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Comment on mr-2021-58

Anonymous Referee #2

Referee comment on "Rapid assessment of Watson–Crick to Hoogsteen exchange in unlabeled DNA duplexes using high-power SELOPE imino ^{1}H CEST" by Bei Liu et al., Magn. Reson. Discuss., https://doi.org/10.5194/mr-2021-58-RC2, 2021

The article entitled « Rapid measurement of Watson-Crick to Hoogsteen exchange in unlabeled DNA duplexes using high-power SELOPE amino 1H CEST « submitted by Liu et al. is an important contribution to the study of Watson-Crick - Hoogsteen exchange occurring in DNA duplexes. The main achievement of the study is the application of a recently found new pulse sequence SELOPE (Schlagniweit et al., 2018) by the group of K.Petzold to DNA duplexes and WC-HG equilibrium. The work is also of a methodological nature with a systematic study of the possible artifacts related to the ^{1}H-^{1}H cross-correlation in the study of systems in equilibrium exchange. There is really a huge wealth of data that are very convincing and that support the main message of the work that is the interest of the application of SELOPE sequence to unlabelled DNA duplexes permitting to obtain large quantity of data about HG-WC equilibrium at a lower cost and with improved efficiency, additionally the method permits to characterize HG-WC equilibrium with a lower HG population and faster kinetics that it was possible using the previously used R1ρ Relaxation dispersion ^{13}C/^{15}N methodology. The method, because it permit to obtain rather easily a lot of data on many DNA base pairs, is well adapted to the study of WC-HG equilibria whose the dependence from sequence is quite complex.

We have just some comments about specific points

Legend of Figure 1 the delay d1 is not explicitly defined

To be clearer , we suggest to make mention earlier in the text that the minor shoulder stated in l 297-298 is indicated with the black line ES in the figure 3B

There is no comments on the large variations observed in rχ^2 in figure 4 (and also Fig S2,

S3) by example why so large variations between U9H3 (498-476) and U5H3 (7.2-6.9) with or without exchange while the experimental data shown with the fit appear similar, additionally for proton T9-H3 or G10H1 while a very significant reduction in reduced $r\chi^2$ is observed when considering or not the existence of WC-HG exchange, justifying clearly the existence of exchange processes for these protons, the reduced $r\chi^2$ for the correct model (with exchange) remain rather elevated considering what is expected generally (Rangadurai et al. Prog. In Nuclear Magn .Res., 2019). If this results from a peculiar definition of the reduced chideux, the error bars or any other reason is not clear and needs some explanations.

Lines 374 not clear -6ppm is repeated