Numerical methods for the microscopic cardiac electrophysiology model

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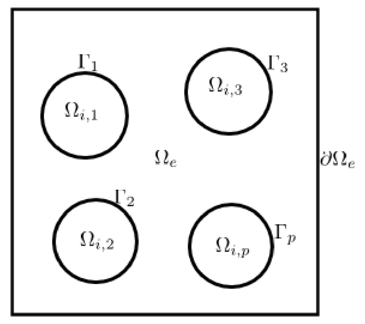
Introduction

At the microscopic level, the cardiac tissue can be viewed as two separate domains: the intra-cellular and extra-cellular domains, Ω_i and Ω_e, respectively, separated by cellular membranes Γ. Although several mathematical models are available for the simulation of the cardiac electrical activity at various scales, we focus on the numerical solution of the microscopic model. An operator splitting method is used at each time step to solve two separate problems,namely the nonlinear ODE models representing the ionic activity on Γ and coupled linear space propagation problems on Ω_i and Ω_e. To handle the non-standard transmission conditions coupling the solutions on Ω_i and Ω_e, we propose a non-overlapping domain decomposition method (DDM). Then, we address convergence issues of this DDM and present some numerical results.

Microscopic model

The microscopic model consists in a set of Poisson equations, one for each sub-domain Ω_i and Ω_e, coupled on interfaces Γ with nonlinear transmission conditions involving a system of nonlinear ODEs. We solve for u_i and u_e the system



$$\Omega_i = \cup_{j=1}^{p} \Omega_{i,j}, \quad \Gamma = \cup_{j=1}^{p} \Gamma_j, \quad \Omega = \Omega_i \cup \Omega_e \cup \Gamma,$$

$$-\nabla\cdot(\sigma_i \nabla u_i) = 0 \quad \text{in } \Omega_i, \tag{1}$$
$$-\nabla\cdot(\sigma_e \nabla u_e) = 0 \quad \text{in } \Omega_e, \tag{2}$$
$$\mathrm{I}_m := C_m \frac{\partial v}{\partial t} + \mathrm{I}_{\text{ion}}(v,t) \quad \text{on } \Gamma, \tag{3}$$
$$\sigma_e \nabla u_e \cdot n_e = -\sigma_i \nabla u_i \cdot n_i = \mathrm{I}_m \quad \text{on } \Gamma, \tag{4}$$
$$\sigma_e \nabla u_e \cdot n_e = \mathrm{I}_{stim}(t) \quad \text{on } \partial\Omega_e \setminus \Gamma, \tag{5}$$
$$v = u_i - u_e \quad \text{on } \Gamma, \tag{6}$$

- $u_{i,e}$ and $\sigma_{i,e}$ are the intra and extracellular potentials and conductivities, respectively;
- v is the membrane potential; $n_{i,e}$ are normal vectors to the boundary of $\Omega_{i,e}$;
- C_m is the electrical capacitance of the membrane Γ per unit area;
- I_{ion} is the ionic current per unit membrane area;
- $\mathrm{I}_{stim}(t)$ is an externally applied electrical stimulus.

Microscopic Model: Godunov Splitting

The microscopic model is difficult to solve due to the non-linear ODE on the interface Γ. For this reason, we use the operator splitting method to subdivide the problem into two sub-problems:

- **Sub-problem 1:** Given the solution v^{n-1} at time $t = t_{n-1}$ on Γ, we solve

$$\frac{v^{n-1/2} - v^{n-1}}{\Delta t} = -\frac{1}{C_m} \mathrm{I}_{\text{ion}}(v^{n-1}) \quad \text{on } \Gamma,$$

- **Sub-problem 2:** Then, we solve for u_i^n, u_e^n the system:

$$\begin{aligned}
-\nabla\cdot\sigma_e \nabla u_e^n &= 0 && \text{in } \Omega_e,\\
-\nabla\cdot\sigma_i \nabla u_i^n &= 0 && \text{in } \Omega_i,\\
\frac{v^n - v^{n-1/2}}{\Delta t} &= \frac{1}{C_m} I_m^n && \text{on } \Gamma,\\
n_e \cdot \sigma_e \nabla u_e^n &= -n_i \cdot \sigma_i \nabla u_i = I_m^n && \text{on } \Gamma,\\
n_e \cdot \sigma_e \nabla u_e^n &= \mathrm{I}_{stim}(t) && \text{in } \partial\Omega_e \setminus \Gamma,\\
v^n &= u_i^n - u_e^n && \text{on } \Gamma.
\end{aligned}$$

Numerical Methods: Time-Splitting DDM

The algorithm for the DDM reads

$$\frac{v^{n-1/2} - v^{n-1}}{\Delta t} = -\frac{1}{C_m} \mathrm{I}_{\text{ion}}(v^{n-1}) \quad \text{on } \Gamma, \tag{7}$$

$$\begin{cases} -\nabla\cdot\sigma_i \nabla u_i^n = 0 & \text{in } \Omega_i,\\ \frac{\Delta t}{C_m} \sigma_i \nabla u_i^n \cdot n_i + u_i^n - u_e^n = v^{n-1/2} & \text{on } \Gamma, \end{cases} \tag{8}$$

$$\begin{cases} -\nabla\cdot\sigma_e \nabla u_e^n = 0 & \text{in } \Omega_e,\\ \frac{\Delta t}{C_m} \sigma_e \nabla u_e^n \cdot n_e + u_e^n - u_i^n = -v^{n-1/2} & \text{on } \Gamma,\\ \sigma_e \nabla u_e^n \cdot n_e = 0 & \text{on } \partial\Omega_e \setminus \Gamma. \end{cases} \tag{9}$$

For a given tolerance, we solve the problem (7)- (9) by iterating between the subproblems on subdomains Ω_i and Ω_e, till convergence. In the following, we focus on the behavior of a single cell Ω_i surrounded by a connected extracellular space Ω_e.

Numerical Results: Model Parameters

To model the ionic current, I_{ion} in (7), we chose the Mitchell-Schaeffer (MS) model:

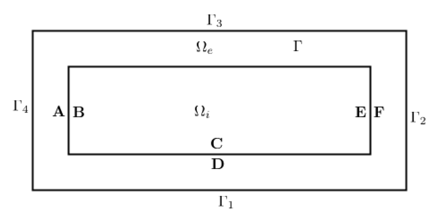
$$\frac{\partial v}{\partial t} = \frac{1}{\tau_{in}} w v^2 (1-v) - \frac{1}{\tau_{out}} v,$$

$$\frac{\partial w}{\partial t} = \begin{cases} \frac{1}{\tau_{open}}(1-w) & \text{if } v < v_{gate},\\ -\frac{1}{\tau_{close}} w & \text{if } v \geq v_{gate}, \end{cases}$$

- v and w are the membrane potential and gating variable, respectively;
- v_{gate} is the activation threshold potential;
- $\tau_{in}, \tau_{out}, \tau_{open}$ and τ_{close} are the four time constants characterizing the four main phases of the membrane action potential. In our computations,
- $\tau_{in} = 0.3ms$, $\tau_{out} = 6ms$, $\tau_{open} = 120ms$, $\tau_{close} = 150ms$, $v_{gate} = 0.13$;
- $\sigma_i = 1.7mS/cm$, $\sigma_e = 3.0mS/cm$, $\mathrm{C_m} = 1\mu\mathrm{F}/cm^2$.

Numerical Results

Ω_i and Ω_e are rectangles of size $100\mu m \times 20\mu m$ and $120\mu m \times 40\mu m$, respectively.



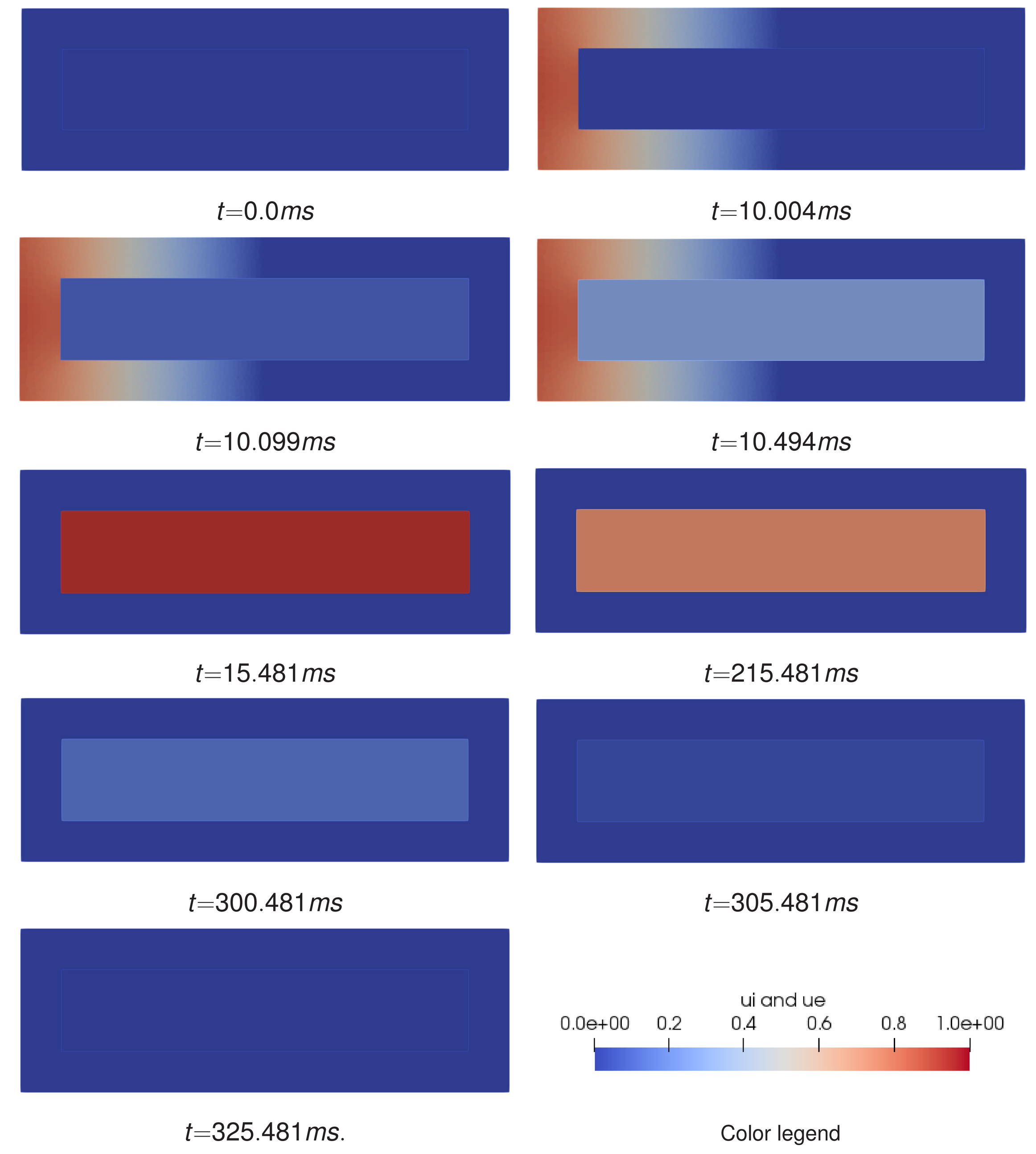
Domain Ω with points A&B, C&D, and E&F

$$\mathrm{I}_{stim}(t) = \begin{cases} 2.25 \times 10^4 & \text{if } 10 < t < 10.5 \quad \text{on } \Gamma_4,\\ 0 & \text{otherwise} \quad \text{on } \Gamma_4, \end{cases}$$

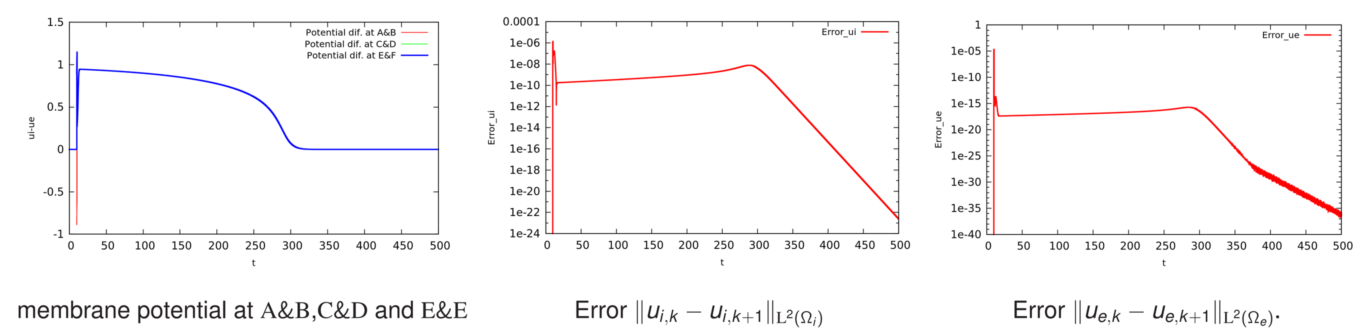
$$\mathrm{I}_{stim}(t) = \begin{cases} -2.25 \times 10^4 & \text{if } 10 < t < 10.5 \quad \text{on } \Gamma_2,\\ 0 & \text{otherwise} \quad \text{on } \Gamma_2. \end{cases}$$

- The total simulation time is $\mathrm{T} = 500ms$. The simulation is triggered at $10.001ms$.
- The time step is $\Delta t = 0.001ms$, then switches to $\Delta t = 0.01ms$ from $t = 10.502$.
- We record the potential difference over time between points A&B, C&D, and E&F.
- We compute the L^2-norm of errors, $\|u_{i,k+1} - u_{i,k}\|$ and $\|u_{e,k+1} - u_{e,k}\|$, between two successive iterates of DDM.

Evolution of the potentials u_i and u_e



Membrane potential and error in DDM over time



Concluding Remarks

- The cell undergoes an action potential and nearly simultaneously depolarizes at points A&B, C&D, and E&F.
- The error is less that 10^{-10} for most time steps. The iteration of the DDM may not be needed at each time-step.
- Future works: Improve the numerical method; increase the number of cardiac cell, and choose more realistic ionic models.

References

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