**General Comments**

Overall, this is a very interesting proposal to read. It seems well thought out and innovative. And its impact is potentially significant. Congrats! I hope you find my comments helpful.

1. Initial word count is 6540. Edited word count is 6376.

2. My approach was to first review the proposal without reading any reviewer comments to look at the structure, content and style and other generic aspects. I then looked at the reviewer comments. I will discuss these in Reviewer Comments.

3. I have altered some text to read as first person rather than second and third person as written. Over time, first person has become the trend in writing manuscripts and grants. One advantage of first person is that it clarifies what you are proposing versus to what is known in the literature. Grants are in reality a combination of first person and third person because third person is useful to describe methods and some other technical details. Plus, a grant written only in first person or only in third person can be tedious to read.

4. Throughout, I have tried to compact the writing for clarity and to provide space for new text. Please read carefully to ensure I have not altered any intent. For clarity, I also separated some compound sentences into single sentences and removed words or phrases that seemed redundant.

5. In the Intro, I highlighted in yellow all instances where you are actually proposing something. This seems a bit unusual for the organization of a proposal. For overall organization and clarity for reviewers, I relocated most of those statements to the end of paragraphs. This will make it more obvious what you are planning to do and what tools you will use.

6. The Preliminary Results is rather long and can feel cumbersome to read and absorb. I suggest adding in two to three subheadings to separate the sections. Please see my comments in the margins.

7. I suggest moving or restating parts of the Gaps in Research section to the end of the Preliminary Results as a transition to the Research Objectives. This will frame the questions being addressed in Research Objectives. Please note the comments at the appropriate lines.

8. Overall, as a friendly reviewer, I would ask what is being proposed that is new and warrants an additional two years of funding? Placing Preliminary Results prior to the Research Objectives led to some of my confusion. The grant results are presented followed by the proposal objectives. This tends to intermingle the objectives of the existing grant with the objectives of the new proposal. I suggest emphasizing at every opportunity that the hypotheses and proposed objectives are derived from the existing grant results. Thus, the objectives proposed are new (or mostly new), even if they are addressed using methodology you have begun to develop through the three years of grant funding. Furthermore, I suggest that your new hypotheses and objectives be derived from the results of the funded grant. To achieve these new goals you will require two years of additional funding. I suggested in the margins where such clarity may be helpful for reviewers. I think this strategy is important. If reviewers are not clear on what is new, they may conclude that you are proposing two more of years of funding for what was already funded for three, which seems unlikely to succeed.

9. **Important.** The proposal as written does not have a specific timeline for the proposed research. This seems critical because to the number of studies proposed. Additionally, a timeline will serve to again distinguish what you have done as part of the funded grant compared to what you are proposing.

