POLITECNICO
MILANO 1863

A HIGH-ORDER DISCONTINUOUS GALERKIN METHOD FOR THE BIDOMAIN PROBLEM OF CARDIAC ELECTROPHYSIOLOGY

Project N° 2

Supervisors: Christian Vergara, Paola Antonietti

Federica Botta, Matteo Calafà

Course of Numerical Analysis for Partial Differential Equations

A.Y. 2020/2021

The mathematical model for the cardiac electrophysiology

Bidomain model + FitzHugh-Nagumo with Neumann B.C.

$$\begin{cases} \chi_m C_m \frac{\partial V_m}{\partial t} - \nabla \cdot (\Sigma_i \nabla \phi_i) + \chi_m I_{ion}(V_m, w) = I_i^{ext}, & \text{in } \Omega_{mus} \times (0, T], \\ -\chi_m C_m \frac{\partial V_m}{\partial t} - \nabla \cdot (\Sigma_e \nabla \phi_e) - \chi_m I_{ion}(V_m, w) = -I_e^{ext}, & \text{in } \Omega_{mus} \times (0, T], \\ I_{ion}(V_m, w) = k V_m (V_m - a)(V_m - 1) + w, & \text{in } \Omega_{mus} \times (0, T], \\ \frac{\partial w}{\partial t} = \epsilon (V_m - \gamma w), & \text{in } \Omega_{mus} \times (0, T], \\ \Sigma_i \nabla \phi_i \cdot n = b_i, & \text{on } \partial\Omega_{mus} \times (0, T], \\ \Sigma_e \nabla \phi_e \cdot n = b_e, & \text{on } \partial\Omega_{mus} \times (0, T], \\ \text{Initial conditions for } \phi_i, \phi_e, w, & \text{in } \Omega_{mus} \times \{t = 0\}. \end{cases}$$

Unknowns: $\phi_i, \; \phi_e, \; V_m = \phi_i - \phi_e, \; w$

Our achievements

What had already been done:

- Implementation of a DG method with FEM basis for the Bidomain problem.
- Implementation of a Semi-Implicit temporal scheme.

What we did:

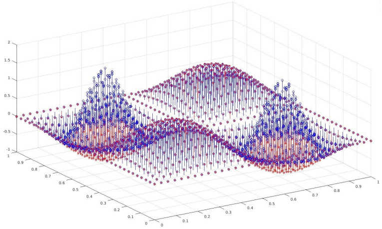
- Implementation of a DG method with **Dubiner** basis for the Bidomain problem.
- Implementation of further temporal schemes.
- Bugs corrections and optimizations.
- Pseudo-realistic simulations.

Previous implementations were not satisfactory from the point of view of stability and convergence, in particular when parameters are chosen as realistic and not unitary.

It was in part due to an inverted sign in the *FitzHugh-Nagumo* model

$\Downarrow$

Risk for the well-posedness of the problem.



Semi-discrete Discontinuous Galerkin formulation

For any $t \in [0, T]$ find $\Phi_h(t) = [\phi_i^h(t), \phi_e^h(t)]^T \in [V_h^p]^2$ and $w_h(t) \in V_h^p$ such that:

$$
\begin{cases}
\displaystyle\sum_{\mathcal{K}\in\tau_h}\int_{\mathcal{K}} \chi_m C_m \frac{\partial V_m^h}{\partial t} v_h d\omega + a_i(\phi_i^h, v_h) + \sum_{\mathcal{K}\in\tau_h}\int_{\mathcal{K}} \chi_m k(V_m^h - 1)(V_m^h - a)V_m^h v_h d\omega + \\
\qquad\displaystyle + \sum_{\mathcal{K}\in\tau_h}\int_{\mathcal{K}} \chi_m w_h v_h d\omega = (I_i^{ext}, v_h), \qquad \forall v_h \in V_h^p, \\
\displaystyle -\sum_{\mathcal{K}\in\tau_h}\int_{\mathcal{K}} \chi_m C_m \frac{\partial V_m^h}{\partial t} v_h d\omega + a_e(\phi_e^h, v_h) - \sum_{\mathcal{K}\in\tau_h}\int_{\mathcal{K}} \chi_m k(V_m^h - 1)(V_m^h - a)V_m^h v_h d\omega + \\
\qquad\displaystyle - \sum_{\mathcal{K}\in\tau_h}\int_{\mathcal{K}} \chi_m w_h v_h d\omega = (-I_e^{ext}, v_h), \qquad \forall v_h \in V_h^p, \\
\displaystyle\sum_{\mathcal{K}\in\tau_h}\int_{\mathcal{K}} \frac{\partial w_h}{\partial t} v_h d\omega = \sum_{\mathcal{K}\in\tau_h}\int_{\mathcal{K}} \epsilon(V_m^h - \gamma w_h) v_h d\omega, \qquad \forall v_h \in V_h^p,
\end{cases}
$$

where:

- $$a_l(\phi_l^h, v_h) = \sum_{\mathcal{K}\in\tau_h} \int_{\mathcal{K}} (\Sigma_l \nabla_h \phi_l^h) \cdot \nabla_h v_h d\omega - \sum_{F\in\mathcal{F}_h^I} \int_F \{\{\Sigma_l \nabla_h \phi_l^h\}\} \cdot [\![v_h]\!] d\sigma +$$
$$- \delta \sum_{F\in\mathcal{F}_h^I} \int_F \{\{\Sigma_l \nabla_h v_h\}\} \cdot [\![\phi_l^h]\!] d\sigma + \sum_{F\in\mathcal{F}_h^I} \int_F \Gamma [\![\phi_l^h]\!] \cdot [\![v_h]\!] d\sigma \qquad l = i, e,$$
- $$(I_i^{ext}, v_h) = \sum_{\mathcal{K}\in\tau_h} \int_{\mathcal{K}} I_i^{ext} v_h d\omega + \int_{\partial\Omega} b_i v_h d\sigma,$$
- $$(-I_e^{ext}, v_h) = - \sum_{\mathcal{K}\in\tau_h} \int_{\mathcal{K}} I_e^{ext} v_h d\omega + \int_{\partial\Omega} b_e v_h d\sigma.$$

Dubiner basis: analytical definition

Definition (Dubiner basis)

The Dubiner basis that generates the space $\mathbb{P}^p(\hat{K})$ of polynomials of degree p over the reference triangle is the set of functions:

$$\phi_{ij} : \hat{K} \to \mathbb{R},$$

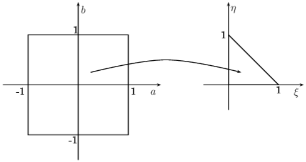
$$\phi_{ij}(\xi, \eta) = c_{ij}\, 2^j (1-\eta)^j J_i^{0,0}\left(\frac{2\xi}{1-\eta} - 1\right) J_j^{2i+1,0}(2\eta - 1),$$

for $i, j = 0, \ldots, p$ and $i + j \leq p$, where $c_{ij} := \sqrt{\frac{2(2i+1)(i+j+1)}{4^i}}$
and $J_i^{\alpha,\beta}(\cdot)$ is the i-th Jacobi polynomial.

Properties

- They consist in a pseudo tensor-product of Jacobi polynomials if the following transformation is then applied:

$$\xi = \frac{(1+a)(1-b)}{4}, \eta = \frac{(1+b)}{2}.$$



- They are $L^2(\hat{K})$ orthonormal ($\hat{K}$ is the reference triangle).

Main works

Remark

Dubiner basis coefficients of a discretized function have ***modal*** *meaning instead of a nodal meaning.*

Then, our main works regarded:

- Methods for the evaluation of the Dubiner functions and gradients in the reference points.
- Methods for the evaluation of the FEM coefficients of a discretized function starting from its Dubiner coefficients and viceversa.
  1. FEM $\rightarrow$ Dubiner is needed to convert u_0 initial data.
  2. FEM $\leftarrow$ Dubiner is needed to plot the solution and do error analysis.

FEM-Dubiner conversion strategies

Consider:

- An element $\mathcal{K} \in \tau_h$
- $\{\psi_i\}_{i=1}^{p}, \{\varphi_j\}_{j=1}^{q}$ as the FEM and Dubiner functions with support in $\mathcal{K}$.
- $\{\hat{u}_i\}_{i=1}^{p}, \{\tilde{u}_j\}_{j=1}^{q}$ as the FEM and Dubiner coefficients of a function u_h.

FEM $\leftarrow$ Dubiner

Exploiting the nodal meaning of FEM, we compute its value in a point:

$$\hat{u}_i = \sum_{j=1}^{q} \tilde{u}_j \varphi_j(x_i),$$

FEM $\rightarrow$ Dubiner

Exploiting the L^2-orthonormality of Dubiner, we compute its Fourier coeff.:

$$\tilde{u}_j = \int_{\mathcal{K}} u_h(x)\varphi_j(x)\,dx = \int_{\mathcal{K}} \sum_{i=1}^{p} \hat{u}_i \psi_i(x)\varphi_j(x)\,dx$$

Semi-implicit scheme

Idea:

- treat most of the terms of the PDE implicitly,
- treat the non-linear term semi-implictly,
- treat the ODE implictly with the exception of the term V_m.

Semi-implicit discretized system

$$\begin{cases} \left(\frac{\chi_m C_m}{\Delta t} \begin{bmatrix} M & -M \\ -M & M \end{bmatrix} + \begin{bmatrix} A_i & 0 \\ 0 & A_e \end{bmatrix} + \begin{bmatrix} C(V_m^n) & -C(V_m^n) \\ -C(V_m^n) & C(V_m^n) \end{bmatrix} \right) \begin{bmatrix} \phi_i^{n+1} \\ \phi_e^{n+1} \end{bmatrix} = \\ \begin{bmatrix} F_i^{n+1} \\ F_e^{n+1} \end{bmatrix} - \chi_m \begin{bmatrix} M & 0 \\ 0 & -M \end{bmatrix} \begin{bmatrix} w^{n+1} \\ w^{n+1} \end{bmatrix} + \frac{\chi_m C_m}{\Delta t} \begin{bmatrix} M & 0 \\ 0 & -M \end{bmatrix} \begin{bmatrix} V_m^n \\ V_m^n \end{bmatrix}, \\ (\frac{1}{\Delta t} + \epsilon\gamma) M w^{n+1} = \epsilon M V_m^n + \frac{M}{\Delta t} w^n. \end{cases}$$

POLITECNICO MILANO 1863

Godunov operator-splitting scheme

The main feature is the sub-division of the problem into two different problems to be solved sequentially, such that $L(u) = L_1(u) + L_2(u)$. In our case:

1:

$$\begin{cases} \chi_m C_m M \frac{\hat{V}_m^{n+1} - V_m^n}{\Delta t} + C(V_m^n) V_m^n + \chi_m M w^n = 0, \\ \frac{w^{n+1} - w^n}{\Delta t} = \epsilon(V_m^n - \gamma w^n). \end{cases}$$

2:

$$\begin{cases} \chi_m C_m M \frac{V_m^{n+1} - \hat{V}_m^{n+1}}{\Delta t} + A_i \phi_i^{n+1} = F_i^{n+1}, \\ -\chi_m C_m M \frac{V_m^{n+1} - \hat{V}_m^{n+1}}{\Delta t} + A_e \phi_e^{n+1} = F_e^{n+1}. \end{cases}$$

Godunov operator-splitting discretized system

$$\begin{cases} \left(\frac{\chi_m C_m}{\Delta t} \begin{bmatrix} M & -M \\ M & -M \end{bmatrix} + \begin{bmatrix} A_i & 0 \\ 0 & -A_e \end{bmatrix} \right) \begin{bmatrix} \phi_i^{n+1} \\ \phi_e^{n+1} \end{bmatrix} = \begin{bmatrix} F_i^{n+1} \\ -F_e^{n+1} \end{bmatrix} + \\ -\chi_m \begin{bmatrix} M & 0 \\ 0 & M \end{bmatrix} \begin{bmatrix} w^n \\ w^n \end{bmatrix} + \left(\frac{\chi_m C_m}{\Delta t} \begin{bmatrix} M & 0 \\ 0 & M \end{bmatrix} - \begin{bmatrix} C(V_m^n) & 0 \\ 0 & C(V_m^n) \end{bmatrix} \right) \begin{bmatrix} V_m^n \\ V_m^n \end{bmatrix}, \\ w^{n+1} = (1 - \epsilon\gamma\Delta t) w^n + \epsilon \Delta t V_m^n. \end{cases}$$

Quasi-implicit operator-splitting scheme

Idea:

- sub-division of the operator as Godunov operator-splitting
- treat implicitly all the terms except the non-linear one

1:

$$\begin{cases} \chi_m C_m M \frac{\tilde{V}_m^{n+1} - V_m^n}{\Delta t} + C(V_m^n) V_m^{n+1} + \chi_m M w^{n+1} = 0, \\ \frac{w^{n+1} - w^n}{\Delta t} = \epsilon (V_m^{n+1} - \gamma w^{n+1}). \end{cases}$$

2:

$$\begin{cases} \chi_m C_m M \frac{V_m^{n+1} - \tilde{V}_m^{n+1}}{\Delta t} + A_i \phi_i^{n+1} = F_i^{n+1}, \\ -\chi_m C_m M \frac{V_m^{n+1} - \tilde{V}_m^{n+1}}{\Delta t} + A_e \phi_e^{n+1} = F_e^{n+1}. \end{cases}$$

Quasi-implicit operator-splitting discretized system

$$\begin{cases} \left(\begin{bmatrix} Q_n & -Q_n \\ Q_n & -Q_n \end{bmatrix} + \begin{bmatrix} A_i & 0 \\ 0 & -A_e \end{bmatrix} \right) \begin{bmatrix} \phi_i^{n+1} \\ \phi_e^{n+1} \end{bmatrix} = \begin{bmatrix} R_n \\ R_n \end{bmatrix} + \begin{bmatrix} F_i^{n+1} \\ -F_e^{n+1} \end{bmatrix}, \\ w^{n+1} = \frac{w^n + \epsilon \Delta t (\phi_i^{n+1} - \phi_e^{n+1})}{1 + \epsilon \gamma \Delta t}. \end{cases}$$

Uniqueness of the potentials

ϕ_i, ϕ_e appear in the system only through their difference V_m or their gradient. This means that there cannot be uniqueness. Namely:

$$\phi_i, \phi_e \ \text{ solutions} \Rightarrow \phi_i + \varphi, \phi_e + \varphi \ \text{ solutions}$$
$$\forall \varphi : [0, T] \to \mathbb{R}$$

Uniqueness strategies

Theorem

The classical solutions ϕ_i, ϕ_e are unique up to a constant depending only on time.

STRATEGIES

1. Imposition of the value of the function in a specific point (m).
$$\phi_i(\bar{x}, t) = \varphi(t) \quad \forall t \in [0, T] \quad \xrightarrow{\text{Numerical version}} \quad u_m^n = \varphi(t^n) \quad \forall n \in \{1, N\}$$

2. Imposition of the function mean value.
$$\int_\Omega \phi_i \, dx = \varphi(t) \quad \forall t \in [0, T] \quad \xrightarrow{\text{Numerical version}} \quad \sum_{j=1}^{N_h} u_j^n \, w_j = \varphi(t^n) \quad \forall n \in \{1, N\}$$

Imposition of the value in a specific point / first coefficient

Remark

The aim is to impose the condition before or directly into the system to avoid ill-conditioning.

Choosing $m = 1$, we want to impose $u_1^n = c$, $c \in \mathbb{R}$. Therefore we apply the following transformation to the system $Au^n = b$.

$$A = \begin{bmatrix} a_{11} & a_{12} & \dots & a_{1N_h} \\ a_{21} & a_{22} & \dots & a_{2N_h} \\ a_{31} & a_{32} & \dots & a_{3N_h} \\ \dots & \dots & \dots & \dots \\ a_{N_h1} & a_{N_h2} & \dots & a_{N_hN_h} \end{bmatrix} \quad \rightarrow \quad \tilde{A} = \begin{bmatrix} 1 & 0 & \dots & 0 \\ 0 & a_{22} & \dots & a_{2N_h} \\ 0 & a_{32} & \dots & a_{3N_h} \\ \dots & \dots & \dots & \dots \\ 0 & a_{N_h2} & \dots & a_{N_hN_h} \end{bmatrix}$$

$$b = \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ \dots \\ b_{N_h} \end{bmatrix} \quad \rightarrow \quad \tilde{b} = \begin{bmatrix} c \\ b_2 - a_{21}c \\ b_3 - a_{31}c \\ \dots \\ b_{N_h} - a_{N_h1}c \end{bmatrix}$$

An anaytical motivation for the mean-value imposition

Remark

The previous strategy modifies directly the system and keeps the symmetry of the matrix. This is not possible for the mean-value imposition, we should look for a different method.

Lemma

The two following problems are both well-posed and have the same solution u, moreover $\lambda = 0$.

Find $u \in H^1(\Omega)$ such that:

$$\begin{cases} \int_\Omega \nabla u \cdot \nabla v = \int_\Omega fv, \quad \forall v \in H^1(\Omega), \\ \int_\Omega u = 0. \end{cases}$$

Find $u \in H^1(\Omega), \lambda \in \mathbb{R}$ such that:

$$\begin{cases} \int_\Omega \nabla u \cdot \nabla v + \lambda \int_\Omega v = \int_\Omega fv, \quad \forall v \in H^1(\Omega), \\ \int_\Omega u = 0. \end{cases}$$

Imposition of the mean-value

Let us define $d_i = \int_\Omega \psi_i$, where ψ_i is the i-th basis function. Moreover, consider c as the imposed value for the mean. The discretized problem turns out to be:

Find $\{u_i\}_{i=1\ldots N_h}, \lambda$ such that:

$$\begin{cases} \displaystyle\sum_{i=1}^{N_h} u_i \int_\Omega \nabla\psi_i \cdot \nabla\psi_j + \lambda\, d_j = \int_\Omega f\psi_j, \quad \forall j = 1 \ldots N_h, \\ \displaystyle\sum_{i=1}^{N_h} u_i\, d_i = c. \end{cases}$$

Remark

An equivalent formulation to the Laplace problem with Neumann B.C. and null mean has been found (the very motivation passed through the Lagrange Multipliers). We can now generalize it for the Bidomain.

Setting $\lambda = u_{N_h+1}$, the original system $Au^n = b$ is then transformed:

$$A = \begin{bmatrix} a_{11} & a_{12} & \dots & a_{1N_h} \\ a_{21} & a_{22} & \dots & a_{2N_h} \\ \dots & \dots & \dots & \dots \\ a_{N_h1} & a_{N_h2} & \dots & a_{N_hN_h} \end{bmatrix} \quad \rightarrow \quad \tilde{A} = \begin{bmatrix} a_{11} & a_{12} & \dots & a_{1N_h} & d_1 \\ a_{21} & a_{22} & \dots & a_{2N_h} & d_2 \\ \dots & \dots & \dots & \dots & \dots \\ a_{N_h1} & a_{N_h2} & \dots & a_{N_hN_h} & d_{N_h} \\ d_1 & d_2 & \dots & d_{N_h} & 0 \end{bmatrix}$$

$$b = \begin{bmatrix} b_1 \\ b_2 \\ \dots \\ b_{N_h} \end{bmatrix} \quad \rightarrow \quad \tilde{b} = \begin{bmatrix} b_1 \\ b_2 \\ \dots \\ b_{N_h} \\ c \end{bmatrix}$$

Strategies choices

Most of the times the two strategies are equivalent even if the second one is computationally more expensive. On the other hand, for very ill-posed systems, first strategy might have an overshooting effect and then a global strategy is needed.

This is why we choose to adopt:

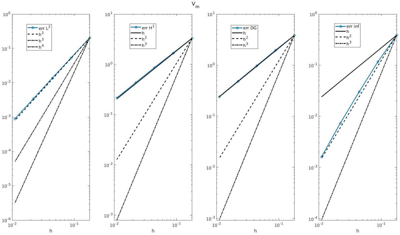
- The first coefficient imposition for error analysis studies.
- The mean value imposition for realistic simulations (where many terms are null).

Error analysis data

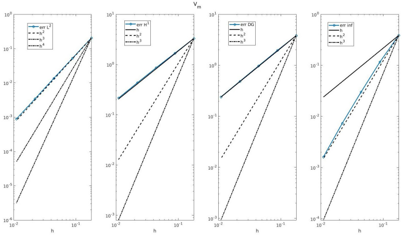
Domain (m)	$\begin{bmatrix} 0 & 1 \\ 0 & 1 \end{bmatrix}$
dt (s)	0.0001
T (s)	0.001
χ_m (m^{-1})	10^5
Σ_i (Sm^{-1})	$\begin{bmatrix} 0.12 & 0 \\ 0 & 0.12 \end{bmatrix}$
Σ_e (Sm^{-1})	$\begin{bmatrix} 0.12 & 0 \\ 0 & 0.12 \end{bmatrix}$
C_m (Fm^{-2})	10^{-2}

k	19.5
ε	1.2
γ	0.1
a	$13 \cdot 10^{-3}$
V_m	$\sin(2\pi x)\sin(2\pi y)e^{-5t}$
w	$\frac{\varepsilon}{\varepsilon\gamma - 5}\sin(2\pi x)\sin(2\pi y)e^{-5t}$

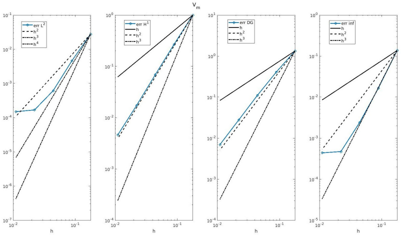
Comparison between FEM and Dubiner



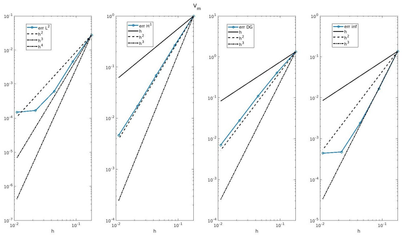
D1



P1

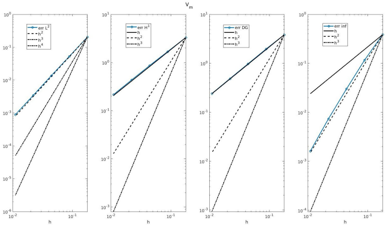


D2

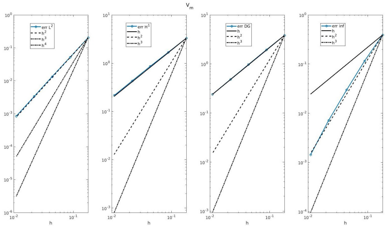


P2

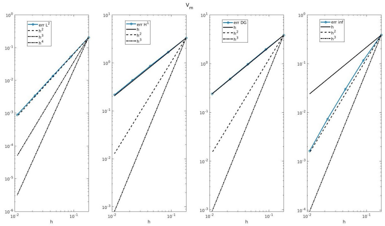
Comparison between temporal schemes



Semi-implicit



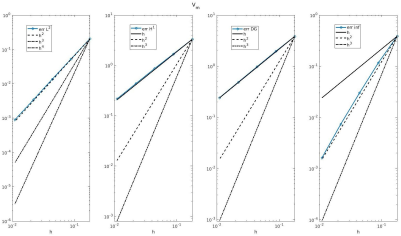
Godunov OS



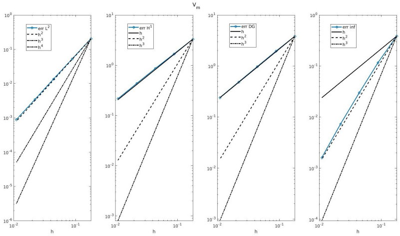
Quasi-implicit OS

POLITECNICO MILANO 1863

Comparison between uniqueness imposition strategies



First coefficient imposition



Mean value imposition

Moreover, condition number passes from $\approx 10^{17}$ to $\approx 10^{7}$.

Realistic simulations data

Domain (m)	$\begin{bmatrix} -0.025 & 0.035 \\ -0.025 & 0.035 \end{bmatrix}$
Temporal scheme	Semi-implicit
Polynomials space	D1
dt (s)	0.0001
$nREF$	5
Initial condition for V_m (V)	0
Initial condition for w	0

b_i (Am^{-2})	0
b_e (Am^{-2})	0
χ_m (m^{-1})	10^5
C_m (Fm^{-2})	10^{-2}
Σ_i (Sm^{-1})	$\begin{bmatrix} 0.34 & 0 \\ 0 & 0.06 \end{bmatrix}$
Σ_e (Sm^{-1})	$\begin{bmatrix} 0.62 & 0 \\ 0 & 0.24 \end{bmatrix}$

The applied currents are:

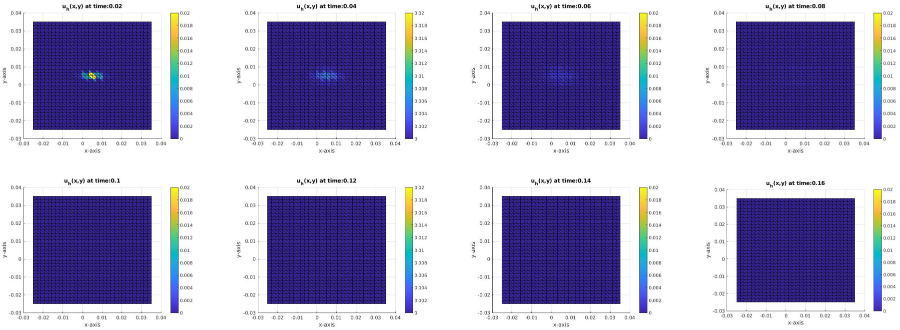
- $I_i^{ext} = I \cdot \chi_{[0.001,0.002]}(t)\,\chi_{[0.0045,0.0055]}(x)\,\chi_{[0.0045,0.0055]}(y)$,
- $I_e^{ext} = I \cdot \chi_{[0.001,0.002]}(t)\,\chi_{[0.0045,0.0055]}(x)\,\chi_{[0.0045,0.0055]}(y)$.

With I positive value to be chosen.

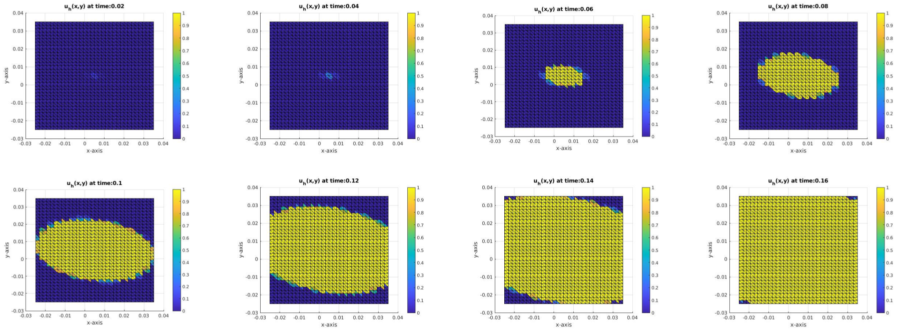
Moreover, the FitzHugh-Nagumo parameters have the previous values:

k	19.5
ϵ	1.2
γ	0.1
a	$13 \cdot 10^{-3}$

Missed activation, $I = 500 \cdot 10^3 Am^{-3}$



Achieved activation, $I = 700 \cdot 10^3 Am^{-3}$



Conclusions

Regarding **error analysis**:

- Excellent outcomes: every result was indeed consistent with the theory.

Regarding **pseudo-realistic simulations**:

- Very good results, they truthfully represent the physical phenomenon: the threshold value for the activation, the propagation, the constant height etc.
- However, the rest and activation values are 0 and 1, different from the physiological values. Moreover, the repolarization phase misses. This is probably due to the ionic model that is too poor and a too coarse mesh.

Further researches might:

1. Do a mesh-adaptivity study.
2. Adopt and compare different ionic models.

References I

[1] V. Anaya et al. "A Virtual Element Method for a Nonlocal FitzHugh-Nagumo Model of Cardiac Electrophysiology". In: *IMA Journal of Numerical Analysis* 40 (2020), pp. 1544–1576.

[2] F. Andreotti and D. Uboldi. *Discontinuous Galerkin approximation of the monodomain problem*. Politecnico di Milano, 2021.

[3] P. F. Antonietti and P. Houston. "A Class of Domain decomposition Preconditioners for hp-Discontinuous Galerkin Finite Element Methods". In: *Journal of Scientific Computing* 46 (2011), pp. 124–149.

[4] M. Bagnara. *The Inverse Potential Problem of Electrocardiography Regularized with Optimal Control*. Politecnico di Milano, 2020.

[5] Y. Bourgault, Y. Coudière, and C. Pierre. "Existence and uniqueness of the solution for the bidomain model used in cardiac electrophysiology". In: *Nonlinear Analysis: Real World Applications* 10 (2009), pp. 458–482.

[6] P. Colli Franzone and L. F. Pavarino. "A parallel solver for reaction-diffusion systems in computational electrocardiology". In: *Mathematical Models and Methods in Applied Sciences* 14 (2004), pp. 883–911.

POLITECNICO MILANO 1863

References II

[7] P. Colli Franzone, L. F. Pavarino, and S. Scacchi. *Mathematical Cardiac Electrophysiology*. Cham: Springer-Verlag, 2014.

[8] M. Dubiner. “Spectral Methods on Triangles and Other Domains”. In: *Journal of Scientific Computing* 6 (1991), pp. 345–390.

[9] A. Ferrero, F. Gazzola, and M. Zanotti. *Elementi di analisi superiore per la fisica e l’ingegneria*. Bologna: Società editrice Esculapio, 2015.

[10] L. Marta and M. Perego. *Discontinuous Galerkin approximation of the bidomain system for cardiac electrophysiology*. Politecnico di Milano, 2021.

[11] A. Quarteroni. *Modellistica Numerica per Problemi Differenziali*. Milan: Springer-Verlag, 2016.

[12] A. Quarteroni, A. Manzoni, and C. Vergara. “The cardiovascular system: Mathematical modelling, numerical algorithms and clinical applications”. In: *Acta Numerica* (2017), pp. 365–590.

[13] R. Sadleir and C. Henriquez. “Estimation of Cardiac Bidomain Parameters from Extracellular Measurement: Two Dimensional Study”. In: *Annals of Biomedical Engineering* 34 (2006), pp. 1289–1303.

[14] S. Salsa. *Equazioni a derivate parziali*. Milan: Springer-Verlag, 2016.

POLITECNICO MILANO 1863

References III

[15] S. J. Sherwin and G. E. Karniadakis. “A new triangular and tetrahedral basis for high-order finite element methods”. In: *Internation journal for numerical methods in engineering* 38 (1995), pp. 3775–3802.

[16] R. Spiteri and S. Torabi Ziaratgahi. “Operator splitting for the bidomain model revisited”. In: *Journal of Computational and applied Mathematics* 296 (2016), pp. 550–563.

[17] L. Zhu and Q. Du. “Mesh dependent stability and condition number estimates for finite element approximations of parabolic problems”. In: *Mathematics of Computation* 83 (2014), pp. 37–64.