

# The calculation of spin–spin coupling constants in large molecules

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## Overview

- the mechanisms responsible for nuclear spin–spin couplings
- the calculation of indirect nuclear spin–spin couplings
- comparison of theoretical methods
  - what  $N$ -electron models and basis sets are needed?
  - are the results in qualitative or quantitative agreement with experiment?
  - how does DFT perform relative to wave-function theory?
- Application to large molecules
  - spin–spin coupling constants at large distances

## Nuclear spin–spin coupling

- With each nuclear spin  $\mathbf{I}_P$  in a molecule, there is an associated magnetic moment:

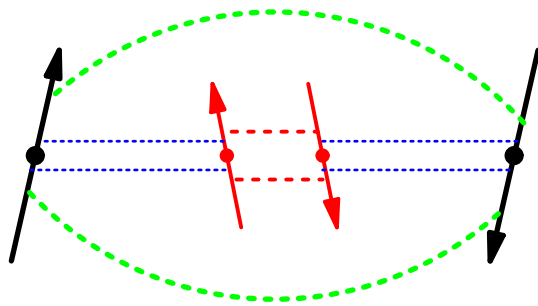
$$\mathbf{M}_P = \gamma_P \hbar \mathbf{I}_P \approx 10^{-4} \text{ a.u.}$$

- These moments interact **directly** with one another, by a classical dipole mechanism:

$$\mathbf{M}_P^T \mathbf{K}_{PQ}^{\text{direct}} \mathbf{M}_Q = \alpha^2 \frac{R_{PQ}^2 (\mathbf{M}_P \cdot \mathbf{M}_Q) - 3(\mathbf{M}_P \cdot \mathbf{R}_{PQ})(\mathbf{R}_{PQ} \cdot \mathbf{M}_Q)}{R_{PQ}^5} \approx 10^{-12} \text{ a.u.}$$

- the direct coupling is anisotropic and vanishes in isotropic media (gases and liquids)

- However, there is also an **indirect** contribution to the coupling, arising from **hyperfine interactions** with the intervening electrons:



- the indirect coupling is exceedingly small:

$$\approx 10^{-16} \text{ a.u.} \approx 1 \text{ Hz}$$

- it does not vanish in isotropic media
- fine structure of high-resolution NMR spectra

- Analogy with molecular electrostatic interactions may be helpful:

- the bare nuclei repel one another by a classical Coulomb mechanism
- this interaction is modified by the intervening electrons, which couple to the nuclei
- the combined interactions may provide stable molecular structures

## Indirect nuclear spin–spin coupling tensors

- To second order in the nuclear moments, the change in the **electronic energy** is described in terms of the (reduced) indirect spin–spin coupling tensors  $\mathbf{K}_{PQ}$ :

$$E(\mathbf{M}_P) = E(\mathbf{0}) + \sum_{P>Q} \mathbf{M}_P^T \mathbf{K}_{PQ} \mathbf{M}_Q + \mathcal{O}(\mathbf{M}^3)$$

- for closed-shell molecules, there are no first-order contributions
- the  $\mathbf{K}_{PQ}$  are simply the second derivatives of  $E(\mathbf{M}_P)$  at  $\mathbf{M}_P = \mathbf{0}$
- they may be calculated by standard techniques for second-order molecular properties
- In what manner is the electronic energy affected by the magnetic moments?
- The nuclear moments set up a magnetic **vector potential** and a **field** ( $\approx 10^{-8}$  a.u.):

$$\mathbf{A}(\mathbf{r}) = \alpha^2 \sum_P \frac{\mathbf{M}_P \times \mathbf{r}_P}{r_P^3}, \quad \mathbf{B}(\mathbf{r}) = \nabla \times \mathbf{A}(\mathbf{r})$$

- In the presence of  $\mathbf{A}$  and  $\mathbf{B}$ , the **kinetic-energy operator** is modified and becomes:

$$H_{\text{kin}} = \frac{1}{2} p^2 + \underbrace{\mathbf{A}(\mathbf{r}) \cdot \mathbf{p} + \frac{1}{2} A(\mathbf{r})^2}_{\text{orbital hyperfine}} + \underbrace{\mathbf{B}(\mathbf{r}) \cdot \mathbf{s}}_{\text{spin hyperfine}}$$

- In nonrelativistic theory, therefore, there are two distinct contributions to the coupling:
  - hyperfine coupling to the **orbital motion** of the electrons
  - hyperfine coupling to the **spin** of the electrons

## Orbital-hyperfine interactions

- The orbital hyperfine or spin-orbit (SO) coupling represents the interaction of charged particles (electrons) moving in the vector potential  $\mathbf{A}(\mathbf{r})$  generated by the nuclei.
- There are two types of orbital hyperfine operators:

$$\frac{1}{2}A^2 = \sum_{PQ} \mathbf{M}_P^T \mathbf{h}_{PQ}^{\text{DSO}} \mathbf{M}_Q, \quad \mathbf{h}_{PQ}^{\text{DSO}} = \alpha^4 \frac{\mathbf{r}_P^T \mathbf{r}_Q \mathbf{I}_3 - \mathbf{r}_P \mathbf{r}_Q^T}{r_P^3 r_Q^3} \leftarrow \text{diamagnetic SO (DSO)}$$

$$\mathbf{A} \cdot \mathbf{p} = \sum_P \mathbf{M}_P^T \mathbf{h}_P^{\text{PSO}}, \quad \mathbf{h}_P^{\text{PSO}} = \alpha^2 \frac{\mathbf{r}_P \times \mathbf{p}}{r_P^3} \leftarrow \text{paramagnetic SO (PSO)}$$

- Whereas the second-order real DSO operator contributes to the expectation value, the first-order imaginary PSO operator contributes to second order in perturbation theory:

$$\mathbf{K}_{PQ}^{\text{SO}} = \langle 0 | \mathbf{h}_{PQ}^{\text{DSO}} | 0 \rangle + 2 \sum_{n_S \neq 0} \frac{\langle 0 | \mathbf{h}_P^{\text{PSO}} | n_S \rangle \langle n_S | (\mathbf{h}_Q^{\text{PSO}})^T | 0 \rangle}{E_{n_S} - E_0}$$

- The DSO contribution is calculated by numerical quadrature.
- The PSO contribution is calculated using linear response theory, in much the same manner as we calculate for example static polarizabilities.
- The SO contributions (especially DSO) are usually but not invariably small.
- For large internuclear separations, the DSO and PSO contributions cancel.

## Spin-hyperfine interactions

- To treat the spin-hyperfine interactions  $\mathbf{B} \cdot \mathbf{s}$ , we need the nuclear magnetic field:

$$\mathbf{B}(\mathbf{r}) = \nabla \times \mathbf{A}(\mathbf{r}) = \frac{8\pi\alpha^2}{3} \sum_P \delta(\mathbf{r}_P) \mathbf{M}_P + \alpha^2 \sum_P \frac{3\mathbf{r}_P(\mathbf{r}_P \cdot \mathbf{M}_P) - r_P^2 \mathbf{M}_P}{r_P^5}$$

- This magnetic field  $\mathbf{B}(\mathbf{r})$  then gives rise to two distinct **first-order triplet operators**:

$$\mathbf{B} \cdot \mathbf{s} = \sum_P \mathbf{M}_P^T (\mathbf{h}_P^{\text{FC}} + \mathbf{h}_P^{\text{SD}}), \quad \left\{ \begin{array}{ll} \mathbf{h}_P^{\text{FC}} = \frac{8\pi\alpha^2}{3} \delta(\mathbf{r}_P) \mathbf{s} & \text{Fermi contact (FC)} \\ \mathbf{h}_P^{\text{SD}} = \alpha^2 \frac{3\mathbf{r}_P \mathbf{r}_P^T - r_P^2 \mathbf{I}_3}{r_P^5} \mathbf{s} & \text{spin-dipole (SD)} \end{array} \right.$$

where FC represents interaction **at the nucleus** and SD interaction **at a distance**.

- The FC and SD operators both contribute to second order in perturbation theory:

$$\mathbf{K}_{PQ}^{\text{FC+SD}} = 2 \sum_{n_T} \frac{\langle 0 | \mathbf{h}_P^{\text{FC}} + \mathbf{h}_P^{\text{SD}} | n_T \rangle \langle n_T | (\mathbf{h}_Q^{\text{FC}})^T + (\mathbf{h}_Q^{\text{SD}})^T | 0 \rangle}{E_{n_T} - E_0}$$

– The  $\mathbf{K}_{PQ}^{\text{FC+SD}}$  are evaluated by linear response theory, just like the  $\mathbf{K}_{PQ}^{\text{PSO}}$ .

- Relative importance of the terms:
  - the isotropic FC/FC term often dominates short-range coupling constants
  - the FC/SD and SD/FC terms often dominate the anisotropic part of  $\mathbf{K}_{PQ}$

## Spin–spin coupling constants by linear response theory

- In linear response theory, we may express the  $\alpha\beta$  Cartesian component of the spin–spin coupling tensor  $\mathbf{K}_{PQ}$  in this manner:

$$K_{P\alpha,Q\beta} = \left\langle h_{P\alpha,Q\beta}^{\text{DSO}} \right\rangle - [\mathbf{F}_{P\alpha}^{\text{PSO}}]^T [\mathbf{G}_{\text{ii}}^{\text{ss}}]^{-1} \mathbf{F}_{Q\beta}^{\text{PSO}} - \sum_{\gamma} [\mathbf{F}_{P\alpha\gamma}^{\text{FC+SD}}]^T [\mathbf{G}_{\text{rr}}^{\text{tt}}]^{-1} \mathbf{F}_{Q\gamma\beta}^{\text{FC+SD}}$$

- Right-hand side elements:

$$[\mathbf{F}_P^{\text{PSO}}]_{ai} = 2\alpha^2 \left\langle a \left| \frac{\mathbf{l}_P}{r_P^3} \right| i \right\rangle, \quad [\mathbf{F}_P^{\text{FC+SD}}]_{ai} = \alpha^2 \left\langle a \left| \frac{8\pi}{3} \delta(\mathbf{r}_P) \mathbf{I} + \frac{3\mathbf{r}_P \mathbf{r}_P^T - r_P^2 \mathbf{I}}{r_P^5} \right| i \right\rangle$$

- Leading Hessian terms are diagonal orbital-energy differences:

$$\begin{aligned} [\mathbf{G}_{\text{ii}}^{\text{ss}}]_{ai,bj} &= \delta_{ij} \delta_{ab} (\varepsilon_a - \varepsilon_i) + \gamma (g_{ajib} - g_{abij}) \quad \leftarrow \text{diagonal in pure DFT} \\ [\mathbf{G}_{\text{rr}}^{\text{tt}}]_{ai,bj} &= \delta_{ij} \delta_{ab} (\varepsilon_a - \varepsilon_i) - \gamma (g_{ajib} + g_{abij}) + \int \frac{\partial^2 f}{\partial \rho_t^2} \phi_a \phi_i \phi_b \phi_j \mathbf{dr} + \dots \end{aligned}$$

- In practice, Hessian inversion is avoided by the solution of linear equations:

$$\mathbf{G}_{\text{rr}}^{\text{tt}} \boldsymbol{\lambda}_{Q\gamma\beta}^{\text{FC+SD}} = -\mathbf{F}_{Q\gamma\beta}^{\text{FC+SD}}$$

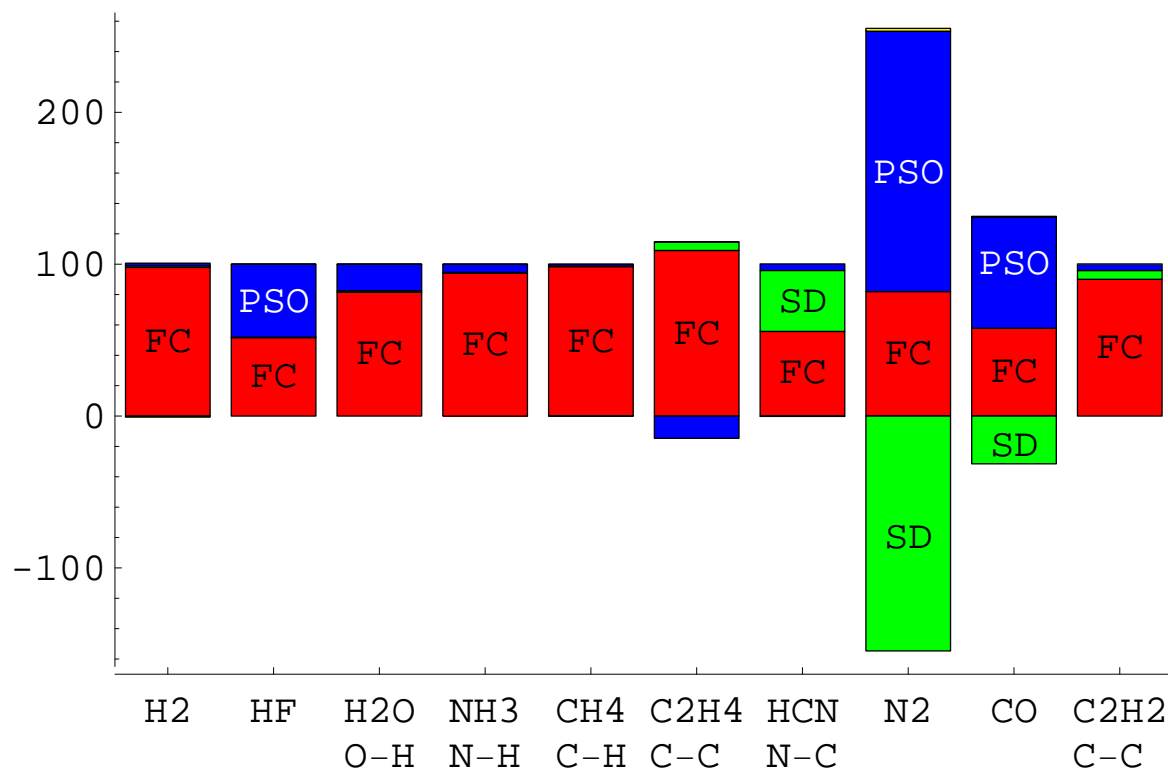
- There are a total of 9 (10) such equations to be solved for each nucleus.

## Relative importance of the contributions to spin–spin coupling constants

- The isotropic indirect spin–spin coupling constants can be uniquely decomposed as:

$$\mathbf{K}_{PQ} = \mathbf{K}_{PQ}^{\text{DSO}} + \mathbf{K}_{PQ}^{\text{PSO}} + \mathbf{K}_{PQ}^{\text{FC}} + \mathbf{K}_{PQ}^{\text{SD}}$$

- The spin–spin coupling constants are often dominated by the FC term.
- Since the FC term is relatively easy to calculate, it is tempting to ignore the other terms.
- However, none of the contributions can be *a priori* neglected (N<sub>2</sub> and CO)!

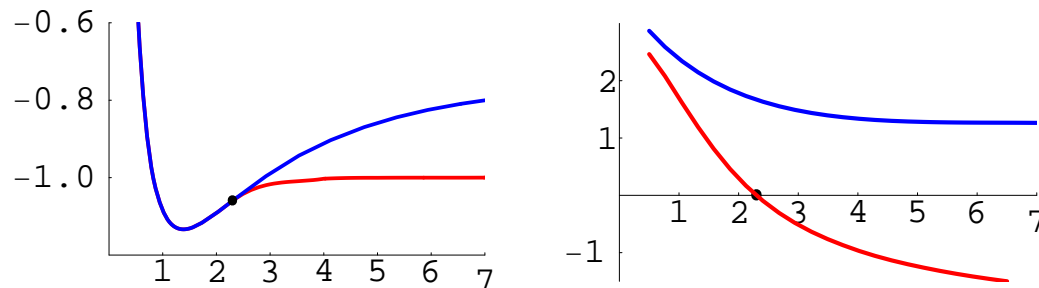


## RHF and the triplet instability problem

- RHF **does not** in general work for spin–spin calculations:
  - the RHF wave function often becomes triplet unstable
  - at or close to such instabilities, the RHF description of spin interactions becomes unphysical
  - the spin–spin coupling constants of  $C_2H_4$ :

Hz	$^1J_{CC}$	$^1J_{CH}$	$^2J_{CH}$	$^2J_{HH}$	$^3J_{cis}$	$^3J_{trans}$
exp.	68	156	–2	2	12	19
RHF	1270	755	–572	–344	360	400
CAS	76	156	–1	3	14	21

- Triplet instability in  $H_2$ :



- Indeed, any method **based on the RHF reference state** may have problems!

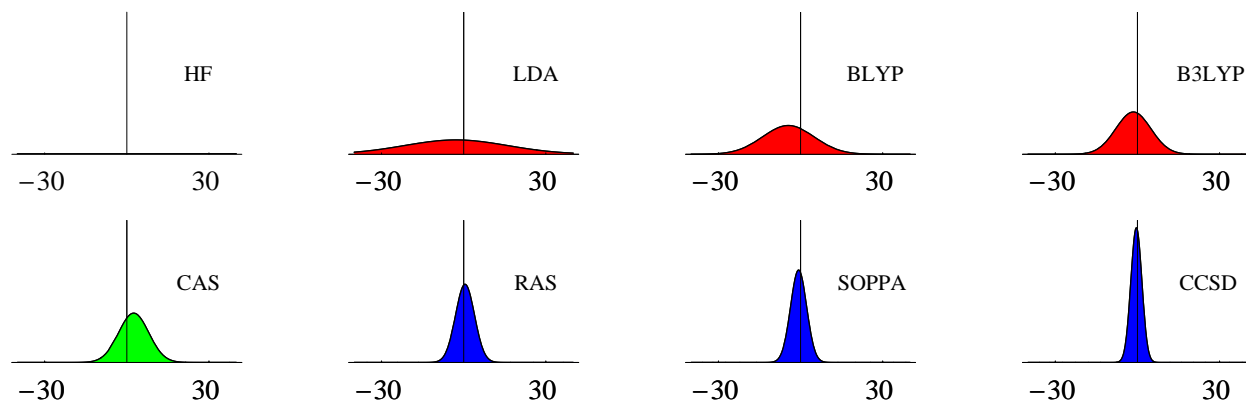


## Correlated methods for spin–spin calculations

- The calculation of spin–spin coupling constants is a challenging task:
  - singlet and triplet perturbations—Hartree–Fock theory fails
  - a large number of response equations are involved
  - large basis sets are needed
  - vibrational corrections are often large
- There is clearly a need for efficient **correlated** methods.
- Traditional **wave-function methods** used for spin–spin calculations:
  - SOPPA (1984), MCSCF (1992), CCSD (1994), CC3 and CCSDT (2001)
  - typical errors are a few Hz in small systems, but often 10%–20% for small couplings
  - however, all of these methods are (at least for now) restricted to **small systems**
- **DFT methods** offer an alternative approach to spin–spin calculations:
  - LDA and GGA without SD, finite perturbation theory (1994)
  - LDA, GGA, hybrid theory, all terms by response theory (2000)
  - errors are somewhat larger and less predictable than for the most accurate wave-function methods
  - much less susceptible to triplet instabilities than Hartree–Fock theory
  - DFT calculations are less expensive and applicable to large systems

## Comparison of density-functional and wave-function theory

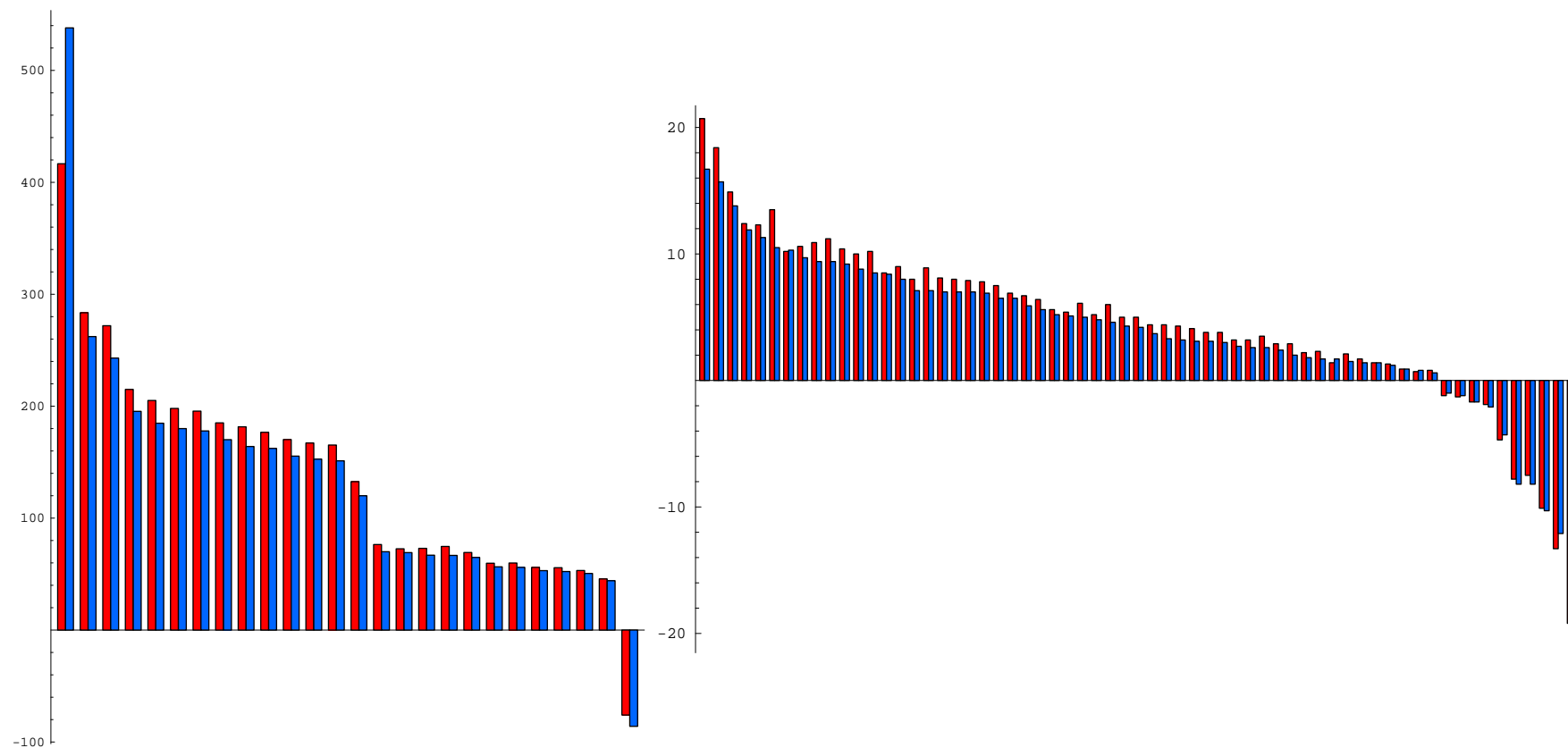
- normal distributions of errors for these molecules and some other systems for which vibrational corrections have been made:



- some observations:
  - HF has a very broad distribution and overestimates strongly
  - LDA underestimates only slightly, but has a large standard deviation
  - BLYP reduces the LDA errors by a factor of two
  - B3LYP improves upon GGA (but not as dramatically as for other properties)
  - B3LYP errors are similar to those of CASSCF and about twice those of the dynamically correlated methods RASSCF, SOPPA, and CCSD
  - the most accurate method appears to be CCSD
  - the situation is much less satisfactory than for geometries and atomization energies

## B3LYP vs. experimental spin-spin coupling constants

- Comparison of B3LYP (red) and experimental (blue) spin-spin coupling constants
  - plotted in order of decreasing experimental value



- Trends are quite well reproduced by B3LYP, in particular for large couplings.

## DFT failures

- DFT failures: couplings to electronegative and lone-pair atoms
- Fluorine couplings, in particular, are strongly underestimated:

		RHF	LDA	BLYP	B3LYP	CCSD	exp
HF	$^1J_{\text{HF}}$	669	396	390	417	522	538
FHF <sup>-</sup>	$^2J_{\text{FF}}$	657	-175	-113	25	439	≈ 274

- This is obviously a failure of the functionals rather than of DFT as such!
- The KT1 functional of Keal and Tozer gives the following one-bond couplings:

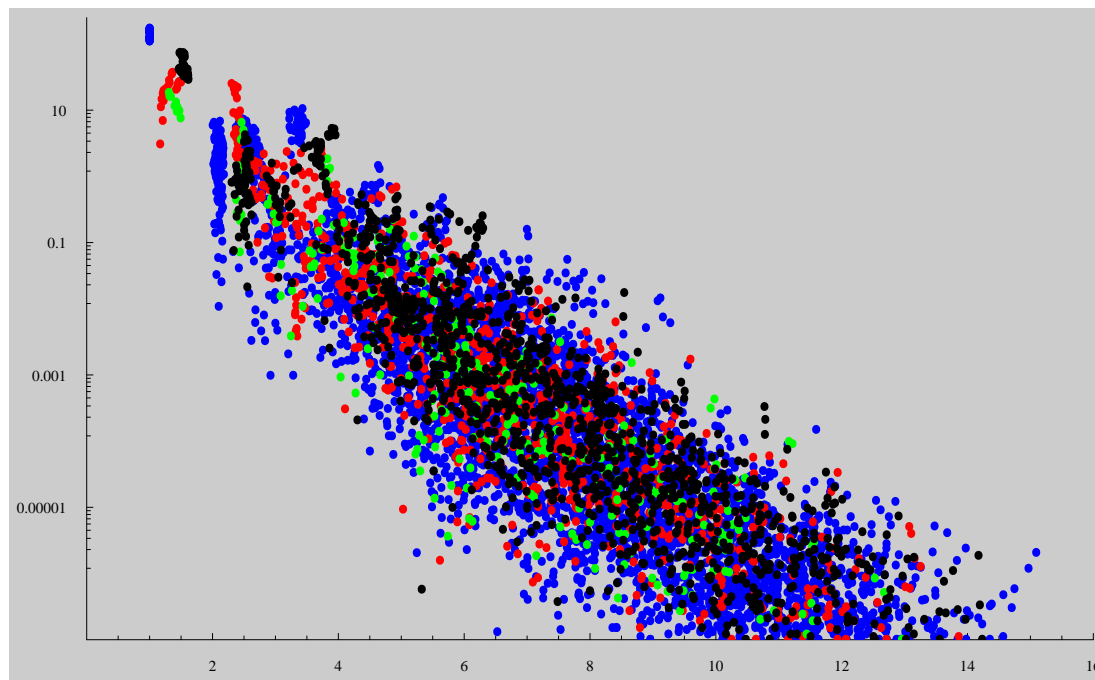
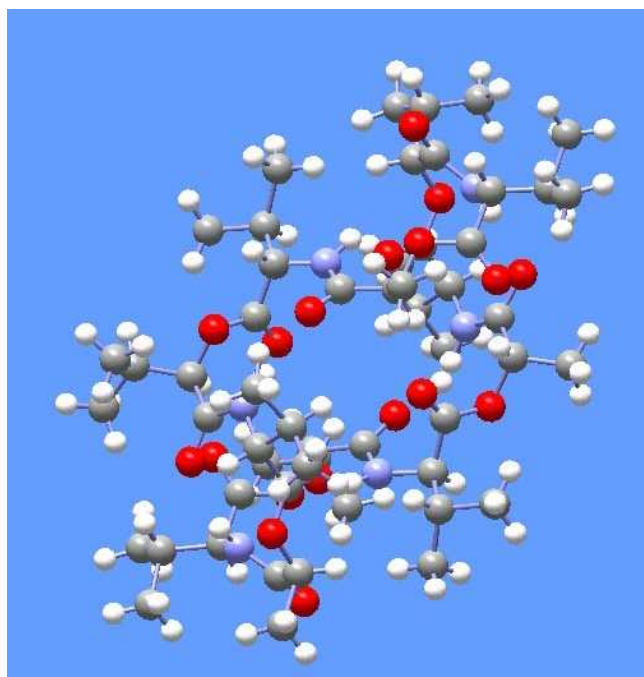
	HF	CO	NN	OH	NH	CC <sup>a</sup>	CH	CC <sup>b</sup>
KT1	507	19	1	-81	44	51	147	13
exp.	538	16	2	-86	44	67	151	35
B3LYP	417	18	3	-76	46	75	165	33

<sup>a</sup> CC in C<sub>2</sub>H<sub>4</sub>; <sup>b</sup> CC in C<sub>2</sub>H<sub>6</sub>

- For high accuracy, it is essential to develop new functionals:
  - self-interaction free functionals
  - current-density functionals
- Nevertheless, the standard functionals of DFT are sufficiently accurate to be useful!

## Valinomycin $C_{54}H_{90}N_8O_{18}$

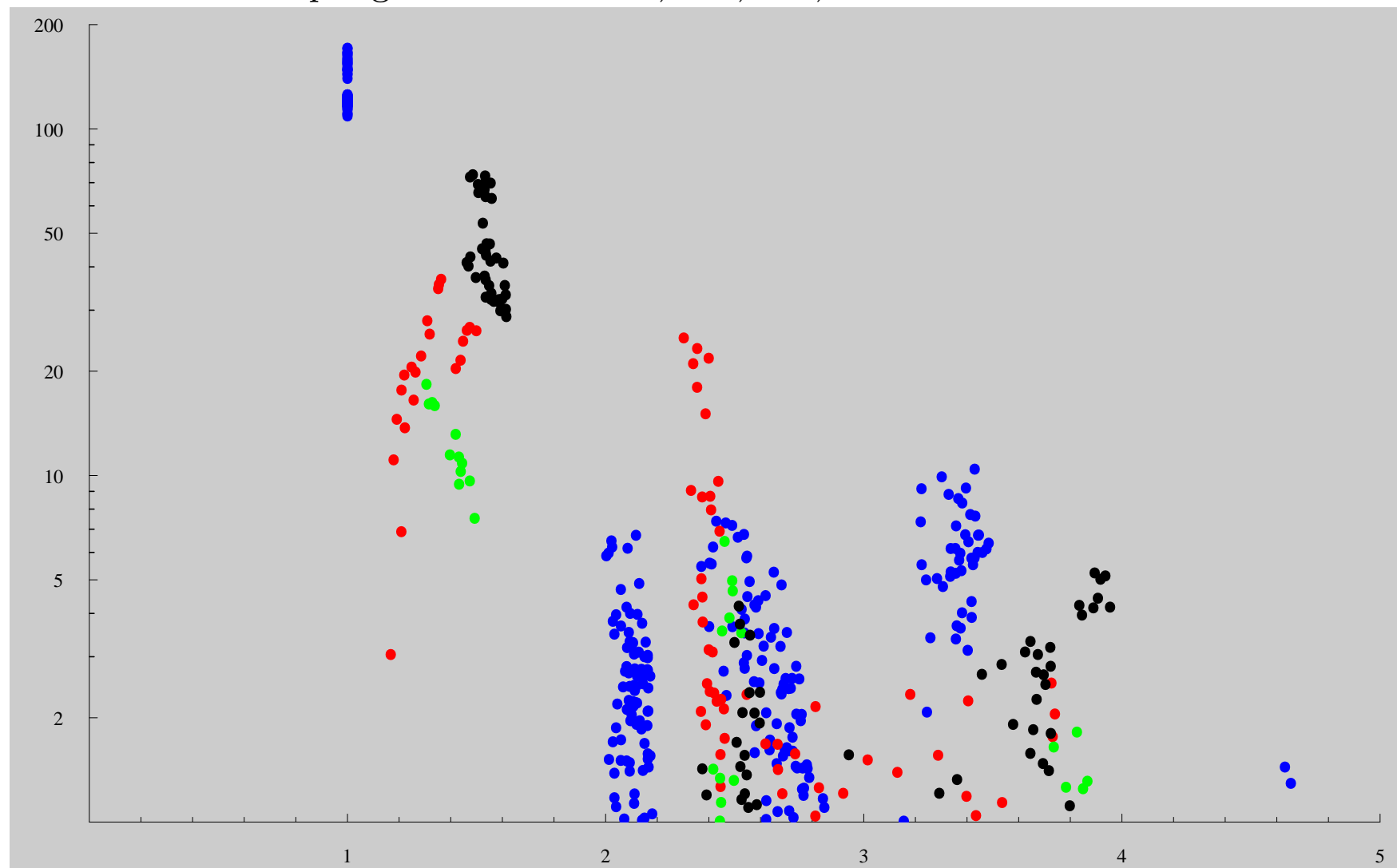
- DFT can be applied to large molecular systems such as valinomycin (168 atoms)
  - There are a total of 7587 spin–spin couplings to the carbon atoms in valinomycin.
  - We have calculated the FC contributions at the LDA/6-31G level of theory.
  - Below, we have plotted the magnitude of the coupling constants on a logarithmic scale, as a function of the internuclear distance.



- The FC contributions fall off exponentially with increasing separation.
- Most of the indirect couplings are small and cannot be detected.

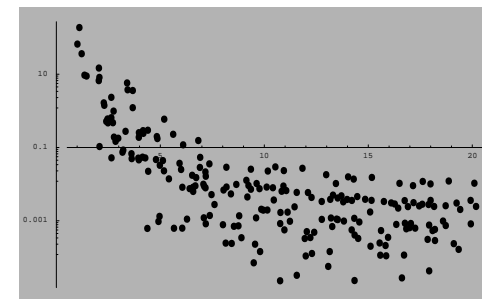
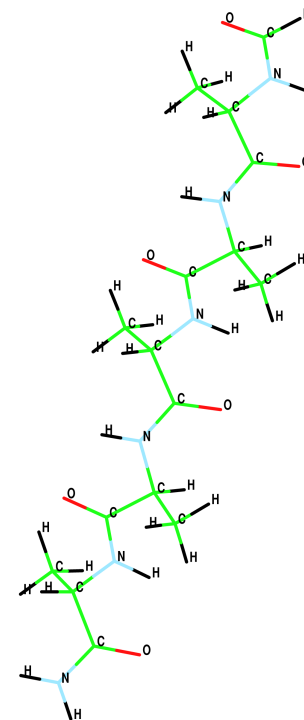
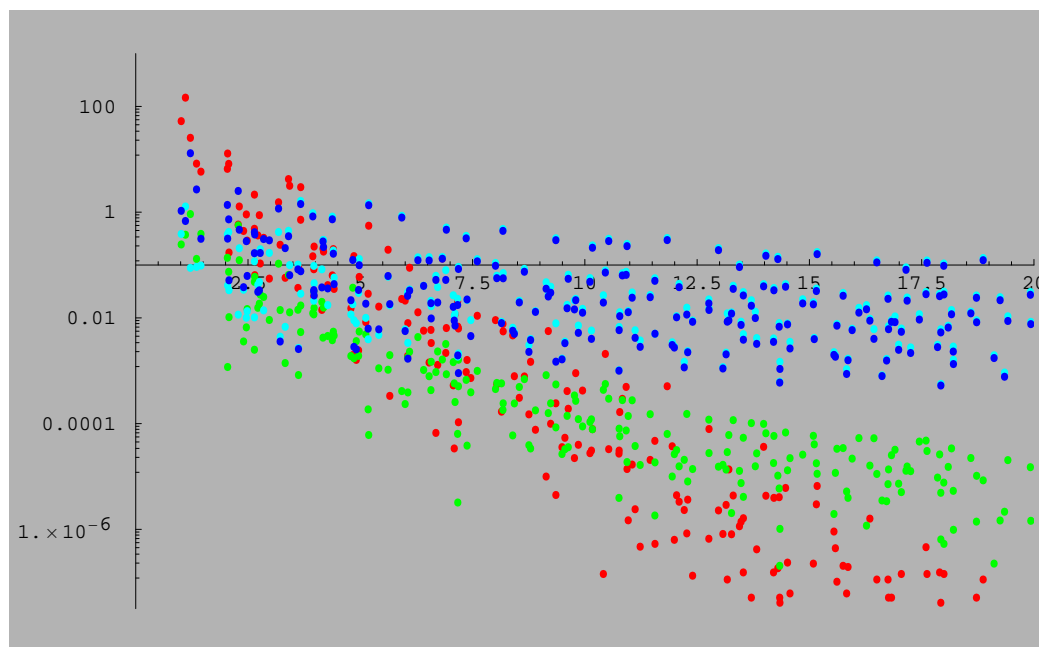
Valinomycin spin-spin couplings  $|J| > 0.1$  Hz

- All observable couplings to carbon: CH, CO, CN, CC



## Hexapeptide

- The FC contribution does not always dominate.
- Below we have plotted, on a logarithmic scale, the different contributions to the spin-spin couplings involving the four top atoms in hexapeptide, at the BLYP/HII level.
- Total = FC + SD + DSO + PSO

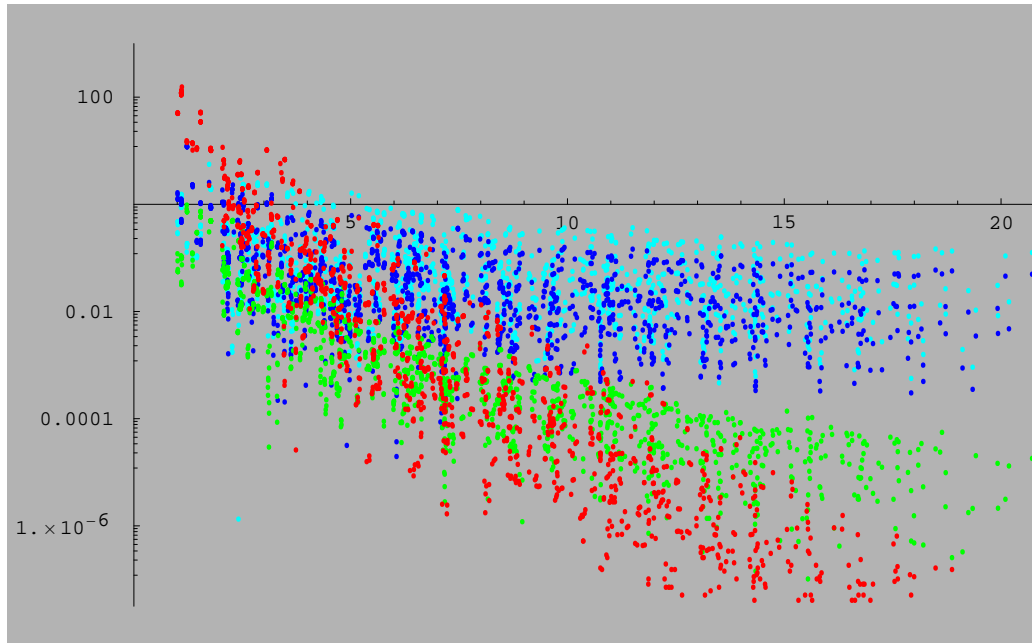


## Long-range behaviour of spin–spin couplings

- The different contributions to the spin–spin couplings decay differently.
- Placing the origin at center of the product Gaussian  $G_a G_b$ , we obtain

$$\begin{aligned} \langle G_a | h_P^{\text{FC}} | G_b \rangle &\propto \exp(-\mu R_P^2), & \langle G_a | h_P^{\text{SD}} | G_b \rangle &\propto R_P^{-3} \\ \langle G_a | h_{PQ}^{\text{DSO}} | G_b \rangle &\propto R_P^{-2} R_Q^{-2} & \langle G_a | h_P^{\text{PSO}} | G_b \rangle &\propto R_P^{-2} \end{aligned}$$

- Placing the origin at one of the nuclei in Ramsey's expression, we find that



- FC decays exponentially
- SD decays as  $R_{PQ}^{-3}$
- DSO decays as  $R_{PQ}^{-2}$
- PSO decays as  $R_{PQ}^{-2}$

- Overall, the indirect nuclear spin–spin coupling constants decay at least as  $R_{PQ}^{-3}$ .



## Cancellation of DSO and PSO at large distances

- Separately, DSO and PSO decay as:

$$\mathbf{J}_{PQ}^{\text{DSO}} \approx -\mathbf{J}_{PQ}^{\text{PSO}} \propto R_{PQ}^{-2}$$

- However, the total SO decays faster:

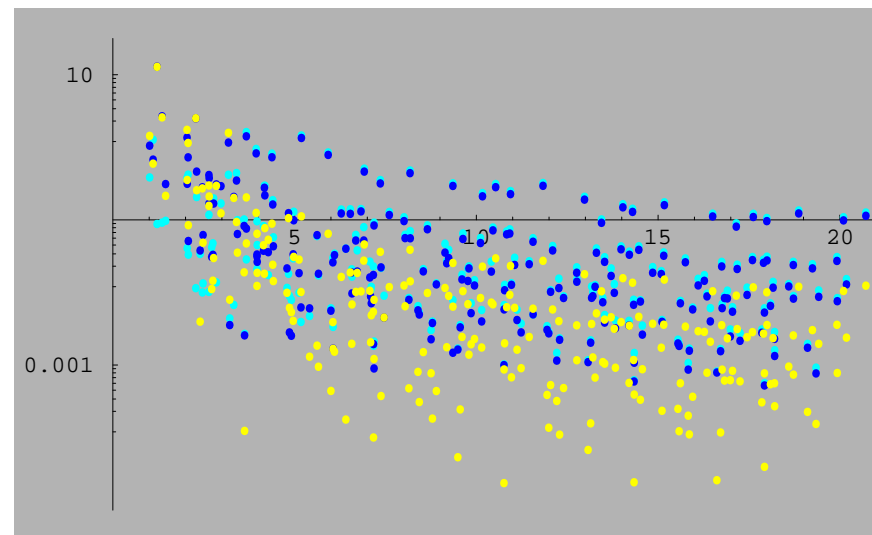
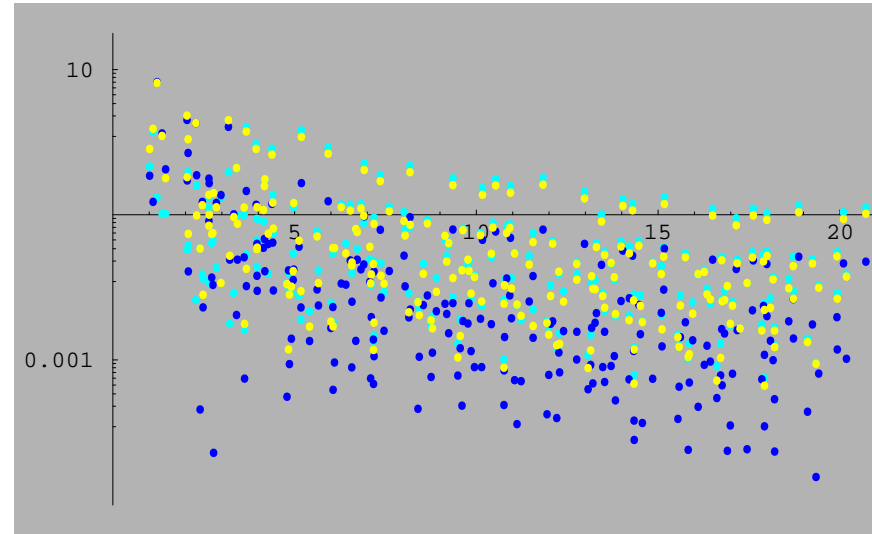
$$\mathbf{J}_{PQ}^{\text{DSO}} + \mathbf{J}_{PQ}^{\text{PSO}} \propto R_{PQ}^{-3}$$

- To the right, we have plotted

$$\text{SO} = \text{DSO} + \text{PSO}$$

for hexapeptide at the LDA/STO-3G and LDA/HII levels of theory.

- Near cancellation of DSO and PSO is only observed in large basis sets.



## Conclusions

- The calculation of spin–spin coupling constants is a challenging task, requiring the solution of 9 or 10 linear equations for each magnetic nucleus.
- The calculation of spin-spin constants can be carried out a variety of levels of theory:
  - wave-function theory: RHF, CASSCF, RASSCF, SOPPA, CCSD
  - density-functional theory: LDA, GGA, hybrid DFT
- Because of triplet-instability problems, the RHF model is unsuitable for spin–spin calculations.
- The most accurate results are provided by the correlated wave-function methods, although these are mostly restricted to rather small systems.
- Whereas LDA provide results of low accuracy, BLYP and in particular B3LYP provide results of almost the same quality as RASSCF, SOPPA, and CCSD.
  - current functionals have difficulties with highly electronegative elements
  - on the other hand, they work very well for hydrocarbons
- DFT can be applied to large systems, using linear-scaling techniques, opening up the possibility of studying couplings in molecules of biological interest.
  - for small internuclear separations, the couplings are dominated by the FC interaction
  - for large separations, DSO and PSO almost cancel but dominate the couplings