Validate your CEST simulation!

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Introduction:

CEST MRI provides a contrast sensitive to exchange processes between solute and water protons, which provides new contrasts for clinical MRI. Recently, quantitative CEST approaches, providing access to the exchange rate and solute concentrations, are gaining interest. This includes Bloch-McConnell fits (1,2), ratiometric approaches (3,4) or CEST MR fingerprinting (5). All of them have in common that, for a limited number of proton pools, the effects can be described quantitatively by Bloch-McConnell simulations. If these simulations differ between groups, the quantitative results will differ as well.

We initiated a simple platform to compare and ultimately validate Bloch-McConnell simulations of different CEST research groups. In this work, we present the first preliminary results of our comparison for four cases with different well-defined continuous-wave saturation schemes and pool models. Our comparison already showed significant differences for a 5 pool WM system including semisolid MT.

Methods:

Until now, 8 groups participated in the Bloch-McConnell simulation comparison. General simulation settings are provided on a public GitHub repository (6), and simulation results are collected in an open google docs sheet to keep participation as simple as possible.

The general settings/assumptions were: a fully relaxed initial magnetization (Zi = 1) for every offset, a post-preparation delay of 6.5 ms representing a typical gradient spoiler duration, a gyromagnetic ratio of exactly 42.5764 MHz/T, a field strength of 3T and thus a Larmor frequency of exactly 127.7292 MHz/T, and a preceding fully-relaxed normalization scan at -300 ppm

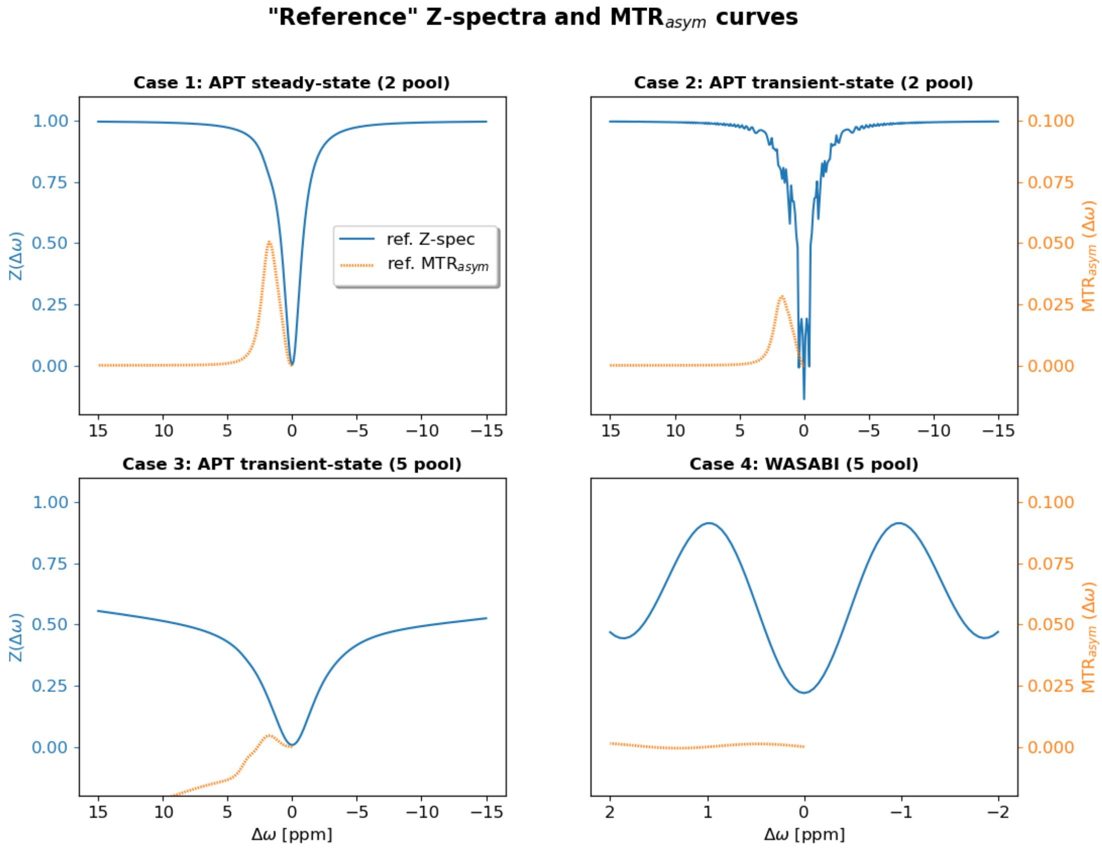
The four simulation cases were chosen as follows:

- Case 1: APTw steady-state (2µT, 15s cw) in a 2 pool model
- Case 2: APTw transient-state (2µT, 2s cw (7)) in a 2 pool model
- Case 3: APTw transient-state (2µT, 2s cw (7)) in a 5 pool model
- Case 4: WASABI (3.7µT, 5ms cw (8)) in a 5 pool model

The 2 pool model consist of a water pool and a single CEST pool. The 5 pool model consists of 1 water, 1 symmetric MTC, 2 CEST and 1 NOE pool. Exact definitions are provided on the GitHub repository. For this abstract, the Pulseq-CEST simulation (9) results are used as a “reference”. However, in general they are explicitly not considered to be the ground truth!

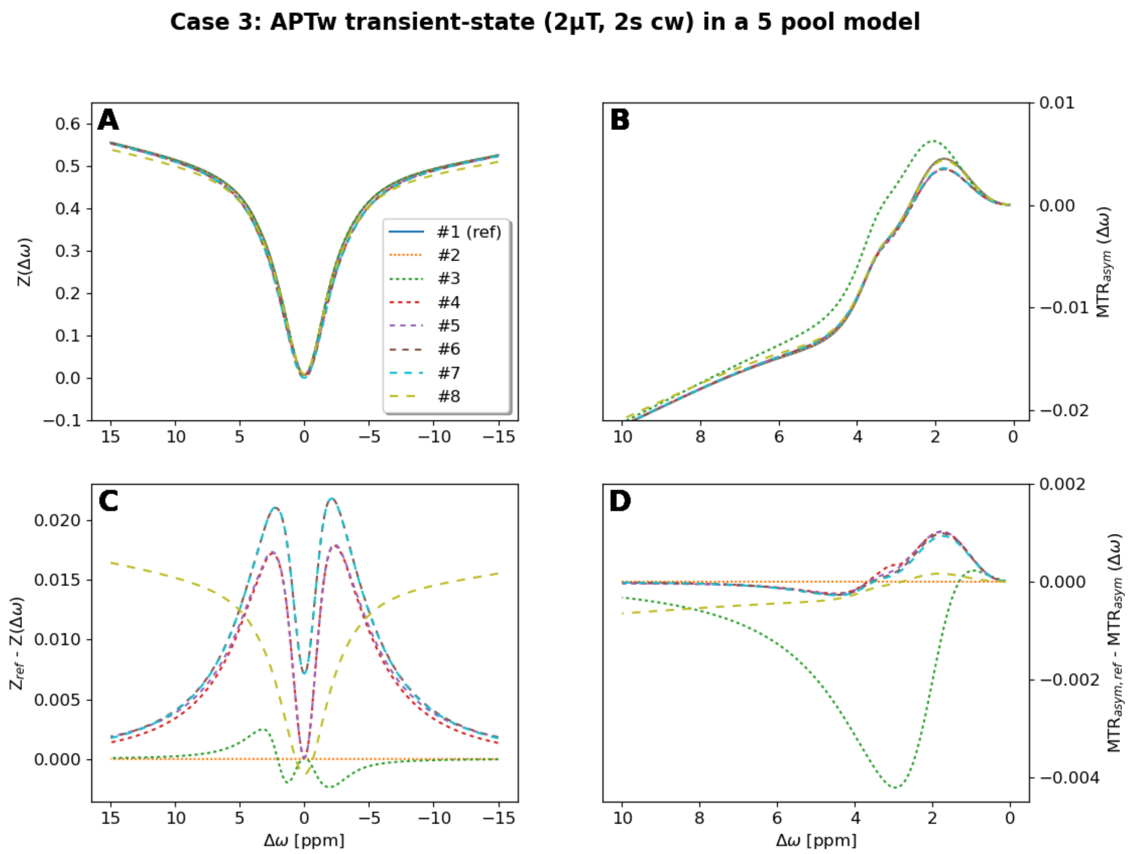
Results:

The “reference” z-spectra and corresponding MTRasym curves for all four cases are shown in figure 1.



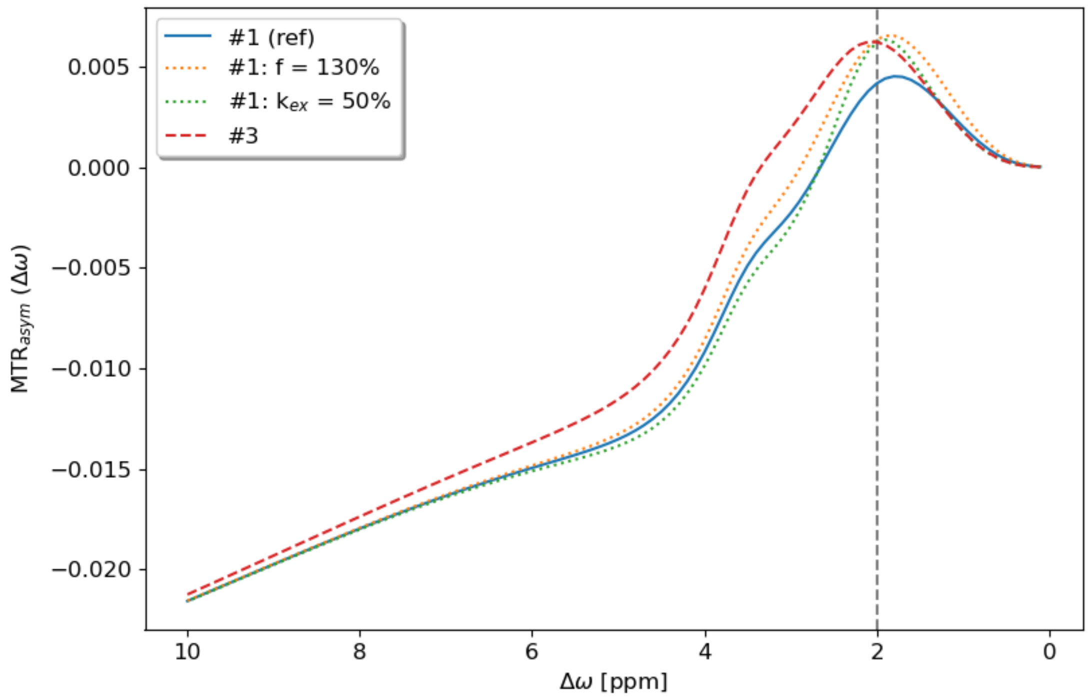
The 2 pool simulations (case 1 and 2) of all groups were in good agreement. Largest deviations in Z-spectra were in the order of 2‰ and are thus not further analyzed or shown here. Larger differences were observed for the 5 pool simulations (cases 3 and 4). For case 3, the Z-spectra of all participating groups are depicted in figure 2A and corresponding MTRasym curves in figure 2B. Figure 2C and 2D show the differences with regard to the Pulseq-CEST simulation.

Interestingly, 5 different results/clusters with essential differences are visible in the Z-spectrum difference plot (Fig. 2C), but due to some symmetric differences only five clusters in the MTRasym curves. With respect to the “reference” MTRasym, the difference range between roughly -20% to +50%, which is surprisingly high. Fitting the same data with different models could therefore generate significant different CEST exchange and concentration parameters.



Discussion

Between the participating groups, we observed differences in both, Z-spectra and MTRasym curves. For case 3, 5 different results out of 8 submitted simulations were observed. The origin of these differences was not yet identified at the time of submission. However, they are a clear indication that previously reported differences in quantitative parameters (5) could originate from differences in utilized simulations. For example, to achieve comparable MTRasym values at 2 ppm between groups #1 and #3, an increase of roughly 30% in the CEST pool size fraction or a 50% decrease of the exchange rate would be necessary (Fig. 3).



Most plausible explanations for the larger deviations in cases 3 and 4 are differences regarding the definition of the MT pool. In particular, the definition of pool size fractions, or the use of x-y-z or only z-components for MT magnetization. However, this cannot be the only reason, because some results match well despite varying simulated MT components.

Furthermore, although the observed deviations for cases 1 and 2 are in the order of 1e-4 and thus comparatively small, they are still several orders of magnitude larger than typical rounding errors. This is a clear indication that the compared simulations must differ in more than just the MT definition.

This project is still open for participation and several discussions about the observed differences are planned. We hope for keen participation and to find the source of differences. The final goal is to realize a consensus on CEST simulationsto and provide a reference that can be used by all groups to validate their CEST simulations.

Conclusion:

Although simple continuous-wave cases were investigated, apparent deviations between participating groups have been observed, leading to large difference in quantifiable parameters. We invite everybody to join and validate their own CEST simulations and plan to generate a solid basis for future quantitative CEST approaches. In upcoming challenges, more sophisticated cases will be included to get better understanding of differences in implementations.

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