Questions to the Audience

Moderated by S. Van Doorslaer

In the second edition of "Your Question to the Audience", two questions were addressed.

The first was raised by Fred Hagen (TUDelft):

How do we deal with symmetry in the spin Hamiltonian of systems that strictly speaking have no symmetry at all (for example metal sites in proteins)?

Fred first introduces the problem: when studying paramagnetic centers in powders or frozen solutions, we classify them as "isotropic", "axial" or "rhombic". However, according to point-group symmetry, there are way more possibilities. The point-group symmetry of a paramagnetic defect determines the number of free spin-Hamiltonian parameters. Many transition metal centers (metalloproteins, e.g.) have "no symmetry at all" (C₁ symmetry), so have a lot of free spin-Hamiltonian parameters. Powder EPR do not provide sufficient information to make unique spin-Hamiltonian analyses in such case. When a good fit to the data is found, how can you be sure that it is physically correct?

A distinction was further made between low-spin (S=1/2) centers with hyperfine interactions and high-spin (S>3/2) where higher order zero-field splitting comes into play.

From the discussion that followed it was clear that the problem of hyperfine interactions, although often overlooked, is the easier one. It can be solved by measuring spectra at several microwave frequencies and/or field-dependent pulsed EPR (ESEEM/HYSCORE) or ENDOR spectra.

The case of high-spin centers with large zero-field splitting is more problematic. For highspin Fe³⁺ (S=5/2) the fourth order zero-field splitting terms are most often ignored but including them sometimes leads to considerably better agreement with experiment and drastic changes in D and E/D parameters (examples given by Fred). This raises the question how reliable published spin-Hamiltonian parameters for these centers are.

At sufficiently high frequency, when zero-field splitting can be considered as a perturbation on the Zeeman Hamiltonian, higher order zero-field splitting does reveal itself to some extent and a limited number of parameters can be extracted from powder EPR spectra. So again, recording spectra at several frequencies, and here preferably high frequencies, presents a solution.

Moreover, unlike the second-order zero-field splitting parameters D and E, which are 0 for "isotropic" centers and can have a very wide range of magnitudes, the fourth (and sixth, for f-block ions) also appear in octahedral, tetrahedral and 8-coordinated cubic ligand fields. So they have an offset "order of magnitude", and should remain in this order of magnitude (determined by the nearest surroundings) even for lower symmetry complexes. This certainly holds true for lanthanide and actinide ion complexes. It should also allow to judge whether fitting results including higher order zero-field splitting parameters for transition metal complexes are realistic. This may require a profound literature review of reliable data (perhaps best single crystal EPR data).

One may further wonder what the harm is in having an incorrect spin-Hamiltonian analysis for transition metal complexes by ignoring the higher-order zero-field splitting terms. If one does not intend to interpret the parameters in terms of detailed structural models, should one really care about the exact value of zero-field splitting parameters and whether all allowed terms are included? Probably the most important thing in spin-Hamiltonian parameter analysis is that later researchers encountering the same paramagnetic species recognize it as the same, based on spectrum simulations. This should be valid for any microwave frequency, and that is where problems can arise if certain terms have been omitted because insufficient experimental data were available at the time. Another danger is that features in spectra that are only reproduced when higher-order zero-field splitting is included, could be interpreted as additional centers (distorted sites). Furthermore, it is important to examine whether different spin-Hamiltonian analyses of the same EPR spectrum would lead to different assessments of concentrations of the paramagnetic species.

The problem of low symmetry for high-spin paramagnetic centers is definitely something that deserves further attention.

The second question was initiated by Peter Leon Hagedoorn:

"What will the AI future mean for EPR? For example https://ai4epr.com/ and other tools for interpretation of EPR spectra, will they be useful?"

Connected to this question (Henk Vrielinck):

"Should we actively support the development of AI for EPR and make our "raw EPR data" publicly available (as training sets)? How/where? Under what format?"

This issue was eventually not really touched upon.

And further also connected, a question from Sabine Van Doorslaer;

"How will EPR of the future look like?"

Bernard Gallez, who could not attend the meeting, asked the last question to ChatGPT, and got the following results

" 1. Biomedical Applications and Clinical Diagnostics:

- 1. **In vivo EPR Imaging**: Developing non-invasive EPR imaging techniques to monitor oxidative stress, inflammation, and tissue oxygenation in real-time in living organisms. This can be pivotal for diagnosing and understanding diseases like cancer, cardiovascular diseases, and neurodegenerative disorders.
- 2. **EPR-based Biosensors**: Creating highly sensitive and specific EPR biosensors for detecting biomarkers and metabolites in biological samples, which could revolutionize early disease detection and monitoring.

2. Materials Science and Nanotechnology:

1. **Characterization of Nanomaterials**: Utilizing EPR to investigate the electronic and magnetic properties of nanomaterials, including quantum dots, nanowires, and graphene. Understanding these properties at the nanoscale can lead to advancements in electronic devices, sensors, and catalysts.

2. **Defects in Advanced Materials**: Studying defects and impurities in advanced materials such as semiconductors, superconductors, and novel magnetic materials. EPR can provide insights into the role of these defects in material performance and stability.

3. Catalysis and Environmental Science:

- 1. **Catalytic Mechanisms**: Applying EPR to elucidate the mechanisms of catalytic reactions, particularly those involving transition metal complexes and radical intermediates. This knowledge can improve catalyst design for industrial processes and green chemistry.
- 2. **Environmental Monitoring**: Developing EPR techniques to detect and quantify environmental pollutants, such as free radicals and transition metal ions in air, water, and soil. EPR can help assess the impact of pollutants on ecosystems and human health.

3. Quantum Computing and Information Science:

- 1. **Quantum Bits (Qubits) and Coherence**: Investigating EPR-active spin systems as potential qubits for quantum computing. EPR can help understand spin coherence and relaxation times, which are crucial for developing stable and efficient qubits.
- 2. **Spintronics**: Exploring spin-based electronics where EPR can characterize spin states and dynamics. This can lead to advances in data storage, transfer, and processing technologies.

4. Methodological and Technological Advancements:

- 1. **High-Resolution EPR**: Developing next-generation EPR spectrometers with higher sensitivity and resolution, including advancements in pulsed EPR and high-frequency EPR techniques. This can expand the range of detectable systems and improve the accuracy of measurements.
- 2. Integration with Other Techniques: Combining EPR with complementary techniques like NMR, X-ray crystallography, and cryo-electron microscopy to provide a more comprehensive understanding of complex biological and material systems. This integrated approach can yield deeper insights into structural and dynamic properties.

These themes represent some of the cutting-edge directions where EPR can make significant contributions to science and technology in the coming years."

The conclusion from this answer is that what ChatGPT sees as future themes are current or already past themes in EPR spectroscopy. This does not mean, though, that AI cannot play a role in finding new directions in EPR research and designing new projects/project proposals. This is already happening at this moment, as well as in the writing of papers.

As for simulating and interpreting spectra with AI, the idea in the audience is that complete EPR spectrum analysis in the most general case is not possible yet at this moment. However, for certain classes of spectra, e.g. for radical adducts to spin traps, it can work already now and be helpful.