Review of: "Depolarization block of interneurons"

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Potential competing interests: No potential competing interests to declare.

The authors Tirozzi et al., provided a manuscript using mathematical model to demonstrate a depolarization block in hippocampal interneurons. The mechanism that the authors are presenting has important implications in considerations in research for conditions of aberrant network activity such as epilepsy. I do think the information in this manuscript will be of interest to the readers, upon revisions.

Major Revision:

1. There are numerous grammatical errors in this manuscript. Some of the contents and concepts are difficult to understand due to the grammatical errors. Because this journal does not use editors, I recommend the authors have this manuscript professionally edited for correct English grammar so reviewers are able to comment on the work and readers can enjoy the full merits of the work performed.

Minor Revisions and comments for consideration.

1. The title is vague and I fear the work in this manuscript will get overlooked. Consider adding more detail to the title such as “A mathematical model of the depolarization block in hippocampal interneurons” or something like that.
2. In the introduction, I recommend adding some additional content to clarify and define depolarization blocks. For example, consider including some language discussing which currents underlie depolarizing blocks (inactivation of fast and slow voltage-gated sodium channels?). Consider introducing the concepts that depolarizing blocks occur during periods of strong and prolonged depolarization. Also consider comparing and contrasting depolarizing blocks with sodium channel inactivation (different kinetics).

Finally consider adding something about what may lead to a breakdown in inhibitory mechanisms that may lead to the need to have a depolarizing block (i.e. GABA depletion). This could easily go into the discuss area instead.

Adding this information will help the reader place your results in a broader physiological context and will also increase the impact and citability of the manuscript.

1. I just wanted to comment that I thought using both the stochastic and deterministic models were thorough and strengthen this article. Well-done.
2. Figure 1- Please define what LP is in figure legend.
3. Figure 1- The graph is beautiful, but hard to interpret fully. For the individual waveforms (in blue) please consider presenting one in a contrasting color so the readers can understand what the relationship looks like. Each individual blue line is not resolvable leaving the relationship between Iex and Veq a mystery.

4. Conclusion- An area that was lacking was the authors underdeveloped the impact of their work. In the last paragraph please consider placing the results found in this study in a larger context with health and disease.
5. Conclusion- I recommend discussing recovery from a depolarizing block. What are the mechanisms necessary? What is the timecourse and or kinetics ?