

A Recursive Cellular Automaton that Reconstructs Transmembrane Voltages with a Range-Adjusted Tikhonov-Method

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Abstract. Tikhonov methods usually lead to solutions of low amplitude that are distributed around zero. When reconstructing transmembrane voltages (TMVs) in the myocardium, the signal is therefore often not in the physiological range of between around $-80mV$ and $10mV$. In this article, we propose an adjusted Tikhonov method that reconstructs TMVs in the correct range, given an estimate of one polarized node in the heart and an estimated set of nodes that have depolarized in the preceding time step. It is shown that when feeding the reconstructed TMVs into a simple cellular automaton recursively, and when using the computed excitation propagation as a prior for the Tikhonov method, it is possible to reconstruct the excitation propagation throughout the ventricular myocardium. The method requires an estimate of the region of initial activation.

Keywords: inverse problem of ECG, electrocardiographic imaging, model-based, extrasystole, body-surface-potential-map

1. Introduction

The pre-interventional localization of extrasystoles and an imaging of the activation sequences of TMVs in the heart could facilitate a treatment planning for ablation therapies. With pre-interventional information on the cardiac electrophysiology available, the duration of invasive therapies could be reduced and their accuracy improved.

Various approaches have been made to reconstruct myocardial activation times or TMVs from body surface potential maps (BSPMs). Among the most established approaches to solve the problem for spatial distributions of sources are the Tikhonov method and the generalized minimal residual regularization [Rudy, 2010]. Another set of methods is available for the reconstruction of activation times in the cardiac muscles, namely the method of critical points and times [Huiskamp and van Oosterom, 1988], wavefront-based approaches [Ghodrati et al., 2006] or the uniform double layer method [Cuppen and van Oosterom, 1984].

This work combines a simple rule-based computer model of excitation propagation with a Tikhonov solver that reconstructs TMVs.

In contrast to the wavefront-based approach by Ghodrati, the proposed recursive solver is only fed with estimates for a single reference node and a set of wavefront nodes. The estimates are used to adjust the range of reconstructed TMVs, which is a new alternative to setting upper and lower bounds [Messnarz et al., 2004].

2. Methods

The excitation pattern of a ventricular extrasystole was simulated on a heart model and the corresponding BSPM calculated. From the BSPM, TMVs in the ventricles were reconstructed using linear least squares optimization, combined with a simple cellular automaton.

2.1. Simulation of the ventricular extrasystole

Anatomical models of the heart and thorax (Fig. 1) were obtained from segmented MRI measurements of a test subject (male, healthy). Electrophysiological models were parameterized with conductivities published by [Gabriel and Gabriel, 1996], and action potential curves were generated with the cell model by [Tusscher et al., 2004]. A rule-based cellular automaton was then used to simulate the excitation conduction in the ventricular myocardium. The automaton assigns the previously generated action potential curves to the activations it has generated [Doessel et al., 2005]. The desired location of an extrasystole in the left ventricle was taken as excitation origin for the automaton, which resulted in the simulated distribution of TMVs shown in Fig. 4 (upper row).

2.2. Forward problem of ECG

A BSPM consists of extracellular potentials Φ_e that are calculated from the simulated TMVs x_{TMV} in the ventricles using a bidomain model [Keller et al., 2010; Henriquez, 1993]. This results in a Poisson problem as stated in Eq. 1, where σ_i and σ_e are the intracellular and extracellular conductivities. The equation was solved in a finite element approach with tetrahedral meshes. The resulting BSPM was overlaid with 30dB additive white Gaussian noise (AWGN) to simulate the conditions of a practical setting. This is shown for the Einthoven ECG leads in Fig. 1.

$$\nabla \cdot ((\sigma_i + \sigma_e) \nabla \Phi_e) = -\nabla \cdot (\sigma_i \nabla x_{TMV}) \quad (1)$$

With the electrophysiological and anatomical model available, a linear relationship can be established between TMVs x_{TMV} as cardiac sources and the resulting BSPM z_{BSPM} :

$$Ax_{TMV} = z_{BSPM} \quad (2)$$

where A is a transfer matrix that is responsible for mapping potentials from the heart volume to the body surface.

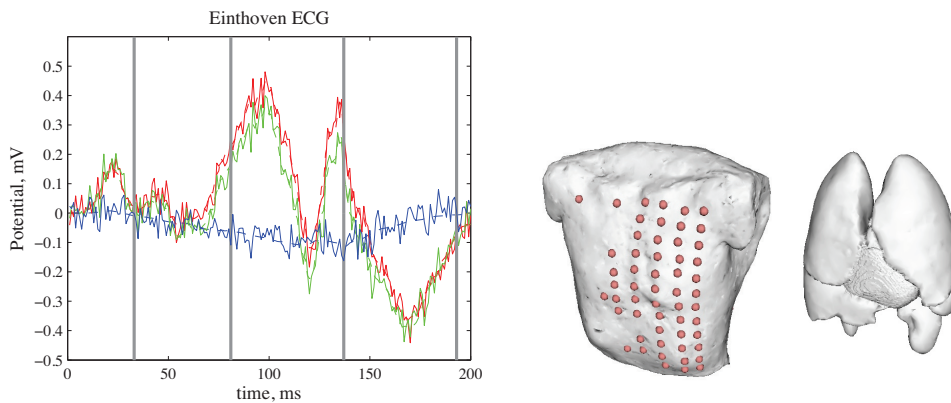


Figure 1. ECG of the simulated extrasystole (Einthoven leads, with and without 30dB additive white Gaussian noise). Anatomical model of the volume conductor, with 63 BSPM electrodes placed on the anterior body surface.

2.3. The linear inverse problem of ECG

Solving Eq. 2 for x_{TMV} would allow for a non-invasive reconstruction of TMVs from BSPMs. The problem, however, is ill-posed, since the solution is not unique and strongly influenced by noise in z_{BSPM} . These obstacles can only be overcome with a regularization of the solution, i.e., by introducing *a-priori* knowledge on the expected source signal. In Tikhonov 2nd order regularization, a linear least squares problem is solved, in which both the equation error and an additional smoothing term are minimized [Hansen, 1998]:

$$\|Ax_{TMV} - z_{BSPM}\|_2^2 + \lambda^2 \|Lx_{TMV}\|_2^2 \rightarrow \min \quad (3)$$

where λ is a weighting factor and L is the Laplace operator.

2.4. Range-adjusted Tikhonov method

In this work, the Tikhonov method shall be given an additional constraint. Although it is well known that the range of TMVs is between $-80mV$ and $10mV$ in myocardial cells, Eq. 3 does not force the solution to stay within its physiological limits. To achieve this, an extended cost term is proposed, in which a subset $\Gamma_{activated}$ of the nodes of the myocardium Ω is pulled towards $10mV$, another subset Γ_{dist} is pulled towards $-80mV$ and all other nodes remain unaffected:

$$\|Ax_{TMV} - z_{BSPM}\|_2^2 + \lambda^2 \|Lx_{TMV}\|_2^2 + m^2 \|S(x_{TMV} - x_{prior})\|_2^2 \rightarrow \min \quad (4)$$

where m is a weighting factor and S is a selection matrix that is diagonal with

$$s_{ii} = \begin{cases} \sqrt{\frac{|\Omega|}{|\Gamma_{activated}|}} & \text{if } i \in \Gamma_{activated} \\ \sqrt{\frac{|\Omega|}{|\Gamma_{dist}|}} & \text{if } i \in \Gamma_{dist} \\ 0 & \text{else} \end{cases} ; \quad \Gamma_{activated} \subseteq \Omega, \Gamma_{dist} \subseteq \Omega, \Gamma_{activated} \cap \Gamma_{dist} = \emptyset,$$

$$x_{prior,i} = \begin{cases} 10mV & \text{if } i \in \Gamma_{activated} \\ -80mV & \text{if } i \in \Gamma_{dist} \\ 0 & \text{else} \end{cases}$$

The least squares solution of the minimization problem yields the following estimate:

$$\hat{x}_{TMV} = (A^T A + \lambda^2 L^T L + m^2 S^T S)^{-1} (A^T z_{BSPM} + m^2 M^T M x_{prior}) \quad (5)$$

2.5. Recursive cellular automaton

The range-adjusted Tikhonov method is applied in combination with a recursive cellular automaton in each time step. After the inverse problem has been solved with Eq. 5 in the previous time step, an *absolute threshold* is applied on all sources of

TMVs to find those undergoing depolarization. After a node in the tetrahedral mesh is classified as depolarizing source, the algorithm looks for neighbors that are already *activated*. If a depolarizing node is in vicinity to the *activated* areas the node itself is permanently classified as *activated*. Otherwise the detected depolarization is ignored and assumed to being caused by noise.

The product of an estimated *excitation conduction velocity (ECV)* and the sampling interval defines the extent of a node's vicinity. Only if a node is within reach of the excitation wavefront, it is considered a neighbor.

2.6. Regularization parameters

In this study, the initial estimate for the recursive algorithm in Sect. 2.5 is taken from the simulation. Reconstructions are produced from the BSPM with a sampling rate of 125Hz . Often the clinician knows for sure that the origin is in the left ventricle. In this case one single node in the right ventricle is assumed to safely produce a TMV of -80mV (Γ_{dist} , see Fig. 4).

In order to find a proper regularization parameter m in Eq. 5, the capability of the cost term to constrain subsets $\Gamma_{\text{activated}}$ and Γ_{dist} to their desired range was assessed in Fig. 2. With λ set to $\lambda = 0.001$, which is a proper choice for Tikhonov 2nd order regularization, m was found to establish the desired conditions at $m = 0.001$.

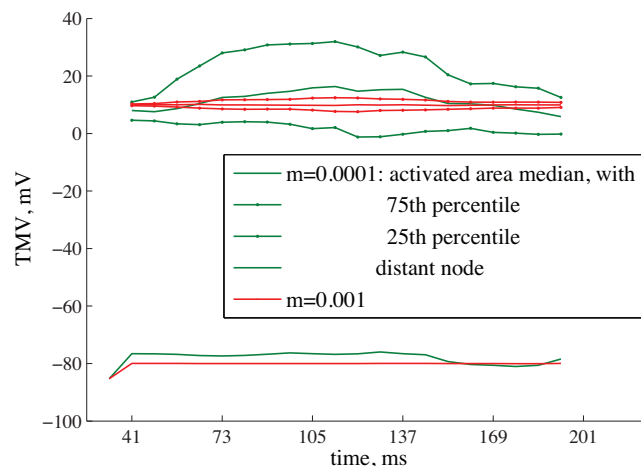


Figure 2. Range of the reconstructed signals belonging to subsets $\Gamma_{\text{activated}}$ (top) and Γ_{dist} (bottom) for different weighting factors m . Reconstruction of TMVs from the BSPM of the simulated extrasystole as obtained with Eq. 5 and the recursive cellular automaton (absolute threshold is -10mV , expected ECV is set to 1000mm/s).

3. Results

3.1. Effect of absolute threshold and estimated excitation conduction velocity

The capability of the algorithm to produce a solution that is not only predetermined by the setup itself but also significantly influenced by the measured BSPM is demonstrated in Fig. 3. It is shown that depolarizations are concentrated along the borderline of the activated area for absolute thresholds greater than -30mV and if a great enough excitation conduction velocity (ECV) is assumed in the recursive algorithm. For the same conditions, it is also shown that depolarizations in the neighborhood of the borderline have indeed a great influence on the spread of the *activated* area, since they occur in only a fraction of the neighborhood that could

possibly be assigned to the *activated* area of the next time step. With lower thresholds, there is an increasing likelihood for depolarizations to occur in areas outside the activated region and its neighbourhood.

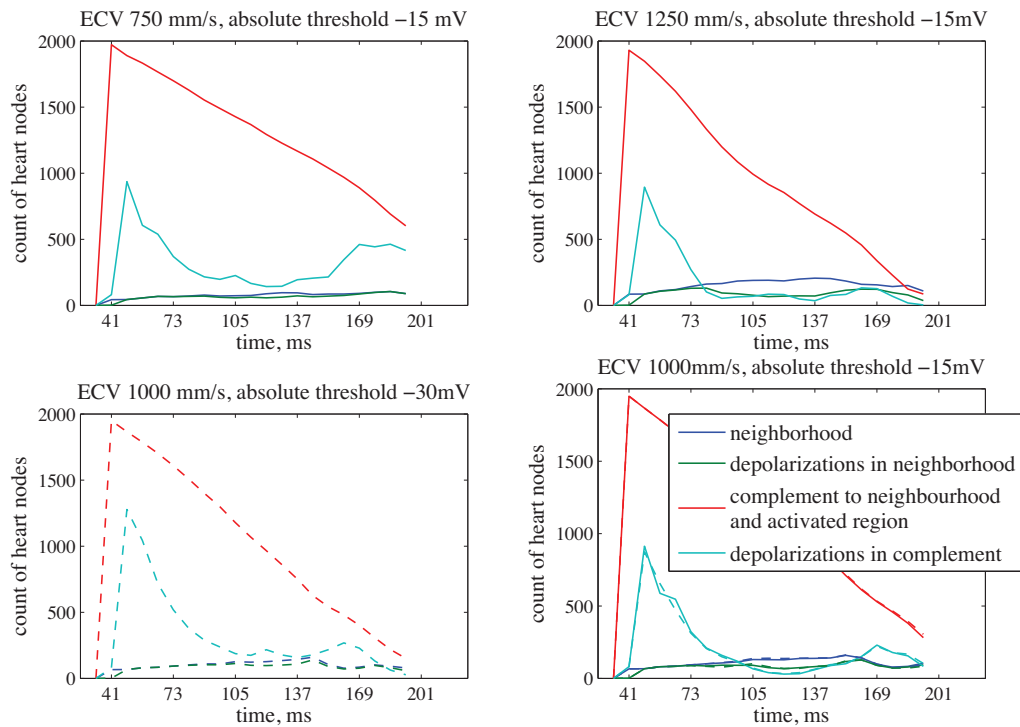


Figure 3. Recursive reconstruction of TMVs from the BSPM of the ventricular extrasystole. Evolution of statistical parameters over time for different assumptions on the excitation conduction velocity and for different absolute thresholds. Dashed lines indicate that the BSPM has not been corrupted with noise before reconstruction; solid lines indicate an AWGN of 30dB.

3.2. Reconstruction of transmembrane voltages

For a setup with an *absolute threshold* of -15mV and the ECV set to 1250 mm/s , the TMVs of the extrasystolic beat were reconstructed (see Fig. 4) using the recursive cellular automaton of Sect. 2.5 and the range-adjusted Tikhonov method of Sect. 2.4. Time samples in Fig. 4 correspond to those in Fig. 1.

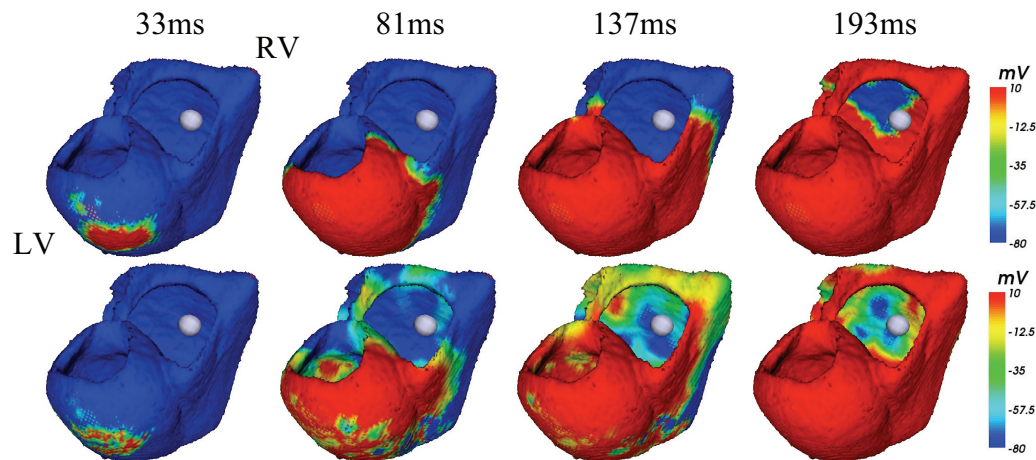


Figure 4. Upper row: simulated extrasystole (ground truth) - lower row: reconstruction from BSPM with AWGN of 30dB using the recursive cellular automaton and range-adjusted Tikhonov method. Absolute threshold: -15mV , estimated ECV: 1250 mm/s (LV: left ventricle, RV: right ventricle, grey marker: node in Γ_{dist}).

4. Discussion and conclusions

Results demonstrate the capability of the proposed algorithm of reconstructing TMVs in their physiological range, with the reconstructed excitation spread closely resembling the simulation.

As this is a model-based method, it is important to discuss the likelihood of committing inverse crimes: if a low *absolute threshold* were chosen for the recursive cellular automaton, together with an excitation conduction velocity in the exact range of the original simulation, the proposed algorithm would produce very similar results to that of the simulation. Both simulation and reconstruction would be based on the same anatomical and physiological model. This aspect, however, has been given particular attention: neither has an *absolute threshold* been chosen that would lead to a domination of the model over the measurements nor is the estimated ECV in a range that would facilitate such domination (see Fig. 3).

In the study, the initial estimate is taken from the simulation itself. In a practical setting, it would have to be derived from an estimate of the excitation origin. In the ventricles, excitation origins can be estimated with accuracy of around 20mm [Ramanathan et al., 2003], and under certain conditions with up to 1.5mm [Liu et al., 2005]. The robustness of the proposed method against errors in the initial estimate is subject to future research. Also, it has to be noted that a personalization of the recursive cellular automaton parameters becomes necessary in the presence of myocardial pathologies that affect thresholds or the spread of excitation. The range of TMVs was found to be robust against the selection of polarized nodes. This causality has to be given particular attention in future studies with the proposed method.

Acknowledgements

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