

Numerical Solution for PDE-Constrained Optimization Problem in Cardiac Electrophysiology

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ABSTRACT

In this paper, we present the numerical solution for the PDE-constrained optimization problem arises in cardiac electrophysiology. The monodomain model, which is a well-established model for simulating electrical behavior of the cardiac tissue, appears as the constraint in our problem. Our objective is to search for the optimal applied current, which is able to dampen out the excitation wavefront of the transmembrane potential during defibrillation process. The modified Dai-Yuan nonlinear conjugate gradient method is employed for computing the optimal applied current, and our numerical results show that the excitation wavefront is successfully dampened out by the optimal applied current.

General Terms

PDE-constrained optimization, Cardiac electrophysiology.

Keywords

Monodomain model, Operator splitting, Optimal control.

1. INTRODUCTION

Sudden cardiac death is an unexpected death of a person in a short time period, and is often attributed to cardiac arrhythmias. During an arrhythmia, the heart may beat too slowly, too rapidly, or irregularly. There are many types of cardiac arrhythmia, and the most common life-threatening arrhythmia is ventricular fibrillation. Currently, the only effective therapy for termination of ventricular fibrillation is through electrical defibrillation [1, 2]. However, there are some adverse effects associated with defibrillation such as myocardial dysfunction and damage [3]. In the effort of minimizing the adverse effects, it is essential to determine the minimal current required for successful defibrillation. As a result, the optimal defibrillation process can be formulated as a PDE-constrained optimization problem, in which the monodomain model appears as the constraint.

The monodomain model is a well-established mathematical model for numerical simulation of cardiac electrical activity [4, 5]. It consists of a parabolic partial differential equation (PDE) coupled with a system of nonlinear ordinary differential equations (ODEs) representing cell ionic activity. In the context of optimally controlled defibrillation process, it is essential to determine the optimal applied extracellular current, which is able to drive the heart rhythm back to normal. In other words, we are trying to search for the optimal current in such a way that it dampens the excitation wavefront of the transmembrane potential during defibrillation process. The main purpose of this paper is therefore to provide a numerical solution for the optimal control problem of the monodomain model.

The structure of the paper is organized as follows. Section 2 presents the optimal control problem of the monodomain model with Rogers-Modified FitzHugh-Nagumo ion kinetic. The numerical approach used to solve the optimal control problem is discussed in Section 3, while the optimization algorithm is presented in Section 4. Next, the numerical results are given in Section 5. Finally, we conclude our paper with a short discussion in Section 6.

2. OPTIMAL CONTROL PROBLEM

Let $\Omega \subset \mathbb{R}^2$ denotes the computational domain, $\Omega_c \subset \Omega$ denotes the control domain and $\Omega_o \subset \Omega$ denotes the observation domain. The optimal control problem for monodomain model is given by

$$\begin{aligned} \min J(V, I_e) &= \frac{1}{2} \int_0^T \left(\int_{\Omega_o} |V|^2 d\Omega_o + \alpha \int_{\Omega_c} |I_e|^2 d\Omega_c \right) dt \\ \text{s.t. } \nabla \cdot (D \nabla V) - \beta C_m \frac{\partial V}{\partial t} - \beta I_{ion} - I &= 0, \text{ in } \Omega \times [0, T] \\ \frac{\partial w}{\partial t} - f &= 0, \text{ in } \Omega \times [0, T] \\ (D \nabla V) \cdot \eta &= 0, \text{ on } \partial \Omega \times [0, T] \\ V(x, 0) &= V_0(x), \text{ on } \Omega \\ w(x, 0) &= w_0(x), \text{ on } \Omega \end{aligned} \quad (1)$$

where

$$D = \frac{\lambda}{1 + \lambda} D_i \quad \text{and} \quad I = \frac{1}{1 + \lambda} I_e$$

Here $\alpha > 0$ is a regularization parameter, T is final simulated time and η is unit normal vector directed outwards from Ω . Moreover, D_i is intracellular conductivity tensor, β is surface-to-volume ratio of the cell membrane, C_m is membrane capacitance per unit area, $I_{ion}(V, w)$ is current density flowing through the ionic channels, $f(V, w)$ is prescribed vector-value functions, λ is a constant scalar used to relate the intracellular and extracellular conductivity tensors, $V(x, t)$ is transmembrane potential, $w(x, t)$ are ionic current variables and $I_e(x, t)$ is extracellular current density stimulus. Both functions $I_{ion}(V, w)$ and $f(V, w)$ depend on the ionic model. In this paper, we adopt Rogers-Modified FitzHugh-Nagumo model [6] which is given by

$$I_{ion}(V, w) = c_1 V \left(1 - \frac{V}{V_{th}} \right) \left(1 - \frac{V}{V_p} \right) + c_2 w V$$

$$f(V, w) = c_3 \left(\frac{V}{V_p} - c_4 w \right)$$

Here V_p is plateau potential, V_{th} is threshold potential, and c_1, c_2, c_3, c_4 are positive parameters. Notice that the optimal control problem in (1) is a PDE-constrained optimization problem with V and w as the state variables, and I_e as the control variable. The control variable is chosen such that it is nontrivial only within the control domain. Also, the control variable is chosen in the best possible way to achieve our control objective, which is to dampen out the excitation wavefront of transmembrane potential in the observation domain.

3. NUMERICAL APPROACH

3.1 First Order Optimality System

We adopt the optimize-then-discretize approach to solve the optimal control problem in (1). For deriving the first order optimality system, Lagrange functional, \mathcal{L} , is formed.

$$\begin{aligned} \mathcal{L} = & \frac{1}{2} \int_0^T \left(\int_{\Omega_o} |V|^2 d\Omega_o + \alpha \int_{\Omega_c} |I_e|^2 d\Omega_c \right) dt \\ & + \int_0^T \int_{\Omega} \left(\nabla \cdot (D\nabla V) - \beta C_m \frac{\partial V}{\partial t} - \beta I_{ion} - I \right) p d\Omega dt \quad (2) \\ & + \int_0^T \int_{\Omega} \left(\frac{\partial w}{\partial t} - f \right) q d\Omega dt \end{aligned}$$

where $p(x, t)$ and $q(x, t)$ are Lagrange multipliers which are used to adjoin the constraints to the cost functional. The first order optimality system is obtained by setting the partial derivatives of (2) equal to zero. As a result, the first order optimality system consists of the following:

$$\left. \begin{aligned} \beta C_m \frac{\partial V}{\partial t} &= \nabla \cdot (D\nabla V) - \beta I_{ion} - I, \\ \frac{\partial w}{\partial t} &= f, \\ (D\nabla V) \cdot \eta &= 0, \\ V(x, 0) &= V_0(x) \text{ and } w(x, 0) = w_0(x), \end{aligned} \right\} \quad (3)$$

$$\left. \begin{aligned} \beta C_m \frac{\partial p}{\partial t} &= -\nabla \cdot (D\nabla p) + \beta [I_{ion}]_v p + [f]_v q - V|_o, \\ \frac{\partial q}{\partial t} &= -\beta [I_{ion}]_w p - [f]_w q, \\ (D\nabla p) \cdot \eta &= 0, \\ p(x, T) &= 0 \text{ and } q(x, T) = 0, \end{aligned} \right\} \quad (4)$$

$$\alpha I_e - \frac{1}{1+\lambda} p = 0, \quad \text{in } \Omega_c \times [0, T] \quad (5)$$

where $[\cdot]_*$ denotes the partial derivative with respect to $*$ and $V|_o$ denotes the transmembrane potential in the observation domain. Here, (3) is known as state system, (4) is known as adjoint system and (5) is the optimality condition.

According to [7], the control-to-state mapping $C \ni I_e \mapsto (V(I_e), w(I_e))$ is well-defined. Thus, the cost functional, $J(V, I_e)$, in (1) can be rewritten as

$$\hat{J}(I_e) = \frac{1}{2} \int_0^T \left(\int_{\Omega_o} |V(I_e)|^2 d\Omega_o + \alpha \int_{\Omega_c} |I_e|^2 d\Omega_c \right) dt$$

where $\hat{J}(I_e)$ is known as reduced cost functional. Furthermore, the gradient of the reduced cost functional is given as

$$\nabla \hat{J}(I_e) = \alpha I_e - \frac{1}{1+\lambda} p$$

3.2 Numerical Discretization

To complete the optimize-then-discretize approach, the optimality system needs to be discretized. In order to reduce the complexity of the optimality system, the operator splitting technique [8] is applied to split (3) and (4) into smaller parts that are easier to solve. After applying the operator splitting technique, the nonlinear PDE in (3) is split into a linear PDE and a nonlinear ODE as follows

$$\beta C_m \frac{\partial V}{\partial t} = \nabla \cdot (D\nabla V)$$

$$\beta C_m \frac{\partial V}{\partial t} = -\beta I_{ion} - I$$

Similarly, the nonlinear PDE in (4) becomes

$$\beta C_m \frac{\partial p}{\partial t} = -\nabla \cdot (D\nabla p)$$

$$\beta C_m \frac{\partial p}{\partial t} = \beta [I_{ion}]_v p + [f]_v q - V|_o$$

For the discretization procedure, the linear PDEs are discretized with Galerkin finite element method in space and Crank-Nicolson method in time. On the other hand, the nonlinear ODEs are discretized with forward Euler method in time. The discretized state system is therefore given as

$$\left. \begin{aligned} \left(\beta C_m \mathbf{M} + \frac{\Delta t_1}{2} \mathbf{K} \right) \mathbf{V}^{n+1} &= \left(\beta C_m \mathbf{M} - \frac{\Delta t_1}{2} \mathbf{K} \right) \mathbf{V}^n \\ \mathbf{V}^{n+1} &= \mathbf{V}^n + \Delta t_2 \left(-\frac{\mathbf{I}_{ion}^n}{C_m} - \frac{\mathbf{I}^n}{\beta C_m} \right), \\ \mathbf{w}^{n+1} &= \mathbf{w}^n + \Delta t_2 \mathbf{f}^n, \\ \mathbf{V}(x, 0) &= \mathbf{V}_0(x), \quad \mathbf{w}(x, 0) = \mathbf{w}_0(x), \end{aligned} \right\} \quad (6)$$

and the discretized adjoint system is given as

$$\left. \begin{aligned} \left(\beta C_m \mathbf{M} + \frac{\Delta t_1}{2} \mathbf{K} \right) \mathbf{p}^n &= \left(\beta C_m \mathbf{M} - \frac{\Delta t_1}{2} \mathbf{K} \right) \mathbf{p}^{n+1} \\ \mathbf{p}^n &= \mathbf{p}^{n+1} + \Delta t_2 \left(\frac{\mathbf{V}^{n+1}|_o}{\beta C_m} - \frac{[\mathbf{I}_{ion}^{n+1}]_v}{C_m} \mathbf{p}^{n+1} - \frac{[\mathbf{f}^{n+1}]_v}{\beta C_m} \mathbf{q}^{n+1} \right) \\ \mathbf{q}^n &= \mathbf{q}^{n+1} + \Delta t_2 \left(\beta [\mathbf{I}_{ion}^{n+1}]_w \mathbf{p}^{n+1} + [\mathbf{f}^{n+1}]_w \mathbf{q}^{n+1} \right), \\ \mathbf{p}(x, T) &= \mathbf{0}, \quad \mathbf{q}(x, T) = \mathbf{0}, \end{aligned} \right\} \quad (7)$$

where \mathbf{M} is the mass matrix, \mathbf{K} is the stiffness matrix, Δt_1 and Δt_2 are the local time-steps.

4. OPTIMIZATION ALGORITHM

The nonlinear conjugate gradient method is an attractive method for solving large-scale unconstrained optimization problem due to its simplicity and low memory requirements [9, 10]. For the previous work, Nagaiah et. al. [11] applied the Dai-Yuan (DY) nonlinear conjugate gradient method [12] for solving the optimal control problem of the monodomain model. For this paper, the modified Dai-Yuan (MDY) method [13] is employed. MDY method is chosen because it not only inherits all the nice properties of DY method, but also proven to converge globally, independent of the line search used. The algorithm for solving the discretized optimal control problem is shown as follows.

Overall Solution Algorithm:

- Step 0. Provide an initial guess \mathbf{I}_e^0 and set $k = 0$.
- Step 1. Set $\mathbf{V}(x, 0) = \mathbf{V}_0(x)$ and $\mathbf{w}(x, 0) = \mathbf{w}_0(x)$. Solve the discretized state system (6).
- Step 2. Evaluate the reduced cost functional \hat{J}^k .
- Step 3. Set $\mathbf{p}(x, T) = \mathbf{0}$ and $\mathbf{q}(x, T) = \mathbf{0}$. Use the result obtained in Step 1 to solve the discretized adjoint system (7).

Step 4. Update the gradient $\nabla \hat{J}^k = \alpha \mathbf{d}^k - \frac{1}{1+\lambda} \mathbf{p}^k$.

Step 5. For $k \geq 1$, check the stopping criteria

$$|\hat{J}^k - \hat{J}^{k-1}| \leq 10^{-4} \quad \text{and} \quad \|\nabla \hat{J}^k\| \leq 10^{-4} (1 + |\hat{J}^k|)$$

If one of them is met, then stop.

Step 6. Compute

$$\mathbf{d}^k = \begin{cases} -\nabla \hat{J}^k, & \text{if } k = 0, \\ -\nabla \hat{J}^k + \theta^k \mathbf{d}^{k-1}, & \text{if } k \geq 1, \end{cases}$$

where

$$\theta^k = \frac{\|\nabla \hat{J}^k\|^2}{(\mathbf{d}^{k-1})^T (\nabla \hat{J}^k - \nabla \hat{J}^{k-1} + \gamma^k \delta^{k-1} \mathbf{d}^{k-1})}$$

$$\gamma^k = 10^{-3} \|\nabla \hat{J}^k\|^2 + \max \left\{ 0, -\frac{(\delta^{k-1} \mathbf{d}^{k-1})^T (\nabla \hat{J}^k - \nabla \hat{J}^{k-1})}{\|\delta^{k-1} \mathbf{d}^{k-1}\|^2} \right\}$$

Step 7. Compute step-length δ^k using Armijo line search.

Step 8. Update the control variable $\mathbf{I}_e^{k+1} = \mathbf{I}_e^k + \delta^k \mathbf{d}^k$. Set $k = k + 1$ and go to Step 1.

5. NUMERICAL EXPERIMENTS

5.1 Experiments Setup

The numerical experiments are carried out on a two-dimensional computational domain $\Omega = [0, 1] \times [0, 1]$ of size $1 \times 1 \text{ cm}^2$ for $T = 3 \text{ ms}$ simulation time. Two control domains are considered, namely $\Omega_{c1} = [0.375, 0.438] \times [0.469, 0.531]$ and $\Omega_{c2} = [0.563, 0.625] \times [0.469, 0.531]$. The observation

domain is defined as the complement of neighborhoods of Ω_{c1} and Ω_{c2} . By taking $\tilde{\Omega}_{c1} = [0.359, 0.453] \times [0.453, 0.547]$ and $\tilde{\Omega}_{c2} = [0.547, 0.641] \times [0.453, 0.547]$ as the neighborhoods of the control domains, the observation domain is therefore given as $\Omega_o = \Omega \setminus (\tilde{\Omega}_{c1} \cup \tilde{\Omega}_{c2})$. The excitation domain is the region where cardiac arrhythmia first occurs, and is denoted as $\Omega_{exi} = [0.498, 0.502] \times [0.498, 0.504] \subset \Omega_o$. The observation domain and the control domain are shown in Figure 1.

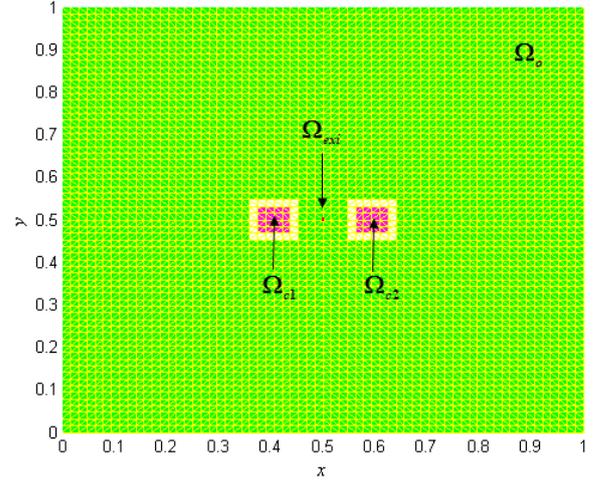


Fig 1: The control and observation domains

Table 1 lists the parameters that we have used in our numerical experiments, with some of them adopted from [14]. Furthermore, the initial conditions for V , I_e and w are given as

$$V(x, 0) = \begin{cases} 105 \text{ mV}, & x \in \Omega_{exi}, \\ 0 \text{ mV}, & \text{otherwise.} \end{cases}$$

$$I_e(x, 0) = \begin{cases} 0 \text{ mA cm}^{-3}, & x \in \Omega_c, \\ 0 \text{ mA cm}^{-3}, & \text{otherwise,} \end{cases}$$

$$w(x, 0) = 0, \quad x \in \Omega$$

Table 1. Parameters used in numerical experiments

Parameter	Value	Units
β	10^3	cm^{-1}
C_m	10^{-3}	mF cm^{-2}
D_i^l	3×10^{-3}	S cm^{-1}
D_i^t	3.1525×10^{-4}	S cm^{-1}
V_{th}	1.3×10^1	mV
V_p	10^2	mV
c_1	1.5	mS cm^{-2}
c_2	4.4	mS cm^{-2}
c_3	1.2×10^{-2}	ms^{-1}
c_4	1	dimensionless
α	10^{-4}	dimensionless
λ	7.062×10^{-1}	dimensionless

5.2 Numerical Results

In this section, we present the numerical results for the optimal control problem of the monodomain model. The uncontrolled solutions and the optimally controlled solutions at times 0.2 ms, 1 ms and 3 ms are illustrated in Figure 2 and Figure 3. Numerical results show the uncontrolled wavefront

of the transmembrane potential spreads from the excitation domain to the rest of the computational domain if no action for controlling is carried out. On the other hand, when the control is switched on, the excitation wavefront is successfully dampened out by the optimal applied current I_e^{opt} during the time interval from 0 ms to 3 ms.

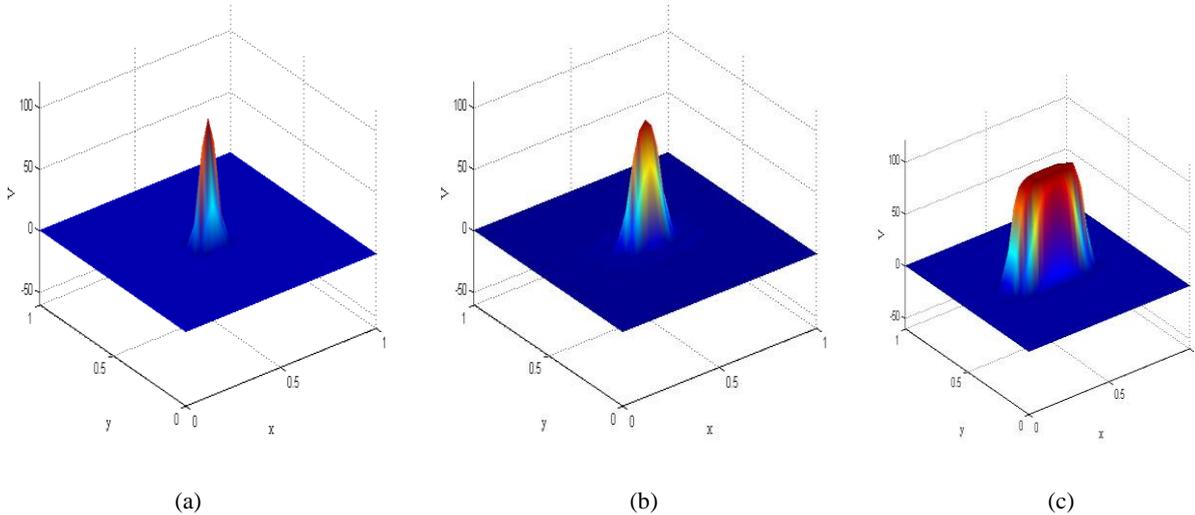


Fig 2: The uncontrolled solutions (V) at (a) 0.2 ms (b) 1 ms and (c) 3 ms

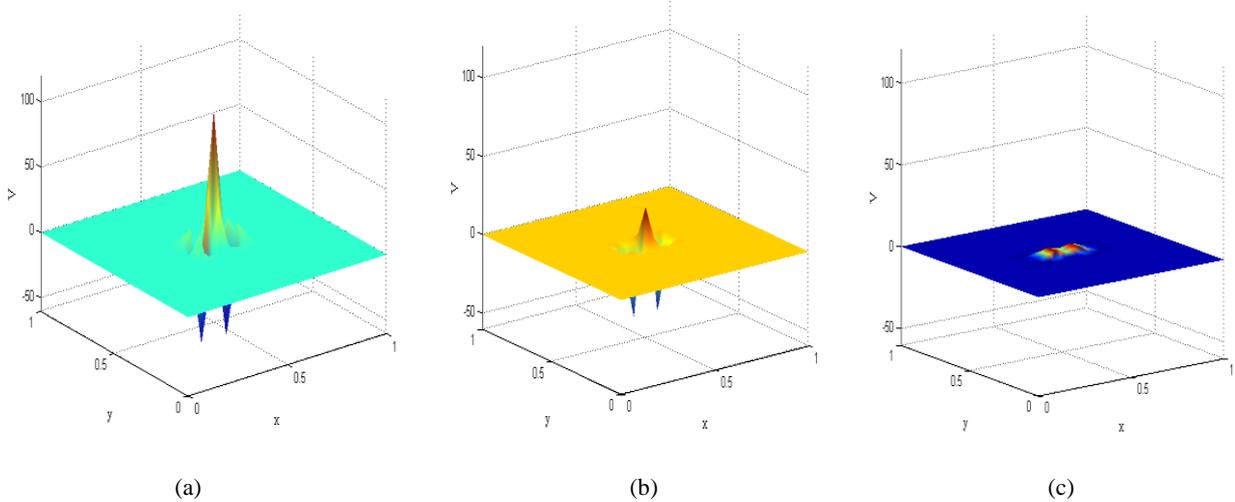


Fig 3: The controlled solutions (V^{opt}) at (a) 0.2 ms (b) 1 ms and (c) 3 ms

Next, we discuss the performance of MDY method for solving the optimal control problem of monodomain model. Figure 4 depicts the minimum value of the reduced cost functional $\hat{J}(I_e)$ along the optimization process. As shown in the figure, the MDY method converges to the minimizer with 38 optimization iterations. Unlike the DY method which descent property depends on the line search [13], the MDY method is well-performed even if the Armijo line search is used in our numerical experiments.

Figure 5 depicts the corresponding norm of gradient of the reduced cost functional, $\|\nabla \hat{J}(I_e)\|$, for 3 ms of simulation time. Note that the logarithmic scale is used in Figure 5 for clear presentation on how the gradient is decreased during optimization process. As shown in Figure 5, the gradient is decreased sharply at the beginning of optimization iterations, followed by a smooth decrease from iteration 15th to the end of iterations.

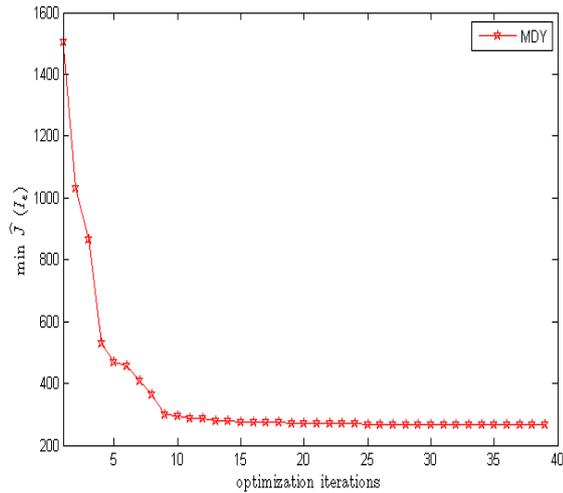


Fig 4: Minimum value of \hat{J} for 3 ms of simulation time

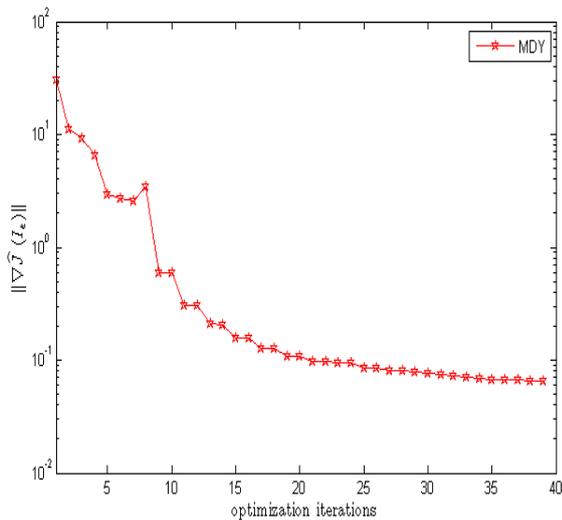


Fig 5: Norm of gradient of \hat{J} for 3 ms of simulation time

6. CONCLUSIONS

In this paper, we have presented the numerical solution for the optimal control problem of monodomain model using the MDY method. Our numerical results indicated that the excitation wavefront of the transmembrane potential has been successfully dampened out by the optimal applied current. Numerical results also indicated that the MDY method perform quite well under Armijo line search. These results motivate us to continue our numerical experiments with different locations and sizes of the control domains using the MDY method.

7. ACKNOWLEDGMENTS

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