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Magn. Reson. Discuss., referee comment RC1
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Comment on mr-2021-42

Anonymous Referee #1

Referee comment on "On the modeling of amplitude-sensitive electron spin resonance (ESR) detection using voltage-controlled oscillator (VCO)-based ESR-on-a-chip detectors" by Anh Chu et al., Magn. Reson. Discuss., https://doi.org/10.5194/mr-2021-42-RC1, 2021

General comments: The authors present a variation on a theme for their VCO-based ESR detection systems, switching from oscillator-frequency to amplitude-based detection of the ESR signal. The manuscript is not written for the general practitioner of EPR spectroscopy; however, documenting and validating the authors' approach in specific sections with relevant equations and assumptions provides important transparency for specialized groups. It would be advisable to tone-down the emphasis on point-of-care EPR spectrometers unless the authors can point to specific medical tests (either FDA/EMA or CLIA assays) that use EPR spectroscopy for diagnostics and/or clinical decision-making. Although my expertise does not extend to review/evaluation of the mathematics and engineering aspects of the manuscript, the work is a meaningful contribution for those developing portable ESR spectrometer systems as the amplitude-detection mode simplifies the experimental setup and does not appear to deteriorate performance (but see notes below on the spin sensitivity calculations).

Specific comments:

Page 1, line 19: True, but I prefer the introduction to EPR presented in Schlecher et al. IEEE SENSORS JOURNAL, VOL. 19, NO. 20, OCTOBER 15, 2019 because it pitches EPR more positively. (EPR seems to be a shrinking community...)

Page 2, line 22: Additional recent references: Dayan et al. Rev. Sci. Instrum. 89, 124707 (2018); https://doi.org/10.1063/1.5063367; Abhyankar et al. Sci. Adv. 28 Oct 2020: Vol. 6, no. 44, eabb0620 https://doi.org/10.1126/sciadv.abb0620

Page 2, line 32: As far as I am aware, there are no EPR spectroscopy-based FDA/EMA approved tests for any diseases/conditions, making the need for such instrumentation extremely aspirational (and not based on documented need). Portable EPR spectrometers are likely most useful for point-of-production food analysis (beer, wine, olive oil) and

oil/gas analysis.

Page 3, line 64: To help those who do EPR spectroscopy, but who aren't EE's: I believe this description is how the "resonator dip" is displayed on commercial systems for tuning purposes. A voltage ramp is applied to a VCO to produce a "frequency window", the center of which is varied so the user can identify the resonator "dip".

Figure 3, page 10: This picture is also shown in https://ieeexplore.ieee.org/document/8310330. Some elements of the AM detection also are presented there: solid DPPH and solid TEMPOL on two different array coils (Figure 21.6.5, right side).

Page 12, line 281: "Since according to the simulation results of Fig. 5, the noise power spectral density around $\Delta\omega = 0$ is heavily plagued by 1/f-noise,…" Not being an EE, it was not clear to me how Figure 5 showed this problem.

Figure 7, page 14: The DPPH linewidth in Figure 7 is about 0.5 mT (5 G), which is a bit larger than I would expect for solid DPPH detected using conventional EPR spectroscopy (2 G, see Yalcin & Boero 2008). An assumption was made that only the imaginary part (absorption) of the magnetic susceptibility is important in this detection scheme (see text before equation 9). Can the authors explain why the linewidth for solid DPPH at room temperature here is broader than expected by more than a factor of 2?

Page 15, lines 295 & 296: The Yalcin & Boero 2008 reference lists N of 2×10^{27} spins/m^3 for DPPH in the caption of Figure 4 and again in the text. There is no reference to how it was calculated. It would be helpful to refer people to one of the original DPPH crystal structure papers (https://cdnsciencepub.com/doi/pdf/10.1139/v91-194 or https://link.springer.com/content/pdf/10.1007/BF01066204.pdf). Note that in these papers, the space group differs and therefore the #spins/volume varies by about 20 %.

Calculation of N_{min}: Using either 1 spin/4.84×10^{-13} pL or 1 spin/5.85×10^{-13} pL (see references cited above for these spin/unit cell volume values; 1 $Å^3 = 1 \times 10^{-15}$ pL) and a 23 pL volume the authors give for the DPPH sample size, the #spins in the sample volume is $(4.3 \pm 0.4) \times 10^{13}$. In eq. 21, assuming an optimal SNR of 3 (typical in analytical chemistry) cancels the 3 in the numerator, so that N_{min} becomes N_{spins}. Dividing 4×10^{13} by the 5 G linewidth measured here, gives 2×10^{12} spins/G sqrt(Hz). Using eq. 11 in Yalcin & Boero 2008, $N_{min} = (1/SNR)(N_{spins} * V_{sample}/\mathrm{sqrt}(f_{BW}))$ gives 1.4×10^{13} spins/sqrt Hz. Dividing that by 5 G, gives approximately 3×10^{12} spins/G sqrt Hz. These two values are very close to one another. From Figure 7, the signal intensity is 1.2 mV and the baseline noise (estimated) is 0.02 mV, which gives an SNR of 60; using that SNR gives an N_{min} of 1.4×10^{11} spins/G sqrt Hz. *My question: how did the authors arrive at $N_{min} = 2 \times 10^{10}$ spins/G sqrt Hz using equation 21?*

Page 15, lines 313-314: Looking at Figure 9, I guesstimated that the linewidth is about 5 mV. Using the VCO gain 0.8 GHz/V and 28 GHz/T gives 1.4 G for the DPPH linewidth in Figure 9, which is closer to the typical 2 G linewidth for DPPH.

Page 16, line 335: Is there a documented need for portable EPR spectrometers for personalized medicine? This claim appears to be strongly investigator-driven and not market-driven.

Technical Corrections: Generally, the written English is excellent. There are few suggestions/corrections below.

Page 2, line 54: sweeping" and "static" are a bit counter to one another. The field is not swept through its resonance (implied with the current wording); it is swept to achieve resonance with the energy splittings in the sample. Although I understand what is meant, perhaps making it two sentences would be useful. "An ESR experiment...reflected power. The externally-applied magnetic field B_0 is swept through the resonance condition where the sample's energy level splittings match the applied frequency.

Page 4, line 75: This sentence, as written, implies that the "very simple experimental setup" is from Handwerker et al. Perhaps revise as follows? "This hardware change simplifies the experimental setup compared to the frequency-sensitive detection described by Handwerker et al. (2016). In that report, the VCO output signal first had to be processed by a chain of frequency dividers to allow for simplified analog-to-digital conversion and subsequent frequency demodulation by a digital phase-locked loop. Fig. 1b shows that such additional elements are not required in the current implementation."

Page 7, line 170: Reference needs parentheses to enclose it.

Page 11, line 247: “defining” should be “to define”

Page 11, line 250: “there is an excellent agreement” should be “there is excellent agreement”

Page 15, line 343: “where” should be “were”