The Radial Point Interpolation Mixed Collocation (RPIMC) Method for the Solution of the Reaction-Diffusion Equation in Cardiac Electrophysiology

Konstantinos A. Mountris and Esther Pueyo

Abstract The Radial Point Interpolation Mixed Collocation (RPIMC) method is developed for the solution of the reaction-diffusion equation in cardiac electrophysiology simulations. RPIMC is an efficient and purely meshfree technique which is expected to be a valuable alternative to the Finite Element Method (FEM) for cardiac electrophysiology applications where models with large number of degrees of freedom and high geometric complexity are common. We propose applying the operator splitting technique to solve the decoupled reaction-diffusion equation. In this way, the reaction (cardiac cell dynamics) and diffusion (action potential propagation) terms are solved independently. We evaluate the RPIMC in a simulation of the cardiac action potential (AP) propagation in a two-dimensional square tissue composed of human ventricular epicardium cells. The state-of-art O'Hara Rudy cell dynamics model is used to solve the reaction term while the diffusion term is solved using the standard forward Euler method. The simulation of the AP propagation using the RPIMC method is compared against a FEM simulation using isoparametric bilinear elements. Comparable results between RPIMC and FEM are obtained for both normal AP propagation and spiral wave generation conditions (expected in arrhythmic events). The convergence of the RPIMC solution to the FEM solution is evaluated for varying nodal spacing and varying dilatation coefficient during support domain nodes identification.

Keywords Radial point interpolation · Mixed collocation · Meshfree · Cardiac electrophysiology

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1 Introduction

The action potential propagation in the human heart (cardiac electrophysiologic function) is a complex multiscale phenomenon [1] that can be described mathematically by the reaction-diffusion Eq. (1a) and the boundary condition Eq. (1b).

$$\partial V/\partial t = -I_{ion}/C + \nabla \cdot (\boldsymbol{D}\nabla V) \qquad in\ \Omega, \tag{1a}$$

$$\boldsymbol{n} \cdot (\boldsymbol{D}\nabla V) = 0 \qquad in\ \partial\Omega, \tag{1b}$$

where Ω and $\partial\Omega$ are the domain of interest and its boundary, $\boldsymbol{n}$ is the outward unit vector to the boundary, V is the action potential (AP), I_{ion} is the sum of the cardiac cell ionic currents, C is the cell capacitance, and D is the diffusivity tensor of the cardiac tissue given by:

$$\boldsymbol{D} = d_0[(1-\rho)\boldsymbol{f} \otimes \boldsymbol{f} + \rho \boldsymbol{I}], \tag{2}$$

where d_0 expresses the conductivity coefficient, $\rho \leq 1$ is the transversal to longitudinal conductivity ratio, $\boldsymbol{f}$ is the fiber direction vector, $\boldsymbol{I}$ is the identity matrix, and $\otimes$ denotes the tensor product operation. The diffusive term $\nabla \cdot (\boldsymbol{D}\nabla V)$ describes the propagation of the cellular AP in the tissue, while the reactive term $-I_{ion}/C$ describes the cellular AP dynamics. Due to the high complexity of the cardiac cell structure, realistic AP models employ a large number of "stiff" ordinary differential equations (ODE) to model accurately the cardiac gate variables and the produced ionic currents [2]. The reaction term "stiffness" requires a time integration step with sufficiently small size to ensure the stability and accuracy of the numerical solution of Eq. (1). To allow for larger time step size without reducing the numerical stability and accuracy, the solution can be decoupled using the operator splitting technique [3]. The two terms of the reaction-diffusion equation are decoupled and solved sequentially. A larger time integration step can be used then for the integration of the diffusion term while the reaction term can be integrated adaptively using a smaller step. State-of-art numerical solvers in cardiac electrophysiology employ the operator splitting approach and use the Finite Element Method (FEM) to derive the numerical solution. However, due to the complexity of the human heart geometry, meshfree methods that alleviate the mesh requirement are of great interest. In this work, we propose the Radial Point Interpolation Mixed Collocation [4] for the simulation of AP propagation in cardiac electrophysiology.

2 Methodology

The Radial Point Interpolation Mixed Collocation (RPIMC) method is a purely meshfree method based on the Meshless Local Petrov Galerkin (MLPG) method [5, 6], where the Radial Point Interpolation (RPI) is used to construct trial functions

and the Dirac delta function is used to construct test functions. Using RPIMC, the weak form of Eq. (1) is evaluated directly on the discretization nodes of the domain of interest and is given in Eq. (3). The use of the Dirac delta function to construct test functions results to reducing the spatial integration of the weak form to nodal summation over the support domain nodes.

$$\sum_{i=1}^{n} \phi^i(\boldsymbol{x_I})\partial V^i/\partial t = -I_{ion}/C + \sum_{i=1}^{n} \nabla \cdot \boldsymbol{D}\nabla^T \phi^i(\boldsymbol{x_I})V^i, \tag{3}$$

where n is the number of support domain nodes of the I^{th} discretization node and $\phi^i(x_I)$ is the RPI basis function given by:

$$\phi^T = \left\{\boldsymbol{r_I}^T \boldsymbol{p_I}^T\right\}\boldsymbol{G_I}^{-1}, \tag{4}$$

where $\boldsymbol{r_I}$ is a radial basis function (RBF) and $\boldsymbol{p_I}$ is the polynomial basis, both evaluated at the I^{th} discretization node. $\boldsymbol{G_I}$ is composed by the RBF and polynomial basis moment matrices, $\boldsymbol{R_I}$ and $\boldsymbol{P_I}$ respectively:

$$\boldsymbol{G_I} = \begin{bmatrix} \boldsymbol{R_I} \boldsymbol{P_I} \\ \boldsymbol{P_I}^T 0 \end{bmatrix}. \tag{5}$$

In this work, we use the linear polynomial basis $\boldsymbol{p_I} = \{1, x_I, y_I\}$ and the polyharmonic RBF ($\boldsymbol{r_I} = r_{Ii}^5, i = 1 \ldots n$) proposed in [7], with r_{Ii} being the radial distance between the I^{th} discretization node and its i^{th} support domain node. Explicit time integration is performed using the forward Euler method and applying the operator splitting technique to decouple the solution of Eq. (3). Applying operator splitting, the solution of Eq. (3) at a time step k is obtained by:

(i) Solving $\partial V_I^{k'}/\partial t = -\boldsymbol{I}_{ion}\left(V_I^{k-1}\right)/C$, and then

(ii) Solving $\sum_{i=1}^{n} \phi^i(\boldsymbol{x_I})\partial V_I^k/\partial t = \sum_{i=1}^{n} \nabla \cdot \boldsymbol{D}\nabla^T \phi^i(\boldsymbol{x_I})V_I^{k'}$.

In the following numerical examples, we consider a tissue composition of human cardiac ventricular epicardium. The O'Hara Rudy model [2] is used to simulate the cell dynamics in step *(i)* of the decoupled RPIMC solution.

3 Numerical Examples

In the first example, we consider a 5 cm × 5 cm square tissue with human cardiac ventricular epicardium composition. The direction of the cardiac fibers is considered perpendicular to the X-axis ($\boldsymbol{f} = [10]^T$). We use conductivity coefficient $d_0 =$ 0.0013 mS/cm and transversal to longitudinal conductivity ratio $\rho = 1/4$.

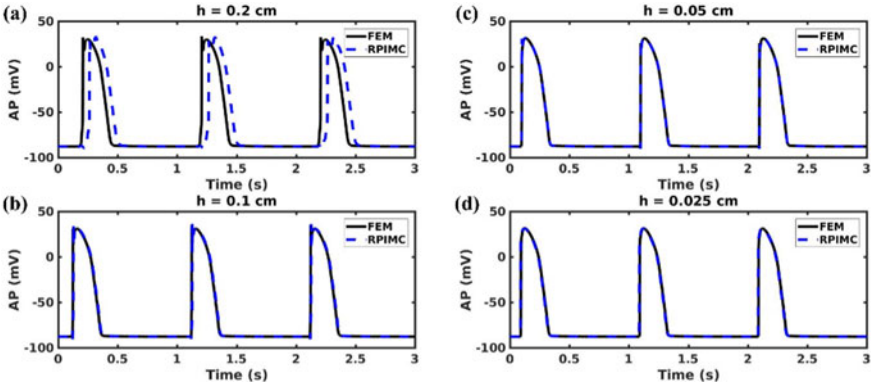

Fig. 1 Comparison of action potential (AP) for time interval $\boldsymbol{t} = [0, 3]$ **s** for nodal spacing (a) $\boldsymbol{h} = 0.2$ **cm**, (b) $\boldsymbol{h} = 0.1$ **cm**, (c) $\boldsymbol{h} = 0.05$ **cm**, (d) $\boldsymbol{h} = 0.025$ **cm**

A periodic stimulus with period $t_T = 1$ s, duration $t_d = 2$ ms, and amplitude (A) of twice diastolic threshold is applied on the left side of the tissue ($x = 0$ cm). The AP propagation is simulated for time ($t_s = 3$ s). We validate the solution of the RPIMC method comparing it with a FEM solution using bilinear isoparametric elements. Regular nodal discretizations and quadrilateral meshes with nodal spacing $h = \{0.2, 0.1, 0.05, 0.025\}$ cm are considered. The support domain size $s_d = \alpha * h$, with $\alpha = 2.8$, is used for the support domain construction in RPIMC. A comparison of the generated AP by RPIMC and FEM in the time interval $t = [0, 3]$ s for all the nodal discretizations is given in Fig. 1.

To further evaluate the quality of the simulated AP we measure the AP duration (APD) metric for 90%, 50%, and 20% repolarization. The APD_{90} metric denotes the time between the maximum value of the potential′s time derivative $(dV/dt)_{max}$ and the time of 90% repolarization from peak amplitude. The APD_{50} and APD_{20} metrics are defined similarly. The highest value of the percentage error of the RPIMC APD compared to the FEM APD is found 0.45%, 2.25%, and 2.27% for the APD_{90}, APD_{50}, APD_{20} and nodal spacing $h = 0.2$ cm. The percentage errors are reduced monotonically for reducing nodal spacing and are equal to zero for nodal spacing $h = 0.025$ cm. We further investigate the effect of the dilatation coefficient α by computing the Normalized Root Mean Square (NRMS) error between the RPIMC solution at $t = 2.2$ s for a nodal discretization with $h = 0.04$ cm and varying dilatation coefficient $a = \{1.2, 1.6, 2.0, 2.4, 2.8\}$ with a FEM solution. The NRMS error is computed using the formula:

$$NRMS = \frac{\left(\sum_{x_i \in \Omega} (u^{RPIMC}(\boldsymbol{x_i}) - u^{FEM}(\boldsymbol{x_i}))^2\right)^{1/2}}{max|u^{FEM}(\boldsymbol{x_i})| - min|u^{FEM}(\boldsymbol{x_i})|}, \tag{6}$$

Where $\boldsymbol{x}_i$ is the vector denoting the spatial coordinates of the i^{th} node in the discretization of the domain Ω, $u^{RPIMC}(\boldsymbol{x}_i)$ is the RPIMC solution at $\boldsymbol{x}_i$, and u^{FEM} is the FEM solution at $\boldsymbol{x}_i$. The NRMS error convergence plot with respect to a is given in Fig. 2.

In the next example, a S1-S2 cross stimulation protocol [8] is simulated to investigate the ability of RPIMC to generate and maintain spiral wave effects that are usually observed in cardiac arrhythmic events. The same tissue geometry and parameters as in the previous example are used with nodal spacing $h = 0.025$ cm. An initial stimulus (S1) is applied at the left edge of the tissue ($x = 0$ cm) at $t = 50$ ms. A second stimulus (S2) is applied at a square region located at the left bottom corner of the tissue with width 1.25 cm and height 2.50 cm at $t = 290$ ms. A spiral wave is generated due to the interaction of the S2 wave front with the S1 wave tail. The spiral wave is considered maintainable if at least 2 spirals are generated during the simulation time $t_s = 1$ s. The spiral wave simulation using RPIMC and FEM at different time intervals is plotted in Fig. 3. Maintainable spiral

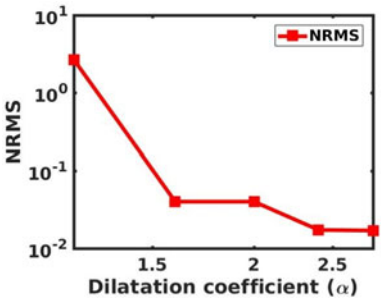

Fig. 2 Normalized Root Mean Square (NRMS) error convergence for varying dilatation coefficient $a = \{1.2, 1.6, 2.0, 2.4, 2.8\}$ and nodal spacing $\boldsymbol{h} = 0.04$ cm

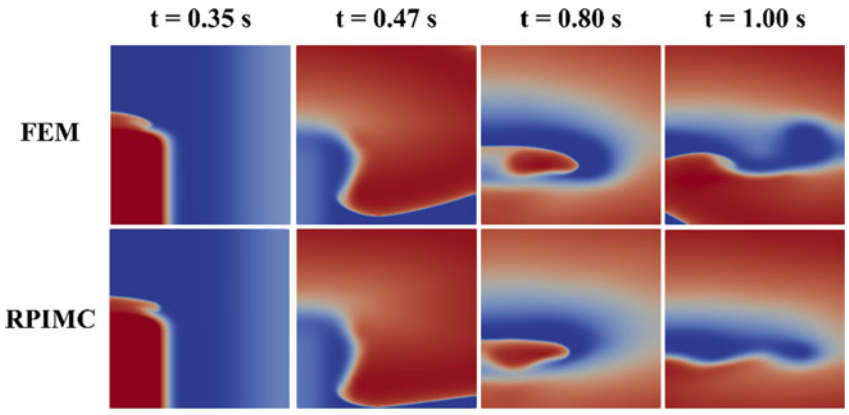

Fig. 3 Spiral wave propagation at different instants in the time interval $t = [0, 1]$ s for the S1-S2 cross stimulation protocol

waves are generated both in RPIMC and FEM with high similarity. The degradation of the similarity between the RPIMC and FEM spiral waves with time may be associated with the slightly slower conduction velocity of the AP in the FEM simulation compared to RPIMC.

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