Discontinuous Galerkin approximation of the bidomain system for cardiac electrophysiology

Authors: *Marta Lorenzo & Perego Matilde*
Supervisors: *Antonietti Paola Francesca & Vergara Christian*

Politecnico di Milano

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Cardiac electrophysiology

Cardiac electrophysiology = propagation of an electrical signal that causes the cells of the myocardium to contract.

- Microscopic scales: ion channels (Na^+, K^+, Ca^-, ...);
- Macroscopic scales: gap junctions.

1. Cell → parallel of series of voltage source and resistance: R_{Na}, V_{Na}, R_K, V_K
2. Cellular membrane → capacitor: C_m
3. Gap junctions → resistance: R_i

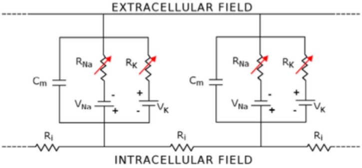


Figure: Electrical circuit for the sequence of two cardiac cells.

Aim of the project

Mathematical and numerical model of the **electrophysiology of the heart**

- **Bidomain model**: systems of partial differential equations
- **Parabolic-parabolic** (PP)
- Model for ionic current: **FitzHugh Nagumo model**
- **Discontinuous Galerkin method**

Why DG methods?

- Solution is the propagation of a steep front $\rightarrow$ high gradients
- Flexibility of mesh design
- Flexibility of polynomial degree

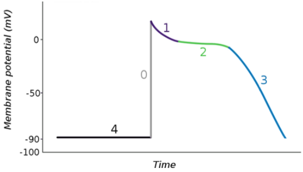


Figure: Propagation of action potential with realistic values

Bidomain equations

The bidomain problem with Neumann boundary condition reads:

$$\begin{cases} \chi_m C_m \dfrac{\partial V_m}{\partial t} - \nabla \cdot (\Sigma_i \nabla \phi_i) + \chi_m I_{ion} = I_i^{ext} & \text{in} \quad \Omega_{mus} \times (0, T] \\ -\chi_m C_m \dfrac{\partial V_m}{\partial t} - \nabla \cdot (\Sigma_e \nabla \phi_e) - \chi_m I_{ion} = -I_e^{ext} & \text{in} \quad \Omega_{mus} \times (0, T] \\ \Sigma_i \nabla \phi_i \cdot \mathrm{n} = b_i & \text{on} \quad \partial\Omega_{mus} \times (0, T] \\ \Sigma_e \nabla \phi_e \cdot \mathrm{n} = b_e & \text{on} \quad \partial\Omega_{mus} \times (0, T] \\ \dfrac{\partial \boldsymbol{\omega}}{\partial t} = \mathrm{g}(V_m, \boldsymbol{\omega}) & \text{in} \quad \Omega_{\mathrm{mus}} \times (0, T] \end{cases}$$

where:

- χ_m is the surface to volume ratio;
- C_m is the the cellular membrane capacitance;
- Σ_i, Σ_e are the intracellular and extracellular conductivity tensors;
- $\phi_i(t, \boldsymbol{x})$ is the intracellular potential;
- $\phi_e(t, \boldsymbol{x})$ is the extracellular potential;
- $V_m(t, \boldsymbol{x}) = \phi_i(t, \boldsymbol{x}) - \phi_e(t, \boldsymbol{x})$ is the trasmembrane potential;
- $I^i_{ext}(t, \boldsymbol{x})$, $I^e_{ext}(t, \boldsymbol{x})$ are the intracellular and extracellular applied currents;
- $I_{ion} = I_{ion}(V_m, \omega)$ is the ionic current;
- b_i, b_e are the intracellular and extracellular potential fluxes;
- ω is the gating variable.

Ionic current

FitzHugh-Nagumo model:

$$\begin{cases} I_{ion}(V_m, \omega) = -kV_m(V_m - a)(V_m - 1) - \omega \\ g(V_m, \omega) = \dfrac{\partial \omega}{\partial t} = \epsilon(V_m - \gamma\omega) \end{cases}$$

with k, a, γ, ϵ suitably chosen parameters.

Semidiscrete DG formulation

$\mathcal{T}_h$ triangulation over Ω_{mus}.

DG space $V_h^k = \{v_h \in L^2(\Omega) : v_h|_{\mathcal{K}} \in \mathbb{P}^k(\mathcal{K})\ \forall \mathcal{K} \in \mathcal{T}_h\}$

For any time $t \in (0, T]$ find $\boldsymbol{\Phi_h}(t) = [\phi_i^h(t), \phi_e^h(t)]^T \in [V_h^k]^2$ and $\omega_h(t) \in V_h^k$:

$$\sum_{\mathcal{K}\in\mathcal{T}_h} \int_{\mathcal{K}} \chi_m C_m \frac{\partial V_m^h}{\partial t} v_h d\omega + a_i(\phi_i^h, v_h) - \sum_{\mathcal{K}\in\mathcal{T}_h} \int_{\mathcal{K}} \chi_m k(V_m^h - 1)(V_m^h - a)V_m^h v_h d\omega \quad + \\ - \sum_{\mathcal{K}\in\mathcal{T}_h} \int_{\mathcal{K}} \chi_m w_h v_h d\omega = (I_i^{ext}, v_h) \qquad \forall\ v_h \in V_h^p$$

$$- \sum_{\mathcal{K}\in\mathcal{T}_h} \int_{\mathcal{K}} \chi_m C_m \frac{\partial V_m^h}{\partial t} v_h d\omega + a_e(\phi_e^h, v_h) + \sum_{\mathcal{K}\in\mathcal{T}_h} \int_{\mathcal{K}} \chi_m k(V_m^h - 1)(V_m^h - a)V_m^h v_h d\omega \quad + \\ + \sum_{\mathcal{K}\in\mathcal{T}_h} \int_{\mathcal{K}} \chi_m w_h v_h d\omega = (-I_e^{ext}, v_h) \qquad \forall\ v_h \in V_h^p$$

$$\sum_{\mathcal{K}\in\mathcal{T}_h}\int_{\mathcal{K}}\frac{\partial w_h}{\partial t}v_h d\omega = \sum_{\mathcal{K}\in\mathcal{T}_h}\int_{\mathcal{K}}\epsilon(V_m^h-\gamma w_h)v_h d\omega \qquad \forall\ v_h\in V_h^p$$

$$a_i(\phi_i^h,v_h)=\sum_{\mathcal{K}\in\mathcal{T}_h}\int_{\mathcal{K}}(\Sigma_i\nabla_h\phi_i^h)\cdot\nabla_h v_h d\omega-\sum_{F\in\mathcal{F}_h^I}\int_F\{\!\{\Sigma_i\nabla_h\phi_i^h\}\!\}\cdot[\![v_h]\!]d\sigma+$$
$$-\delta\sum_{F\in\mathcal{F}_h^I}\int_F\{\!\{\Sigma_i\nabla_h v_h\}\!\}\cdot[\![\phi_i^h]\!]d\sigma+\sum_{F\in\mathcal{F}_h^I}\int_F\gamma[\![\phi_i^h]\!]\cdot[\![v_h]\!]d\sigma$$

$$a_e(\phi_e^h,v_h)=\sum_{\mathcal{K}\in\mathcal{T}_h}\int_{\mathcal{K}}(\Sigma_e\nabla_h\phi_e^h)\cdot\nabla_h v_h d\omega-\sum_{F\in\mathcal{F}_h^I}\int_F\{\!\{\Sigma_e\nabla_h\phi_e^h\}\!\}[\![v_h]\!]d\sigma+$$
$$-\delta\sum_{F\in\mathcal{F}_h^I}\int_F\{\!\{\Sigma_e\nabla_h v_h\}\!\}\cdot[\![\phi_e^h]\!]d\sigma+\sum_{F\in\mathcal{F}_h^I}\int_F\gamma[\![\phi_e^h]\!]\cdot[\![v_h]\!]d\sigma$$

$$(I_i^{ext},v_h)=\sum_{\mathcal{K}\in\mathcal{T}_h}\int_{\mathcal{K}}I_i^{ext}v_h d\omega+\int_{\partial\Omega}bv_h d\sigma.$$

$$(-I_e^{ext},v_h)=-\sum_{\mathcal{K}\in\mathcal{T}_h}\int_{\mathcal{K}}I_e^{ext}v_h d\omega+\int_{\partial\Omega}bv_h d\sigma.$$

Stabilization function and penalty constant

- $\gamma \in L^\infty(\mathcal{F}_h)$ is the **stabilization function**

$$\gamma|_{\mathcal{F}} = \alpha \frac{\tilde{k}^2}{\tilde{h}}$$

  with $\alpha \in \mathbb{R}, \alpha > 0$, $\tilde{k} = \max(k_+, k_-)$ and $\tilde{h} = \max(h_{k_+}, h_{k_-})$, where k_+, k_- are the degrees of the polynomial of the neighbouring elements, while h_{k_+}, h_{k_-} are the characteristic length of those elements.

- δ is the **penalty constant**:
  - $\delta = 1$: SIP i.e. Symmetric Interior Penalty;
  - $\delta = 0$: IIP i.e. Incomplete Interior Penalty;
  - $\delta = -1$: NIP i.e. Non-symmetric Interior Penalty.

Algebraic formulation

Introduce the basis $\{\varphi_j\}_{j=1:N_h}$ of the space V_h^k and decompose the solutions:

$$\mathbf{\Phi}_h(t) = \begin{bmatrix} \phi_i^h(t) \\ \phi_e^h(t) \end{bmatrix} = \begin{bmatrix} \sum_{j=1}^{N_h} \phi_{i,j}(t)\varphi_j \\ \sum_{j=1}^{N_h} \phi_{e,j}(t)\varphi_j \end{bmatrix}$$

$$V_m^h(t) = \sum_{j=1}^{N_h} V_{m,j}(t)\varphi_j = \sum_{j=1}^{N_h} (\phi_{i,j}(t) - \phi_{e,j}(t))\varphi_j$$

$$w_h(t) = \sum_{j=1}^{N_h} w_j(t)\varphi_j$$

Define the matrixes:

$$M_{kj} = \sum_{\mathcal{K}\in\mathcal{T}_h} \int_{\mathcal{K}} \varphi_j \varphi_k d\omega$$ Mass matrix

$$A_i = V - I_i^T - \theta I_i + S \qquad A_e = V - I_e^T - \theta I_e + S$$ Intra and Extra-cellular stiffness matrix

where:

$$V_{kj} = \int_{\Omega} \nabla_h \varphi_j \cdot \nabla_h \varphi_k d\omega \qquad S_{kj} = \sum_{F\in\mathcal{F}_h^I} \int_F \gamma \, [\![\varphi_j]\!] \cdot [\![\varphi_k]\!] d\sigma$$

$$I_{i,kj} = \sum_{F\in\mathcal{F}_h^I} \int_F [\![\varphi_j]\!] \cdot \{\!\{\Sigma_i \nabla_h \varphi_k\}\!\} d\sigma \qquad I_{i,kj}^T = \sum_{F\in\mathcal{F}_h^I} \int_F \{\!\{\Sigma_i \nabla_h \varphi_j\}\!\} \cdot [\![\varphi_k]\!] d\sigma$$

$$I_{e,kj} = \sum_{F\in\mathcal{F}_h^I} \int_F [\![\varphi_j]\!] \cdot \{\!\{\Sigma_e \nabla_h \varphi_k\}\!\} d\sigma \qquad I_{e,kj}^T = \sum_{F\in\mathcal{F}_h^I} \int_F \{\!\{\Sigma_e \nabla_h \varphi_j\}\!\} \cdot [\![\varphi_k]\!] d\sigma$$

$$C(u_h)_{kj} = -\sum_{\mathcal{K}\in\mathcal{T}_h} \int_{\mathcal{K}} \chi_m k (V_m^h - 1)(V_m^h - a) \varphi_j \varphi_k d\omega$$ Non linear matrix

Algebraic formulation

Find a solution $\mathbf{\Phi_h} = [\phi_i^{\boldsymbol{h}}(t), \phi_e^{\boldsymbol{h}}(t)]^T \in [V_h^p]^2$ and $\omega_\mathrm{h} \in V_h^p$ for every $t \in (0, T]$:

$$\chi_m C_m \begin{bmatrix} M & -M \\ -M & M \end{bmatrix} \cdot \begin{bmatrix} \dot{\phi}_{\boldsymbol{i}}^{\boldsymbol{h}}(t) \\ \dot{\phi}_{\boldsymbol{e}}^{\boldsymbol{h}}(t) \end{bmatrix} + \begin{bmatrix} A_i & 0 \\ 0 & A_e \end{bmatrix} \cdot \begin{bmatrix} \phi_{\boldsymbol{i}}^{\boldsymbol{h}}(t) \\ \phi_{\boldsymbol{e}}^{\boldsymbol{h}}(t) \end{bmatrix} +$$

$$- \begin{bmatrix} C(V_m^h) & -C(V_m^h) \\ -C(V_m^h) & C(V_m^h) \end{bmatrix} \cdot \begin{bmatrix} \phi_{\boldsymbol{i}}^{\boldsymbol{h}}(t) \\ \phi_{\boldsymbol{e}}^{\boldsymbol{h}}(t) \end{bmatrix} - \chi_m \begin{bmatrix} M & 0 \\ 0 & -M \end{bmatrix} \cdot \begin{bmatrix} \boldsymbol{\omega_h}(t) \\ \boldsymbol{\omega_h}(t) \end{bmatrix} = \begin{bmatrix} \boldsymbol{F_i^h} \\ \boldsymbol{F_e^h} \end{bmatrix}$$

Temporal discretization

Divide the interval (0,T] into K subinterval $(t^k, t^{k+1}]$ of length $\Delta t = t^{k+1} - t^k$ where $t^k = k\Delta t \qquad \forall k = 0, ..., K-1$.

- time discretization $\rightarrow$ implicit
- non linearity of ionic current $\rightarrow$ semi-implicit

$$I_{ion} = -k(\boldsymbol{V_m}^k - a)(\boldsymbol{V_m}^k - 1)\boldsymbol{V_m}^{k+1} - \boldsymbol{\omega}^{k+1}$$

- ω gating variable $\rightarrow$ implicit

The final system to solve $\forall k = 0, ..., K-1$ is:

$$\begin{cases} \left(\dfrac{1}{\Delta t} + \varepsilon\gamma\right) M\boldsymbol{\omega}^{k+1} = \varepsilon M \boldsymbol{V_m}^k + \dfrac{M}{\Delta t}\boldsymbol{\omega}^k \\ \\ (B + C_{nl}(\phi^k))\phi^{k+1} = \boldsymbol{r}^{k+1} \end{cases}$$

- $$B = \frac{\chi_m C_m}{\Delta t}\begin{bmatrix} M & -M \\ -M & M \end{bmatrix} + \begin{bmatrix} A_i & 0 \\ 0 & A_e \end{bmatrix}$$

- $$C_{nl}(\phi^k) = \begin{bmatrix} C(V_m^k) & -C(V_m^k) \\ -C(V_m^k) & C(V_m^k) \end{bmatrix} \qquad (\ C(V_m^k) = -k\chi_m(\boldsymbol{V_m^k} - a)(\boldsymbol{V_m^k} - 1))$$

- $$\boldsymbol{r}^{\boldsymbol{k}+1} = \begin{bmatrix} \boldsymbol{F_i^{k+1}} \\ \boldsymbol{F_e^{k+1}} \end{bmatrix} + \boldsymbol{\chi_m}\begin{bmatrix} \boldsymbol{M} & 0 \\ 0 & -\boldsymbol{M} \end{bmatrix} \cdot \begin{bmatrix} \boldsymbol{\omega^{k+1}} \\ \boldsymbol{\omega^{k+1}} \end{bmatrix} + \frac{\boldsymbol{\chi_m C_m}}{\boldsymbol{\Delta t}}\begin{bmatrix} \boldsymbol{M} & -\boldsymbol{M} \\ -\boldsymbol{M} & \boldsymbol{M} \end{bmatrix} \cdot \begin{bmatrix} \boldsymbol{\phi_i^k} \\ \boldsymbol{\phi_e^k} \end{bmatrix}$$

Analytical test

In order to test our model we build an exact analytical solution on a square 2D domain $\Omega_{mus} = [0,1]^2$:

- $\tilde{\phi}_i = 2\sin(2\pi x)\sin(2\pi y)e^{-5t} \qquad \forall t \in (0, T]$
- $\tilde{\phi}_e = \sin(2\pi x)\sin(2\pi y)e^{-5t} \qquad \forall t \in (0, T]$

We obtain the following transmembrane potential:

- $\tilde{V}_m = \tilde{\phi}_i - \tilde{\phi}_e = \sin(2\pi x)\sin(2\pi y)e^{-5t} \qquad \forall t \in (0, T]$

Boundary conditions

We impose the following Neumann boundary conditions:

$$\Sigma_i \nabla \tilde{\phi}_i \cdot \boldsymbol{n} = \begin{cases} 2\Sigma_i(-2\pi \sin(2\pi x)\cos(2\pi y)e^{-5t}) & (y=0) \\ 2\Sigma_i(2\pi \cos(2\pi x)\sin(2\pi y)e^{-5t}) & (x=1) \\ 2\Sigma_i(2\pi \sin(2\pi x)\cos(2\pi y)e^{-5t}) & (y=1) \\ 2\Sigma_i(-2\pi \cos(2\pi x)\sin(2\pi y)e^{-5t}) & (x=0) \end{cases}$$

$$\Sigma_e \nabla \tilde{\phi}_e \cdot \boldsymbol{n} = \begin{cases} \Sigma_e(-2\pi \sin(2\pi x)\cos(2\pi y)e^{-5t}) & (y=0) \\ \Sigma_e(2\pi \cos(2\pi x)\sin(2\pi y)e^{-5t}) & (x=1) \\ \Sigma_e(2\pi \sin(2\pi x)\cos(2\pi y)e^{-5t}) & (y=1) \\ \Sigma_e(-2\pi \cos(2\pi x)\sin(2\pi y)e^{-5t}) & (x=0) \end{cases}$$

Applied currents

The applied current is analytically calculated by inserting the exact solutions in the bidomain system:

- $I_i^{ext} = \left[-5\chi_m C_m + 16\pi^2\Sigma_i - \chi_m k(\tilde{V}_m - 1)(\tilde{V}_m - a)\right]\tilde{V}_m - \chi_m\omega$
- $-I_e^{ext} = \left[5\chi_m C_m + 8\pi^2\Sigma_e + \chi_m k(\tilde{V}_m - 1)(\tilde{V}_m - a)\right]\tilde{V}_m + \chi_m\omega$

where:

$$\omega = \frac{\epsilon}{\epsilon\gamma - 5}\tilde{V}_m$$

Choice of parameters

We chose unitary parameter for the PDEs:

- $\chi_m = 1;$
- $C_m = 1;$
- $\Sigma_i = 1;$
- $\Sigma_e = 1;$

and physiological parameters for the gating variable ODE:

- $k = 19.5;$
- $\varepsilon = 1.2;$
- $\gamma = 0.1;$
- $a = 0.013.$

Solution of V_m - Test 1

Test1: k = P1, T = 0.001, dt = 0.0001, nref = 3

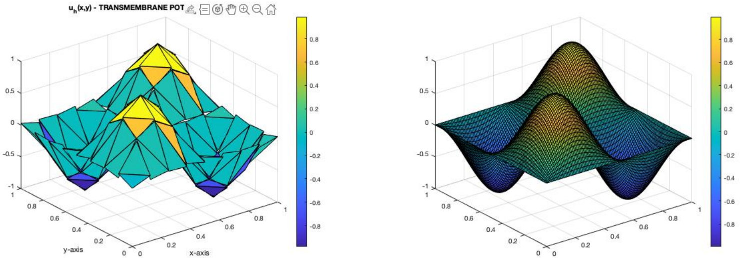


Figure: Numerical solution of V_m (left) and analytical solution of V_m (right)

Error of V_m - Test 1

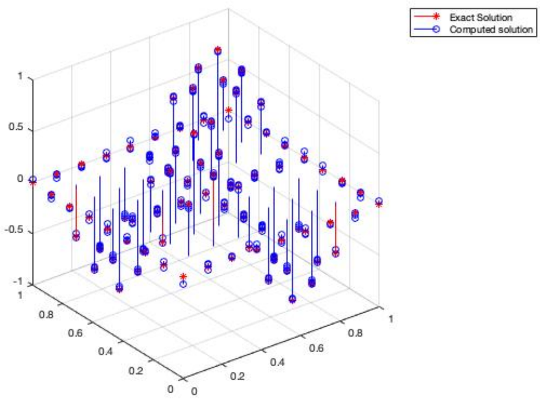
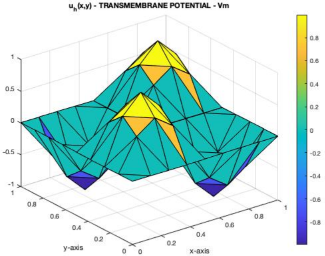


Figure: Computed and exact solution of V_m

Solution of V_m - Test 2

Test2: k = P2, T = 0.001, dt = 0.0001, nref = 3



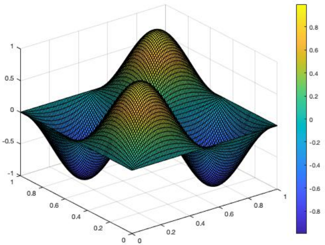


Figure: Numerical solution of V_m (left) and analytical solution of V_m (right)

Error of V_m - Test 2

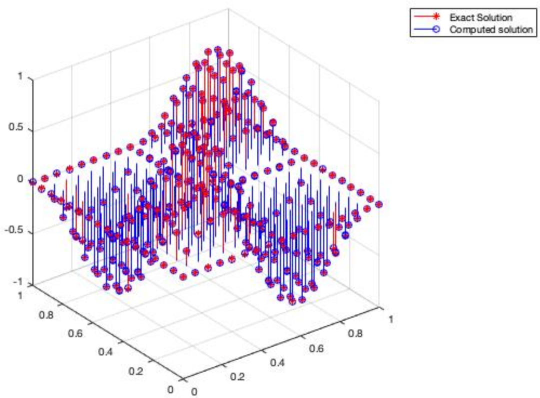


Figure: Computed and exact solution of V_m

Solution of V_m - Test 3

Test3: k = P3, T = 0.001, dt = 0.0001, nref = 3

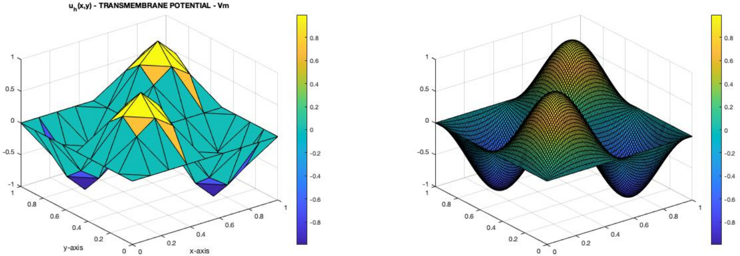


Figure: Numerical solution of V_m (left) and analytical solution of V_m (right)

Error of V_m - Test 3

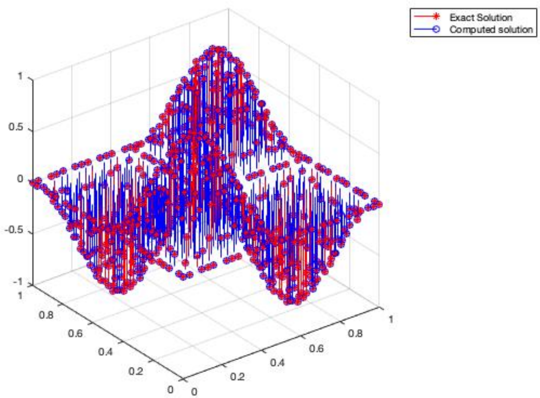


Figure: Computed and exact solution of V_m

Solution of V_m - Test 4

Test4: k = P1, T = 0.001, dt = 0.0001, nref = 4

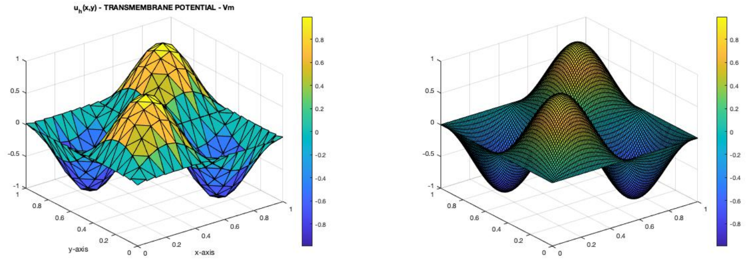


Figure: Numerical solution of V_m (left) and analytical solution of V_m (right)

Error of V_m - Test 4

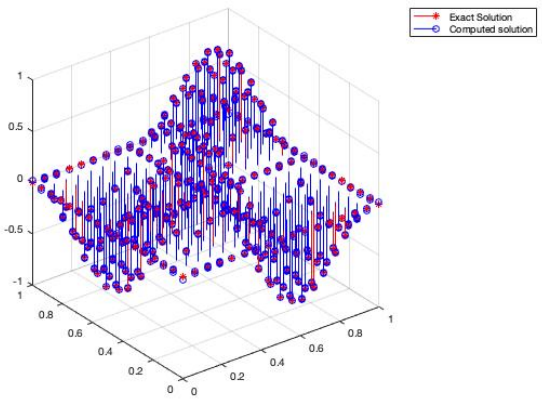


Figure: Computed and exact solution of V_m

Comparison of errors

Error type	**P1** (nref=3)	**P2** (nref=3)	**P3** (nref=3)	**P1** (nref=4)
Error L^2	0.0587	0.0035	2.7682e-04	0.0155
Error semi-H^1	1.3895	0.2280	0.0246	0.7101
Error H^1	1.3907	0.2280	0.0246	0.7103
Error inf	0.0811	0.0076	0.0011	0.0365
Error DG	1.5418	0.2444	0.0254	0.8060

Table: Comparison of errors of Test1, Test2, Test3, Test4

Convergence test of $V_m - Test1$

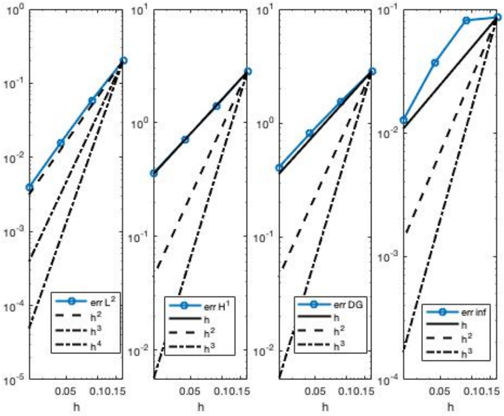


Figure: Convergence test of V_m

Convergence test of V_m − *Test2*

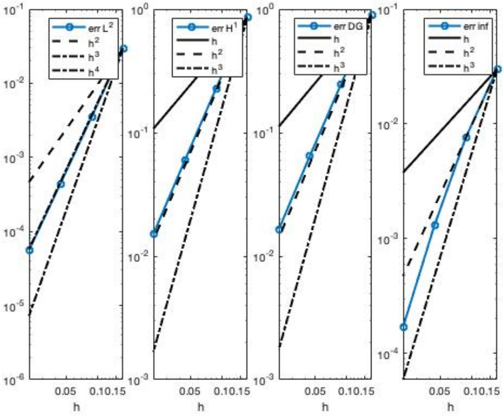


Figure: Convergence test of V_m

Convergence test of $V_m - Test3$

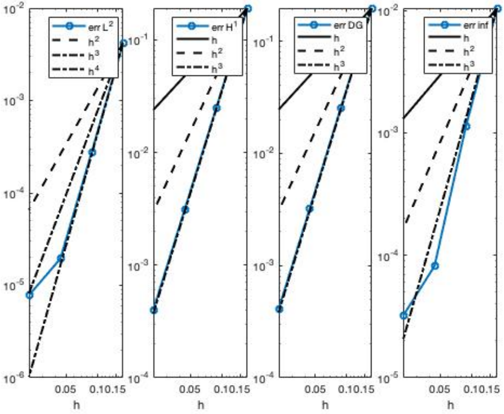


Figure: Convergence test of V_m

Solution of Φ_i - Test 1

Test1 k=P1, T=0.001, dt=0.0001, nref=3

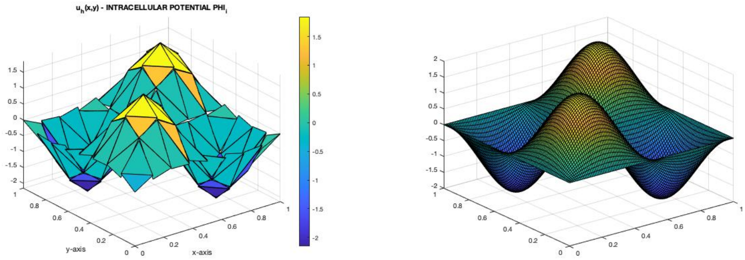


Figure: Numerical solution of Φ_i (left) and analytical solution of Φ_i (right)

Error of Φ_i - Test 1

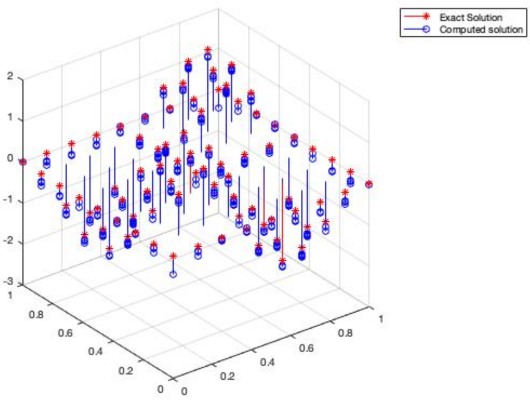
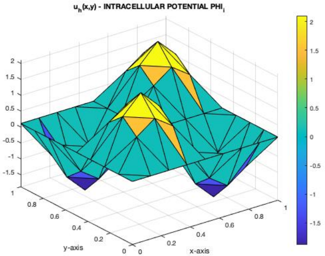


Figure: Computed and exact solution of Φ_i

Solution of Φ_i - Test 3

Test3 k = P3, T = 0.001, dt = 0.0001, nref = 3



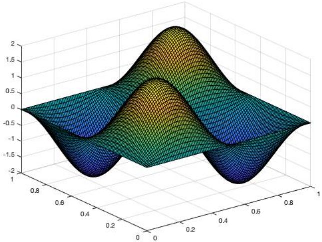


Figure: Numerical solution of Φ_i (left) and analytical solution of Φ_i (right)

Error of Φ_i - Test 3

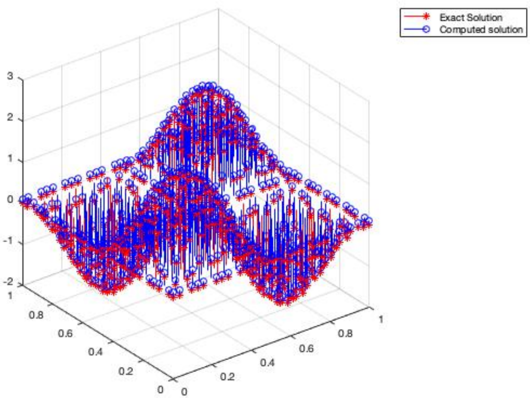


Figure: Computed and exact solution of Φ_i

Convergence test of Φ_i - Test 3

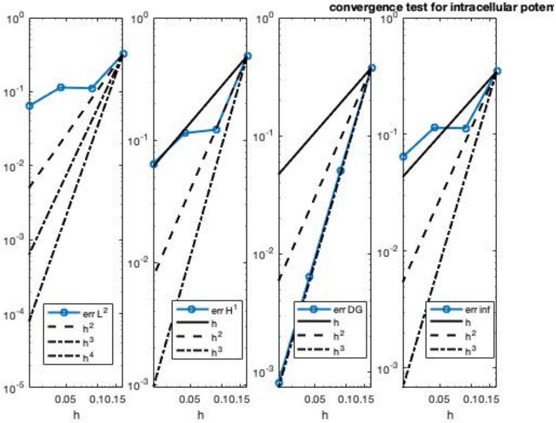


Figure: Convergence test of Φ_i

Solution of Φ_e - Test 1

Test1 k = P1, T = 0.001, dt = 0.0001, nref = 3

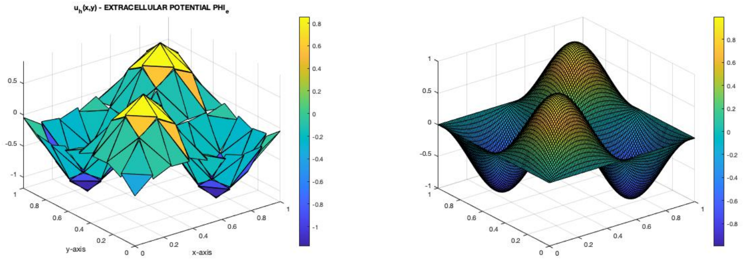


Figure: Numerical solution of Φ_e (left) and analytical solution of Φ_e (right)

Error of Φ_e - Test 1

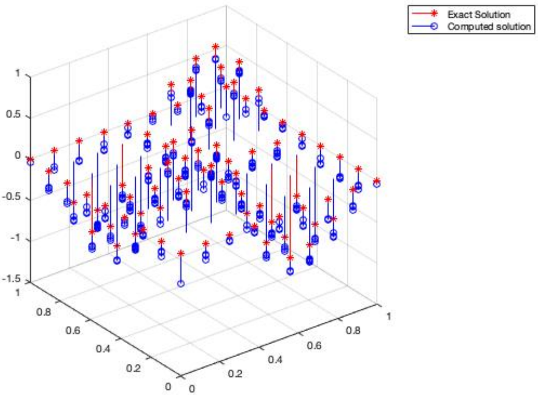


Figure: Computed and exact solution of Φ_e

Solution of Φ_e - Test 3

Test3 k = P3, T = 0.001, dt = 0.0001, nref = 3

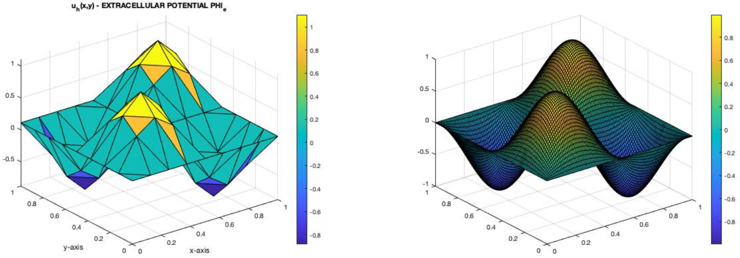


Figure: Numerical solution of Φ_e (left) and analytical solution of Φ_e (right)

Error of Φ_e - Test 3

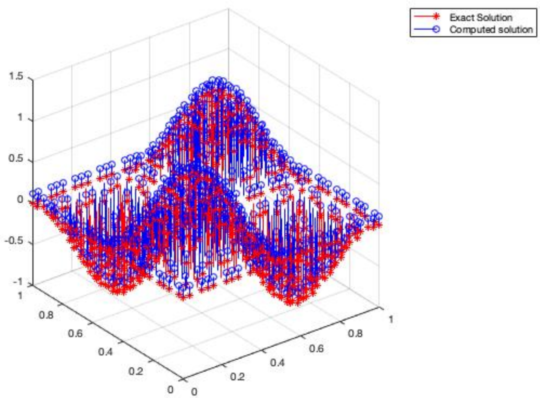


Figure: Computed and exact solution of Φ_e

Convergence test of Φ_e - Test 3

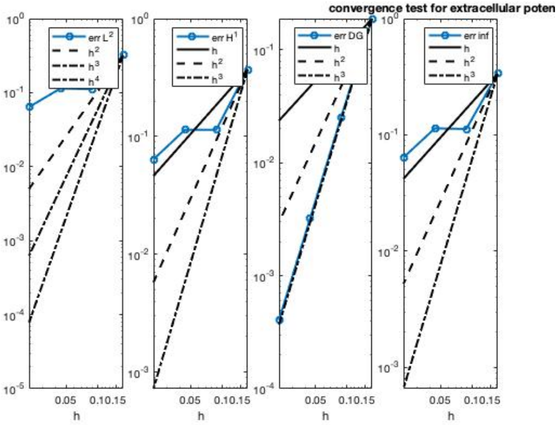


Figure: Convergence test of Φ_e

Convergence test of gating variable - Test 5.a

Test 5.a: k = P1, T = 0.001, dt = 0.0001, nref = 3

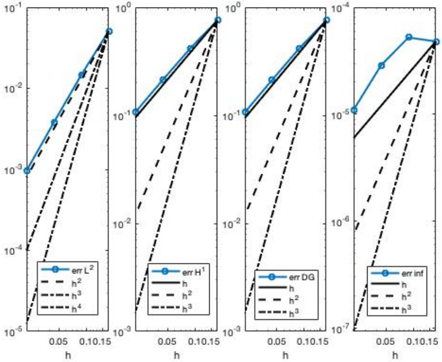


Figure: Convergence test of ω

Convergence test of gating variable - Test 5.b

Test5.b: k = P2, T = 0.001, dt = 0.0001, nref = 3

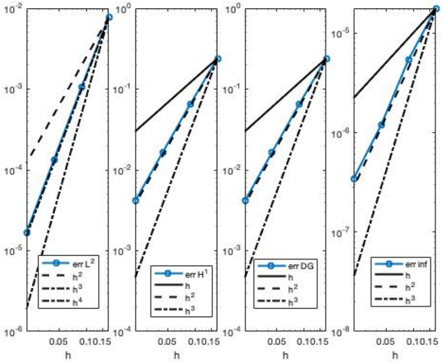


Figure: Convergence test of ω

Convergence test of gating variable - Test 5.c

Test 5.c: k = P3, T = 0.001, dt = 0.0001, nref = 3

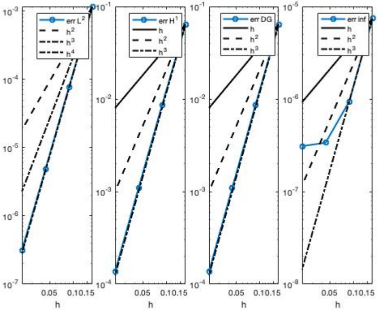


Figure: Convergence test of ω

Thanks for the attention

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