

Review of: "Depolarization block of interneurons"

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Potential competing interests: No potential competing interests to declare.

Comments on the paper by Brunello Tirozzi "Depolarization block of interneurons"

In this paper the author has proposed and discussed Mathematical Models for a hippocampal interneuron and claimed that the model explains its behavior, mainly depolarization block. This is an interesting work dealing with an important phenomenon in neurobiology. However, I have some queries to be satisfactorily answered by the author before the manuscript gets accepted for publication. These are as follows.

1. In Introduction, the description of Hippocampal neurons is too brief & superficial. The author should critically discuss the complex biology of the system.
2. What was the purpose of the mathematical model? What is the ultimate aim of this work. How does it help understanding the complex functioning of the brain, in particular, hippocampus?
3. In page 4, Table (no number), what are the sources of these values? Do these values change from species to species? Would it affect the results?
4. In page 4, the pre-synaptic potential has been modelled as a sigmoid function. What is the rationale behind?
5. In page 5, for implementing a linear postsynaptic summation, the synaptic conductance is given as a sum of normalized double exponential functions. What is the rationale for this equation/ model? Any reference?
6. In page 5, the sentence "In order to reproduce the 100Hz firing frequency of the presynaptic cell, the mean of the Gaussian Distribution has been fixed to $\mu = 10\text{ms}$ and the variance to $\sigma^2 = 0.1\text{ms}^2$." Why? In the context of firing frequency, a Gaussian distribution with a specified mean and variance does not directly represent a 100 Hz firing frequency. It is more appropriate to consider it as a Poisson process, where the occurrence of events (in this case, firing events) take place at a constant rate. The rate parameter represents the average number of events per unit time.
7. Page 6 Fig 1.: What is V_{eq} ? Is it the same as defined in the f^t equation (V). If not, how does the author calculate the V_{eq} ?
8. Page 6 Fig 1: The author has mentioned the Limit cycle as a saddle node, and occurrence of Andronov-Hopf bifurcation. Were the stability tests done for all?
9. Page 6 Fig 1: I think, the statement "Label H denotes a supercritical Andronov-Hopf Bifurcation" is not appropriate. In a supercritical Andronov-Hopf bifurcation, a stable limit cycle emerges as a result of the bifurcation. The term "supercritical" refers to the fact that the bifurcation occurs when a stable equilibrium point loses stability and transits to a stable limit cycle. The author must show all these details.

10. What is the biological relevance or physical consequence of Andronov-Hopf bifurcation in a neuronal system? The author may give more explanation on how Andronov-Hopf bifurcation represents the depolarisation block?
11. The author may use network of neurons (Excitatory and Inhibitory) to see the actual effect of synaptic conductance.
12. The phenomenon of synaptic plasticity is a highly complex one. In order to make his model appropriate for this phenomenon the author should go deep into the biology of synaptic plasticity and tune this model adequately.

I recommend major revision of the manuscript.