How Genetic Algorithms can Improve a Pacemaker Efficiency

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ABSTRACT

In this paper, we propose the use of Genetic Algorithms as a tool for improving a pacemaker efficiency in a defective heart. Such device is generally used when the electrical activity of the heart is deficient and consists in applying electrodes on several points at the surface of the heart. By optimizing the positions of these electrodes with respect to a well chosen criteria, we show the significant gain that can be achieved with this technique compared to a less systematic positioning.

Categories and Subject Descriptors

J.3 [**Computer Applications**]: Life and medical sciences

General Terms

Algorithms

Keywords

optimization, heart, electrical activity

1. INTRODUCTION

The heart is located between the lungs and consists of four parts, the right and left atria and ventricles. The function of the heart involves pumping blood from the lung and the body and ejecting it towards the body allowing the organs to operate. This function is the result of a contraction–relaxation process induced by an electrical impulse moving across the heart. The electrical signal is first induced in the sinus node, the natural pacemaker, then propagates through the atria and reaches the ventricles through the atrioventricular (A-V) node, see Figure 1[1]. In the ventricles, the propagation is led by the bundle of His causing a wavefront which propagates by a cell–to–cell activation. In each cell, a depolarization phase occurs corresponding to the inflow of sodium ions (causing the electrical activation) followed by a plateau phase, and then by a repolarization phase corresponding to the outflow of potassium ions. This phenomenon is illustrated in Figure 1 by the representation of the potential action in different types of cardiac cells.

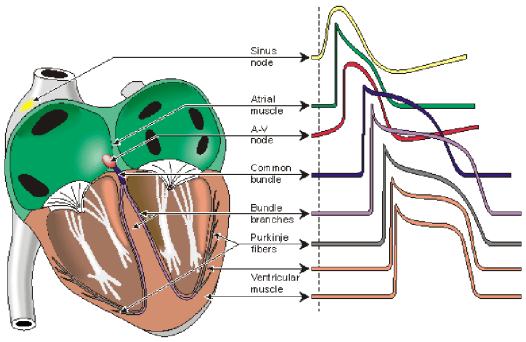

Figure 1: Potential profiles at various points

The electrical activity of the cell membranes is generally modelled by the so–called bidomain equations [1] in which the current term due to ionic exchanges can be modelled by the FitzHugh–Nagumo model [2, 6].

The electrical conduction of heart may be defective causing the heartbeat to be too fast, too slow or irregular. Some pathologies, as for example sinus node dysfunction or bundle branch block are treated with an artificial pacemaker which is used to help the heart to recover a quasi–normal electrical activity. A pacemaker consists of a small battery and electrodes transmitting the electrical impulse. Though today pacemakers give good results, certain questions still arise. How many electrodes should be set? Where the electrodes should be placed? When the electrodes should act? Many experiments are led to give answers to these questions, see [7] and references therein. As experimental measurements are difficult to obtain, numerical simulations may contribute to a better understanding.

Our aim in this paper is to determine the optimal positioning of electrodes of a pacemaker on a disease heart. This can be interpreted as an inverse type optimization problem which can be solved with optimization tools such as Genetic Algorithms. Already used in many other medical applications, cite for instance in the heart domain the classification of ischemic beats [5], Genetic Algorithms are well adapted

[1]Figure from Bembook:
http://butler.cc.tut.fi/ malmivuo/bem/bembook

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when the cost function is not smooth or forms a complex simulation, as it is the case here.

The paper is organized as follows. In Section 2 we present the bidomain/Fitzhugh–Nagumo model used to perform the numerical simulation of the cardiac electrical activity. Section 3 is devoted to the optimization description and in Section 4 and 5, we present and discuss some numerical results on a simplified test case representative of a left bundle branch block in a modelled human heart. We end the paper with some conclusions in Section 6.

2. MODELLING OF THE HEART ELECTRICAL ACTIVITY

2.1 The bidomain model

At the microscopic level, the cardiac muscle, denoted by Ω_H, is made of two distinct and intricate media: the intra and extra-cellular media, respectively called Ω_{Hi} and Ω_{He}, that are separated by a surface membrane Γ_H (see Figure 2).

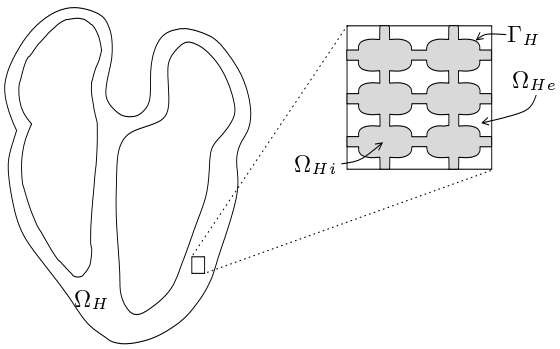

Figure 2: Simplified view of the heart at macro/microscopic level.

After a homogenization process, the corresponding electrical potentials ϕ_i and ϕ_e and the transmembrane potential

$$V_m(t,x) = \phi_i(t,x) - \phi_e(t,x) \tag{1}$$

are defined on the entire domain $x \in \Omega_H$ and satisfy the so–called bidomain model [1], on $[0,T] \times \Omega_H$:

$$A_m \left(C_m \partial_t V_m + I_{\text{ion}}\right) - \text{div}(\sigma_i \nabla V_m) = \text{div}(\sigma_i \nabla \phi_e)\,, \tag{2}$$

$$\text{div}(\sigma_i \nabla \phi_i) = -\text{div}(\sigma_e \nabla \phi_e)\,, \tag{3}$$

with the following boundary condition on the heart boundary $\partial\Omega_H$:

$$\sigma_i \nabla \phi_i \cdot n = \sigma_e \nabla \phi_e \cdot n = 0\,, \tag{4}$$

where n denotes the outward unit normal at $x \in \partial\Omega_H$.

Finally an initial condition is prescribed:

$$V_m(0,x) = V_m^0(x) \quad \text{ in } \Omega_H\,. \tag{5}$$

In this model, the parameters A_m, C_m, σ_i and σ_e respectively denote the average rate of membrane surface per volume area, the membrane capacity and the intra and extracellular conductivity tensors.

The current term due to ionic exchanges, I_{ion}, is evaluated with the help of the simple but non-physiological Fitzhugh-Nagumo model [2, 6]:

$$I_{\text{ion}} = -\frac{1}{\epsilon}(-(V_m - V_r)(V_m - V_s)(V_m - V_a) - u)\,, \tag{6}$$

where the auxiliary variable u satisfy the following ODE:

$$\frac{du}{dt} = k(V_m - V_r) - u\,, \tag{7}$$

and $V_r < V_s < V_a$ respectively represent the potential at rest, the threshold and the activity potential, ϵ and k are positive coefficients.

2.2 Pathologic case

The pathology we consider here is called left bundle branch block. In such situation, the electric signal can not be propagated by the bundle of His in the left ventricle, consequently the depolarization process occurs with delay causing asynchronous contraction–decontraction. In the previous bidomain model, it is simulated by an absence of initial natural stimulation in the left ventricle in equation (5).

In order to help the heart to recover its normal electrical activity, a well known surgery device, called pacemaker, is used. It acts through the application of a certain number of electrodes located at the heart surface that are able to give a local electrical impulse. In the previous bidomain model, the electrodes act like a local (in space and time) current volumic source term in the right hand side of the equation (2).

3. OPTIMIZATION PRINCIPLES

In order to improve the efficiency of a pacemaker, the idea is to optimize the positioning of its electrodes. An error-type cost function between the reference healthy case and the pathologic case with a given position of electrodes has to be defined. The optimization is then achieved by using Genetic Algorithms.

3.1 Definition of an appropriate cost function

The first cost function that has been tested is the quadratic norm in space and time of the difference between the transmembrane potential V_m of a disease heart with a given position of electrodes and its target value $V_{m,target}$ computed for the healthy case:

$$J_1 = \int_0^T \int_{\Omega_H} |V_m - V_{m,target}|^2 dx dt\,. \tag{8}$$

Actually, this first and natural cost function does not give satisfactory results for two reasons. First, it is due to the fact that the electrical activity of electrodes will represent a major obstacle to make V_m converge to $V_{m,target}$ on the whole domain in space and time. Moreover, the right criteria to recover a normal electrical activity is rather to reduce the delay of a characteristic depolarization time. A new and better cost function is thus introduced and is expressed as

$$J_2 = t_d - t_{d,target}\,, \tag{9}$$

where t_d represents the first time for which 95 per cent of the whole heart is depolarized:

$$t_d = \inf\{t \geq 0, \quad \text{Volume}(\Omega_t) \geq 0.95\,\text{Volume}(\Omega_H)\}\,,$$

with:

$$\Omega_t = \{x \in \Omega_H, \quad V_m(t,x) > V_s\}\,.$$

As previously, $t_{d,target}$ denotes the same value for the corresponding healthy heart.

3.2 Optimization by Genetic Algorithms

The cost functions J_1 or J_2 previously described are computed after solving a complex set of coupled PDE and ODE with strong three-dimensional effects. Moreover, due to the complexity of the heart geometry, they display a non-smooth behavior with many local minima. For all these reasons, the minimization of J_1 and J_2 is achieved by using evolutionary algorithms and more precisely Genetic Algorithms.

Inspired from the Darwinian theory of evolution of species, Genetic Algorithms [3] have been applied in the last decade in various applicative domains including the biomedical field, ranging for instance from the aerodynamic optimization of a car shape [4], to the classification of ischemic heart beats [5].

In the present case, a classical real coded Genetic Algorithm is used to optimize the positioning of one or two electrodes of a pacemaker on the internal boundary surface of the heart, also called endocardium. A mapping from the endocardium or a part of it to a simple plane domain, for instance a rectangular domain of $\mathbb{R}^2$, has first been defined in order to simplify the parametric search space.

The selection process used in the Genetic Algorithm is done with a proportionate roulette wheel with respective parts based on the rank of each element in the population. The crossover of two elements is obtained by a barycentric combination with random and independent coefficients in each coordinate whereas the mutation of one element is of non uniform type. Finally, a one-elitism principle is added in order to make sure to keep in the population the best element of the previous generation.

4. DESCRIPTION OF THE TEST CASE

The simulations are performed on a simplified geometry which contains ventricles only, see Figure 3.

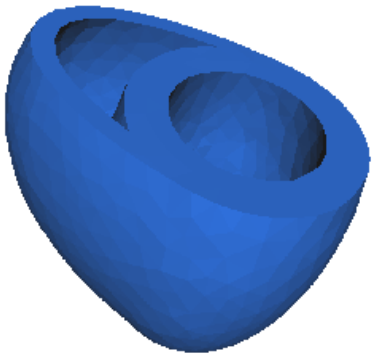

Figure 3: A simplified heart geometry Ω_H.

The domain, closed to a human heart, is analytically defined through its boundary, made of the union of four truncated ellipsoids:

$$(\tfrac{x}{a_{iL}})^2 + (\tfrac{y}{b_{iL}})^2 + (\tfrac{z}{c_{iL}})^2 = 1, \quad (\tfrac{x}{a_L})^2 + (\tfrac{y}{b_L})^2 + (\tfrac{z}{c_L})^2 = 1\,,$$

with $\{a_{iL}\,, b_{iL}\,, c_{iL}\,, a_L\,, b_L\,, c_L\} = \{2.72, 2.72, 5.92, 4, 4, 7.2\}$ cm for the left ventricle internal and external boundary respectively, and

$$(\tfrac{x}{a_{iR}})^2 + (\tfrac{y}{b_{iR}})^2 + (\tfrac{z}{c_{iR}})^2 = 1, \quad (\tfrac{x}{a_R})^2 + (\tfrac{y}{b_R})^2 + (\tfrac{z}{c_R})^2 = 1\,,$$

with $\{a_{iR}\,, b_{iR}\,, c_{iR}\,, a_R\,, b_R\,, c_R\} = \{7.36, 3.36, 6.2, 8, 4, 6.84\}$ cm for the right ventricle.

All these ellipsoids are restricted to the half space $z \leq 2.75$.

In a real surgical case, the electrodes can be placed in the atria and/or in the ventricles. As we only consider here the heart ventricles, we seek for the best positioning of the electrodes in the internal surface of the left ventricle. The chosen cost function to minimize, J_2, is defined in (9).

Two optimization processes are presented in the next section, depending on the allowable number of electrodes, respectively one or two. Note the second computation has been achieved for comparative purposes with the first case, regardless of the surgical constraints to handle it.

In the following section, the numerical results obtained on this test case using the optimization principles presented in Section 3 are described.

5. NUMERICAL RESULTS

We choose the conductivities in (2) and (3) such that the anisotropy of the fibers in the myocardium are taken into account, namely $\sigma_i = \alpha_i^t(I - d_f \otimes d_f) + \alpha_i^l(I - d_f \otimes d_f)$ and $\sigma_e = \alpha_e^t(I - d_f \otimes d_f) + \alpha_e^l(I - d_f \otimes d_f)$, where d_f is the direction of the fibers, I the identity matrix in $\mathbb{R}^3$ and $\alpha_i^t = 5\,10^{-3}\,, \alpha_i^l = 1.5\,10^{-1}\,, \alpha_e^l = 1.\,10^{-1}$ and $\alpha_e^t = 7.5\,10^{-3}$. The parameters in (2)–(7) are choosen as follows: $A_m = C_m = 1$, $V_r = 0$ mV, $V_s = 0.5$ mV, $V_a = 1$ mV, $\epsilon = 3.2\,10^{-3}$ and $k = 2.5\,10^{-2}$.

The intensity of the initial stimulation equals 0.5 mV during 10 ms. The artificial stimulations have the same intensity as the initial stimulation and hold during 40 ms. As we are interested in the depolarization phase only, the final time of computations is actually equal to 100 ms whereas the total duration of depolarization–repolarization process is 300 ms.

The domain Ω_H is discretized with tetrahedra for a total number of nodes equal to 12921. The ionic current is solved by the *cvode*[2] solver, an appropriate solver for stiff nonlinear systems of ODE. The bidomain problem (2)–(5) is approximated by a piecewise finite elements scheme in space and by a second order backward differences scheme in time with a time step equals to 0.5 ms. The simulations are done with the C++ library *LifeV*[3].

We take 40, respectively 80, individuals in the GA population for the optimization of the positioning of one, respectively two electrodes. In both cases, the crossover probability and the mutation probability are respectively chosen

[2]http://llnl.gov/casc/sundials
[3]http://www.lifev.org/

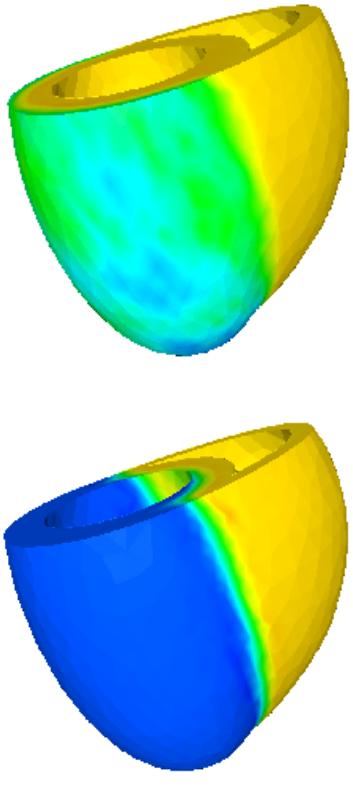

Figure 4: The wavefront in the ventricles at $t = 28.5$ ms in the healthy case (top) and in the pathologic case (bottom)

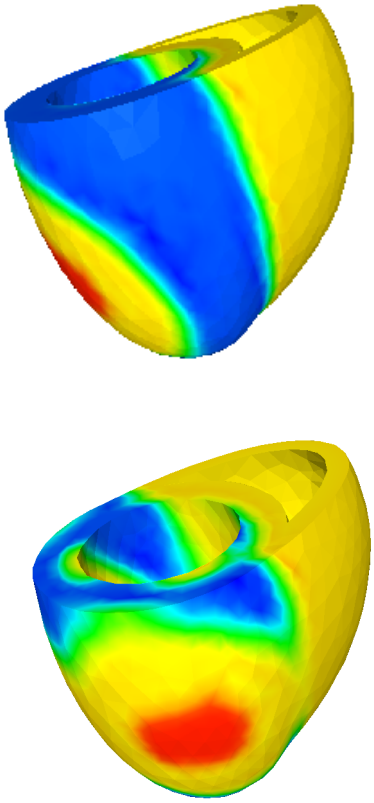

Figure 5: The wavefront in the ventricles at $t = 28.5$ ms in the pathologic case treated with one electrode (top) and two electrodes (bottom)

equal to 0.9 and 0.6. A number of 10 generations is then needed to achieve a near optimal solution.

A very good reproducibility for the obtained optimal solution, has been observed after doing a large number of GA runs (more than 10). The optimal positions that are given below correspond to the mean values after all these runs but can also be obtained after any single run. On the contrary, the convergence history of the GA, not plotted here, can be different from one run to another depending on the quality of the first random generation.

In presence of one electrode, the mean optimal positioning correspond to the value

$$(x, y, z) = (2.54, -0.024, 2.12)\,,$$

and in presence of two electrodes, the mean optimal positioning is:

$$(x_1, y_1, z_1) = (1.64, 2.06, -1.47)$$
$$(x_2, y_2, z_2) = (1.60, -2.08, -1.59).$$

Note that in the second case, the two electrodes are positioned in a symmetric way with respect to $y = 0$, which is not surprising remembering the analytic description of the heart surface boundary. Another interesting observation for clinical purposes is that all the optimal positions are localized in the opposite side of the bundle of His.

In the case of a healthy heart, we obtain $t_{d,target} = 28.5$ ms which means that at this time, 95% of the cells are depolarized whereas in the pathologic case with no electrodes, only 52.4% are depolarized at this time and $t_d = 98$ ms.

Figure 4 and 5 respectively show the wavefront at $t_{d,target}$ for the healthy case, the pathologic case, and the pathologic case treated with one and two optimally located electrodes.

In presence of one electrode the minimal value of t_d reduces to 45 ms, namely $J_2 = 16.5$ ms. Note in this case that at $t_{d,target}$, 71.5% of cells are depolarized. In presence of two electrodes the minimal obtained value is $t_d = 36.5$ ms, namely $J_2 = 8$ ms. In this case, 80.6% of cells are depolarized at $t_{d,target}$.
The corresponding isolines of V_m depicted on Figure 4 and 5 at $t_{d,target}$ clearly corroborate these observations and show that the presence of one or two well positioned electrodes reduce the delay in the depolarization of the whole heart.

When one electrode acts, the optimal value of J_2 namely 16.5 ms, has to be compared with possible values ranging

between 60 and 70 ms when the electrode positioning is done randomly. Similarly, when two electrodes act, the best value of the cost function J_2 after the optimization is equal to 13 ms but this function can reach values higher than 50 ms for a random positioning. This last observation can be summed up by saying that an optimal positioning of electrodes (either 1 or 2) can reduce by a factor up to 3 the delay in the characteristic depolarization time compared to a random positioning.

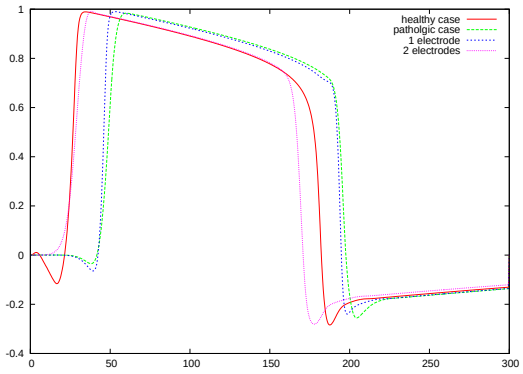

Figure 6: Comparison of potential profiles at a given point in the healthy, pathologic, pathologic with one and two electrodes cases.

Figure 6 gives the potential profiles at the particular point $(x, y, z) = (-2.04, -0.16, -4.19)$ in the healthy and pathologic cases and in presence of one and two optimally located electrodes. We can observe the delay in the activation of the potential at that point and the effect of the two electrodes in bridging this delay. The effect of the two electrodes is observed during the depolarization phase (between 30 ms and 100 ms, depending on the case), and also during the repolarization phase (between 175 ms and 220 ms). At this particular point, the gain obtained when passing from one to two electrodes is rather significant.

Finally, it is interesting to observe that the choice of the current cost function J_2 is also efficient in order to recover a good electrocardiogram. The complete computation of the ECG comes from a coupling, not detailed here, see [8], between the previous bidomain model and a torso domain, considered as a passive conductor.

6. CONCLUSIONS

In this paper we have considered the problem of positioning the electrodes of a pacemaker in a disease heart. To achieve it efficiently, we have proposed a numerical approach based on the use of a cost function linked to the depolarization of the heart cells, which is the major process as it controls the contraction of the heart. The problem can then be treated as an inverse optimization problem and has been solved here by using a Genetic Algorithm. Numerical results clearly show the large influence of the positioning of one or more electrodes on the quality of the electrical activity recovery of the heart and consequently, the crucial need to do the electrode positioning on a systematic way rather than doing it randomly.

6.1 Acknowledgments

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