Computers in Biology and Medicine 63 (2015) 108–117

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Control of cardiac alternans in an electromechanical model of cardiac tissue

Azzam Hazim [a], Youssef Belhamadia [b], Stevan Dubljevic [c,*]

[a] Department of Biomedical Engineering, University of Alberta, Edmonton, AB Canada T6G 2V2
[b] Department of Biomedical Engineering, Department of Mathematics and Campus Saint-Jean, University of Alberta, AB Canada T6C 4G9
[c] Department of Chemical and Materials Engineering, University of Alberta, Edmonton, AB Canada T6G 2V4

ARTICLE INFO

Article history:
Received 22 January 2015
Accepted 13 May 2015

Keywords:
Action potential
Alternans control
Electrical alternans
Mechanical perturbation
Nash–Panfilov model
Pacing periods

ABSTRACT

Electrical alternations in cardiac action potential duration have been shown to be a precursor to arrhythmias and sudden cardiac death. Through the mechanism of excitation–contraction coupling, the presence of electrical alternans induces alternations in the heart muscle contractile activity. Also, contraction of cardiac tissue affects the process of cardiac electric wave propagation through the mechanism of the so-called mechanoelectrical feedback. Electrical excitation and contraction of cardiac tissue can be linked by an electromechanical model such as the Nash–Panfilov model. In this work, we explore the feasibility of suppressing cardiac alternans in the Nash-Panfilov model which is employed for small and large deformations. Several electrical pacing and mechanical perturbation feedback strategies are considered to demonstrate successful suppression of alternans on a one-dimensional cable. This is the first attempt to combine electrophysiologically relevant cardiac models of electrical wave propagation and contractility of cardiac tissue in a synergistic effort to suppress cardiac alternans. Numerical examples are provided to illustrate the feasibility and the effects of the proposed algorithms to suppress cardiac alternans.

1. Introduction

Electrical alternans is a physiological phenomenon manifested as beat-to-beat oscillation (electric wave width alternation) of the cardiac Action Potential Duration (APD) [1]. Alternans has been shown to be a precursor to arrhythmias [2,3] and sudden cardiac death (SCD), which is the most common cause of death in the industrialized world. Experimentally, APD alternans is observed during pacing at high rates so that beyond a critical pacing value a sequence of long and short APDs emerges [4] as presented in Fig. 1. In this figure, APD is defined as the period of time during which the action potential exceeds the given threshold value, while a diastolic time interval (DI) is defined as the period of time during which the action potential is below the threshold value.

The majority of feedback control algorithms [5–10] that have been developed until now to suppress alternans in cardiac tissue utilize the difference between the measurements of the two most recent APDs to make small adjustments to the timing of electrical stimuli. These algorithms are specific implementations of time-delay auto-synchronization [11] and extended time-delay auto-synchronization [12] feedback control techniques. Hall et al. [5] used this approach to successfully control cardiac arrhythmia called an alternans rhythm in an *in vitro* rabbit heart. Similarly, Rappel et al. [6] suppressed alternans in two geometrical models of both 1D and 2D tissues, to conclude that several control electrodes need to be placed on the tissue in order to stabilize normal heart rhythm. Control of atrioventricular-nodal conduction alternans has also been demonstrated *in vivo* human hearts [7] by stabilizing the underlying unstable steady-state conduction. The first experimental attempt to implement the electrical pacing interval technique is due to Hall and Gauthier [9], who succeeded in suppressing alternans in small pieces ($\lesssim 1$ cm) of a bullfrog cardiac muscle. Echebarria and Karma [8] were the first to investigate this approach theoretically in a model of Purkinje fibers. They showed, by using Noble model, that alternans in fibers no longer than ≈ 1 cm could be suppressed using single electrode. Their theoretical results were experimentally verified by Christini et al. [10]. In addition, Dubljevic et al. [13] proved regarding the stated approach, that the failure to suppress alternans completely in tissues exceeding 1 cm in length is due to the lack of information of the spatial evolution of alternans away from the pacing site, and due to finite controllability of actuation at the pacing site.

It has been shown theoretically and experimentally that the above mentioned control technique has a finite degree of controllability, such that alternans stabilization in cardiac tissues of the length above 1 cm cannot be achieved [8,10,13,14]. Although

* Corresponding author. Tel.: +1 780 248 1596; fax: +1 780 492 2881.
E-mail address: Stevan.Dubljevic@ualberta.ca (S. Dubljevic).

http://dx.doi.org/10.1016/j.compbiomed.2015.05.011
0010-4825/

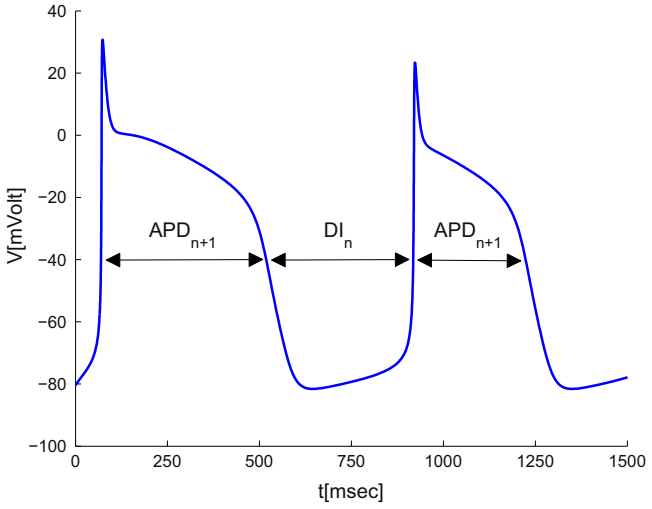

Fig. 1. Time evolution of transmembrane potential in the Noble cardiac cell model.

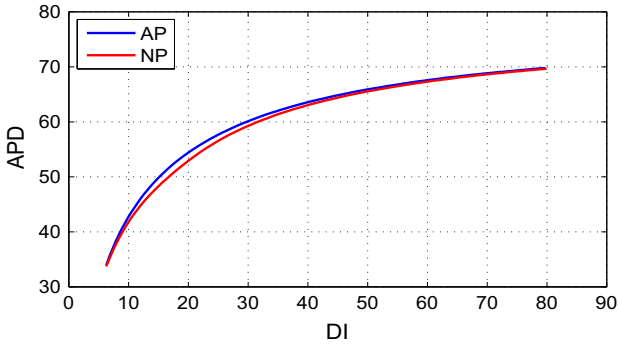

Fig. 2. The dynamic APD restitution curves for the AP and NP models.

Table 1
Parameter values for the electromechanical model employed for small deformation.

$k=8$	$a=0.05$	$\varepsilon=0.1$	$\mu_1=0.12$
$\mu_2=0.3$	$k_{Ta}=0.01$ kPa	$\tilde{c}=16$ kPa	$G_s=1.6$

such algorithms have proved effectiveness of controlling electrical alternans in small tissues, several electrodes need to be implanted along the length of cardiac tissue (≈ 6.25 cm), so that each pacing electrode can suppress alternans in a finite part of the tissue (≈ 1 cm). In addition, to the authors' best knowledge, all the electric-based realization algorithms have not take into account mechanical properties of cardiac tissue, despite the fact that mechanical deformation is shown to influence electrical activity of the heart tissue, and consequently the cardiac alternans. In fact, cardiac electrical waves propagate through cardiac tissue and initiate its contraction via excitation–contraction coupling (ECC), while contraction of the heart causes cardiac tissue deformation which in turn feeds back on the wave propagation and affects electrophysiological properties via mechanoelectrical feedback (MEF) [15–18].

Many studies have shown the importance of the MEF and, for instance, that mechanical impact on the chest, in the area directly over the heart, can either cause Commotio Cordis, when the chest receives a blow [19,20], or terminate cardiac arrhythmia by striking a blow of the fist to the chest in a precordial thump [21,22]. Therefore, in this paper, we explore the feasibility of controlling electrical alternans by manipulating mechanical properties of the cardiac tissue. From mathematical point of view, electromechanical models where the coupling is between electrical and mechanical activity of the heart are more suitable for our study. A variety of these models has been developed to investigate various physical phenomena and they can be mainly classified into two categories. The weakly coupled electromechanical models [23–26] that account only for the effects of electrical activity on the cardiac mechanics, i.e., one way coupling, and the strongly coupled electromechanical models [27–31] that account for the effects of electrical activity on the cardiac mechanics and the effect of mechanical deformation on electrical properties. For more details about the electromechanical models, the reader is referred to [32,33]. In this work, we will use Nash–Panfilov (NP) model [27,28], which is a strongly coupled electromechanical model. This model includes an additional variable to link the electrophysiological properties of the heart tissue which is modelled with the well-known Aliev–Panfilov (AP) model [34], with cardiac tissue's mechanical properties. It has been shown in [4] that APD alternans occurs when the slope of the dynamic APD restitution curve is greater than one. Therefore, for the NP model, APD alternans can be induced by pacing cardiac tissue at a rapid rate as the slope of the dynamic restitution curve (Fig. 2) at high frequencies is greater than one. The dynamic restitution curve, which describes the relationship between action potential duration (APD) and preceding diastolic interval (DI), was constructed using a dynamic pacing protocol [4] and determined by plotting each action potential duration at 90% repolarization against the preceding diastolic interval at incremental pacing rates. The dynamic restitution curve of the NP model is the dynamic restitution curve of the AP when coupled with cardiac contraction. As the NP model is dimensionless, units are not used, refer to Section 4 for details, and the models' parameters used are given in Table 1.

The main goal of this paper is to show that the control of cardiac alternans along a 7 cm cable of cardiac cells can be achieved by control algorithms that use the mechanical perturbation approach. In particular, we consider several electrical pacing and mechanical perturbation strategies with two relevant mechanical deformations being considered. The first one is in small deformation, and therefore the model is governed by the equations of the linear elasticity theory [35,36]. Since the cardiac cells change length by up to 20%, which occurs as a result of cardiac contraction during a normal heart beat [24,27,37,38], the second strategy is therefore when the deformation is large. The model in this case is however governed by nonlinear equations of the finite deformation elasticity theory [35,36,39].

It will be demonstrated that in small deformation, one can suppress alternans along the whole cable of cardiac cells by using mechanical perturbation strategy. The control algorithm proposed for the large deformation, which is an extension of the one used for small deformation, combines electrical boundary pacing and mechanical perturbation strategy. In all proposed algorithms, the electrical pacing is applied at the tissue boundary while the mechanical perturbation control is applied at one place over a small localized region within the cable length of 7 cm. Recently, mechanics-based devices have been developed that can be attached to the membrane of the heart to treat cardiac diseases [40]. The proposed control algorithm is a promising approach that can be possibly incorporated into mechanical-based devices that can be equipped with mechanical patch to apply mechanical perturbation over a small localized region of the heart tissue in order to suppress alternans. Applying this control strategy to control cardiac alternans can potentially improve therapy since it requires that one mechanical patch, in a one-dimensional model, to be placed over a small region (≤ 1 cm), to suppress alternans, while the existing electrical pacing control requires several electrodes to be implanted in the ventricles, which is very difficult to