.  $A_{\text{con}}$  and  $\mathbf{A}_{\text{dip}}$  are the leading isotropic and anisotropic hyperfine terms arising from the nonrelativistic Fermi contact and spin-dipole interactions of the unpaired electron(s) with the magnetic nucleus, respectively.  $A_{\text{PC}}$ ,  $\mathbf{A}_{\text{dip},2}$  and  $\mathbf{A}_{\text{as}}$  are terms of different symmetries arising from special relativistic corrections of the contact and dipolar hyperfine interactions, as well as the orbital contribution.

### 3. Contemporary implementation

The above-sketched methodology from 1970 was implemented in a series of papers during the last 15 years (*e.g.*, Soncini & Van den Heuvel, 2013; Martin & Autschbach, 2015; Vaara, Rouf & Mareš, 2015) in a modern quantum-chemical framework that allows large-scale computations on experimentally relevant systems. Before showing an example of the achievable spectral assignment and prediction potential of the approach, the possibility of breaking down the pNMR shielding and chemical shift into *physically* distinct mechanisms is in place. The  $g$ - and hyperfine coupling tensors can be expanded into terms with different physical background as illustrated in Figure 4.

When placed in the theoretical shielding expression, the decompositions of  $\mathbf{g}$  and  $\mathbf{A}$  give rise to altogether 9 distinct terms up to  $\alpha^4$  (one routinely goes beyond this by using so-called fully relativistic calculations of these molecular property tensors), which lend themselves to analysis of the calculated shieldings (Pennanen & Vaara, 2008). Figure 5 shows such a break-down of the mechanisms of the shielding tensor for an example  $^1\text{H}$  pNMR signal in a cobalt(II) complex. The obtained agreement with experiment allows reliable assignment of the experimental signals, and the term decomposition makes it possible to analyse the physical mechanisms in detail.

While the basic theory of Kurland and McGarvey was well known in the field for decades, only lately have both the development of quantum-chemical methods and the computational capacity allowed an efficient application of the theory for

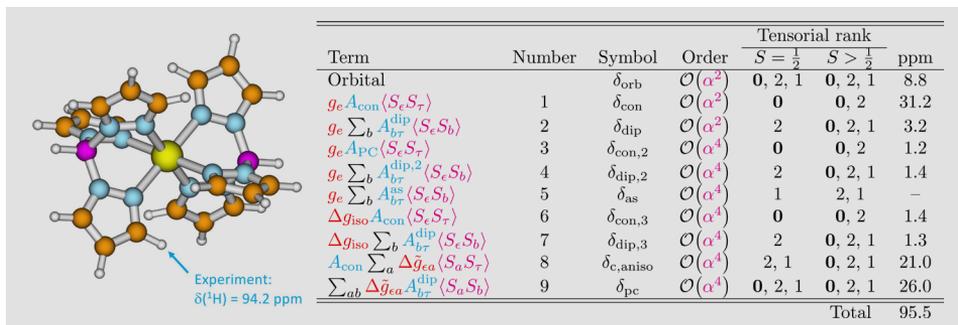


Figure 5. Example analysis of a measured (Dlugopolska, Ruman, Danilczuk & Pogocki, 2008)  $^1\text{H}$  pNMR chemical shift into physical mechanisms. (Left) Co(II) pyrazolyborate complex and the selected proton with its experimental chemical shift. (Right) Table of hyperfine shielding constant contributions resulting from the break-down of the  $g$ - and  $\mathbf{A}$  tensors as in Figure 4, the resulting ranks of tensorial contributions in the case of a single ( $S = \frac{1}{2}$ ) or several ( $S > \frac{1}{2}$ ) unpaired electrons, such as in the present  $S = 3/2$  case. Ranks 0, 1, and 2 correspond to isotropic shielding constant, anisotropic symmetric, and anisotropic antisymmetric tensorial contributions, respectively. In blue, the corresponding calculated chemical shift contributions as well as the total theoretical chemical shift in relation to tetramethylsilane (TMS) reference compound, are presented (Rouf, Mareš & Vaara, 2015).

molecular and materials systems of experimentally interesting size. Figure 6 presents an example workflow of such computations, which have become routine for calculations of predictive value involving models exceeding the size of 100 atoms.

## 4. Point-dipole approximation

Despite the performance of the contemporary computational *modus operandi* of pNMR shift calculations outlined above, many interesting paramagnetic materials and biological systems appear to remain intractably large. That the spin density of the unpaired electrons is often relatively localised around the metal ions of the system, however, offers a clue to a plausible approach for such systems. Whereas the

contact-type hyperfine interactions of the NMR nuclei take place solely within the volume occupied by the spin density, other parts of hyperfine interactions have a long-distance limit that corresponds to a point-dipole approximation (PDA) well outside of the spin-density distribution (Figure 7).

This fact has been traditionally used in the analysis of experimental pNMR spectra taken particularly of biological systems (Bertini, Luchinat & Parigi, 2001). In the approach, the metal centre is assigned a susceptibility tensor that can be determined either experimentally or, as it turns out, to a good approximation, using the modern electronic structure theory from the same  $g$ - and  $\mathbf{Q}$  tensors that are used for the Kurland-McGarvey theory (Figures 2-3). In the external magnetic field of an NMR spectrometer such a centre acquires an induced magnetic moment that, in turn, produces a second-

ary field at the NMR nucleus and, hence, a paramagnetic shift. The great benefit of the method for quantum chemistry is that to calculate from first principles the chemical shifts of paramagnetic systems involving hundreds or thousands of atoms (Figure 7), one needs to explicitly include in the model only the region around the metal centre that is big enough to house the essential spin density distribution. No explicit calculations of the  $\mathbf{A}$  tensors are needed for the distant NMR nuclei, only their positions are needed. An important insight into the method was obtained in recent work (Lang, Ravera, Parigi, Luchinat & Neese, 2020), where it was shown that not only the spin-dipole, but also the orbital hyperfine terms have a surviving long-distance limit, when coupled to the

relativistic spin-orbit term in the electronic Hamiltonian. This finding resolved an earlier ambiguity concerning the use of a symmetric or non-symmetric susceptibility tensor in connection with PDA.

## 5. Fundamental extensions of the theory

As mentioned above, the Kurland-McGarvey theory expresses the pNMR shielding in terms of quantities appearing in the EPR spin Hamiltonian, which are used to parameterise the ground multiplet of an electronically open-shell materials

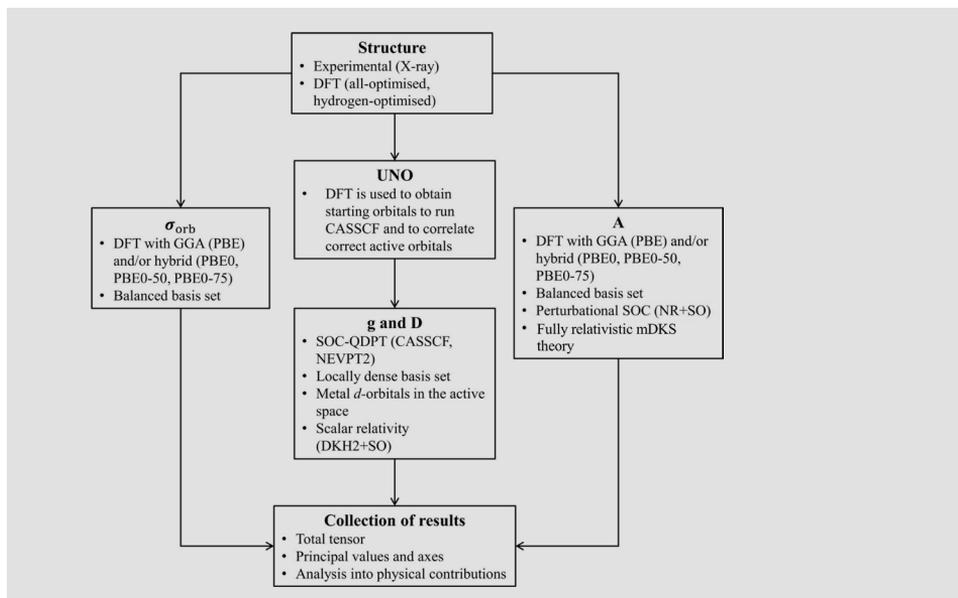


Figure 6. Flow chart of practical quantum-chemical investigation of pNMR shielding tensors (adapted from Rouf, 2017). Details of the calculation of various magnetic property tensors appearing in Figure 2, are shown.

system. The multiplet consists of states that have thermal occupations, and it is assumed that the multiplet is sufficiently far removed in energy from the other, excited multiplets, that the occupation of the latter may be overlooked. This is not generally true. Another usual approximation is in the form of the commonly used EPR Hamiltonian itself, where one limits the electronic Zeeman and ZFS interactions to the leading terms, linear and quadratic, respectively, in the electron spin  $\mathbf{S}$ . While admitting the success of practical Kurland-McGarvey calculations for the case of many unpaired electrons, the approach is, however, formally justified only up to a couple of unpaired electrons (Chibotaru & Ungur, 2012). For strongly spin-orbit coupled systems, such as

lanthanide complexes, as well as cases in which there are low-lying excited multiplets, one needs to abandon the use of the true electron spin angular momentum  $S$ , and use the pseudospin concept instead, to release the above-discussed approximations. In particular, the pseudospin  $\tilde{\mathbf{S}}$  acts in a space of similar dimension  $2S+1$  as the true spin, yet it encompasses the effects of both the orbital and spin angular momenta and is defined only in terms of its matrix elements. A decomposition of the expressions of observables such as the electronic magnetic moment or the ZFS-split structure of the thermally accessible energy levels in terms of the powers of  $\tilde{\mathbf{S}}$ , leads to generalized  $g$ - and ZFS tensors. The concept has already been applied to pNMR shifts within the PDA

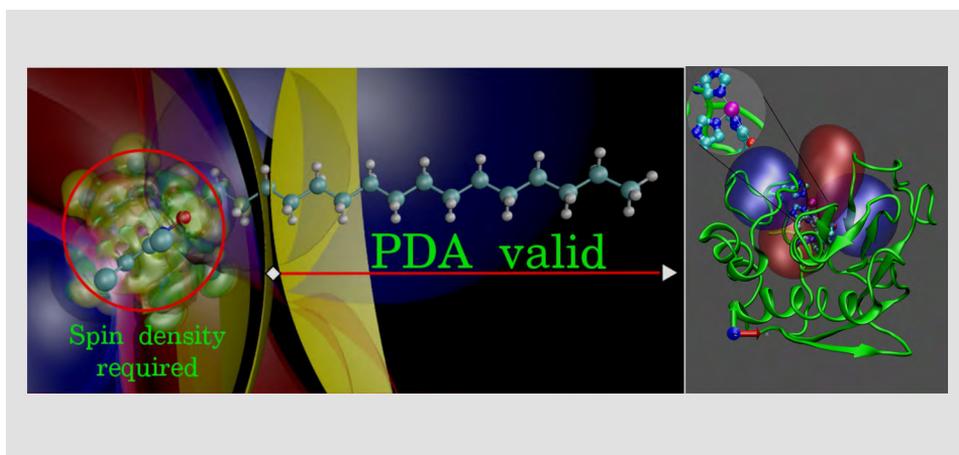


Figure 7. (Left) Schematic division of a paramagnetic molecule into the region within the extent of the spin density distribution, in which the full quantum-mechanical treatment is needed for the calculation of the pNMR shielding tensor, and the more distant region where the explicitly calculated hyperfine tensor is replaced by a point-dipole approximation (PDA) based on the relative atomic positions with respect to the paramagnetic centre. The latter is assigned a susceptibility tensor. (Right) Molecular model of a Co(II)-substituted matrix metalloproteinase, for which PDA makes it possible to compute  $^{13}\text{C}$  pNMR chemical shifts from first principles (Benda et al., 2016; figures courtesy of J. Mareš).

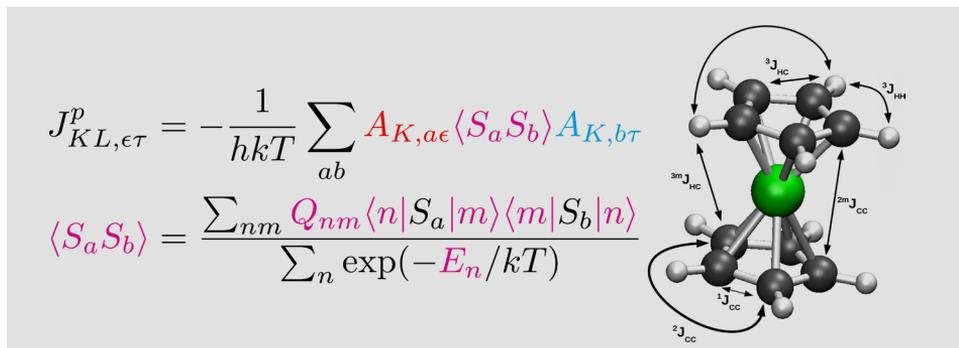


Figure 8. (Left) Kurland-McGarvey formula for the paramagnetic spin-spin coupling enhancement (Cherry, Rouf & Vaara, 2017) involving the hyperfine couplings  $\mathbf{A}_K$  and  $\mathbf{A}_L$  of both the coupled nuclei with the unpaired electron spins, as well as the same dyadic ( $\mathbf{S}\mathbf{S}$ ) of the effective electron spin operator as in the corresponding theory of the shielding tensor (Figure 2). (Right) Nickelocene system ( $S = 1$ ), in which the predicted paramagnetic enhancements of the spin-spin coupling constants greatly exceed the magnitude of the conventional coupling constants for couplings across the metal centre, between nuclei located in the different cyclopentadienyl rings ( $^m J_{KL}$ ).

(Van den Heuvel & Soncini, 2012) and work towards a full implementation using  $\mathcal{A}$ -tensors calculated from first principles is in progress.

A further interesting avenue for progress would be to altogether abandon using an EPR Hamiltonian, be it the standard Hamiltonian as adopted by Kurland and McGarvey, or the generalised one based on  $\tilde{\mathcal{S}}$ , and express the pNMR shielding tensor via second-order perturbation theory expression (featuring the first-order wave function correction) in a full, unparameterised quantum-chemical calculation of the electronic structure of the open-shell system. This would finally render the complicated pNMR situations to be calculable on equal footing with standard closed-shell NMR parameters. So far, the approach has only been implemented (Gendron, Sharkas & Autschbach, 2015) in a sum-over-states formulation involving

the explicit energies and wave functions optimised for the ground state and a few low-lying excited states, a method that is still somewhat cumbersome to apply and does not include a complete response of the system to the magnetic field. Further developments of this excellent idea are, however, to be expected from many groups.

## 6. Solid-state calculations

Often continuous solids, as opposed to materials consisting of a condensed assembly of molecules, are experimentally interesting, and for this end the molecular approach of Kurland-McGarvey has been generalised for periodic boundary conditions (PBC, Mondal & Kaupp, 2018). The

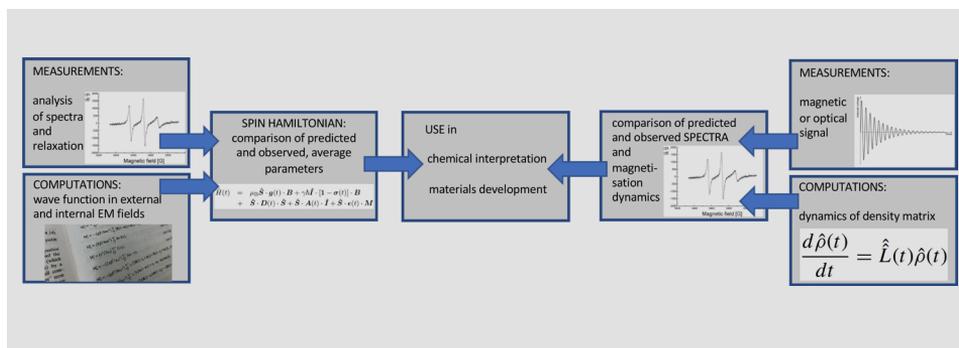


Figure 9. Two different paradigms of theoretical magnetic resonance spectroscopy. (Left) The traditional approach, in which computational and experimentally obtained spectral parameters are compared. (Right) The computational spectroscopy approach, where the experimental observables are directly calculated by solving the Liouville-von Neumann equation for the spin density operator of the system, and comparisons with experiment are made at the level of primary spectra and magnetisation dynamics.

dominating quantum-chemical means of calculating periodic systems is density-functional theory (DFT, Koch & Holthausen, 2012), which readily allows the calculation of  $\sigma^{\text{orb}}$  and  $\mathcal{A}$  in a PBC framework. The DFT performance for the  $g$ -tensor and particularly the ZFS parameters is much worse, however, and, to gain meaningful pNMR predictions, Mondal and Kaupp constructed separate finite cluster models around the transition metal sites of their materials. Calculating the problematic parameters from such clusters using electron-correlated *ab initio* wave function theory methods, and then embedding the results to the Kurland-McGarvey framework, constitutes currently a useful approach for the materials problems in which PBC treatment has to be used.

## 7. Role of hyperfine coupling

Currently the standard approach for obtaining the critically important  $\mathcal{A}$  tensors is DFT, which, however, unfortunately often constitutes a bottleneck in the predictive power of the calculations. This is principally because standard DFT is a so-called single-reference method for dynamic electron correlation, whereas the transition or lanthanide ion-containing molecular and materials systems of pNMR interest regularly have a strong multiconfigurational character. This means that their electronic structure cannot be reliably described by one set of occupied single-electron states, or a single Slater determinant built out of them (Atkins & Friedman, 2005). In practice, modern hybrid DFT functionals lead mostly to satisfactory results for  $^1\text{H}$  and  $^{13}\text{C}$  shifts, which are

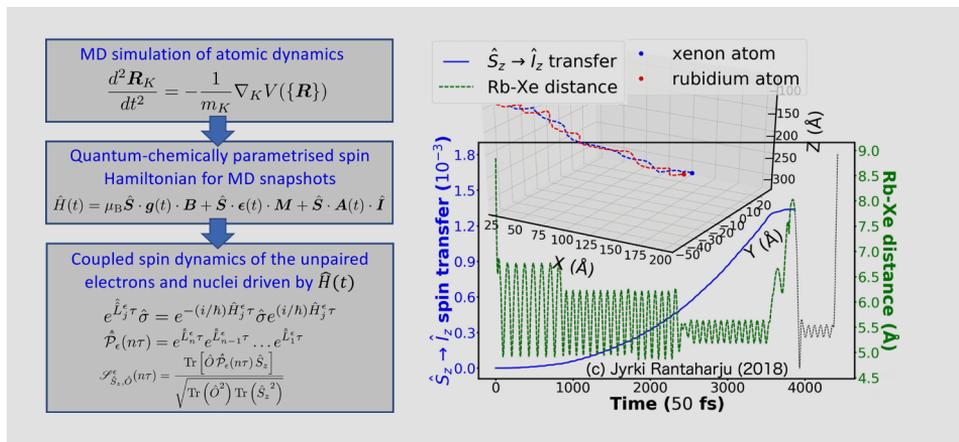


Figure 10. (Left) Steps of the multiscale simulation of magnetic resonance processes. (Right) Simulated spin polarisation transfer from the unpaired electrons of optically polarised Rb vapour to the nuclear spin of  $^{129}\text{Xe}$  in a gaseous van der Waals complex, in a spin-exchange optical pumping experiment (Rantaharju, Hanni & Vaara, 2020).

of central importance for pNMR, but this does not hold for heteroatoms, nor is the performance of hybrid DFT entirely consistent across related systems, or even non-equivalent nuclei of a single system.

Correlated *ab initio* wave function theory approaches that, in principle, render it possible to approach the right answer for the right reason through a hierarchical series of approximations, are so far very limited in the size of molecules for which their application is possible, as well as being still geared towards single-reference systems. Several possible avenues are presently being pursued to improve the quality of the  $\mathbf{A}$  tensors in practical pNMR calculations. They include large-scale *ab initio* restricted active-space multiconfigurational self-consistent field theory approaches with the crucial orbitals for modelling spin polarisation hand-picked to the active space (Sharkas, Pritchard & Autschbach, 2015), efficient, fully relativis-

tic multireference configuration interaction calculations (Knecht, Jensen & Fleig, 2010), combination of DFT with the multiconfigurational ansatz (Hedegård, Toulouse & Jensen, 2018), and the novel local hybrid DFT functionals (Schattenberg, Maier & Kaupp, 2018).

## 8. Exchange-coupled systems

The final extension to the pNMR shielding theory that needs to be mentioned here is the case of multiple magnetic centres. Many interesting pNMR systems, *e.g.*, in biology, contain two or more paramagnetic metal ions. Such centres interact via the so-called exchange coupling - the same interaction that underlies ferromagnetic and antiferromagnetic behaviour of materials - causing that, at sufficiently low measurement temperatures, the shielding

contributions from paramagnetic ions cannot any longer be assumed additive. Instead, one needs to formulate the theory based on, besides ZFS, also exchange coupling entering the definition of the states  $|m\rangle$  in the Kurland-McGarvey formulation (Figure 2). This work is currently in progress.

## 9. Spin-spin coupling in paramagnetic NMR

The indirect spin-spin coupling,  $J$ , is a phenomenon that causes *e.g.*, the fine structure of the spectral lines of conventional liquid-state NMR. It arises from the fact that the magnetic field at the position of the NMR nucleus, hence the resonance frequency of that nucleus, are also affected by the presence of other magnetic nuclei in the sample (Levitt, 2008). The effect is used, *e.g.*, in the investigation of molecular conformations. The calculation of  $J$  is well established for diamagnetic systems, although it is methodologically more demanding than that of  $\sigma$ , due to the many simultaneous physical interactions and the particular demand that they place on the quality of the wave function models (Helgaker, Jaszunski & Ruud, 1999). In contrast, little is known about how  $J$  is changed in paramagnetic systems. Two reasons thereto can be seen. As mentioned above, the paramagnetic relaxation enhancement often renders the fine structure of the resonances invisible. On the other hand, in regions far from the spin density distribution, the spin-spin coupling may be to a good approximation be assumed unaffected by paramagnetism.

With the rapid progress in experimental pNMR techniques, particularly via the sc. ultrafast magic angle spinning (Bertini, Emsley, Lelli, Luchinat, Mao & Pintacuda, 2010), nuclei in the blind zone and the fine structure of lines in closer proximity to the paramagnetic centre than before are becoming increasingly interesting. This raises the question of the effects of paramagnetism on  $J$ . Such a paramagnetic ‘ $J$ -coupling enhancement’ was formulated (Cherry, Rouf & Vaara, 2017) by a straightforward generalisation of the Kurland-McGarvey shielding theory (Figure 8). It is noteworthy that in some cases quite large changes are predicted as compared to the  $J$ -couplings of isostructural diamagnetic complexes. Another feature of the results is that the paramagnetic enhancement reflects mainly the simultaneous couplings of the two nuclei to the unpaired electron spin, and not so much a direct coupling of the formally coupled nuclei. On account of this, pNMR  $J$  close to the paramagnetic sites may be less valuable in the determination of molecular structure than in corresponding diamagnetic systems.

## 10. Outlook

The topic of this overview article has been the calculation of NMR spectral parameters, *i.e.*, quantities appearing in the NMR spin Hamiltonian, particularly in electronically open-shell paramagnetic molecules and materials. In a lot of the contemporary NMR-based materials research, the results of such computations are compared with the outcome of experimental measurements of spectra and relaxation rates that, in turn, are analysed in terms of theoretical

model. Such analyses involve assumptions of the relevant spin system and the motional state of the molecule, resulting in ‘experimental’ spectral parameters. In favourable cases such a comparison allows a cohesive picture of the physics and chemistry of the system of interest, enabling useful conclusions to be drawn for applications work (Figure 9).

Lately, the present author has been interested in a more complete and direct modelling of, instead of spectral parameters, complete experimental processes, in an approach that may be termed *computational spectroscopy* (Figure 9). In this paradigm, the theorist strives to meet the experimentalist in the ballpark of the latter, and computes directly the time dependence of the primary experimental observables, generally the magnetisation dynamics of the different spins involved. In the optimal case, this enables a more detailed understanding of the underlying physics of the dynamic NMR processes than in the conventional approach. In practice, this means using a multiscale model (Figure 10), in which (1) the atomic motion is followed in a molecular dynamics simulation, (2) time series of spin Hamiltonians is calculated quantum-

chemically from the instantaneous atomic positions and (3) the Hamiltonians are used to drive the coupled dynamics of the spins of nuclei and unpaired electrons, by integrating the Liouville-von Neumann equation. The solution of the latter, the time-dependent spin density matrix allows calculating the magnetisation dynamics of relevance to spectra, relaxation and polarisation transfer processes occurring in modern magnetic resonance, retaining full microscopic detail.

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