Review of: "Pacemaking function of two simplified cell models"

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The article deals with the simulation of electric propagation of systems consisting of two types of cells. One cell type, called pacemaker, is self excitatory, i. e., it depolarizes periodically without the influence of the neighboring cells. The second type, called excitable, depolarizes only by receiving an external stimulus. The external stimulus may be provided by the depolarization of any type of cell: pacemaker or excitable. In the article, the self excitatory cells are associated with pacemaker cells found in some biological systems such as the Sino Atrial Node (SAN) in the heart. On the other hand, excitable cells (A) are associated with the surrounding tissue of the pacemakers, for example, the one found in the right atrium of the heart.

The authors use two variables mathematical models to simulate the electric activity of tissue consisting of both types of cells: pacemaker, and excitable cells; and they claim that they can reproduce some of the results presented in [47], [33], and [57] according to the numbers in their bibliography. For instance, in lines 340 to 342, the authors claim that their simulations presented in the plot in Fig 8C *are close* to those in Fig 11 in [47]. In the cited bibliography the models of several variables of Severi et al. for SAN cells and Malecker et al. for A cells were used (see bibliography within [47]). Unfortunately, the authors do not indicate how they compare the figures, and it seems that the electric current propagating through the tissue is the only aspect relevant to the authors. However there are many aspects that the authors could compare, for instance, the speed of propagation of the current through the tissue, but they do not show any measurable comparison.

Taking into account the last and the following observations the article can not be considered a contribution to the state of the art:

1. Having the objective of reproducing the figures of very rudimentary model simulations (not of experimental data) using models with only two variables cannot be considered relevant.
2. Even if the simulations obtained were equivalent to those that the authors intend to reproduce, the use of the rudimentary *explicit Euler method* to integrate the equations would make the results questionable. The use of Euler's method is not justified given the number of variables utilized and since

the authors used matlab, and this software includes much more precise and stable methods. In any case, the authors should mention why they do not use other methods in comparing, as an example, the computational time of some of the arrays, (for instance, in the one-dimensional case).

3. The authors do not mention the limitations of their models, as an example, it is not possible to simulate the influence of the nervous system that, as shown in [47], can be implemented by modifying, in the several variables models, some parameters of the I_f current.

To conclude, the study of the propagation of the current in a system formed with pacemaker oscillator's and with excitable cells by using only two variables models could be relevant to understand many physiological phenomena, but it is not enough to model the propagation of a wave if it is not compared in measurable ways with more physiologically accurate cellular models which include more than two variables.