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Magn. Reson. Discuss., referee comment RC1
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Comment on mr-2020-38

Anonymous Referee #1

Referee comment on "Protein dynamics insights from 15N-1H HSQC" by Erik R. P. Zuiderweg, Magn. Reson. Discuss., https://doi.org/10.5194/mr-2020-38-RC1, 2021

The article tries, and fails, to correlate measured line widths with line widths calculated from crystal structures, assuming dipolar relaxation as the dominant relaxation mechanism.

The ultimate conclusion is that amides with narrower line widths than average are mobile, whereas amides with broader line widths reflect us – ms dynamics. This is not at all new and the conclusion in line 215 is trivial.

Using M = 3 in equation 1 is inappropriate for a sensitivity-enhanced HSQC, as magnetization is not transverse throughout all delays of the PEP scheme.

Equation 4 applies to indistinguishable spins. It does not apply to amide protons with distinguishable chemical shifts (see Bothner-By et al., JACS 106, 811 (1984)

or equations 79 and 89 in Abragam, Chapter VIII).

As admitted by the author, Figure 4 shows no correlation. Figure 6 doesn't show a significant correlation either, again as admitted by the author. This indicates failure of the entire concept. If coordinate precision is a major problem (line 222), the concept cannot be salvaged.

Line 167: The line width of the amide proton of Asp3 could very well be due to enhanced H-exchange, as the N-terminus is positively charged and the exchange base-catalyzed.

Line 187: Much more is known about the dynamics in BPTI than suggested by the manuscript, see, e.g., Grey et al., JACS 125, 14324 (2003).

Line 225: water molecules on protein surfaces are not known to contribute to dipolar relaxation.

Line 235: detailed dynamical data have been obtained for large proteins from methyl relaxation.

Line 280: independent movement of a domain relative to the rest of the protein produces narrower lines. This is not novel: there are countless examples, such as calmodulin, trigger factor etc.

Figure 3 does not specify the acquisition times used in the spectrum - too short acquisition times would cause artificial line broadening to a variable degree for amide protons with different intrinsic line width.

Legend of Fig. 1: EM and cosine not explained

Line 57: equal to what?

Line 94: us is not a unit.

Line 155: what is meant by flattered comparison?

Line 269: what is meant by ATP conformation?

In the opinion of this reviewer, the manuscript falls far short of the criteria of Magnetic Resonance in terms of scientific impact (absence of a clear advance) or scientific quality (wrong equations used, data mostly not provided and, hence, the conclusions of the manuscript cannot be reproduced independently). It would be unexpected if it were to pass the review process of any NMR journal.