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Scroll-wave dynamics in the presence of ionic and conduction inhomogeneities in an anatomically realistic mathematical model for the pig heart

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Nonlinear waves occur in excitable media of physical, chemical, and biological origin. Such waves can form vortices in two and three dimensions; these are called spiral and scroll waves, respectively, and they are involved in the spatiotemporal organization of wave dynamics in various complex systems. Therefore, the study of such waves is a subject of interest in a broad area of research. One of the most important applications of such studies is the formation of vortices in cardiac tissue, which is associated with the onset and development of lethal cardiac arrhythmias [1–3]. Cardiac arrhythmias, such as ventricular tachycardias (VT) are generally associated with stationary, meandering, or drifting, periodic or quasiperiodic scroll waves; whereas, ventricular fibrillation (VF) is associated with scroll-wave break up. The dynamical behaviour of scroll waves in cardiac tissue is affected significantly by the presence of inhomogeneities [2–9], which can occur in the heart in many forms. However, biophysically, they can be grouped into two major classes: 1) conduction-type, i.e., inexcitable obstacles; and 2) ionic-type, i. e., inhomogeneities in the properties of different cells that constitute the system. An in-depth knowledge of the role of these inhomogeneities is essential for understanding the mechanisms that underlie most cardiac arrhythmias.

In experiments, it is often difficult to study systematically the role of these inhomogeneities in the development of arrhythmias, with regard to the nature, position, and distribution of these inhomogeneities within the heart. Fortunately, mathematical modelling provides an important tool here; it has been used extensively, with outstanding success, in interdisciplinary science. Mathematically, the excitable cardiac-tissue medium is described by a reaction-diffusion (RD) equation of the type:

$$\frac{\partial v}{\partial t} = \nabla(\mathcal{D}\nabla v) + \mathcal{F}(g, v), \qquad (1)$$

with the reaction part $\mathcal{F}(g, v)$ accounting for properties of cardiac cells and the diffusion part $\nabla(\mathcal{D}\nabla v)$, for the connection of cells to tissue. In this setting, an ionic inhomogeneity represents a modification of $\mathcal{F}$, whereas a conduciton inhomogeneity involves a modification of $\nabla(\mathcal{D}\nabla v)$. In this Letter, a modified version of the original Luo-Rudy I model [10], namely, the mLRI [11], was used to model the electrophysiological properties of the pig cardiac cell. The transmembrane potential (V) of a cardiac cell was calculated according to the following partial differential equation:

$$\frac{\partial V}{\partial t} = \nabla(\mathcal{D}\nabla V) - \frac{I_{\rm ion} + I_{\rm stim}}{C}, \qquad (2)$$

where C is the specific membrane capacitance of the cell. The diffusion tensor $\mathcal{D}$ is a 3×3 matrix [12, 13] with elements

$$\mathcal{D}_{ij} = D_{\parallel}\delta_{ij} + (D_{\parallel} - D_{\perp})\alpha_i\alpha_j. \qquad (3)$$

In the absence of inhomogeneities, we obtain a single stable periodically rotating scroll, with an average frequency 12 Hz. We find that solitary, large-scale conduction inhomogeneities did not have any pronounced effect on scroll-wave dynamics, with the scroll wave remaining insensitive to the presence of the obstacle at all 3 positions: P, P2 and P3 (Fig. 1a). However, small-scale conduction inhomogeneities can change the characteristics of the scroll wave substantially, thereby causing its breakup. At all distributions of small-scale conduction inhomogeneities that we have considered, namely,

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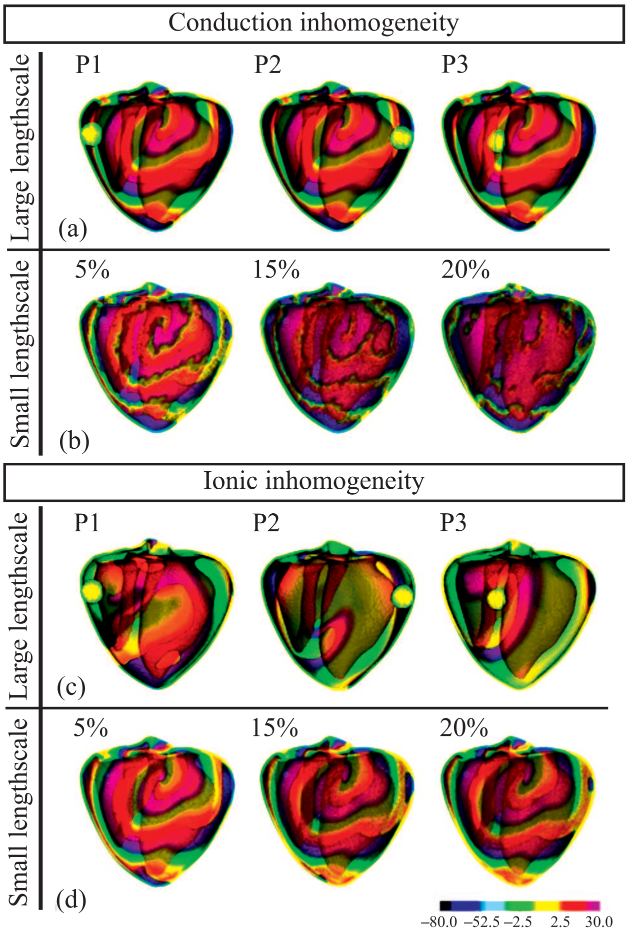

Fig. 1. (Color online) Representative snapshots of scroll-wave dynamics in anatomically realistic pig hearts in the presence of (a) & (c) large- and (b) & (d) small-scale, conduction and ionic inhomogeneities

5, 10, 15, and 20% inhomogeneity, we observe a shortening of the spatial wavelength of the scroll, and scroll-wave breakup at inhomogeneities $\gtrsim 15\,\%$ (Fig. 1b). On the contrary, with solitary, large-scale ionic inhomogeneities, we observe interesting dynamical behaviour, such as, scroll-wave breakup (Fig. 1c: **P1**) and anchoring **P3**), whereas, small-scale ionic inhomogeneities did not lead to qualitatively interesting dynamics (Fig.1d). Our results demonstrate that large-scale conduction inhomogeneities do not affect scroll-wave dynamics in the pig heart. However, large-scale ionic inhomogeneities can lead to scroll-wave breakup. On the contrary, small-scale conduction inhomogeneities generally lead to some decrease in the spatial wavelength of the scroll wave and initiate scroll-wave breakup. Small-scale ionic inhomogeneities, however, prove to be protective against breakup.

Our principal, qualitative result that small-scale inhomogeneities are important in the diffusion part is a consequence of the effect of the diffusion processes on the reaction part (called the electrotonic effect in electrophysiology) [14]. However, we have also found that small-scale conduction inhomogeneities are not averaged out by the diffusion. Therefore, their mean-field consideration, e.g., by using homogenization techniques, should be done with caution. For large-scale heterogeneities, our results are in line with findings for human cardiac-tissue simulations [15]. However, these have been performed on a completely different cardiac geometry, different cell models, and for substantially different values of scroll wavelengths. In addition to dynamical anchoring (via the transient-breakup phase) described in Ref. [15] we have also observed anchoring of the other type resulting from a drift of the scroll for qualitatively different positions of the heterogeneity: in particular, we have placed heterogeneity inside the septum and have found that it can attract scroll waves and thus lead to interesting new dynamics.

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