Review of: "Depolarization block of interneurons"

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Potential competing interests: No potential competing interests to declare.

Tirozzi, Lecian, and Politi find that a published conductance-based model of hippocampal interneurons exhibits depolarization block for sufficiently large constant injected current. This loss of repetitive firing occurs through a supercritical Hopf bifurcation. Additionally, an arbitrarily small firing frequency can occur at the onset of repetitive firing showing that this neuron model is in Hodgkin's excitability class 1. There is considerable room for improvement in the exposition, grammar, and the methodology of the manuscript. Most significantly, the bifurcation analysis of the model is incomplete and the importance of the results is not clear. The manuscript needs to be improved before publication.

Here are some specific comments:

1) Tirozzi should list an institutional email.

2) Abstract: "of an hippocampal" → “of a hippocampal”, “deterministic the” → “deterministic and the”, “our results proved” → “our results show”, "are a in" → “are in a”, “such mechanism” → “such a mechanism”, "activity of the neurons" → “activity of neurons”.

3) Introduction: “interneuron” → “interneurons”, “In whole generality” → “In general, ”, “biological neural network” → “biological neural networks”, “and used considered model” → “used the model in”, “potentials goes” → “potentials go”, “no such a decrease” → “no such decrease”.

4) Provided references for the biological facts listed in the last sentence of the first paragraph.

5) In the introduction, mention the organism of this model. Humans? Also, mention that you are performing numerical bifurcation analysis.

6) Materials and Methods: “we considered” → “we consider”, “dynamic” → “dynamics”, “dynamic of this variable is much quicker than that one of” → “dynamics of this variable are much quicker than that of”, “dynamic” → “dynamics”, “We remark that in this equation the presynaptic conductance V_syn is involved in the” → “The presynaptic conductance V_syn affects the activation rate through a”, “MatLab” - > “Matlab”

7) Describe how MatCont works.

8) To improve the reproducibility of this work, post an m-file with the right-hand side of the ODE and anything else needed to produce the MatCont output shown in figure 1. ModelDB might be appropriate.

9) Table 1 and 2: “Unity of measure” → “Units”; Table 3: use English titles.

10) What about the parameters values in Table 1 makes this neuron model behave like a hippocampal interneuron? E_Na looked strangely small. Checking with [5], the value should be 55mV, not -55mV.

11) In a plot, show V(t) for I_syn deterministic and a comparable stochastic value of I_syn. This plot will help facilitate the discussion for comment 10.

12) I don't think you want Gaussian distributed T_i. Those random variables could be negative, which is admitted unlikely for mu=10, \sigma=0.1. I assume that you are rejecting negative T_i. If so, you should state this. Is each interspike interval independent? If so, state that T_i are iid. A better model for interspike intervals in the hippocampus might be exponentially distributed or perhaphs gamma distributed. Either way, provide a reference for your choice for the distribution of T_i.

13) Figure 1: Continue the stable equilibirum to smaller I_ext (show at least until -10); the superimposed trajectories are difficult to understand since there are too many of them; define LP as “limit point” or change the labels to something defined in the caption; “LP a saddle node bifurcation” what about the other LP involving two unstable equilibria? Also, how have you confirmed that the lower LP point is a saddle node bifurcation? Is this part of the MatCont output or have you compared against a normal form?

14) Results: “an infinite train” → “a train”, Figure 2 caption “Action potential” → “The number of action potentials”, “In this figures” → “In these figures”, “of spike for” → “of spikes for”, “of the graphics are” → “is”

15) Figure 2: Why have you selected 100ms? How do you detect a spike? Is it any maximum or does it need to be sufficient narrow and/or with a high enough V value? Inset plots of V(t) at a couple of different values of I_ext would help a lot. What initial condition are you using for each I_ext?

16) Figure 3: Use more values of g_syn to reveal the ‘staircase’ due to the discretness of the number of spikes. The x-axis label needs a bar on g_syn.

17) The result that the bifurcation is a SNIC seems important. Show the “further graphical investigation”.

18) Figure 4: Have you made repeated samples of the spiketimes? Also, use more values of g_syn. The x-axis label needs a bar on g_syn.

19) Discussion: “interneuron” → “interneurons”

20) Make the case that your result that the interneuron model exhibits depolarization block is important. Perhaps this would be aided by a simulation of a network of hippocampal neurons.