Connexin Dynamics Induce Conductance Dispersion in Cardiac Tissue

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Constant conductances are often considered when modeling cardiac tissue. However experimental evidences have proven differently [1]. Gap junctions connect adjacent cardiac myocytes to enable ion selective diffusion amongst neighboring cells. Gap junctions are complex proteins of the connexin family. In mammals, the most common type of proteins conforming the gap junctions in cardiac cells are the Cx43 and Cx45 (the number in the denomination of the protein comes associated with its molecular mass).

Gap junctions posseses their own dynamics which interacts with the propagating action potential (AP) by remodeling the conductivities of the cardiac tissue (in analogy to the plastic behavior of the brain cells). The aim of the present paper is to get a better understanding of gap junction dynamics and its influence on the conductance in the tissue during stimulations.

We have simulated a one dimensional strand of cardiac tissue using the membrane model of four currents proposed by Peñaranda et al. [2] and included the connexins dynamics following the work of Desplantez et al. [1] with some slight modifications. We have considered asymmetrical gap junctions such as Cx43-Cx45, and also symmetrical cases such as Cx43-Cx43 and Cx45-Cx45 in separated simulations (see Fig. 1).

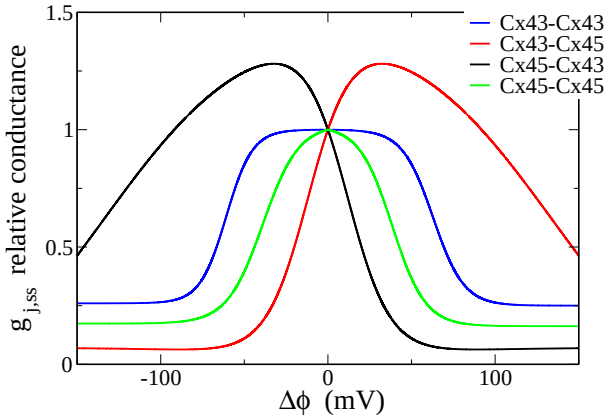

Figure 1: Stationary state conductances as a function of potential difference $\Delta\phi$ of neighbouring cells for the different gap junctions studied in this paper. The relative conductances for gap junctions formed with Cx43-Cx43 and Cx45-Cx45 are symmetrical.

The values of the conductances are initially uniform in the tissue but after a certain time (which depends on the system parameters) the conductances vary significantly from one cell to its neighbour. For long simulations the conductance between each cell will eventually reach a stationary state. We observed two different fixed values to which the conductances converge. The convergence to a fixed value is influenced by the spatial distribution of the cell conductances. In conclusion, we have observed a dynamical dispersion of the conductance among neighbouring cells in the tissue (as illustrated in Fig. 2). This effect is observed in the asymmetrical as well as in the symmetrical gap junction type of connexins.

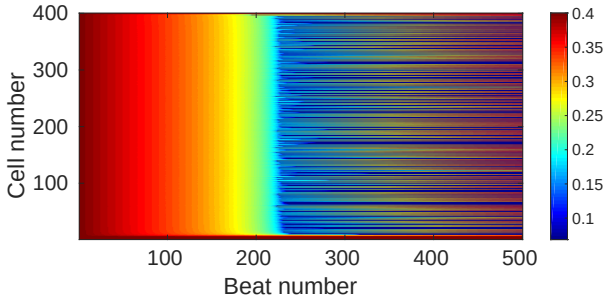

Figure 2: Space-time plot showing the dispersion of the conductance in a strand of tissue formed by 400 cardiac myocytes (4 cm).

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[1] Desplantez T, Halliday D, Dupont E. Weingart R. *Cardiac connexins Cx43 and Cx45: formation of diverse gap junction channels with diverse electrical properties* (European Journal Physiology, 2004).

[2] Peñaranda A, Cantalapiedra IR, Bragard J, Echebarria B., *Cardiac dynamics: a simplified model for action potential propagation.* (Theoretical Biology and Medical Modelling, 2012 9:50).