Multistability and stochastic effects in the dynamics of coupled cardiac gap junctions

Jean Bragard[1], Pau Lopez[2], Blas Echebarria[2],
[1]Dept Fsica y Matemtica Aplicada, Universidad de Navarra
[2]Dept Fsica, Universitat Politcnica de Catalunya

Gap junctions are intercellular channels that allow electrical coupling through the cell to cell transfer of ions. They play an important role in the transmission of electrical impulses in nerve and muscle excitable tissue. In this contribution, we present results regarding the propagation of the cardiac action potential in a one-dimensional fiber, where cells are electrically coupled through gap junctions (GJs). Instead of considering a constant conductance between cells, we consider first deterministic gap junctional gate dynamics that depend on the intercellular potential

$$\frac{dg}{dt} = \frac{g_\infty(\Delta\phi) - g}{\tau_g(\Delta\phi)} \quad (1)$$

where $\Delta\phi$ is the difference in transmembrane potential between two adjacent cells. Once we include the dynamics, we find that, after a large number of stimulations, different GJs in the tissue can end up in two different states [1]: a low conducting state and a high conducting state (see Fig. 1). The conductance dispersion usually occurs on a large time scale, i.e., hundreds or thousands of heartbeats.

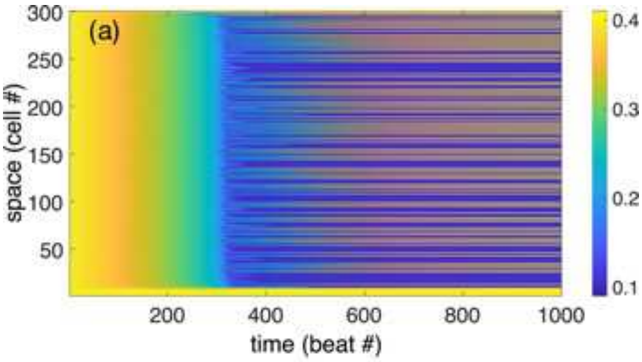

Fig. 1. Evolution of the intercellular conductivity as a function of the stimulation number, showing a final state with up and down states.

We first present evidence of the dynamical multistability that occurs by setting specific parameters of the GJ dynamics [2]. Subsequently, we explain how the multistability is a direct consequence of the GJ stability problem by reducing the dynamical systems dimensions.

Then, we study the effect of stochasticity in the dynamics of the gap junctions. The deterministic description of the gap junctional dynamics in Eq. (1) can be considered as the limit of a large set of GJs, where is of them behaves as a two-state system with transition rates depending on the intercellular potential difference. When the number of GJs becomes small (typically there are of the order of 50-100 in each junction) stochastic effects can become relevant and affect the multistability of the system.

[1] C. Hawks, J. Elorza, A. Witt, D. Laroze, I. R. Cantalapiedra, A. Pearanda, B. Echebarria, and J. Bragard, *Gap Junction Dynamics Induces Localized Conductance Bistability in Cardiac Tissue*, International Journal of Bifurcation and Chaos **29**, 1930021 (2019).

[2] J. Bragard, A. Witt, D. Laroze, C. Hawks, J. Elorza, I.R. Cantalapiedra, A. Pearanda, B. Echebarria, *Conductance heterogeneities induced by multistability in the dynamics of coupled cardiac gap junctions*, Chaos 31, 073144 (2021).