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Interactive comment on "Paramagpy: Software for Fitting Magnetic Susceptibility Tensors Using Paramagnetic Effects Measured in NMR Spectra" *by* Henry William Orton et al.

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We much appreciate the reviewer taking the time to test our software and are glad to hear that it performed stably. We have modified the manuscript, taking into account all the referee's suggestions. Below are our detailed responses in plain type underneath the original comments in bold type.

They claim, as the biggest advantage of this software with respect to the previous ones, that Paramagpy can use CCR effects to improve the calculation. In Fig. 4 they show one example where they compare the results taking and not taking into account CCR effects but only the correlation plot is presented without any

statistical analysis. As the effect seems to be important I think that a statistical analysis of the improvement offered by this new approach should be presented with some examples, which they already have. For example, just showing the Pearson correlation coefficients (R) or Q-factors with and without CCR.

In the revised version of the manuscript, the magnitudes of Curie-spin/CSA cross-correlated relaxation effects and the anisotropic contributions to PREs are illustrated in a correlation plot that includes error bars. Q-factors are given too. See Figure 1 attached to the final page, which now has the following caption:

Paramagpy GUI showing R_1(^{15}N) PRE data for calbindin D_{9k} loaded with Tb^{3+}. The correlation plot shows calculated vs. experimental values. Blue: SBM and isotropic Curie-spin theory are used for calculating PREs (Q-factor 1.01). Red: Taking into account also the cross-correlation between Curie spin and CSA relaxation (Q-factor 0.49). Green: Including the additional correction arising from the anisotropy of the χ tensor (Q-factor 0.47).

In addition they could explain in which cases the consideration of cross-correlated relaxation can have a strongest effect on the tensor prediction.

The main text now includes a description of when these effects are expected to be of significance to the experimentalist (see text below in blue).

The CSA tensors of ^{15}N spins are much larger than those of ^{1}H spins, so that Curie-spin/CSA cross-correlation effects can dominate the PRE to the point that even negative PREs can be observed ((Orton 2016) Figure 4). These CCR effects are predicted to be most pronounced for ^{15}N spins located about 10 Å from the metal ion. In contrast, the CSA of ^{1}H spins is much smaller, so that their CCR effects are predicted to be most significant in the range of 20-25 Å and therefore too small to be easily observed experimentally (Pintacuda 2004a).

They also say that the software includes some additional options for PCS and

PRE calculations not offered by PyParaTools, the other program that can integrate PCS, RDC and PRE effects in the calculations. It would be nice if they specify which are these options.

The introduction of the main text now includes a description of the additional features of PCS and PRE calculations that Paramagpy offers over PyParaTools which will replace the paragraph at line 12 page 2 of the original submission. The text we propose for the revised version is shown below:

NMR spectra of biomolecules labelled with paramagnetic metal ions with fast electronic relaxation rates, as afforded by lanthanide tags, simultaneously display PCS, RDC, PRE and CCR effects in the same spectrum (Pintacuda 2004b). Due to their common origin in the paramagnetism of the metal ion, all these effects are interrelated. For example, the $\Delta\chi$-tensor determined from PCS measurements can, in principle, be used to predict RDCs, and RDCs arising from paramagnetic alignment allow predictions of some of the $\Delta\chi$-tensor parameters. The software PyParaTools offers convenient integration of all of these effects, but it lacks many refinements, such as the computation of RACS effects which may affect PCS measurements (John 2005), explicit routines for calculating PREs based on Solomon-Bloembergen-Morgan or Curie-spin relaxation theory including anisotropic effects arising from non-vanishing $\Delta\chi$-tensors, calculation of cross-correlated Curie-spin/CSA PRE effects or Curie-spin/dipole-dipole CCR involving anisotropic $\Delta\chi$-tensors, or anisotropic SBM (Suturina 2018) calculations.

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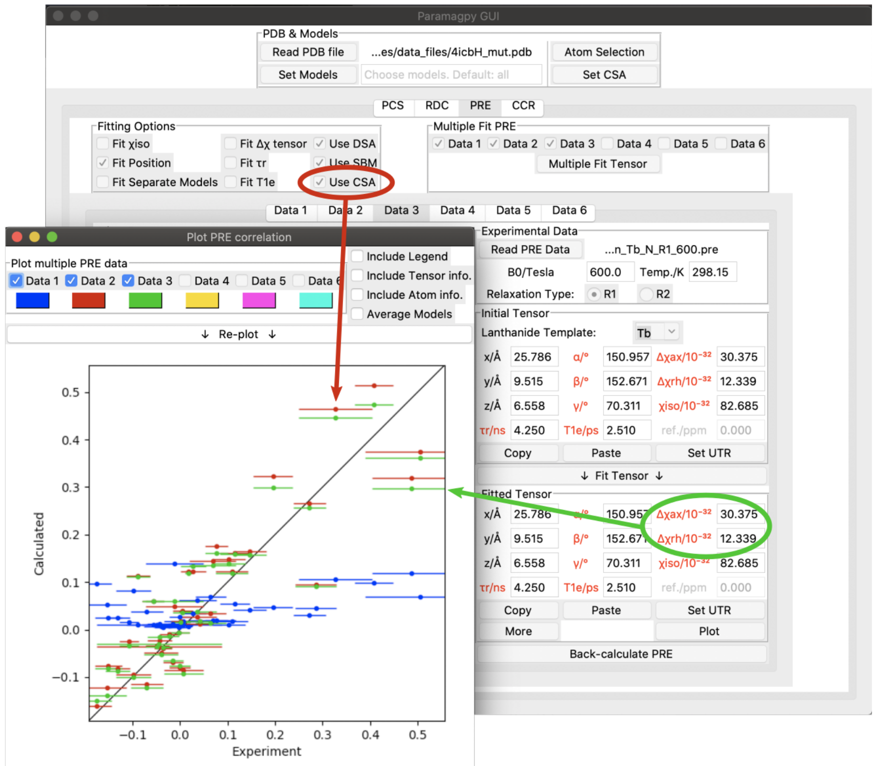

Fig. 1. Revised figure 4 for manuscript