Feedback Control of Resonant Drift as a Tool for Low Voltage Defibrillation

IV Biktasheva[1], SW Morgan[1], G Plank[2], VN Biktashev[1]

[1]University of Liverpool, Liverpool, UK
[2]Medical University Graz, Graz, Austria

Abstract

Resonant drift of re-entry occurs in response to repetitive stimulation with period equal to that of the re-entry. Feedback controlled resonant drift drives re-entry out from excitable tissue, so may be used as antiarrthymic or defibrillation strategy. To test it in realistic computer simulations, we used monodomain and bidomain description of the tissue, rectangular 2D and 3D geometry, and anatomically realistic rabbit ventricles geometry, with Barkley, Drouhard-Roberge-Beeler-Reuter, and Courtemanche-Ramirez-Nattel kinetics models. Re-entries terminated at a fraction of the conventional shock strength. The success depends on the detailes of the feedback protocol. The simulations motivate experimental testing of the proposed low-voltage defibrillation method, which will be most productive in conjunction with simulations.

1. Introduction

Timely application of an electric shock, particularly with implantable cardioverters/defibrillators (ICDs), is the only reliable therapy to prevent sudden cardiac death. However, the strong shocks have serious adverse effects, e.g. electroporation and mechanical dysfunction. The shocks are above the pain threshold and psychological effects on patients play a non-negligible role, so patients suffering from arrhythmias which are not immediately life-threatening do not tolerate ICD therapy.

Here, we consider a method which employs feedback-controlled pacing to eliminate re-entrant circuits, by moving them towards inexcitable obstacles or each other, and annihilate. The method relies on the resonant drift of re-entrant waves when repetitive low energy shocks are applied in resonance with the period of the re-entry [**?**, **?**]. The feedback helps to maintain the resonance [**?**, **?**]. The method can also eliminate multiple re-entrant sources [**?**].

Resonant drift and its feedback control have been studied experimentally in the Belousov-Zhabotinsky reaction medium and in numerical simulations of simplified mathematical models (e.g. [**?**, **?**, **?**]). Here, we investigate its effectiveness for low-voltage defibrillation in a bidomain model of cardiac tissue with microscopic inhomogeneities and realistic cellular kinetics. As heart is essentially 3D, we also investigate effectiveness of the resonant suppression the scroll wave turbulence with spontaneous of multiplication of the scroll filaments. Finally, we present a case study demonstrating the work of the method in a bidomain, three-dimensional, anatomically detailed model of rabbit ventricles with microscopic inhomogeneities.

2. Methods

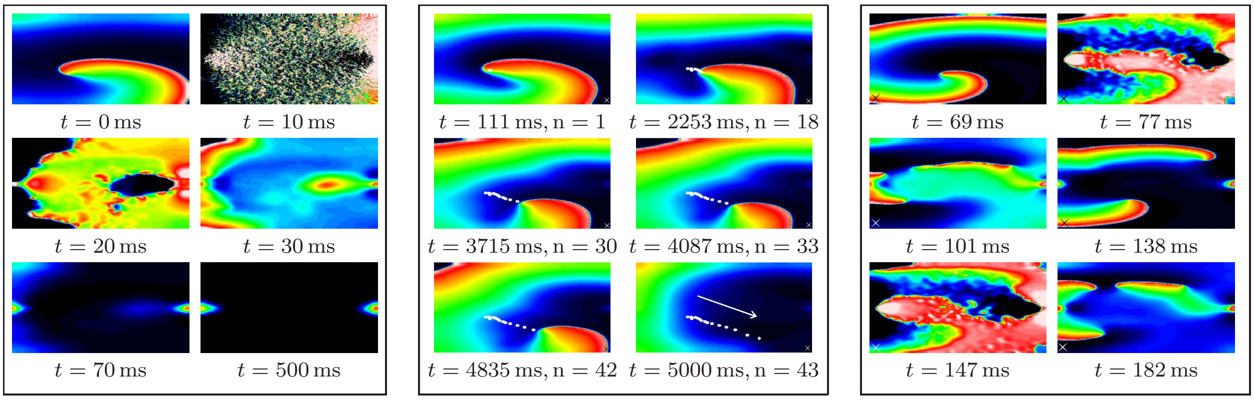
2.1. 2D bidomain model

We used the finite-element bidomain solver Cardiac Arrythmia Research Package (CARP) [**?**], with the numerical setup as in [**?**], for a thin sheet of cardiac tissue $40 \times 20 \times 0.2\,\mathrm{mm}^3$ with fibres oriented along the x-direction, no-flux boundary conditions and no surrounding bath. As in [**?**], the components of the intracellular conductivity tensor were fluctuating at the level of 50% of their mean values.

To describe the ionic kinetics, we used Courtemanche *et al.* human atrial model [**?**] with two additions, electroporation current (EP), and acetylcholine-dependent potassium current, $I_{K(ACh)}$, as in [**?**]. This mode produces meandering spirals which have a tendencey to self-terminate within about 20 seconds. In some simulations, we also applied a 65% block of the slow inward L-type Ca^{2+} current coupled with a nine-fold increase in the slow delayed outward K^+ current and the rapid delayed outward K^+ current as suggested by Xie *et al.* [**?**]. This variant of the model produces stationary persistent spirals.

Re-entries were initiated using the usual S1-S2 protocol.

For defibillation, we used stimulating electrodes of the size $1\times1\times0.2\,\mathrm{mm}^3$ centered along the left and right edges of the slab to inject current into, and withdraw from, the extracellular space. We applied repetitive low-amplitude $5\,\mathrm{ms}$ rectangular monophasic shocks via these electrodes, at the instants determined by signals from a "feedback"



(a) (b) (c)

Figure 1. 2D bidomain model. (a) Single shock defibrillation. (b) Feedback resonant drift defibrillation. (c) Failure of the feedback resonant drift defibrillation.

registration electrodes.

2.2. 3D monodomain model

The simulations were done with EZscroll solver by Barkley *et al.* [**?**], suitably modified to implement resonant drift. We used Barkley [**?**] kinetic model with parameters $a = 1.1$, $b = 0.19$, and $\epsilon = 0.02$, a 19-points finite difference approximation of the Laplacian on equidistant Cartesian mesh. The time and space units are non-dimensional, and their relation to real time and space is a matter of convention. We performed simulations in a box of $60 \times 60 \times 60$ space units with no-flux boundary conditions. With the chosen parameters, an initial condition in the shape of a scroll ring leads to a developed scroll wave turbulence within 200 dimensionless time units.

The stimulation was done in two different ways. "Modulation of excitability" was achieved by varying the excitation threshold parameter b as $b(t) = b_0 + B\cos(\omega_f t)$, $b_0 = 0.19$, as in [**?**]. The alternative way was "extra transmembrane current" stimlation, via an extra time-dependent term in the activator equation, in the form of a series of rectangular pulses of duration 0.3 time units, varying amplitude E and timing synchronized with signals from a feedback electrode.

2.3. Whole-ventricles model

As in Study 1, we used CARP to do the calculations, with similar methods including fluctuations of the intracellular conductivities. Now the geometry was that of the rabbit ventricles [**?**], placed in a surrounding bath of the size $29 \times 31 \times 28\,\mathrm{mm}^3$ with no-flux boundary conditions. The stimulating current was injected and withdrawn through plate electrodes of the thickness of $0.1\,\mathrm{mm}$ along the lateral faces of the bath. The shocks were of monophasic truncated exponental profiles with time constant of $10\,\mathrm{ms}$ and duration $8\,\mathrm{ms}$, synchronized with a signal from a feedback electrode near the apex. We used a variant of Drouhard-Roberge modified Beeler-Reuter model kinetics described in [**?**].

3. Results

3.1. 2D bidomain model

Fig. 1(a) shows an episode of a successful single shock defibrillation. Microscopic conductivity fluctuations enable the far-field action of the electric field. With the moment of application of the shock varied, the 50% probability of defibrillation was achieved at the shock amplitudes of $14 \times 10^6\,\mu\mathrm{A/cm}^3$ and $18 \times 10^6\,\mu\mathrm{A/cm}^3$ for meandering and stationary spirals, respectively. Fig. 1(b) illustrates a successful elimination of a meandering spiral via feedback-controlled resonant drift. The feedback electrode is in the bottom right corner, the white dots show the positions of the spiral tips in every 3 rotations, to compensate for the meandering of the spirals. The spiral drifts along nearly a straight line and vanishes within 5 sec. This has been achieved by $1 \times 10^6\,\mu\mathrm{A/cm}^3$ shocks, *i.e.* 18 times weaker than the single shock defibrillation threshold (only relative values of the currents are meaningful as the effect of the stimulating current depends very much on the stimulation electrode geometry). We varied the position and geometry of the feedback electrode (the four corners and horizontal and vertical middle lines), and the termination of meandering spirals by $2 \times 10^6\,\mu\mathrm{A/cm}^3$ shocks within 10 sec was achieved for all electrodes.

With the stationary spirals, some feedback electrodes performed consistently worse than others: termination by $6 \times 10^6\,\mu\mathrm{A/cm}^3$ shocks within 10 sec was achieved for 3 out of the 6 electrodes. A typical failure is illustrated

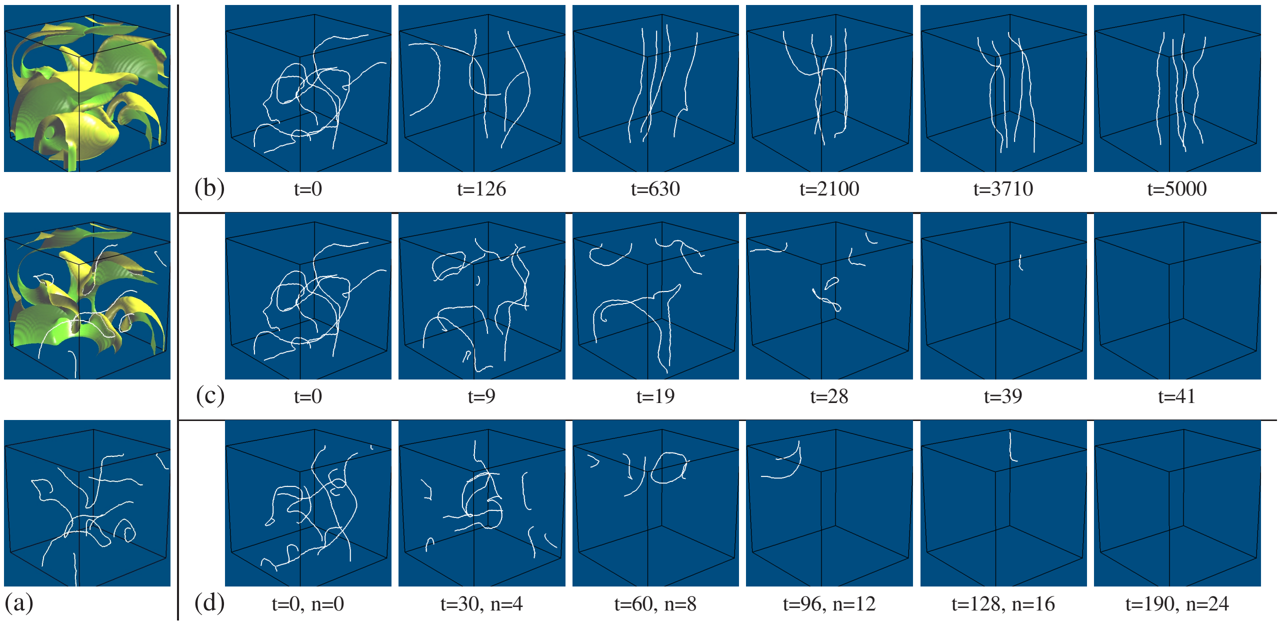


Figure 2. 3D monodomain model. (a) Scroll turbulence snapshot: fronts and filaments. (b) Excitability modulation, above-resonant frequency. (c) Excitability modulation, resonant frequency. (d) Extra current feedback-driven stimulation.

by Fig. 1(c) (feedback electrode in the bottom left corner): new spirals are generated by high gradients of the external field, which leads to an infinite loop of termination and creation of spirals. A delay in the feedback loop changes the drift direction and positions of the wavefronts during the shocks, so can disrupt the vicious circle. *E.g.* a feedback delay of $30\mathrm{ms}$ in the simulation shown in Fig. 1(c) led to termination of all activity within 3 sec.

3.2. 3D monodomain model

Fig. 2(a) illustrates the concept of the scroll filament. The negative tension of filaments causes their multiplication in this conceptual model of fibrillation. It was previously suggested [**?**] that a periodic stimulation with a frequency higher than the own frequency of the scroll waves can effectively change the filament tension from negative to positive and thus eliminate the fibrillation. The latter is not necessarily true, though: in Fig. 2(b) at $\omega_f = 1.13$, $B = 0.03$, the filaments get positive tension and straighten, but do not disappear. In contrast, Fig. 2(c) shows the effect of stimulation with the same amplitude but with $\omega_f = 0.80$, which equals the average de-facto frequency of the scrolls: all the activity is eliminated within a few scroll rotations. Fig. 2(d) illustrates the work of the feedback-controlled stimulation by more realistic "extra current" stimuli of amplitude $E = 0.03$, much smaller than the single shock defibrillation threshold of $E = 4.3$. The main impediment to the fast elimination of the scrolls was due to contribution of the Doppler effect in the feedback loop, which was significant due to the large size of the box (several wavelengths). Clearly this aspect is unlikely to be essential in real hearts.

3.3. Whole-ventricles model

The calculations involved are very time consuming and here we present only a case study demonstrating viability of the method. Fig. 3 presents a videogram of a simulation of successful elimination of fibrillation, achieved within a fraction of a second, by three feedback-controlled $2 \times 10^5 \mu\mathrm{A}/\mathrm{cm}^3$ shocks, which produced external electric field of about $2\,\mathrm{V}/\mathrm{cm}$. For comparison, [**?**] reported "defibrillation strength" electric fields in a similar numerical model with the same anatomy in the range of 10 to $20\,\mathrm{V}/\mathrm{cm}$.

4. Discussion and conclusions

Termination of re-entries can be achieved with high probability at a fraction of the shock strength used for conventional single-shock defibrillation, by moving the re-entry cores towards an anatomical boundary or towards each other. The movement depends on the electrodes' location and details of the feedback protocol. Simulations reveal reasons when the protocol has not been successful and can suggest modifications to it to overcome the difficulties. The evidence from simulations motivates experimental testing of the proposed low-voltage defibrillation method. Such testing will be most productive if done in conjunction with simulations.

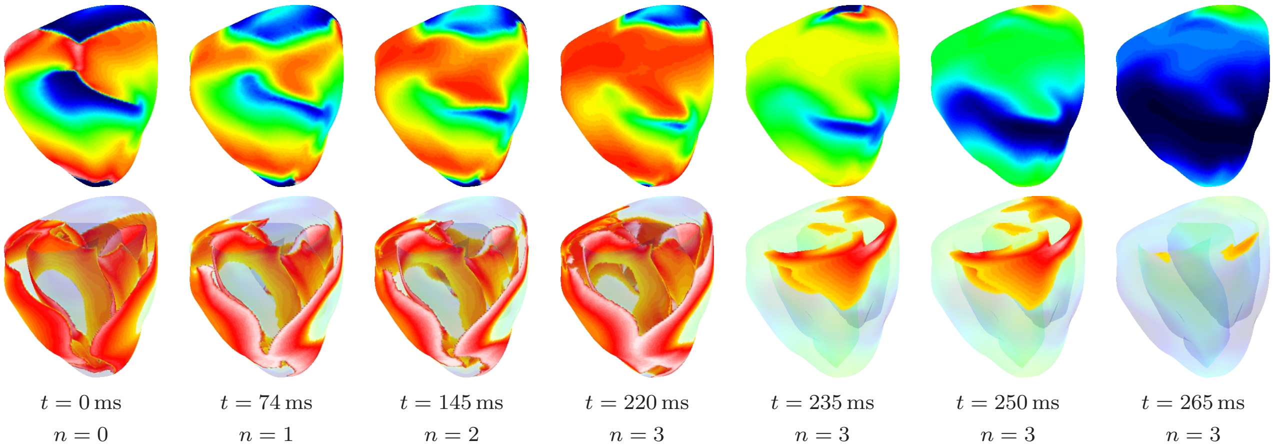


Figure 3. Whole-ventricles model. Successful defibrillation by feedback stimulation, surface and semi-transparent views. The moments 74, 145 and 220 ms are 17 ms after beginning of a shock.

Acknowledgements

This study has been supported by EPSRC (grant EP/D500338/1).

Address for correspondence:

I. V. Biktasheva
Department of Computer Science
University of Liverpool
Liverpool L69 3BX
UK
E-mail address ivb@liv.ac.uk