Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Biomedical Engineering

Personalized imaging and modeling strategies for arrhythmia prevention and therapy

Natalia A. Trayanova, Patrick M. Boyle and Plamen P. Nikolov

Abstract

The goal of this article is to review advances in computational modeling of the heart, with a focus on recent non-invasive clinical imaging- and simulation-based strategies aimed at improving the diagnosis and treatment of patients with arrhythmias and structural heart disease. Following a brief overview of the field of computational cardiology, we present recent applications of the personalized virtual-heart approach in predicting the optimal targets for infarct-related ventricular tachycardia and atrial fibrillation ablation, and in determining risk of sudden cardiac death in myocardial infarction patients. The hope is that with such models at the patient bedside, therapies could be improved, invasiveness of diagnostic procedures minimized, and health-care costs reduced.

Addresses

Institute for Computational Medicine, Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD, USA

Corresponding author: Trayanova, Natalia A, Institute for Computational Medicine, Johns Hopkins University, 3400 N. Charles Street, 208 Hackerman Hall, Baltimore, MD 21218, USA. Fax: +1 410 516 5294. (ntrayanova@jhu.edu)

Current Opinion in Biomedical Engineering 2018, **5**:21–28

This review comes from a themed issue on **Futures of Biomedical Engineering: Cardiovascular Bioengineering**

Edited by **George A. Truskey**

Received 13 November 2017, revised 21 November 2017, accepted 29 November 2017

https://doi.org/10.1016/j.cobme.2017.11.007

Keywords

Atrial arrhythmia, Ventricular arrhythmia, Computational modeling, Catheter ablation, Sudden cardiac death risk stratification, Myocardial infarction.

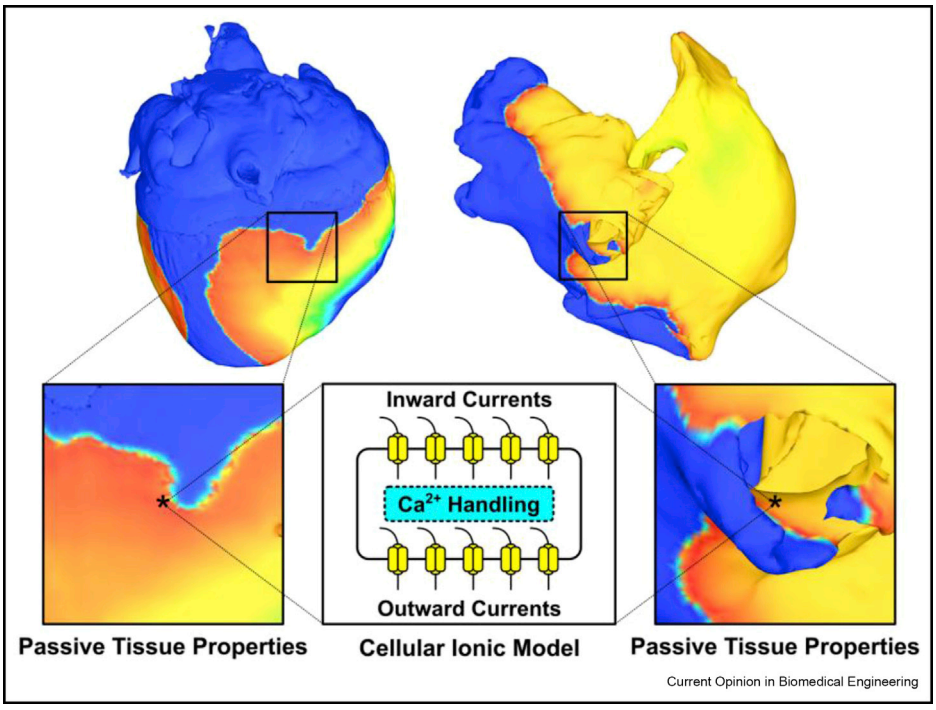
Cardiovascular disease is a major burden to the US health care system. It is the number one killer in the US, and is expected to become the most common cause of death in the world by 2020. As the population ages, prevention, diagnosis, and treatment of cardiovascular disease will be one of the most pressing clinical needs in this century. As the foremost health care problem in the industrialized world, cardiovascular diseases present tremendous challenges to medicine, and these challenges have grown larger in the post-genomic biologic world.

Computational modeling of the heart has a long and glorious history, pioneering the use of quantitative models to understand the mechanisms of, and the interactions associated with, altered cardiac structure and function in disease. The goal of this brief review is to present recent developments in personalized clinical imaging-based modeling strategies intended for use in the clinic for arrhythmia prevention and therapy. While earlier efforts and developments in heart modeling, specifically those for the human heart, are noted but not exhaustively reviewed, the focus of this article is on the path cardiac modeling is taking towards clinical implementation.

As summarized in recent reviews [1,2], biophysically detailed cardiac simulations incorporating multiscale interactions from the sub-cellular to the entire organ, and frequently representing the realistic geometry of the organ (Fig. 1), have been widely used to explain experimental observations, revealing the mechanisms of organ-scale arrhythmogenic phenomena and contractile dysfunction emerging from pathological effects at the tissue, cell and protein levels. Notably, recent cardiac models have been constructed with unprecedented structural and biophysical detail, including cardiac electromechanics [3,4], even integrating from the levels of cellular electrophysiology and electromechanics to fluid dynamics of blood flow [5]. Models of the human ventricles have been used to gain insights into the mechanisms of ventricular arrhythmia resulting from dynamic instabilities such as alternans [6,7], myocardial ischemia [8,9], and channelopathies [10,11]. Models have also been applied to investigate improved methods for cardiac resynchronization therapy in dyssynchronous heart failure [12,13]. Defibrillation and understanding the response of the heart to electric shocks has been a major staple in ventricular modeling [14,15], culminating in the development of biophysically-detailed heart torso-models to assess defibrillator deployment in patients with congenital heart disease [16]. An important novel development in computational modeling of the heart is its use to elucidate mechanisms of arrhythmia termination and to guide new developments in the emergent field of cardiac optogenetics [17–19].

As atrial arrhythmias, particularly atrial fibrillation (AF), are the most prevalent cardiac arrhythmia and have become an emerging global health crisis, with about 1–2% of the global population currently suffering from AF [20], cardiac computational modeling has recently placed a major focus on understanding how atrial remodeling affects action potential dynamics and turbulent propagation

Figure 1



Multiscale approach to image-based modeling of cardiac electrophysiology. Passive electrical coupling of cardiac cells mediates the tissue-scale propagation of bioelectric impulses that originate at the membrane level (action potentials). 3-D geometrical models are reconstructed from images. (Modified with permission from Trayanova et al. [57] under the Creative Commons CC BY 4.0 license https://creativecommons.org/licenses/by/4.0/).

associated with human AF. Atrial computational models have made major contributions in understanding how intrinsic atrial structural and electrophysiological heterogeneities predispose to atrial arrhythmias [21–24]. Investigating the role of pulmonary vein triggers in the establishment of paroxysmal AF [25], determining the mechanisms of lone paroxysmal AF arising from inherited ion channel dysfunction [26], and elucidating the role of the ganglionic plexi in initiating AF [27] are examples of such contributions. The recent understanding of the role of fibrosis in maintaining persistent AF has led to a number of new computational studies aimed at teasing out how the remodeled structural substrate alters AF dynamics, among which assessment of the different representations of fibrosis [28,29] and the spatial resolution of clinical measurement needed to detect reentrant drivers, which sustain AF [30]; additional developments are described in recent reviews [31,32].

A major thrust in computational cardiology has been the use of heart models as a test bed for evaluation of new antiarrhythmic drug therapies. It is now possible to collect the experimental data needed to constrain models of ion channel gating and drug binding, and use these data to test hypotheses regarding mechanisms of drug action on heart cells and tissues [33,34] as well as whole heart [35]. Furthermore, multiscale heart models of antiarrhythmic drug interactions with ion channels have provided insights into why certain pharmacological interventions result in proarrhythmia, whereas others do not [35]. This work has the potential to more effectively guide the drug development pipeline—a process that is well known to have high failure rate and expense. The identification of novel therapies through computational models have yet to be translated to clinical applications [36]. The use of computer models as a tool for screening cardiac toxicity is spearheaded by the Comprehensive In Vitro Proarrhythmia Assay (CiPA) initiative, led by the US Food and Drug Administration and others [37,38], with the aim to utilize biophysical cardiac simulations to predict the functional response of the heart to novel compounds. Examples of the use of simulations in this field include predict drug effects on arrhythmogenic risk [39], role of biological variation in model predictions [40] and linking binding assay data to clinical information [41].

The recent emphasis on precision medicine in many aspects of health care, including cardiovascular medicine, has provided a significant impetus for the development of predictive approaches combining clinical imaging and computational modeling that can be applied to the diagnosis and treatment of heart rhythm disorders in patients with heart disease [42,43]. A major avenue in this direction is the creation and translation into clinical practice of novel clinical imaging- and