Numerical Solutions for Optimal Control of Monodomain Equations in Cardiac Electrophysiology

Ch. Nagaiah[1], K. Kunisch[1], and G. Plank[2]

[1] Institute of Mathematics and Scientific Computing, University of Graz, Heinrichstr. 36, Graz, A-8010, Austria.
nagaiah.chamakuri@uni-graz.at,karl.kunisch@uni-graz.at
[2] Institute of Biophysics, Medical University of Graz, Harrachgasse 21, Graz, A-8010, Austria. gernot.plank@meduni-graz.at

Summary. In this article, we present computational techniques for optimal control of monodomain equations which are a well established model for describing wave propagation of the action potential in the heart. The model consists of a non-linear parabolic partial differential equation of reaction-diffusion type, where the reaction term is a set of ordinary differential equations which characterize the dynamics of cardiac cells.

Specifically, an optimal control formulation is presented for the monodomain equations with an extracellular current as the control variable which must be determined in such a way that wavefronts of transmembrane voltage are smoothed in an optimal manner. Numerical results are presented based on the optimize before discretize and discretize before optimize techniques. Moreover, the derivation of the optimality system is given for both techniques and numerical results are discussed for higher order methods to solve the optimality system. Finally, numerical results are reported which show superlinear convergence when using Newton's method.

1 Introduction

The bidomain equations are considered to be among the most accurate descriptions of cardiac electric activity at the tissue and organ level. They characterize cardiac tissue as a syncytial continuum, derived via a homogenization procedure, that consists of two interpenetrating domains, intracellular and extracellular, separated by a cellular membrane at any given point in space. The equations state that current leaving one domain, by traversing the cellular membrane, acts as source of current density in the other domain. Mathematically, this leads to a degenerate parabolic problem that can be recast as an elliptic partial differential equation (PDE) coupled to a parabolic PDE.The elliptic PDE expresses the extracellular potential distribution, Φ_e, as a function

M. Diehl et al. (eds.), *Recent Advances in Optimization and its Applications in Engineering*,
DOI 10.1007/978-3-642-12598-0_35,

of the transmembrane voltage distribution, V_m whereas the parabolic PDE models cellular activation and recovery processes (reaction term) and how they affect adjacent tissue by diffusion. We refer to [8, 2] for more detailed derivation of the bidomain model and further discussions. The numerical solution of the bidomain equations is computationally expensive owing to the high spatio-temporal resolution required to resolve the fast transients and steep gradients governing wavefront propagation in the heart. Assuming that the anisotropy ratios of the two spaces are equal leads to a reduced bidomain model, referred to as monodomain, which can be solved at a much cheaper cost by avoiding the time consuming solution of the elliptic PDE [7]. Under most circumstances of practical relevance the monodomain model can be set up to approximate the bidomain model fairly well [9, 6].

Under pathological conditions regular activation sequences may decay into complex and irregular patterns which impair the heart's capability to pump blood. If sufficiently fast and disorganized, such patterns, referred to as cardiac arrhythmias, may lead to death if not treated immediately. Electrical defibrillation, i.e. the delivery of a strong electrical shock to the heart, is the only known therapy to reliably restore a normal rhythm. During defibrillation shocks extracellular currents are injected via electrodes to establish an extracellular potential distribution which acts to reduce the complexity of the activity. This is achieved either by extinguishing all electrical activity, i.e. the entire tissue returns to its quiescent state, or gradients in V_m are smoothed out to drive the system to a less heterogeneous state which reduces the likelihood of triggering new wavefronts via "break" mechanisms when switching off the applied field. To optimally control cardiac arrhythmias, it is essential to determine the control response to an applied electric field as well as the optimal extracellular current density that acts to damp gradients of transmembrane voltage in the system. The present article is devoted to the development of efficient numerical techniques to solve this optimal control problem for the monodomain equations.

The finite element method is chosen for the spatial discretization and higher order linearly implicit Runge-Kutta time stepping methods for the temporal discretization. Numerical techniques for solving optimal control problems typically require combining a discretization technique with an optimization method. We will give a brief description of the optimize before discretize technique, that is write the continuous optimality system first before discretizing them, and discretize before optimize, that is first discretize the differential equations before discretizing the optimality system to solve the monodomain equations. To the authors knowledge this is the first attempt to combine the linearly implicit time stepping methods with the discretize before optimize technique to solve the optimality system. The optimal control approach is based on minimizing a properly chosen cost functional $J(V_m, I_e)$ depending on the extracellular current I_e as input and on the transmembrane potential V_m as one of the state variables.

The organization of this article is as follows: in the next section the governing equations for the action potential and the behavior of the ionic current variables using ionic models are described. In section 3 the control problem is posed for the monodomain equations and the optimality system is derived for the two discretization approaches. Numerical results are presented in section 4. Finally concluding remarks are given.

2 The monodomain equations

The monodomain model consists of the equations for the transmembrane potential and ionic current variables. We set $Q = \Omega \times [0, t_f]$ where $\Omega \subset \mathbf{R}^d$, $d = 2$, denotes the cardiac tissue sample domain.

$$\nabla \cdot \bar{\sigma_i} \nabla V_m = \frac{\partial V_m}{\partial t} + I_{ion}(V_m, w) - I_e \quad \text{in } Q \tag{1}$$

$$\frac{\partial w}{\partial t} = g(V_m, w) \quad \text{in } Q \tag{2}$$

where $V_m : Q \to \mathbf{R}$ is the transmembrane voltage, $w : Q \to \mathbf{R}^n$ represents the ionic current variables, $\bar{\sigma_i} : \Omega \to \mathbf{R}^{d \times d}$ is the intracellular conductivity tensor, I_e is an extracellular current density stimulus, and I_{ion} is the current density flowing through the ionic channels. The function $g(V_m, w)$ determines the evolution of the gating variables. Eq. (1) is a parabolic equation and Eq. (2) is a set of ordinary differential equations which can be solved independently for each node. Here the initial and boundary conditions are chosen as

$$\bar{\sigma_i} \nabla V_m \cdot \eta = 0 \quad \text{on } \partial Q = \partial \Omega \times [0, t_f] \tag{3}$$

$$w(0) = w_0 \quad \text{and } V_m(0) = V_0 \quad \text{in } \Omega\,. \tag{4}$$

Ionic model

The ionic activity is modeled by nonlinear ordinary differential equations. For the present paper we use the modified FitzHugh-Nagumo (FHN) model based on the work of Rogers and McCulloch [10] and the simulation parameters are taken from Colli Franzone et al. [1].

$$I_{ion}(V_m, w) = G V_m (1 - \frac{V_m}{v_{th}})(1 - \frac{V_m}{v_p}) + \eta_1 V_m w\,. \tag{5}$$

$$g(V_m, w) = \eta_2 (\frac{V_m}{v_p} - \eta_3 w)\,. \tag{6}$$

where $G, \eta_1, \eta_2, \eta_3$ are positive real coefficients, v_{th} is a threshold potential and v_p the peak potential.

3 Optimal control framework and numerical discretization

In this section we set forth the optimal control problem, for which the numerical experiments were carried out. We consider

$$\text{(P)} \qquad \begin{cases} \min J(V_m, I_e)\,, \\ \\ e(V_m, w, I_e) = 0 \quad \text{in} \quad Q\,, \end{cases} \tag{7}$$

where V_m and w are the state and I_e is the control variable. The coupled PDE and ODE constraints (1-2) for the monodomain equation together with initial and boundary conditions for V_m are expressed as $e(V_m, w, I_e) = 0$. The control variable I_e is chosen such that it is nontrivial only on the control domain Ω_{con} of Ω and I_e equals zero on $(\Omega \setminus \Omega_{con}) \times (0, T)$.

The cost functional which is used to optimize the potentials and currents is given by

$$J(V_m, I_e) = \frac{1}{2} \int_0^T \left(\int_{\Omega_{obs}} |V_m - Z|^2 \, \mathrm{d}\Omega_{obs} + \alpha \int_{\Omega_{con}} |I_e|^2 \, \mathrm{d}\Omega_{con} \right) dt, \tag{8}$$

where α is the weight of the cost of the control, Ω_{obs} is the observation domain and Ω_{con} is the control domain. If $Z = 0$ then the interpretation of the cost-functional J for the problems to be considered is such that by properly applying I_e excitation waves are suppressed in the region Ω_{obs}. The inclusion of the tracking type term Z in the cost functional serves code-validation purposes.

Due to their size and complexity PDE based optimization problems are generally challenging to solve in practice. The interplay of optimization and infinite dimensionality of the problem is a crucial one. There are essentially two approaches to deal with it. In the optimize before discretize (OBD) approach, first a minimization strategy is applied to the continuous optimal control problem, (this may consist of deriving the optimality system), and subsequently the resulting formalism is discretized. Alternatively, in the discretize before optimize (DBO) approach, first the differential equations as well as the cost J in (P) are discretized and subsequently the optimization procedure for solving the finite-dimensional minimization problem is fixed.

3.1 Optimize before discretize

In this subsection we follow an OBD technique to solve the monodomain model. More specifically for the problem under consideration the Lagrangian is defined by

$$\begin{aligned} \mathcal{L}\ (V_m, w, I_e, p, q) = J(V_m, I_e) + \int_0^T \int_\Omega \left(\frac{\partial w}{\partial t} - g(V_m, w) \right) q \ \mathrm{d}\Omega \, \mathrm{d}t \\ + \int_0^T \int_\Omega \left(\nabla \cdot \bar{\sigma_i} \nabla V_m - \frac{\partial V_m}{\partial t} + I_{ion}(V_m, w) - I_e \right) p \ \mathrm{d}\Omega \, \mathrm{d}t, \end{aligned} \tag{9}$$

where the initial conditions are kept as explicit constraints. The first order optimality system is obtained by formally setting the partial derivatives of $\mathcal{L}$ equal to 0. We find

$$\mathcal{L}_{V_m}: \quad (V_m - Z)_{\Omega_{obs}} + \nabla \cdot \bar{\sigma_i} \nabla p + p_t - (I_{ion})_{V_m} p - g_{V_m} q = 0\,, \tag{10}$$

$$\mathcal{L}_w: \quad -(I_{ion})_w p - q_t - g_w q = 0\,, \tag{11}$$

where the subscripts V_m and w denote partial derivatives with respect to these variables. Further we obtain the

$$\text{terminal conditions: } p(T) = 0, \quad q(T) = 0, \tag{12}$$

$$\text{boundary conditions: } \bar{\sigma_i} \nabla p \cdot \eta = 0 \quad \text{on} \quad \partial Q\,, \tag{13}$$

$$\text{and the optimality condition: } \mathcal{L}_{I_e}: \quad \alpha I_e + p = 0\,, \quad \text{on} \quad \Omega_{con}\,. \tag{14}$$

To solve (P) numerically we need to solve the coupled system of primal equations (1-2), adjoint equations (10-11), together with initial conditions (4), boundary conditions (3,13), terminal conditions (12), and the optimality system (14). The optimality system serves as a gradient of the cost functional for our computations.

In this study, we have chosen the finite element method for the spatial- and higher order linearly implicit Runge-Kutta time stepping methods for the temporal discretizations, specifically a 2-stage Rosenbrock type method [3]. We now give a brief description of spatial and temporal discretizations for the primal and adjoint equations. For further details we refer to Nagaiah et al. [4].

Discretization of primal and adjoint problems

In computations, the primal problem is solved by decoupling the parabolic part from the ordinary differential equation. In a first step we use the Euler explicit time stepping method to solve the ODE part. In a second step, using the new solution of the gating variables w, we solve the parabolic part by employing a Rosenbrock time stepping method, refer to [4, 5] for more details. After the space and time discretization for the primal problem, the system of linear equations can be expressed as follows:

$$\begin{aligned}
\mathbf{w}_n &= \mathbf{w}_{n-1} + \delta t \eta_2 \left(\frac{\mathbf{v}_{n-1}}{v_p} - \eta_3 \mathbf{w}_{n-1} \right) \\
\mathbf{J}_1 \mathbf{k}_1^n &= -\mathbf{K} \mathbf{v}_{n-1} - \mathbf{M} \mathbf{I}_{ion}(\mathbf{v}_{n-1}, \mathbf{w}_n) + \mathbf{M} \mathbf{I}_e\,, \\
\mathbf{J}_1 \mathbf{k}_2^n &= -\mathbf{K} \left(\mathbf{v}_{n-1} + \alpha_{21} \mathbf{k}_1^n \right) - \mathbf{M} \mathbf{I}_{ion}(\mathbf{v}_{n-1} + \alpha_{21} \mathbf{k}_1^n, \mathbf{w}_n) + \mathbf{M} \mathbf{I}_e - \frac{c_{21}}{\delta t} \mathbf{M} \mathbf{k}_1^n \\
\mathbf{v}_n &= \mathbf{v}_{n-1} + m_1 \mathbf{k}_1^n + m_2 \mathbf{k}_2^n, \qquad \text{for } n = 1, \ldots, N_t,
\end{aligned} \tag{15}$$

where $\mathbf{K}$ is the stiffness matrix, $\mathbf{M}$ is the mass matrix, $\mathbf{J}_1 = (\frac{1}{\delta t \gamma} \mathbf{M} + \mathbf{K} + \mathbf{M}[\mathbf{I}_{ion}(\mathbf{v}_{n-1}, \mathbf{w}_n)]_{\mathbf{v}})$, N_t is the maximum number of time steps, the coefficients $\gamma, \alpha_{ij}, c_{ij}$ are constants and the subscript $\mathbf{v}$ denotes the partial derivative with respect to this variable. For solving the linear system the BiCGSTAB

method with ILU preconditioning is used. We use the same discretization techniques to solve the adjoint problem. After spatial discretization by FEM and time discretization by a 2-stage Rosenbrock type method for the adjoint problem the system can be written as follows:

$$
\begin{aligned}
\mathbf{q}_n &= (1-\delta t\eta_2\eta_3)\mathbf{q}_{n+1} + \delta t\eta_1\mathbf{v}_{n+1}\mathbf{p}_n \\
\mathbf{J}_2\mathbf{l}_1 &= \mathbf{K}\mathbf{p}_{n+1} + \mathbf{M}[\mathbf{I}_{ion}(\mathbf{v}_{n+1})]_{\mathbf{v}}\mathbf{p}_{n+1} + \frac{\eta_2}{v_p}\mathbf{M}\mathbf{q}_n - \mathbf{M}(\mathbf{v}_{n+1}-\mathbf{z}_{n+1})_{\Omega_{obs}}\,, \\
\mathbf{J}_2\mathbf{l}_2 &= \mathbf{K}\left(\mathbf{p}_{n+1}+\alpha_{21}\mathbf{l}_1\right) + \mathbf{M}[\mathbf{I}_{ion}(\mathbf{v}_{n+1})]_{\mathbf{v}}\left(\mathbf{p}_{n+1}+\alpha_{21}\mathbf{l}_1\right) + \frac{\eta_2}{v_p}\mathbf{M}\mathbf{q}_n \\
&\qquad -\mathbf{M}(\mathbf{v}_{n+1}-\mathbf{z}_{n+1})_{\Omega_{obs}} - \frac{c_{21}}{\tau}\mathbf{M}\mathbf{l}_1 \\
\mathbf{p}_n &= \mathbf{p}_{n+1} + m_1\mathbf{l}_1 + m_2\mathbf{l}_2\,, \text{ for } n = 1,\ldots,N_t-1\,, \\
&\text{where } \mathbf{J}_2 = -\left(\frac{1}{\tau^n\gamma}\mathbf{M} - (\mathbf{K}+\mathbf{M}[\mathbf{I}_{ion}(\mathbf{v}_{n+1})]_{\mathbf{v}_{n+1}})\right)
\end{aligned}
\tag{16}
$$

3.2 Discretize before optimize

In this subsection we explain a discretize before optimize (DBO) technique to solve the monodomain model. This technique first transforms the original continuous problem into a finite dimensional optimization problem by discretizing in space and time. Then the fully discretized optimization problem is solved by existing optimization solvers. First, in this process the objective functional is written as follows

$$
\begin{aligned}
J(\mathbf{v},\mathbf{I_e}) = \frac{\delta t}{2}\Big(&\sum_{n=1}^{N_t-1}(\mathbf{v}_n-\mathbf{z}_n)^\top\mathbf{M}(\mathbf{v}_n-\mathbf{z}_n) + \alpha(\mathbf{I}_e^n)^\top\mathbf{M}\mathbf{I}_e^n\Big) \\
+ \quad &\frac{\delta t}{4}\left[(\mathbf{v}_{N_t}-\mathbf{z}_{N_t})^\top\mathbf{M}(\mathbf{v}_{N_t}-\mathbf{z}_{N_t}) + \alpha(\mathbf{I}_e^{N_t})^\top\mathbf{M}\mathbf{I}_e^{N_t}\right] + \frac{\delta t}{4}\alpha(\mathbf{I}_e^0)^\top\mathbf{M}\mathbf{I}_e^0.
\end{aligned}
$$

To solve the monodomain problem with the DBO approach we discretize the problem first in space and time. For the space discretization we used piecewise linear FEM, and for the temporal discretization a 2 stage Rosenbrock type method. The resulting algebraic system can be obtained as in Eq. (15). The corresponding Lagrangian is given by

$$
\begin{aligned}
&\mathcal{L}(\mathbf{w},\mathbf{v},\mathbf{I}_e,\mathbf{k}_1,\mathbf{k}_2,\mathbf{p},\mathbf{q},\phi,\psi) \\
&= J(\mathbf{v},\mathbf{I}_e) + \sum_{n=1}^{N}\mathbf{q}_n^\top\left(\mathbf{M}\mathbf{w}_n - \mathbf{M}\mathbf{w}_{n-1} - \delta t\ \mathbf{M}g(\mathbf{v}_{n-1},\mathbf{w}^{n-1})\right) \\
&\quad + \sum_{n=1}^{N}\phi_n^\top\left(\mathbf{J}_1\mathbf{k}_1^n + \mathbf{K}\mathbf{v}_{n-1} + \mathbf{M}\mathbf{I}_{ion}(\mathbf{v}_{n-1},\mathbf{w}_n) - \mathbf{M}\mathbf{I}_e^n\right) \\
&\quad + \sum_{n=1}^{N}\psi_n^\top\Big(\mathbf{J}_1\mathbf{k}_2^n + \mathbf{K}\left(\mathbf{v}_{n-1}+\alpha_{21}\mathbf{k}_1^n\right) + \mathbf{M}\mathbf{I}_{ion}(\mathbf{v}_{n-1}+a_{21}\mathbf{k}_1^n,\mathbf{w}_n)
\end{aligned}
$$

$$-\mathbf{M}\mathbf{I}_e^n + \mathbf{M}\frac{c_{21}}{\delta t}\mathbf{k}_1^n\Big) + \sum_{n=1}^{N} \mathbf{p}_n^\top(\mathbf{v}_n - \mathbf{v}_{n-1} - m_1\mathbf{k}_1^n - m_2\mathbf{k}_2^n)\,.$$

The first order optimality system is obtained by formally setting the partial derivatives of $\mathcal{L}$ equal to 0. We find

$$\begin{aligned}
\mathcal{L}_{\mathbf{w}^n}: \quad & \mathbf{q}_n^\top - \mathbf{q}_{n+1}^\top + \delta t\eta_2\eta_3\mathbf{q}_{n+1}^\top + \phi_n^\top\eta_1\mathbf{v}^{n+1} + \psi_n^\top\left(\mathbf{v}^{n+1} + a_{21}\mathbf{k}_1^n\right)\eta_1 = 0 \\
\mathcal{L}_{\mathbf{k}_2^n}: \quad & \psi_n^\top\mathbf{J}_1 - m_2\mathbf{p}_n^\top = 0 \\
\mathcal{L}_{\mathbf{k}_1^n}: \quad & \phi_n^\top\mathbf{J}_1 + \psi_n^\top\mathbf{K}a_{21} + \psi_n^\top\mathbf{M}(\mathbf{I}_{ion})_{\mathbf{k}_1} + \frac{c_{21}}{\delta t}\psi_n^\top\mathbf{M} - m_1\mathbf{p}_n^\top = 0 \\
\mathcal{L}_{\mathbf{v}}: \quad & \delta t[\mathbf{M}(\mathbf{v}_n - \mathbf{z}_n)_{\Omega_{obs}} - \frac{\eta_2}{v_p}\mathbf{M}\mathbf{q}_{n+1}^\top] + \phi_{n+1}^\top\mathbf{K} + \phi_{n+1}^\top\mathbf{M}(\mathbf{I}_{ion}(\mathbf{v}))_v \\
& + \psi_{n+1}^\top\mathbf{K} + \psi_{n+1}^\top\mathbf{M}\left(\mathbf{I}_{ion}(\mathbf{v}^{n+1} + a_{21}\mathbf{k}_1, \mathbf{w}^n)\right)_v + \mathbf{p}_n^\top - \mathbf{p}_{n+1}^\top = 0 \quad (17) \\
\mathcal{L}_{\mathbf{v}_{Nt}}: \quad & \mathbf{p}_{Nt} = -\frac{\delta t}{2}\mathbf{M}(\mathbf{v}_{Nt} - \mathbf{z}_{Nt}) \quad (18) \\
\mathcal{L}_{\mathbf{I}_e}: \quad & \delta t\alpha\mathbf{M}\mathbf{I}_e^n = \mathbf{M}(\phi_n + \psi_n)\,, \qquad \text{where } n = N-1, \ldots, 1 \quad (19) \\
\mathcal{L}_{\mathbf{I}_e^{Nt}}: \quad & \frac{\delta t}{2}\alpha\mathbf{M}\mathbf{I}_e^{Nt} = \mathbf{M}(\phi_{Nt} + \psi_{Nt}). \quad (20)
\end{aligned}$$

In this case eqs. (19) and (20) serve as a gradient of the cost functional in computations.

3.3 Comparison of optimization methods

If we observe the first derivative of the cost functional, it involves the adjoint stage solutions ϕ_n and ψ_n of time stepping method in the DBO case and in the OBD case it involves the adjoint variable of the primal solution. The terminal solution to solve the adjoint problem is different in the DBO from the OBD case. Also, one needs to evaluate two extra matrix times vector products in the DBO case, see eq. (17), in comparison to algebraic system of the OBD. If one uses Newton's method to solve the optimality system, the DBO case requires more memory than the OBD case, because the stage solutions of primal problem are involved in the linearized primal and adjoint equations.

A nonlinear conjugate gradient (NCG) method and Newton's method are adopted to solve the optimality system. In both cases a line search is required. For this purpose we use the strong Wolfe conditions with a back tracking strategy. A more in-depth description will be found in [4, 5] to solve the current optimization problem.

4 Results

In this section numerical results are presented to demonstrate the capability of dampening an excitation wave of the transmembrane potential by properly applying an extracellular current stimulus. In this note the numerical

results for the OBD and DBO approaches are compared for 1D examples, see [5] for 2D results. Also comparisons with respect to the NCG and Newton optimization algorithms are given. The computational domain is $\Omega = (0, 1)$. The relevant subdomains are depicted in Figure 1. The observation domain is $\Omega_{obs} = \Omega \backslash (\Omega_{f1} \cup \Omega_{f2})$, the excitation domain is Ω_{exi} and the control domain is $\Omega_{con} = \Omega_{con1} \cup \Omega_{con2}$.

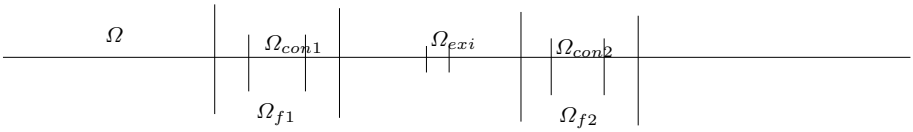

Fig. 1. Control and excitation region at the cardiac domain

The choice $Z = 0$ corresponds to the desire to dampen the wave in Ω_{obs}. For the computations the simulation time is set to 4 $msec$. A uniform spatial mesh consisting of 100 nodes, and 200 equidistant time steps are used. Also we assume that the initial wave excitation takes place on the excitation domain. In all simulations the weight of the cost of the control is fixed at $\alpha = 5 \cdot 10^{-3}$ and the optimization iterations were terminated when the following condition is satisfied: $\|\nabla J_k\|_\infty \leq 10^{-3}(1 + |J_k|)$ or difference of the cost functional between two successive optimization iterations is less than 10^{-3}. The code is implemented using MATLAB-7.4 version.

The continuous L^2 norm of the gradient and the minimum value of the cost functional with respect to the optimization iterations are depicted in Figure 2 for OBD and DBO, using the NCG and Newton optimization algorithms. The norm of the gradient and the minimal values of the cost functional decrease more rapidly for Newton's method. In this case both OBD and DBO take 7 optimization iterations to reach the stopping criterion. The DBO algorithm is bit faster and takes 13 sec of CPU time. The OBD algorithm takes 1.04 times of CPU time more than the DBO case. Indeed, there is no big difference between the OBD and DBO techniques for this particular problem. Also, similar behavior between the OBD and DBO is observed using the NCG algorithm. For all methods the cost functional value is approximately 102 at the optimal state solution. The optimal state solution of transmembrane voltage is shown in Figure 3 at time $t = 0.04$ msec and $t = 1.40$ msec and we can observe that excitation wave is completely dampened.

The line search algorithm takes small step lengths at the beginning of optimization iterations and full steps towards the end of the iterations. In Table 4 the optimization iterations, the norm of the gradient of the cost functional and the order of convergence for the OBD method using Newton's algorithm is presented. From this table we can conclude that the OBD technique based on the Newton method shows super linear convergence from iteration 3 to 6.

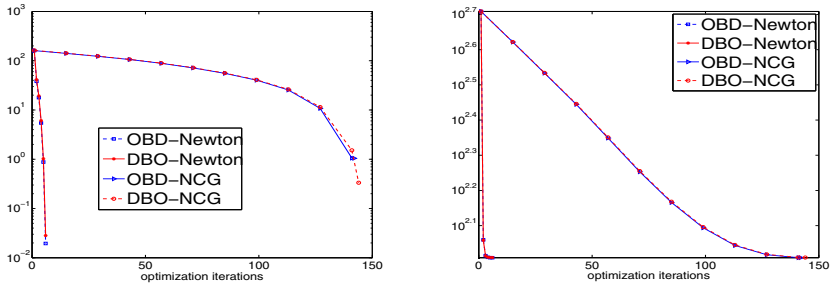

Fig. 2. The norm of the gradient and minimum value of the cost functional are shown on left and right respectively for $T = 4$ msec of simulation time.

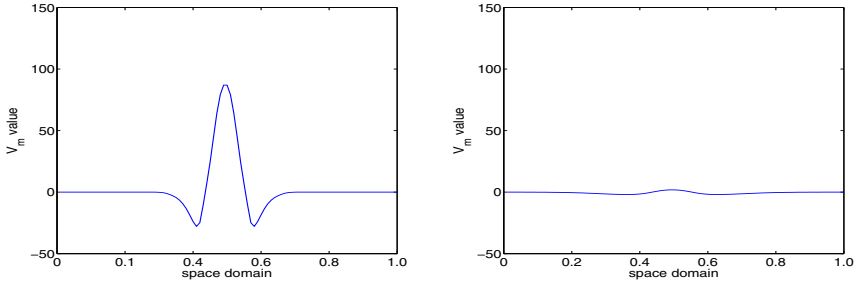

Fig. 3. The optimal state solution of V_m at time $t = 0.04$ msec and $t = 1.80$ msec for $T = 4$ msec of simulation time.

opt.iters	$\|\|\nabla J(V_m, I_e)\|\|$	$\frac{\|\|\nabla J(V_m,I_e)\|\|_{i+1}}{\|\|\nabla J(V_m,I_e)\|\|_i}$
1	160.4675668	
2	38.2739193	0.2385
3	17.7594672	0.4640
4	5.4176392	0.3051
5	0.4178937	0.0771
6	0.0064591	0.0155
7	0.0001882	0.0291

Table 1. Optimization iterations, norm of gradient of cost functional and order of convergence for the OBD technique with Newton's algorithm are presented.

5 Conclusions

In this note, two concrete realizations of the OBD and the DBO approaches for optimal control of the action potential in cardiac electrophysiology based on the monodomain equation were discussed and numerical results are presented for a one-D example. For the current problem there is no significant difference for these two techniques. However, there is a significant difference between

the NCG and the Newton methods. Due to the strong nonlinearities in the model, it appears to be difficult to observe a second order convergence. In this respect we were more successful to achieve a superlinear convergence for both discretization methods. The results motivate us to continue our investigations for the bidomain model. The computational results, with extracellular control dampening the complete wave propagation of the transmembrane potential, suggest to also strive for more insight into longer time horizons, with complete simulations of several heart beats, and more realistic geometries and finer meshes.

Acknowledgement: The authors gratefully acknowledge the Austrian Science Foundation (FWF) for financial support under SFB 032, "Mathematical Optimization and Applications in Biomedical Sciences".

References

1. P. Colli Franzone, P. Deuflhard, B. Erdmann, J. Lang and L. F. Pavarino, Adaptivity in Space and Time for Reaction-Diffusion Systems in Electrocardiology, *SIAM Journal on Numerical Analysis*, **28(3)**, 942-962, 2006
2. C. S. Henriquez, Simulating the electrical behavior of cardiac tissue using the bidomain model, *Crit. Rev. Biomed. Eng.*, **21**, 1 77, 1993.
3. J. Lang, Adaptive Multilevel Solution of Nonlinear Parabolic PDE Systems, *Lecture Notes in Computational Science and Engineering*, **16**, 2001.
4. Ch. Nagaiah, K. Kunisch and G. Plank, Numerical solution for optimal control of the reaction-diffusion equations in cardiac electrophysiology, *to appear in Computational Optimization and Applications* doi:10.1007/s10589-009-9280-3.
5. Ch. Nagaiah and K. Kunisch, Higher order optimization and adaptive numerical solution for optimal control of monodomain equations in cardiac electrophysiology, *Applied Numerical Mathematics*, **accpeted** .
6. B. F. Nielsen, T. S. Ruud, G. T. Lines and A. Tveito, Optimal monodomain approximations of the bidomain equations, *Applied Mathematics and Computation*, **184(2)**, 276-290, 2007.
7. G. Plank, M. Liebmann, R. Weber dos Santos, EJ. Vigmond, G. Haase, Algebraic multigrid preconditioner for the cardiac bidomain model, *IEEE Trans Biomed Eng.*, **54(4)**, 585-596, 2007.
8. R. Plonsey, Bioelectric sources arising in excitable fibers (ALZA lecture), *Ann. Biomed. Eng.*, **16**, 519 546, 1988.
9. M. Potse, B. Dube, J. Richer, A. Vinet and R. M. Gulrajani, A Comparison of Monodomain and Bidomain Reaction-Diffusion Models for Action Potential Propagation in the Human Heart, *IEEE Transactions on Biomedical Engineering*, **53(12)**, 2425-2435, 2006.
10. J. M. Rogers and A. D. McCulloch, A collocation-Galerkin finite element model of cardiac action potential propagation, *IEEE Trans. Biomed. Eng.* , **41**,743-757, 1994.
11. E. J. Vigmond, R. Weber dos Santos, A. J. Prassl, M. Deo, and G. Plank, Solvers for the cardiac bidomain equations, *Prog Biophys Mol Biol*, **96(1-3)**, 3-18, 2008.