Spin–Spin Coupling Pathways

Visualization of Nuclear Spin–Spin Coupling Pathways by Real-Space Functions[**]

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Indirect nuclear spin–spin coupling constants are amongst the most important magnetic resonance parameters, invaluable in establishing molecular structure from NMR spectroscopy. Their detailed understanding in terms of molecular and electronic structure is thus of central importance in many fields of research and has been pursued since the advent of NMR spectroscopy more than 50 years ago. For example, questions of "through-space" versus "through-bond" mechanisms,[1,2] the coupling pathways in polycyclic systems, and most recently, spin–spin couplings through hydrogen bonds[3] have stimulated intensive discussions. Today, the quantum-chemical calculation of coupling constants has in many cases reached predictive accuracy.[4] This has, in turn, enhanced the interest in interpretation, that is, to go from accurate numbers to deeper insight.

Various types of analyses were used to obtain further information about different contributions to spin–spin coupling[2,5–8] in terms of localized or canonical molecular orbitals (MOs).[9] While these approaches can provide a very useful insight, their conclusions depend on MO transformations and are thus strongly model-dependent; different MO schemes may lead to conflicting interpretations.[8] Recently the analysis of spin–spin coupling constants based on Weinhold's natural bond orbital (NBO)[5] scheme has become popular. However, its language of localized MOs does not always appear natural for the interpretation of coupling constants, as the coupling may involve the interaction between the spins of two often remote nuclei and thus a delocalized depiction of the pathways of scalar couplings would be more sensible. Here we will show that a model-independent description of spin–spin coupling is possible, based on real-space functions in three-dimensional space, which is appropriate for both localized and delocalized bonding situations.

The indirect spin–spin coupling (J_{MN}) may be expressed as the energy splitting between states with parallel and antiparallel nuclear spins:

$$J_{\mathrm{MN}} = \frac{\hbar}{2\pi}\gamma_{\mathrm{M}}\gamma_{\mathrm{N}}K_{\mathrm{MN}} = \frac{1}{2}[E(\uparrow\uparrow) - E(\uparrow\downarrow)] \tag{1}$$

where K_{MN} is the reduced coupling constant (the M and N labels represent the two coupled nuclei). Since both of these energies may be written as an integral over an energy density *ε(r)*, it is also possible to express the coupling itself in this form:

$$J_{\mathrm{MN}} = \frac{\hbar}{2\pi}\gamma_{\mathrm{M}}\gamma_{\mathrm{N}}K_{\mathrm{MN}} = \frac{1}{2}\int[\varepsilon^{\uparrow\uparrow}(r) - \varepsilon^{\uparrow\downarrow}(r)]\mathrm{d}V = \frac{\hbar}{2\pi}\gamma_{\mathrm{M}}\gamma_{\mathrm{N}}\int\varepsilon_{\mathrm{MN}}(r)\mathrm{d}V \tag{2}$$

where $\varepsilon_{\mathrm{MN}}(r)$ is the coupling energy density (CED).[10] The integral of CED over all space is equal to the reduced coupling constant. The concept of CED does not involve any approximation and thus is model-independent. CED is a real-space function and can be visualized easily in 3D space.[11] It contains all the information about the propagation of the nuclear spin–spin interaction throughout a molecule. To calculate CED we use double finite perturbation theory (DFPT). The Fermi-contact (FC) operators on both coupled nuclei are included simultaneously in the Hamiltonian, and the coupling between nuclei M and N is calculated in two steps. First, one calculates the total energy for a system with parallel nuclear spins (that is, both FC operators have the same sign). In a second separate calculation, the FC perturbations corresponding to antiparallel nuclear spins (opposite signs) are included. The difference between these two total energies is proportional to the coupling constant. This is in fact a faithful description of the underlying physics; the coupling constant probes the energy difference between these two states. Many years ago, Kowalewski et al. used this elegant idea for the simple implementation of spin–spin coupling constant calculations at the configuration–interaction level of theory.[12] Recently, a related implementation based on density functional theory (DFT) has been reported by Contreras et al.[13] An obvious disadvantage of the DFPT approach in actual numerical calculations of couplings is that for each pair of coupled nuclei two separate self-consistent calculations are required. Therefore, the DFPT approach is not often used in practice. To our knowledge, the enormous potential of this scheme for the interpretation of couplings has not been realized. Note that, in addition to providing the CED, the approach also affords a coupling electron deformation density (CDD) in a straightforward manner, defined as:

$$\rho_{\mathrm{MN}}(r) = \frac{\rho^{\uparrow\uparrow}(r) - \rho^{\uparrow\downarrow}(r)}{\lambda_1\lambda_2} \tag{3}$$

where λ_1 and λ_2 are the perturbation parameters used in DFPT.[12,14]

The calculation of CDD (which is practically the scaled difference of the electron densities obtained from two separate SCF calculations) does not require any additional programming, but the evaluation of CED does.[15] As shown below, CDD provides similar information on the coupling as CED. However, in contrast to CED the integration of CDD over space gives exactly zero. The present concept is not restricted to any particular quantum-chemical method. CED and CDD can in the same fashion be obtained from

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Hartree–Fock (HF) calculations, many post-HF methods and DFT. In the present implementation in our program ReSpect,[16] DFT is used.[17] Further implementation and computational details will be published elsewhere.[18] Here we will use a few representative examples to demonstrate the abilities of the new method. In the following plots, blue and red colors correspond to positive and negative function values, respectively (isosurfaces or isolines are shown). The relative importance of different pathways may be judged by intensities and volumes.

Figure 1 shows isosurfaces of CED for $^3J_{H,H}$ coupling in benzene. It can be seen that the spin–spin interaction dominantly propagates through the three intervening bonds, whereas other mechanisms, for example, through space, are not apparent. Note however, that CED has significant values also in areas outside the direct pathway (near neighboring C–C bonds; isoline plots not shown here exhibit even more detailed features near neighboring hydrogen atoms). This is not surprising in view of the delocalized π system of benzene, and it suggests that substituents at these neighboring positions may also affect the coupling constant (in agreement with experimental evidence[19]). CDD for the same $^3J_{H,H}$ coupling is provided in Figure 2, which strongly resembles the CED plot in all important topological features, but also shows small differences (for example, the volume of the areas around the coupled hydrogen atoms). It should be remembered that the integral of CDD over space is equal to zero whereas the integral of CED gives the reduced coupling constant.[20] The close topological resemblance of CDD and CED is consistent with the cornerstone of DFT, that is, that the electron density contains all the information about a molecule. The analysis of CDD is slightly more straightforward than that of CED, as it mirrors directly the changes in electronic structure due to the coupling interactions. A deeper analysis of CDD will be provided elsewhere.[18]

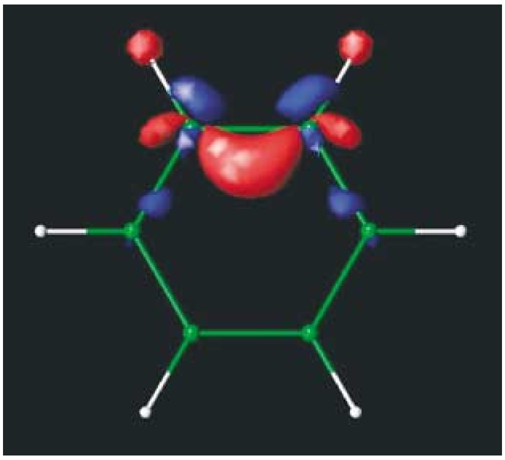

Figure 1. Visualization of the $^3J_{H,H}$ coupling energy density (CED) in benzene.

While the $^3J_{H,H}$ coupling in benzene may be taken as an example of a through-bond interaction, the $^3J_{P,P}$ coupling in $C_2H_2(PH_2)_2$ is frequently considered as a typical case of a through-space interaction.[2] However, up to now the relative role of through-bond versus through-space interactions could not be established. The CED for $^3J_{P,P}$ in $C_2H_2(PH_2)_2$ is shown in Figure 3. The through-bond pathway resembles the $^3J_{H,H}$ coupling in benzene (Figures 1 and 2). Yet, the through-space interaction between the two phosphorus nuclei dominates clearly. The interaction is due to the overlap of the phosphorus lone pairs in space, which provides an efficient spin-polarization pathway (notwithstanding the fact that molecular orbitals may be orthogonal). To obtain further insight, Figure 4 provides CED for the P-P coupling in a model $H_3P\cdots PH_3$ system. The molecular structure of the model complex is taken to be as in $C_2H_2(PH_2)_2$, but with hydrogen atoms replacing the backbone (the P–H distance was taken to be 1.427 Å, as for the other P–H bonds). The clear result of this plot may be somewhat unexpected; the P-P coupling interaction is stronger than in $C_2H_2(PH_2)_2$! This conclusion is supported by the calculated values of the coupling constants (calculated via integration of CED): 289 Hz for the model

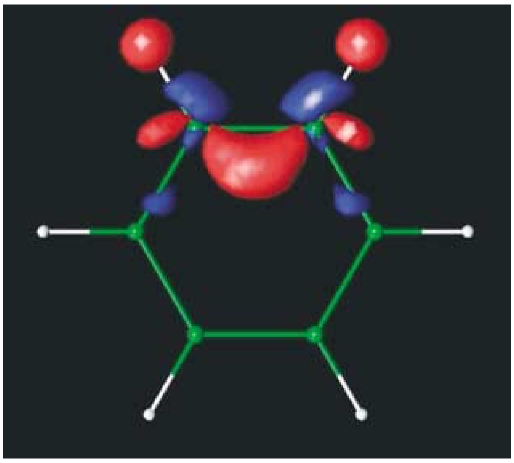

Figure 2. Visualization of the $^3J_{H,H}$ coupling electron deformation density (CDD) in benzene.

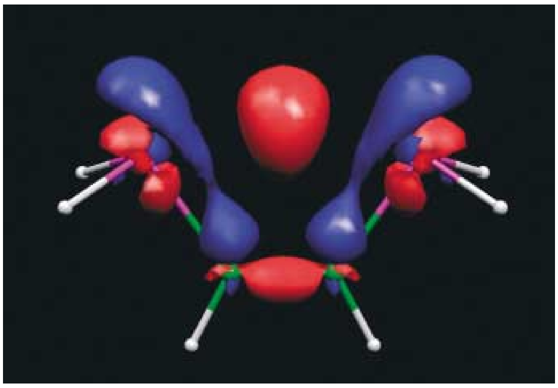

Figure 3. Visualization of the $^3J_{P,P}$ coupling energy density (CED) in the $C_2H_2(PH_2)_2$ molecule.

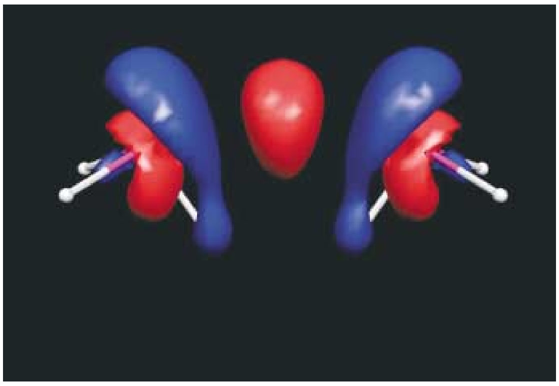

Figure 4. Visualization of $J_{P,P}$ coupling energy density (CED) in the model $H_3P\cdots PH_3$ system.

system versus 180 Hz for $C_2H_2(PH_2)_2$ (to the best of our knowledge, no experimental value is available).

In the context of the topical field of couplings through hydrogen bonds, Figure 5 shows the CDD for a formal $^2J_{C,N}$ coupling in the hydrogen-bonded model complex $NCH\cdots NH_3$. In this case, we decided to show isolines of CDD in a plane containing the hydrogen bond. Interestingly, the polarization propagates throughout the entire system with significant amplitude of CDD on the far-left (as-depicted) nitrile nitrogen atom, which is outside of the direct coupling pathway. This suggests that the C≡N bond plays a role in the coupling despite the overall obvious σ character of the pathway.

In conclusion, the newly proposed and implemented real-space functions allow unprecedented insight into the pathways of indirect nuclear spin–spin couplings. Further analysis of CED and CDD is possible along several lines, for example, the analysis of MO contributions to the functions, or the topological analysis of bond or lone-pair contributions, based on auxiliary real-space functions; this work is underway. Very recently, Soncini and Lazzeretti[21] reported findings that may be related to the CED proposed by us.[22] The definition differs from ours, and apparently so does the computational implementation. Unfortunately, not enough details were given in this report to judge how exactly the two methods are related. Probably, the DFPT approach proposed here is more applicable to systems of chemically relevant size, and the inclusion of electron correlation via DFT provides a more quantitative analysis.

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[9] Usually only the dominant Fermi-contact term is analyzed. We will follow this line throughout the paper, though all other important terms can be visualized along the same lines.

[10] Probably the first attempt to visualize chemical-shift density (as an example of a property density) was made by C. J. Jameson, A. D. Buckingham, *J. Chem. Phys.* **1980**, *73*, 5684.

[11] To calculate CED we used the following alternative equation for the reduced coupling constant: $K_{MN} = -[2\langle\Psi^{11}|\mathscr{H}^0|\Psi^0\rangle + \langle\Psi^{01}|\mathscr{H}^0|\Psi^{10}> + \langle\Psi^{10}|\mathscr{H}^0|\Psi^{01}\rangle]$. This allows us to avoid visualization of an integrand containing delta functions (Fermi-contact operators). Here $\mathscr{H}^0$ is the ground-state Hamiltonian, and Ψ^0, Ψ^{10}, Ψ^{01},and Ψ^{11} are unperturbed, single-perturbed (by the first and second perturbations), and bilinear-perturbed

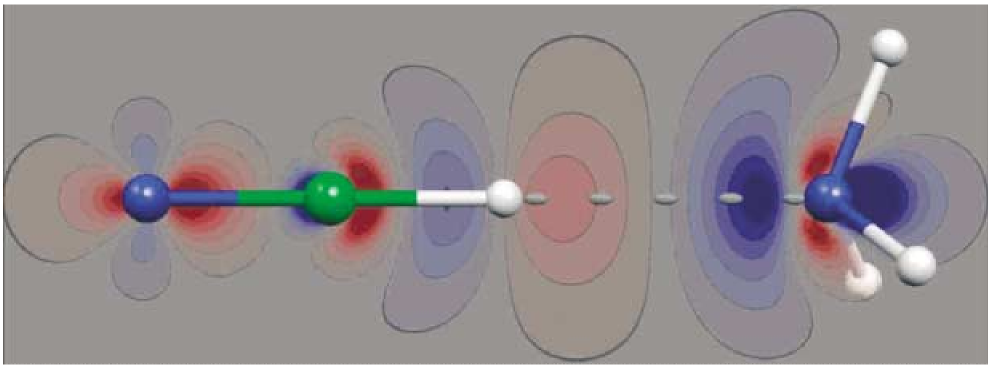

Figure 5. Visualization of $^2J_{C,N}$ coupling electron deformation density (CDD) for coupling through hydrogen bonds in the model $NCH\cdots NH_3$ system.

wavefunctions, respectively. The corresponding double-perturbed density matrix is easily available in DFPT.

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[14] One can consider λ_1 and λ_2 as an analogy of nuclear *g*-values. Usually the values λ_1 and λ_2 are chosen to be about 10^{-2} au to avoid numerical noise in the calculations.

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[17] The calculations were made with Perdew/Wang exchange[17a] and Perdew correlation functionals.[17b] Basis set BII of Kutzelnigg et al.,[17c] perturbation parameters $\lambda_1 = \lambda_2 = 0.01$, and an extensive grid (with about 24000 points per atom) was employed throughout this work for the numerical calculation of couplings. A much smaller grid (about 2000 points per atom) is already sufficient for visualization purposes. Visualization of CED and CDD was achieved using the MOLEKEL program.[17d] a) J. P. Perdew, Y. Wang, *Phys. Rev. B* **1986**, *33*, 8800; b) J. P. Perdew, *Phys. Rev. B* **1986**, *33*, 8822; J. P. Perdew, *Phys. Rev. B* **1986**, *34*, 7406; c) W. Kutzelnigg, U. Fleischer, M. Schindler *in NMR-Basic Principles and Progress, Vol. 23* (Eds.: P. Diehl, E. Fluck, H. Günther, R. Kosfeld, J. Seelig), Springer, Heidelberg, **1990**, p. 165; d) MOLEKEL 4.0, P. Flükiger, H. P. Lüthi, S. Portmann, J. Weber, Swiss Center for Scientific Computing, Manno, Switzerland, **2000**.

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[20] The CED coupling (calculated by integration) is equal to 7.4 Hz, which is in good agreement with the experimental value of 7.5 Hz (see D. L. Beveridge in *Semiempirical Methods of Electronic Structure Calculations* (Ed.: G. A. Segal), Plenum, New York, **1977**, p. 163).

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[22] See footnote [**].