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Data-driven estimation of cardiac electrical diffusivity from 12-lead ECG signals

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ABSTRACT

Diagnosis and treatment of dilated cardiomyopathy (DCM) is challenging due to a large variety of causes and disease stages. Computational models of cardiac electrophysiology (EP) can be used to improve the assessment and prognosis of DCM, plan therapies and predict their outcome, but require personalization. In this work, we present a data-driven approach to estimate the electrical diffusivity parameter of an EP model from standard 12-lead electrocardiograms (ECG). An efficient forward model based on a mono-domain, phenomenological Lattice-Boltzmann model of cardiac EP, and a boundary element-based mapping of potentials to the body surface is employed. The electrical diffusivity of myocardium, left ventricle and right ventricle endocardium is then estimated using polynomial regression which takes as input the QRS duration and electrical axis. After validating the forward model, we computed 9500 EP simulations on 19 different DCM patients in just under three seconds each to learn the regression model. Using this database, we quantify the intrinsic uncertainty of electrical diffusion for given ECG features and show in a leave-one-patient-out cross-validation that the regression method is able to predict myocardium diffusion within the uncertainty range. Finally, our approach is tested on the 19 cases using their clinical ECG. 84% of them could be personalized using our method, yielding mean prediction errors of 18.7 ms for the QRS duration and 6.5° for the electrical axis, both values being within clinical acceptability. By providing an estimate of diffusion parameters from readily available clinical data, our data-driven approach could therefore constitute a first calibration step toward a more complete personalization of cardiac EP.

1. Introduction

1.1. Clinical rationale

With around 17.3 million deaths per year (Mendis et al., 2011), the global burden of cardiovascular diseases remains high and causes a significant social and economic impact. According to recent estimates, about 2% of adults in Europe (McMurray et al., 2012) and 2.4% of adults in the US (Roger et al., 2012) suffer from heart failure alone, with the prevalence rising to more than 10% among persons 70 years of age or older. One of the most common causes of heart failure is dilated cardiomyopathy (DCM), a condition with weakened and enlarged ventricles and atria, leading to an ineffective pump function that can directly and indirectly affect the lungs, liver, and other organ systems. The prevalence of DCM amounts to around 0.9% of adults in the US (Ferri, 2013), and the disease is the leading indication for heart transplantation in younger adults. Due to a large variety of individual causes and disease stages, diagnosis and treatment of DCM remains an open challenge.

Cardiac arrhythmia, i.e. irregular electrical activity of the heart, occurs frequently in heart failure patients, particularly in those with DCM (McMurray et al., 2012). But also beyond DCM, the prevalence of cardiac rhythm disorders has increased significantly in the last decade following an improvement in patient care (Marcus et al., 2013). Depending on the kind of rhythm disorder, which is commonly diagnosed using electrocardiography (ECG),

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the treatment of arrhythmia includes drug therapies, radio frequency ablation and the implantation of artificial pacemakers and cardioverter-defibrillators. Unfortunately, around 30% of patients are non-responders to these invasive treatments, and in up to 50% of the cases, recurrences are identified (Auricchio et al., 2011).

As a result, tools for a more predictive assessment of cardiac electrophysiology (EP) are needed. Computational assistance is not only required for a superior patient management and diagnosis but could also benefit therapy planning, outcome prediction and intervention guidance. While improved risk stratification could help avoiding unnecessary surgeries, the potential of optimizing invasive procedures, for instance by choosing optimal electrode locations, can potentially lead to an increased success rate and fewer non-responders. For this purpose, computational models can be employed to study and evaluate patient-specific electrophysiology in silico.

1.2. Technical background: computational models of cardiac electrophysiology

1.2.1. Models of cardiac action potential

A wide range of computational models of cardiac EP with different biological scales and theoretical complexity has been proposed since the seminal work of Hodgkin and Huxley (1952). Especially in the last decade, the community has witnessed tremendous progress in modeling efforts (Clayton et al., 2011). Depending on their level of detail, EP models can be classified into three groups: Biophysical, phenomenological and Eikonal models.

Biophysical cellular models capture cardiac electrophysiology directly at cell level by describing biological phenomena responsible for myocyte depolarization and repolarization. More precisely, ionic interactions within the cell and across the cell membrane (ion channels) are considered (Noble, 1962; Luo and Rudy, 1991; Noble et al., 1998; Ten Tusscher et al., 2004) and lead to complex equations, commonly one per molecular process. Although it has been shown that biophysical models can reproduce different electrophysiological behaviors such as action potential restitution and conduction velocity, the large amount of parameters limits their usage in clinical applications due to the difficulty of personalization.

Cell models are then integrated at the organ level using reaction–diffusion partial differential equations (PDEs). Two major categories can be distinguished. While mono-domain approaches neglect interstitial effects and consider the myocardium as single excitable tissue (Coudière and Pierre, 2006), bi-domain strategies superimpose intra- and extra-cellular domains and take different electrical properties into account (Bourgault et al., 2009). In the absence of external stimuli, mono-domain models have been shown to produce almost identical results as their bi-domain counterparts (Potse et al., 2006).

Phenomonological models, historically the first models to be proposed by FitzHugh (1961), work at a more macroscopic level. Derived from experimental observations, the action potential is described by a small number of parameters with direct influence on its shape, disregarding the underlying ionic interactions (Aliev and Panfilov, 1996; Mitchell and Schaeffer, 2003). Having only few parameters with direct effect on measurable output facilitates model personalization, and the lower computational cost when compared to biophysical models offers a reasonable compromise between modeling capacity and performance. The distinction between mono-domain organ level integration schemes such as in Aliev and Panfilov (1996), Fenton and Karma (1998), Mitchell and Schaeffer (2003) and bi-domain approaches such as in Clayton and Panfilov (2008) can be applied to phenomonological models, too. Recent numerical advances based on Lattice-Boltzmann methods (Rapaka et al., 2012) or Finite Element methods (Talbot et al., 2013) exploit the massively parallel architecture of modern graphics processing units, and allow near real-time performance and user interaction.

Eikonal models (Franzone et al., 1990; Keener and Sneyd, 1998; Sermesant et al., 2007) solely concentrate on the propagation of the electrical wave to stimulate muscle activation. The formation as well as the shape of the action potential in myocytes is neglected. Governed only by the anisotropic speed of wave propagation, the local time of wave arrival throughout the myocardium, can be computed very efficiently using fast marching methods (Sethian, 1999; Wallman et al., 2012). While it has become possible to simulate wave reentry phenomena with Eikonal models (Pernod et al., 2011), capturing other complex pathological conditions such as arrhythmias, fibrillations or tachycardia is more challenging.

1.2.2. Model personalization

In order to apply the aforementioned EP models in clinical settings, patient-specific physiology has to be captured by personalized model parameters. Finding those is challenging in the clinical workflow as the estimation from patient data implies solving an inverse problem. In this context, the *forward model* denotes the computation of the electrical wave propagation from the heart to the point of measurement (catheter electrode, body surface), and the *inverse model* the back-projection of measurement data onto the heart and the inference of model parameters (Gulrajani, 1998).

Inverse problem techniques are computationally demanding because they comprise an optimization problem and therefore require a large quantity of forward model runs (Modre et al., 2002; Chinchapatnam et al., 2008; Dössel et al., 2011). Alternatively, data-driven algorithms have been investigated to tackle model personalization. Linking activation patterns with the resulting cardiac motion that can be observed in clinical images, Prakosa et al. (2013) train a machine-learning algorithm to estimate depolarization times for cardiac segments from regional kinematic descriptors. Jiang et al. (2011) apply statistical learning to map body surface potentials onto the epicardium. Konukoglu et al. (2011) derive a surrogate EP model based on polynomial chaos theory to personalize an Eikonal model. Wallman et al. (2014) infer tissue conduction properties using Bayesian inference to be patient-specific. The advantage of these statistical methods is the possibility to quantify uncertainty and to optimize the location of measurements. Machine learning techniques could therefore constitute efficient strategies for model personalization. However, a sufficient sampling of the parameter space is needed for these approaches to yield meaningful results. In this study, we aim to achieve an estimation of model parameters only from sparse electrocardiogram data.

1.2.3. Models of electrocardiogram and torso potential

From the perspective of data acquisition, endocardial mapping (Sermesant et al., 2009; Relan et al., 2011) facilitates the parameter estimation as it provides dense potential measurements but it is pre-operatively often avoided as it is invasive. A non-invasive alternative is to back-project electrical potentials measured at the body surface in the form of electrocardiograms (ECG), to the epicardium. Considering the ill-posedness of the parameter estimation, the use of body surface mapping (BSM) has been investigated (Dössel et al., 2011; Wang et al., 2011; Han et al., 2013). In contrast to standard 12-lead ECG, BSM is however not yet widely available as diagnostic modality.

If body surface ECG data is used for parameter estimation, regardless of the number of traces, a model of electrical potentials at the surface of the torso is needed. In terms of the forward model, current approaches employ both Finite Element (FEM) and Boundary Element (BEM) methods. While the former intrinsically