The manuscript is well written and of good scientific quality. All experimental data is well presented and documented, and reproduction seems possible given the provided information. The content is of general interest to a broad magnetic resonance community and therefore suitable for publication in MR. Before publication, however, I ask the authors to comment on several specific points and perform minor revisions of the manuscript accordingly.
We thank the reviewer for the positive assessment of our work and for helpful suggestions on how to improve our manuscript. The point by point response to the reviewer's comments is below.

In line 40, the authors state that "modest gains have been detected for membrane proteins with ε=4-10 (Wylie et al., 2015)". This statement reads like a general observation, however, the referenced work covers a rather special case of membrane proteins labeled with single nitroxide tags which come into dipolar contact. In my experience, DNP enhancement of 40-60 can be routinely achieved for membrane proteins.
We have thoroughly revised the paragraph in question to more clearly delineate parallel discussions of DNP at high magnetic field and DNP in biological systems. We have added a wider range of enhancement factors, 20-100, that can be achieved at lower field based on an overview of available literature – these numbers can vary greatly depending on the precise details of the sample.

The following sentence ("Recently, large DNP signal...") is confusing. The first part deals with impregnated microcrystalline histidine, the second part is in no way generally applicable and seems to be specifically limited to the highest available field. Even in this regard, the sentence is misleading because it implies that no soluble polarizing agents are available for biological systems.
We agree that the original sentence was confusing and have revised it.

The authors use "build-up time, Tb" interchangeably for both the time constant as well as the experimentally chosen polarization time period (c/f lines 127, 129, 142, and Figure 2). These two different parameters have to be clearly distinguished by an unambiguous choice of symbol and naming.
We agree with the reviewer and have changed the notations for the time constant of polarization buildup and the experimentally chosen polarization transfer time period to T_B and the "recycle delay", respectively.

In Figure 2, it is not clear, which graphs the subpanels abc are referring to. Also, in the lower left graph, epsilon(-) seems to be missing a negative sign (-4).
We have revised the figure caption to clarify what the individual subpanels are referring to and added a negative sign to epsilon(i) to the bottom left panel.

When discussing the build-up dynamics in Figure 2, it should be clarified that SCREAM-DNP magnetization is emerging from the methyl groups and the spreading through the 13C network by spin diffusion. This explains the quick inversion of Ile resonances, and the delayed response of the other resonances.
Thank you for this suggestion; we have added this clarification to the discussion.

On the bottom of page 5, it is stated that "Heteronuclear decoupling has no effect...". I am wondering by what means turning off the decoupling is expected to effect a sign inversion? Heteronuclear decoupling is used when the 13C magnetization is already in the transverse plane, so it is unclear to me how this can influence the sign of polarization. For SCREAM-DNP 1H saturation during the build-up period mostly destroys the incoherent pathway, but this is independent from decoupling. This part should be revised, it should either be explained why decoupling may be expected to change the outcome of the experiment, or it should be clarified if indeed decoupling is mistaken for saturation
The intention here was to test whether, by simply decoupling H from C NMR spins, the heteronuclear cross-relaxation effect (SCREAM-DNP) can be suppressed. Clearly, it cannot, nor would we necessarily have expected it to be. We have therefore removed the reference to sign inversion but left the note about decoupling, since we feel it is nonetheless important to state that it has no effect on the SCREAM-DNP mechanism, consistent with predictions. The revised sentence is: "As expected, heteronuclear decoupling has no effect on these time dependencies, as shown in Figure 3a (bottom panel): turning the decoupling off only results in broadening of the signals."

In line 204, "with the with line..." seems to contain an additional "with"
We corrected this typo.