# Second order numerical solution for optimal control of reaction-diffusion systems in electrophysiology

**Chamakuri Nagaiah**[1]

Subproject: OPTIM
Direction: Prof. Karl Kunisch[1], Prof. Stefan Volkwein[1]
Collaboration with HEART group: Dr. Gernot Plank[2]

[1]Institute of Mathematics and Scientific Computing
Karl-Franzens University of Graz.
[2]Institute of Biophysics, Medical University of Graz.

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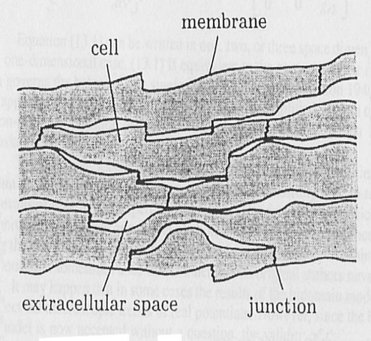
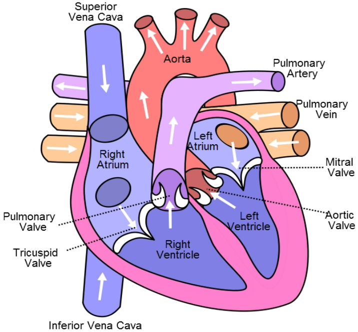
# Outline

# The electrical activity of the heart




- The cardiac tissue comprises of two anisotropic superimposed media, one intracellular and the other extracellular which occupy the same volume and are separated by the cellular membrane.
- The bioelectric activity of cardiac cells is due to the flow of various ionic currents through the cellular membrane.

# The electrical activity of the heart

- The cardiac arrhythmia is any deviation from the normal heart rhythm due to disturbances of the normal sequence of impulse propagation through the heart.
- The bidomain equations are widely used for describing the electrical activity of the cardiac tissue.
- Challenging to find the accurate and efficient numerical solutions.
- Goal : Determine the control response of an electrical field which can be able to drive the system from arrhythmia pattern to a uniform pattern.

Mathematical derivation: Tung 78; Plonsey 89; Henriquez 93; Keener, Panfilov 96

# Bidomain model

$$-\nabla\cdot(\bar{\sigma_i}+\bar{\sigma_e})\nabla\phi_e-\nabla\cdot\bar{\sigma_i}\nabla V_m=I_e(x,t)\text{ in }Q_c\quad\text{where }Q_c=\Omega_c\times[0,t_f]\quad(1)$$

$$\nabla\cdot\bar{\sigma_i}\nabla V_m+\nabla\cdot\bar{\sigma_i}\nabla\phi_e=\beta\left(C_m\frac{\partial V_m}{\partial t}+I_{ion}(V_m,v)-I_{tr}(x,t)\right)\text{ in }Q_c\quad(2)$$

$$\frac{\partial v}{\partial t}=g(V_m,v)\quad\text{in }Q_c\quad(3)$$

- $\phi_e, V_m : Q_c \to \mathbb{R}$ are the extracellular potential and transmembrane voltage
- $v : Q_c \to \mathbb{R}^n$ represents the ionic current variables
- $I_{ion}(V_m, v)$ : the current density flowing through the ionic channels.
- $\bar{\sigma_i},\ \bar{\sigma_e} : \Omega_c \to \mathbb{R}^{d\times d}$ are respectively the intracellular and extracellular conductivity tensors
- $\beta$ - the surface to volume ratio, $C_m$ - the capacitance per unit area, $I_{tr}$ - the transmembrane current density stimulus and $I_e$ - an extracellular current density stimulus

# Membrane model

- Some of the most well-known ionic models.
  - FitzHugh-Nagumo, Aliev-Panfilov, Beeler-Reuter , Luo-Rudy ... etc.

**The simplified FitzHugh-Nagumo system (Roger and McCulloch,1994)**

$$I_{ion}(V_m, v) = GV_m(1 - \frac{V_m}{v_{th}})(1 - \frac{V_m}{v_p}) + \eta_1 V_m v \, ,$$

$$g(V_m, v) = \eta_2(\frac{V_m}{v_p} - \eta_3 v)$$

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

[P. Colli Franzone, P. Deuflhard, B. Erdmann, J. Lang, L. Pavarino, 2006]

# Optimal control problem

- Constrained optimal control problem

$$\begin{cases} \min \ J(V_m, I_e), \\ \text{s.t.} \ \ e(\phi, V_m, v, I_e) = 0 \quad \text{in} \ \ Q_c\,, \\ \text{B.C: homogeneous Neumann BC} \end{cases} \tag{4}$$

where $e(\phi, V_m, v, I_e)$ represents the PDE constraints.

→ The choice of the cost functional which is suitable to optimize the potentials

$$J(V_m, I_e) = \min \frac{1}{2} \int_0^T \left( \int_{\Omega_{obs}} |V_m|^2 \, d\Omega_{obs} + \alpha \int_{\Omega_{con}} |I_e|^2 \, d\Omega_{con} \right) dt \tag{5}$$

→ The Lagrangian related to the primal problem is given by

$$\mathcal{L}(\phi_e, V_m, v, I_e, p, q, \zeta) = J(V_m, I_e) + < e(\phi, V_m, v, I_e), X > \tag{6}$$

- In computations monodomain equations are used (replace $\sigma_e = \lambda \sigma_i$ in bidomain equations) [Potse et.al. 06; Nielsen et.al. 07].

# Mono-domain problem

Primal system:

$$\nabla \cdot \bar{\sigma}_i \nabla V_m = \beta \left( C_m \frac{\partial V_m}{\partial t} + I_{ion}(V_m, v) - I_e(x,t) \right) \quad \text{in } Q_c$$

$$\frac{\partial v}{\partial t} = g(V_m, v) \quad \text{in } Q_c$$

Adjoint system:

$$\left.\begin{aligned} -\nabla \cdot \nabla V_m + \nabla \cdot \bar{\sigma}_i \nabla q + \beta(C_m q_t - (I_{ion})_{V_m} q) - g_{V_m}\zeta = 0 \\ -\beta (I_{ion})_v q - \zeta_t - g_v^T(V_m, v)\zeta = 0 \end{aligned}\right\}$$

Initial and terminal conditions:

$$V_m(0) = V_0, \quad v(0) = V_0, \quad q(T) = 0, \quad \zeta(T) = 0\,.$$

Optimality condition:

$$\mathcal{L}_{I_e} : \ \alpha I_e + q = 0\,,$$

# Numerical approach

- Piecewise linear finite element method for the space discretization of the primal and dual problem
- Linearly implicit Runge-Kutta methods (ROS2,ROS3P) for the time dicretization
- In computations the primal problem is solved by decoupling the system as follows,

$$\text{step-1}: \qquad \mathbf{v}^{\mathbf{n}+1} = \mathbf{v}^{\mathbf{n}} + \Delta t \mathbf{g}(\mathbf{V}_{\mathbf{m}}^{\mathbf{n}}, \mathbf{v}^{\mathbf{n}})\,. \tag{7}$$

$$\text{step-2}: \qquad \mathbf{M}\frac{\partial \mathbf{V}_{\mathbf{m}}}{\partial t} = -\frac{1}{\beta C_m}\mathbf{A}_{\mathbf{i}}\mathbf{V}_{\mathbf{m}} - \frac{1}{C_m}(\mathbf{I}_{\mathbf{ion}}(\mathbf{V}_{\mathbf{m}}, \mathbf{v}) - \mathbf{I}_{\mathbf{e}})\,. \tag{8}$$

- BiCGSTAB method with ILU preconditioner to solve linear system
- Nonlinear conjugate gradient and Newton method method to solve the optimization
- Line search method is based on the strong Wolfe conditions

# NCG algorithm

primal variables: $V_m, v$ and dual variables : $p, q$

choose $I_{tr}^{exi} := I_{tr}^{0}$ and solve once the primal and dual problem. Set $\hat{J}_0 := J(V_{m_0}(I_{e_0}), I_{e_0}),\ \nabla\hat{J}_0 := \nabla J(V_{m_0}(I_{e_0}), I_{e_0})$ and $d_0 := -\nabla\hat{J}_0,\ k \leftarrow 0$

**while** $\left\|\nabla\hat{J}\right\| > tol$ **do**

  set $\beta_0 := 0.9$ and compute $\beta_k$ using back tracking method

  **while** $\hat{J}(I_{e_k} + \beta_i d_k) \geq \hat{J}(I_{e_k}) + c_1\beta_i\nabla\hat{J}(I_{e_k})^T d_k$

    and $\nabla\hat{J}(I_{e_k} + \beta_i d_k)^T d_k \geq c_2 \left|\nabla\hat{J}(I_{e_k})^T d_k\right|$ **do**

    solve the primal and dual problem for update the gradient

    set $\beta_i := \beta_i/2$

  **end while**

  update $I_{e_{k+1}} \leftarrow I_{e_k} + \beta_k d_k$ using modified $\beta_i$, evaluate $\nabla\hat{J}_{k+1}$

  evaluate $\gamma_{k+1}$ (using one of the update) and set $d_{k+1} \leftarrow -\nabla\hat{J}_{k+1} + \gamma_{k+1} d_k,\ k \leftarrow k+1$

  set $V_m(0) := V_m^0, v(0) := v^0$ and solve the primal problem to obtain $V_m(t), v(t)$

  solve the dual problem for $p(t), q(t)$ using terminal conditions $p(T) := 0, q(T) := 0$

**end while**

# Newton method

The computation of the Newton system expressed as

$$\hat{J}^{''}\delta I := (T^{*}\nabla^{2}\mathcal{L}T)\delta I = -\hat{J}^{'}(I_e^n)\,. \qquad (9)$$

where

- $\hat{J}^{'}(I_e^n)$ is the gradient of the reduced cost functional $\hat{J}(I_e^n)$
- $T(x)$ is the matrix operator
- $\delta I$ is a direction

[Hinze and Kunisch 2001]

# Newton method

1. Compute the $\hat{J}'(I^n)$ obtained by one solve of the primal and dual equations.
2. Iteratively solve (9). In each step the action of $\hat{J}''(I^n)$ on a direction $\delta I^n$ has to be evaluated by means of
   - solve the linearized primal equation for $V_l$, $v_l$ using $\delta I_j^k$.

$$\begin{pmatrix} \nabla \cdot (\bar{\sigma}_i \nabla V_l) - \beta \left( C_m V_{l_t} + \nabla I_{ion}(V_l, v_l) \right) \\ v_{l_t} - \nabla g(V_l, v_l) \end{pmatrix} = \begin{pmatrix} -\beta \delta^k \\ 0 \end{pmatrix}$$

   - evaluate the $(z_1, z_2)$ as follows.

$$\nabla^2 \mathcal{L}(V_l, v_l, \delta I) = \begin{pmatrix} \begin{pmatrix} V_l - \beta (I_{ion})_{V_m V_m}(V_l) q - \beta \eta_1 v_l q \\ -\beta \eta_1 V_l q \end{pmatrix} \\ \alpha \delta I \end{pmatrix} =: \begin{pmatrix} \begin{pmatrix} z_1 \\ z_2 \end{pmatrix} \\ \alpha \delta I \end{pmatrix}$$

# Newton method

- solve the adjoint equation with $(z_1, z_2)$ as r.h.s as follows.

$$-e_{I_e}^{*}(e_{(V_m,v)}^{-1})^{*}\begin{pmatrix} z_1 \\ z_2 \end{pmatrix} = \begin{pmatrix} w_1 \\ w_2 \end{pmatrix}$$

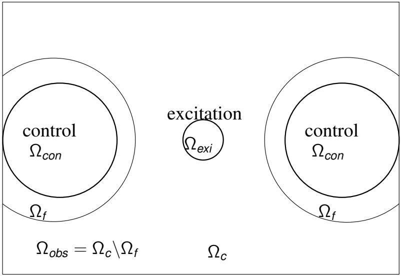
- finally compute the action of $\hat{J}''(I^k)$ on $\delta I_j^k$.

$$\hat{J}''(I) = (T^{*}\nabla^{2}\mathcal{L}T)\delta I := -\beta w_1 + \alpha\delta I$$

1. An iterative algorithm like a CG method is used.
2. Code is implemented using DUNE, a public domain package (see P. Bastian et.al. 2008)

[Kunisch and Nagaiah (*in preparation*)]

# Numerical results




- The computational domain size $\Omega_c = [0, 1] \times [0, 1]$
- The observation domain is $\Omega_{obs} = \Omega_c \backslash \Omega_f$, the excitation domain is $\Omega_{exi}$ and the control domain is $\Omega_{con}$.
- The weight of the cost of the control is $\alpha = 10^{-3}$
- The iterations were terminated by $\|\nabla J_k\|_\infty \leq 10^{-3}(1 + |J_k|)$

# Numerical results : Test case 1

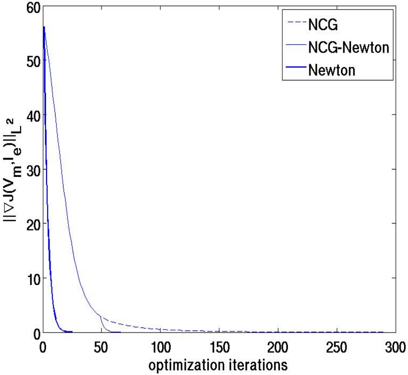
- The choice of the cost functional

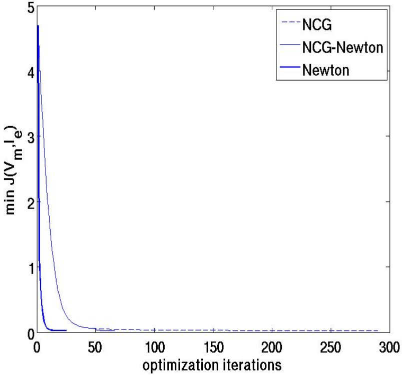
$$J(V_m, I_e) = \min \frac{1}{2}\int_0^T \left( \int_{\Omega_{obs}} |V_m - V_d|^2 \mathrm{d}\Omega_{obs} + \alpha \int_{\Omega_{con}} |I_e|^2 \mathrm{d}\Omega_{con} \right) \mathrm{d}t,$$

  where $V_d$ is the desired state.
- The desired trajectory ($V_d$) of the transmembrane voltage solution is computed using the following initial conditions,

$$\begin{aligned} V_d(0) &= \begin{cases} 105.0 & \text{in} \quad \Omega_{exi} \\ 0 & \text{otherwise} \end{cases} \\ v(0) &= 0 \quad \text{in } \Omega_c. \\ I_e &= \begin{cases} 15 & \text{in} \quad \Omega_{con} \times [0, T] \\ 0 & \text{otherwise.} \end{cases} \end{aligned}$$

# Numerical results : Test case 1




| | NCG | NCG-Newton | Newton |
|---|---|---|---|
| iterations | 291 | 67 (50+17) | 26 |
| CPU time (*s*) | 643.876 | 375.711 | 410.726 |

see [Nagaiah, Kunisch, Plank (in preparation)]

# Numerical results : Test case 2

- The choice of the cost functional which is suitable to optimize the potentials

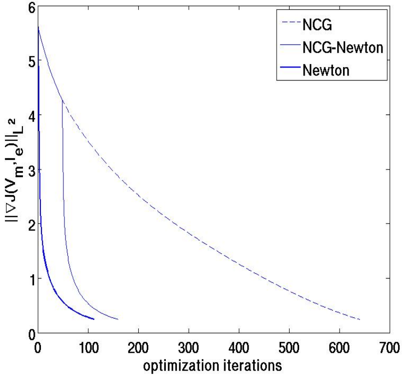
$$J(V_m, I_e) = \min \frac{1}{2} \int_0^T \left( \int_{\Omega_{obs}} |V_m|^2 \, d\Omega_{obs} + \alpha \int_{\Omega_{co'n}} |I_e|^2 \, d\Omega_{con} \right) dt$$

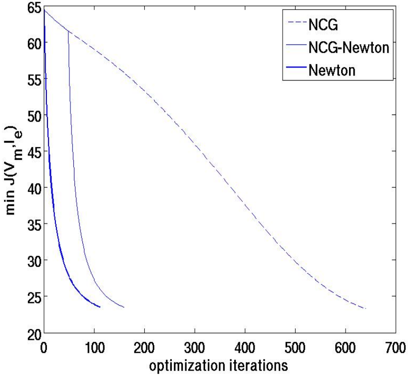
- The initial solution is considered for this test case as follows:

$$\begin{aligned} V_m(0) &= \begin{cases} 105.0 & \text{in} \quad \Omega_{exi} \\ 0 & \text{otherwise} \end{cases} \\ v(0) &= 0 \quad \text{in } \Omega_c \, . \\ (I_e)_0 &= 0 \quad \text{in } \Omega_{con} \times [0, T] \, . \end{aligned}$$

# Numerical results : Test case 2

→ For $T = 1$ *msec* of simulation time.

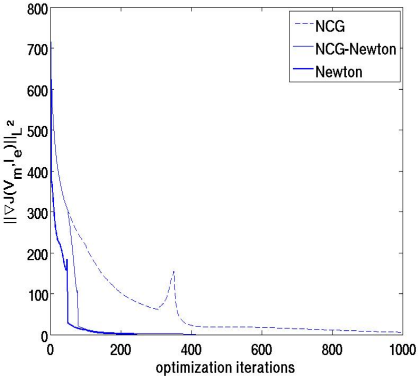


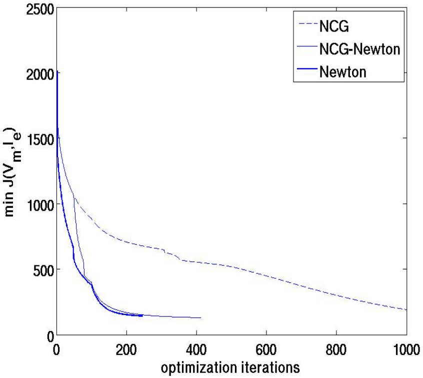




| | NCG | NCG-Newton | Newton |
|---|---|---|---|
| iterations | 641 | 160 (50+110) | 113 |
| CPU time ($s$) | 1351.4 | 1545.22 | 1431.47 |

# Numerical results : Test case 2

→ For $T = 8$ *msec* of simulation time.




| | NCG | NCG-Newton | Newton |
|---|---|---|---|
| iterations | 1000 | 414 (50+364) | 247 |
| CPU time | 4.5575 *h* | 12.1688 *h* | 7.8316 *h* |

# Numerical results : Test case 2

movies for the initial state and optimal state solutions.

# Summary

- Good results obtained for optimal control of the mono-domain equations.
  - Specifically, with tracking type and minimization of transmembrane voltage.
- Second order methods are faster to converge to the solutions for long time horizons.
- Cost functional involving gradient of transmembrane voltage.
- Mathematical analysis of the optimal control of bidomain equations.

# Outlook

- Improve the efficiency of the codes for the primal and adjoint equations by utilizing adaptivity.
- Do longer time horizons with complete simulations of several heart beats.

Movie file