Ab-initio prediction of cw-EPR spectra of organic radicals in (any?) kind of matrix

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Virtual Italian Laboratory for Large-scale Applications in a Geographically distributed Environment (VILLAGE)
Molecular dynamics & reactivity

- Molecular motions time-scales encompass
  - global dynamics (ms),
  - domains dynamics (ns),
  - localized fluctuations (ps and fs).

- Molecular properties depend on the synergetic action of different motions at several time and length scales.

Information on molecular multiscale dynamics can be gained DIRECTLY from CW-ESR, ELDOR, ENDOR etc.
Quantum Mechanical calculation pursued by Density Functional Theory (DFT) via adoption of mixed quantum-mechanical / molecular mechanical (QM/MM) methods

Molecular Geometry

Interpretation based on Stochastic Liouville Equation (SLE) defined by the direct inclusion of motional dynamics via stochastic operators plus super Hamiltonian $H$

Spectrum

Diffusion Tensor

In double labeled systems, determination of dipolar interaction based on the molecular structures beyond the point approximation

Dipole-Dipole Tensor

Dissipative parameters, e.g. rotational diffusion tensors, can be determined via hydrodynamic modelling
Stochastic Liouville Equation

\[
\frac{\partial \rho(Q,t)}{\partial t} = -i \left[ \hat{H}(Q), \rho(Q,t) \right] - \hat{\Gamma}(q) \rho(Q,t) = -\hat{L} \rho(Q,t)
\]

The ESR line is proportional to the spectral density, the real part of the Fourier – Laplace transform of the correlation function of the physical observable

\[
I(\omega - \omega_0) = \frac{1}{\pi} \Re \left\{ \left\langle v \left[ i(\omega - \omega_0)1 + \left( \hat{\Gamma} + i\hat{H}^\times \right) \right]^{-1} \left| v \right\rangle \right\}
\]

\[
\left| v \right\rangle = \left[ I \right]^{-1/2} \left| \hat{S}_X \otimes 1_I \otimes P_{eq}^{1/2} \right\rangle
\]

The calculation of the ESR spectrum is reduced to the solution of a set of coupled linear equations by spanning the stochastic Liouville operator on a set of basis functions

\[
I(\omega - \omega_0) = \frac{1}{\pi} \Re \left\{ \mathbf{v}^\dagger \mathbf{A}(\Delta \omega) \mathbf{v} \right\}
\]
Polar solvent increase $A_N$ through the relative stabilization of the “more polar” resonance structure.

<table>
<thead>
<tr>
<th></th>
<th>Exp</th>
<th>TEMPO</th>
<th>TEMPO+1S</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Gas-phase</td>
<td>Solution</td>
</tr>
<tr>
<td>Benzylic Alcohol</td>
<td>15.91</td>
<td>14.94</td>
<td>15.12</td>
</tr>
<tr>
<td>(cyclohexane)</td>
<td></td>
<td>(cyclohexane $\varepsilon=2.0$)</td>
<td>(benzylic alcohol $\varepsilon=10$)</td>
</tr>
<tr>
<td>Phenol</td>
<td>16.58</td>
<td>14.94</td>
<td>15.16</td>
</tr>
<tr>
<td>(toluene)</td>
<td></td>
<td>(toluene $\varepsilon=2.4$)</td>
<td>(phenol $\varepsilon=13$)</td>
</tr>
</tbody>
</table>
Constrained and unconstrained forces and velocities can be related via geometric considerations to molecular geometry and solvent viscosity.

\[ \mathbf{D} = \begin{pmatrix} D_{TT} & D_{TR} & D_{TI} \\ D_{TR}^{tr} & D_{RR} & D_{RI}^{tr} \\ D_{TI}^{tr} & D_{RI}^{tr} & D_{II} \end{pmatrix} = k_B T \Xi^{-1} \]
Stochastic modeling of CW-ESR spectroscopy of [60]fulleropyrrolidine bisadducts with nitroxide probes in toluene

- Stochastic model: Brownian rotator (1B model)
- Geometry & shape: MM level calculation (Tinker)
- Diffusion tensor: hydrodynamic model (rigid spheres in fluid)
Interpretation of CW-ESR spectroscopy of \( p \)-(methyl thio) phenyl nitroxylnitroxide (MTPNN) in toluene

\[ \text{Stochastic model: Brownian rotator + conformational dynamics (2B model)} \]
\[ \text{Geometry & shape: QM level calculation in vacuo (Gaussian, DFT-B3LYP)} \]
\[ \text{Diffusion tensor: hydrodynamic model (rigid spheres in fluid)} \]
CW-ESR spectroscopy of Fmoc-(Aib-Aib-TOAC)$_2$-Aib-OMe in acetonitrile

The oligopeptide is labeled with two nitroxide radicals, in the form of $\alpha$-amino acid TOAC (2,2,6,6-tetrametyl-1oxyl-4amino-4-carboxylic acid)

Molecular structure of eptapeptide 1: Fmoc-(Aib-Aib-TOAC)$_2$-Aib-OMe

- Fmoc = fluoren-9-yloxy carbonyl
- Aib = $\alpha$-aminoisobutyric acid
- OMe = methoxy group.
Numerical solution of Stochastic Liouville Equation

\[ \hat{H} = \frac{\beta_e}{\hbar} \sum_i \vec{B}_0 \cdot \vec{g}_i \cdot \hat{\mathcal{S}}_i + \gamma_e \sum_i \hat{I}_i \cdot \vec{A}_i \cdot \hat{\mathcal{S}}_i - 2\gamma_e J \hat{\mathcal{S}}_1 \cdot \hat{\mathcal{S}}_2 + \hat{\mathcal{S}}_1 \cdot \vec{T} \cdot \hat{\mathcal{S}}_2 \]

\[ \hat{\Gamma} = D_x \hat{J}_x^2 + D_y \hat{J}_y^2 + D_z \hat{J}_z^2 \]

\[ G(\omega - \omega_0) = \frac{1}{\pi} \Re \left\{ \langle \nu | [i(\omega - \omega_0) + (i\hat{H}^x + \hat{\Gamma})]^{-1} | \nu_{eq} \rangle \right\} \]
Simulations of cw-ESR spectra of the peptide in four different solvents. Red solid line are experimental spectra, black dashed line are theoretical spectra.
CW-ESR spectroscopy of Tempo-Palmitate in 5CB

The tempo-palmitate (TP) spin probe is derivated from the TEMPO spin probe by the adjoint of a 15 carbons alkyl chain.

5CB is highly employed in liquid crystals displays. It forms a nematic phase under 35 °C. The graph on the left shows the temperature dependence of the order parameter.
Tempo- Palmitate: combined use of anisotropic PCM and hybrid methods

Selected $g$ and $A$ results at PBE1PBE/6-311+G(d,p) level.

<table>
<thead>
<tr>
<th></th>
<th>$g_{xx}$</th>
<th>$g_{yy}$</th>
<th>$g_{zz}$</th>
<th>$a_{xx}$</th>
<th>$a_{yy}$</th>
<th>$a_{zz}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>in vacuum: full TP</td>
<td>2.00870</td>
<td>2.00642</td>
<td>2.00380</td>
<td>-8.71</td>
<td>-8.43</td>
<td>17.14</td>
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<tr>
<td>in vacuum: model TP</td>
<td>2.00870</td>
<td>2.00642</td>
<td>2.00380</td>
<td>-8.71</td>
<td>-8.43</td>
<td>17.15</td>
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<tr>
<td>5CB: $\varepsilon_{</td>
<td></td>
<td>}$ along Z</td>
<td>2.00836</td>
<td>2.00635</td>
<td>2.00375</td>
<td>-9.19</td>
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<tr>
<td>6CB: $\varepsilon_{</td>
<td></td>
<td>}$ along Z</td>
<td>2.00839</td>
<td>2.00635</td>
<td>2.00375</td>
<td>-9.15</td>
</tr>
<tr>
<td>6CB: experimental</td>
<td>2.00978</td>
<td>2.00763</td>
<td>2.00273</td>
<td>-9.60</td>
<td>-9.50</td>
<td>19.10</td>
</tr>
</tbody>
</table>
\[ \hat{\Gamma} = -\left[ \frac{\hat{M}}{\partial / \partial \theta} \right]^+ \begin{bmatrix} D_{RR} & D_{RI} \\ D_{IR} & D_{II} \end{bmatrix} P_{eq}(\Omega, \theta) \left[ \frac{\hat{M}}{\partial / \partial \theta} \right] P_{eq}^{-1}(\Omega, \theta) \]

\[ P_{eq}(\Omega, \theta) \propto \exp\left[ -V(\Omega, \theta) / k_B T \right] \]

\[ V(\Omega, \theta) \approx V(\Omega) + V(\theta) \]
Experimental (red solid line) and theoretical (black dashed line) cw-ESR spectra of tempo-palmitate in 5CB in the temperature range 316.09 K (isotropic phase) to 299.02 K (nematic phase)
E-SpiReS
Network

Università degli Studi di Padova (1)
Modeling & software development
• Antonino Polimeno
• Mirco Zerbetto
• Silvia Carlotto

Università “Federico II” di Napoli
QM / MM software development (Gaussian)
• Vincenzo Barone
• Paola Cimino
• Orlando Crescenzi

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CW-ESR, ENDOR experiments
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• M. Brustolon
• Lorenzo Franco
• Alfonso Zoleo

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Multi-frequency CW-ESR and 2D-ELDOR
• Jack H. Freed
• ACERT staff

Synthesis: C. Toniolo, M. Maggini (Padova U)