This paper describes the theoretical underpinnings and an experimental approach for obtaining insight into the dynamics of IDPs. Information of this sort is important as the experimental toolkit for IDPs is not as well established as for folded proteins. The authors suggest measuring a pair of cross correlated spin interactions, longitudinal and transverse, from which a factor of Q is calculated. Simulations are provided to establish the information content of Q. The paper is more a description of a conceptual idea – the authors state that pulse sequences for Ca-C' dipolar, C' CSA cross-correlation measurements are still in progress and they don’t present experimental data. Therefore, it is difficult for this reviewer to evaluate the utility of the proposed method/idea. For example, in the case of an IDP where little residual structure is present and conformations are in rapid flux, and where diffusion anisotropy could well be present on a per-residue basis, will this method be able to detect this qualitatively? Will a per-residue “feel” (even qualitative) of the dynamics be attainable? Could the authors present some experimental data to try to answer these questions, or the general question of what insights we might be able to obtain practically.

Can the authors comment on whether interactions involving other 13C spins in a U-13C labeled IDP would be predicted to influence the extracted cross-correlation rates, especially in cases where rates are small.