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A macro finite element formulation for cardiac electrophysiology simulations using hybrid unstructured grids

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Abstract

Electrical activity in cardiac tissue can be described by the bidomain equations whose solution for large scale simulations still remains a computational challenge. Therefore, improvements in the discrete formulation of the problem which decrease computational and/or memory demands are highly desirable. In this study, we propose a novel technique for computing shape functions of finite elements. The technique generates macro finite elements (MFEs) based on the local decomposition of elements into tetrahedral sub-elements with linear shape functions. Such an approach necessitates the direct use of hybrid meshes composed of different types of elements. MFEs are compared to classic standard finite elements with respect to accuracy and RAM memory usage under different scenarios of cardiac modeling including bidomain and monodomain simulations in 2D and 3D for simple and complex tissue geometries. In problems with analytical solutions, MFEs displayed the same numerical accuracy of standard linear triangular and tetrahedral elements. In propagation simulations, conduction velocity and activation times agreed very well with those computed with standard finite elements. However, MFEs offer a significant decrease in memory requirements. We conclude that hybrid meshes composed of MFEs are well suited for solving problems in cardiac computational electrophysiology.

Keywords

Bidomain equations; conduction velocity; numerical accuracy

I. INTRODUCTION

RECENTLY, significant progress has been made in computational modeling of cardiac bioelectric activity at the organ level [1]. Initial attempts to construct anatomically realistic heart models were based on digitally imaged serial histological sections[2], [3]. Today, much faster tomographic imaging techniques deliver anatomical information at unprecedented resolution [4]. Such imaging modalities, in combination with the ease of use of image-based model generation pipelines, have lowered the barrier for constructing individualized heart models [1], [5], [6]. Concomitantly, concerns related to increased computational costs associated with high resolution models have been somewhat alleviated with the advent of Peta FLOPS computers and optimal highly scalable numerical techniques [7].

In general, the cardiac bidomain equations are considered the most complete framework to describe electric behavior at the tissue and organ levels. Among finite element method based modeling studies, tetrahedral elements using linear shape functions are common [8], [9], [10], but isoparametric trilinear hexahedral elements [7] and cubic-hermite hexahedral elements [11], [12] have also been used. In general, tetrahedral meshes have the advantage over hexahedra of being better able to follow complex geometries. Alternatively, it has been demonstrated that faithful representations of complex geometries can be generated by tessellating the myocardial volume into a combination of tetrahedra, hexahedra, prisms and pyramids [13]. Such hybrid meshes (HMs) are hex-dominant within the volume distant from any surfaces, but along the organ boundaries other element types are required for padding the clefts and producing a smooth surface. Such meshes can be split up into purely tetrahedral meshes automatically [13], with reasonably small overhead in terms of additional vertices required, making it suitable for standard techniques since none of the finite element techniques reported in the bidomain literature make direct use of HMs.

The objective of this study is to introduce the use of HMs for solving the bidomain equations. A novel macro finite element (MFE) approach for HM is first developed and then compared against the established standard FE techniques used in the field, i.e., linear triangular and bilinear quadrilateral elements in 2D, as well as linear tetrahedral and trilinear hexahedral elements in 3D, but also against more standard Lagrangian hybrid FE techniques which make use of linear shape functions on tetrahedral elements, trilinear shape functions on hexahedral elements, bilinear shape functions on prisms [14], and conformingly matching rational shape functions on pyramids [15]. Accuracy when solving analytical problems is compared, as well as solutions to propagation scenarios.

II. METHODS

A. A macro finite element approach

The basic idea of the MFE approach is to break down elements into a set of sub-elements wherein linear weighting functions are used. In 2D, any convex polygon can be split into a set of sub-triangles and in 3D any convex polyhedron can be subdivided into sub-tetrahedra. The minor difference between 2D and 3D is that quadrilateral faces of polyhedra have to be split first into triangles to facilitate the construction of sub-tetrahedra. Linear weighting functions used in each sub-element are piece-wise added to create a C^0 continuous weighting functions within the macro element. The MFE can be applied in the same way to

any tessellation that uses convex polygons in 2D and convex polyhedra in 3D without any adjustments to the FE routines as long as the virtual sub-triangles do not degenerate.

The 2D case of a quadrilateral element is best suited to elucidate the basic concept. A quadrilateral spanned by four nodes, p_1, p_2, p_3 and p_4 , is subdivided into four triangles using the center of the quadrilateral, located at $p_5 = (p_1 + p_2 + p_3 + p_4)/4$, as a vertex shared between the virtual sub-elements. The value assigned to the weighting function at center is set to $1/n$, where n is the number of points generating the virtual mid-point, 4 in this example. The weighting function associated with vertex p_1 is 1 at p_1 , $1/4$ at the virtual center p_5 , and zero at the remaining nodes (see Fig. 1). It is important to note that this is different from actually splitting the element into triangles since the virtual center is used for constructing the weighting function only, and does not create an additional degree of freedom in the assembly of FE matrices.

Analogously, 3D polyhedra can be split into tetrahedra; however, in a first step, quadrilateral faces of polyhedra have to be split as explained above into triangles to facilitate the construction of sub-tetrahedra. This also ensures continuity of the constructed weighting functions over element interfaces. Although the method can be applied to *any* convex polyhedron we will restrict ourselves to the four element types which are considered as standard element topologies in many FE engineering applications, i.e., tetrahedra, pyramids, prisms and hexahedra. Tetrahedra are dealt with in the standard way, i.e., linear tetrahedral weighting functions are employed and no macro approach is required. A formal definition of the MFE shape functions is given in the appendix §A.

B. Standard Lagrange finite elements for common element topologies

To investigate the numerical properties of the MFE approach a detailed comparison with first-order Lagrange finite elements [14] was performed. This involved the hat functions for simplicial elements, isoparametric bilinear weighting functions for quadrilaterals, as well as isoparametric trilinear weighting functions for hexahedra. Less-known/Less-used were bilinear tensor-product weighting functions for prisms (as suggested in [14]) as well as non-polynomial first-order weighting functions on pyramids (as suggested in [15]). A formal definition is given in appendix §B.

C. FE analysis of macro and Lagrange elements

Based on FE analysis [14], MFE discretizations and standard Lagrange FE discretizations are first order approximations which should show the same asymptotic convergence behavior. The optimal discretization error estimate in the L_2 -norm in terms of the spatial discretization, h , is given by

$$\|u - u_h\| \leq C_0 h^2$$

where u denotes the exact solution and u_h the discrete FE solution, assuming u and the underlying problem are sufficiently regular. The parameter C_0 is a problem dependent constant. The theoretically predicted convergence rates were confirmed by considering Poisson problems of dimension η ($=2$ or 3)

$$-\nabla u(x) = \prod_{i=1}^{\eta} \sin(\pi x_i) \quad \text{in } \Omega \quad (1)$$

$$u=0, \quad \text{on } \partial\Omega \quad (2)$$

which has an analytical solution given by

$$u(x) = \frac{1}{\eta\pi^2} \prod_{i=1}^{\eta} \sin(\pi x_i) \quad (3)$$

Numerically, convergence rates with respect to $\|u - u_h\|$ were determined by discretizing a unit square in 2D and a unit cube in 3D. Starting from a uniform mesh with an h of 0.2, successive refinements doubled the number of elements along each axes, halving h . A total of six refinement levels were examined. The problem was solved numerically at each refinement level using both MFEs and standard first-order FEs. In 2D, MFE quadrilaterals were compared with triangular discretizations, and in 3D, MFE hexahedral and prismatic discretizations with standard Lagrange tetrahedral discretizations. Meshes of different element types were constructed using the exact same regular nodal lattices. Thus, pyramidal meshes were excluded from comparisons with standard Lagrange elements since additional nodes have to be inserted into the nodal lattice to construct a purely pyramidal mesh. The L^2 norm of the error, $\|u - u_h\|$, was computed and used as a measure for the quality of the numerical approximation. The rate of convergence in the L^2 norm $\|u - u_h\| \sim Ch^p$ with respect to h was determined as the slope of the graph of $\log \|u - u_h\|$ versus $\log h$ (see Figure 2).

D. Macro FE for the cardiac bidomain equations

The bidomain equations [16] in their elliptic-parabolic form [17] are given as

$$\begin{bmatrix} -\nabla \cdot (\sigma_i + \sigma_e) \nabla \phi_e \\ -\nabla \cdot \sigma_b \nabla \phi_e \end{bmatrix} = \begin{bmatrix} \nabla \cdot \sigma_i \nabla V_m \\ I_e \end{bmatrix} \quad (4)$$

$$\begin{aligned} \beta C_m \frac{\partial V_m}{\partial t} &= (\nabla \cdot \sigma_i \nabla \phi_i) \\ -\beta (I_{ion}(V_m, \eta) - I_{tr}) \end{aligned} \quad (5)$$

$$V_m = \phi_i - \phi_e \quad (6)$$

where σ_i and σ_e are the intracellular and extracellular conductivity tensors (respectively), σ_b is the conductivity of the surrounding medium in which the tissue is immersed, β is the surface to volume ratio of myocytes, I_{tr} is the current density of the transmembrane stimulus, I_e is the extracellularly applied current density, C_m is the membrane capacitance per unit area, V_m is the transmembrane voltage, i.e. the difference between intracellular potential ϕ_i and extracellular potential, ϕ_e across the membrane, and I_{ion} is the density of the total current flowing through the membrane ionic channels, pumps and exchangers, which in turn depends on the transmembrane voltage and on a set of state variables, η . In the absence of a conductive bath, electrical isolation of intracellular and interstitial space is assumed along the tissue surfaces, which is accounted for by imposing no-flux boundary conditions on ϕ_e and ϕ_i . Otherwise, in the presence of a conductive bath, no-flux boundary conditions imposed on ϕ_e are assumed along the boundaries of the conductive medium, whereas continuity of the normal component of the extracellular current and continuity of ϕ_e are enforced at the tissue-bath interface. The no-flux boundary conditions for ϕ_i remain the same in both cases.

The absence of analytical solutions of the bidomain equations renders assessing numerical accuracy a difficult exercise. As an alternative, inaccuracies due to spatial discretization can be investigated via convergence experiments where simulations are repeated on successively refined grids. A solution is considered as converged at a particular discretization level, h , if

the difference to a solution obtained at the next finer discretization level $h/2$, is below a given tolerance. For such convergence experiments, the conduction velocity, ϑ , of propagating wavefronts is a sensitive cumulative metric for assessing of numerical inaccuracies.

Spatial discretization errors arise mainly along the steep depolarization wavefronts and, to a much lesser extent, along the much smoother repolarization wavebacks. The steepness of a wavefront depends on the upstroke velocity of a particular cellular model and ϑ . On theoretical grounds, the upstroke time, ΔT_{up} , is independent of ϑ in the case of uniform propagation and the spatial extent of a wavefront, ΔX_{up} , is given via $\vartheta \times \Delta T_{up}$. Spatial approximation errors depend critically on the ratio $h/\Delta X_{up}$, which is direction dependent owing to the dependency of ϑ on the propagation direction relative to the principal orthotropic axes of the tissue, ξ , where ξ is either the direction along the fibers, i.e. the long axis of the prevailing myocyte orientation, l , transverse to the fibers within a laminar sheet, s , or along the sheet normal, n [18]. Since ϑ_ξ is, in turn, proportional to the space constant, λ_ξ , (see Appendix §D), by measuring approximation errors as a function $H = h/\lambda_\xi$, we provide a direction and velocity independent metric for assessing numerical accuracy.

1) Conduction velocity based analysis of numerical accuracy—Monodomain wavefront propagation was simulated in thin tissue strands of 2cm length using both 2D and 3D MFE as well as standard Lagrangian elements. Reference solutions were computed using the established standard discretization, that is, linear Lagrangian elements on triangles in 2D and on tetrahedra in 3D, at a fine grid resolution of $10\mu\text{m}$. A temporal resolution of $10\mu\text{s}$ was chosen which resulted in sufficient accuracy with the employed IMEX method (see §C in the Appendix). Two recent models of the cellular dynamics, the Mahajan-Shiferaw (MSH) rabbit ventricular cell model [19] and the ten Tusscher (TNNP) human ventricular cell model [20], were considered. Wavefront propagation was initiated by stimulating the left edge (2D) or face (3D) of the strand. For each ionic model the monodomain conductivities

$$\sigma_{m\xi} = \frac{\sigma_{i\xi}\sigma_{e\xi}}{\sigma_{i\xi} + \sigma_{e\xi}} \quad (7)$$

determined as the harmonic mean of the bidomain conductivities, were scaled to reproduce reported conduction velocities, $\vartheta_l = 0.6\text{m/s}$, $\vartheta_s = 0.4\text{m/s}$ and $\vartheta_n = 0.2\text{m/s}$ (see Tab. I) which reflect the orthotropic nature of cardiac tissue [18]. Scaling was performed using the finest discretization of the strand at $10\mu\text{m}$. Experimentally measured conductivities [21] were used as initial values in an iterative refinement procedure where $\sigma_{e\xi}$ remained unchanged while $\sigma_{i\xi}$ was modified in each iteration until measured and prescribed conduction velocities matched within a tolerance of 0.5%. The converged $\sigma_{m\xi}$ value was used then for all other experiments.

Each conduction velocity in the strand was tested with isotropic conductivities since the geometry was essentially 1D and the propagation wavefront was planar. Starting from $10\mu\text{m}$, the spatial discretization was coarsened, until the computed ϑ_H deviated by more than 50% from the reference solution, ϑ_0 computed at the finest $10\mu\text{m}$ grid. The time step was kept constant at $10\mu\text{s}$.

The space constant λ_ξ was numerically estimated by applying a weak subthreshold stimulus to a lateral face of the strand until the voltage distribution along the strand became stationary. Then λ_ξ was determined as the exponent of the function $V_m = V_m(x=0) \cdot e^{-\lambda_\xi x}$ which was fitted to the simulated $V_m(x)$ by using a least-square method. Graphs

$\bar{\vartheta}(H) = \vartheta_0 / \vartheta(H)$ were constructed for all conductivity settings and compared between the different element topologies and shape functions. Smaller deviations from $\bar{\vartheta} = 1$ were interpreted as being a better approximation on a coarser grid. It is important to note that for the strands, the nodal lattice was independent of the type of FE formulation used.

2) Anatomically realistic test case—To compare the numerical accuracy of the MFE formulation in an anatomically more realistic scenario, simulations were performed in a micro-anatomically detailed model of a papillary muscle. First, as described in [13], a volumetric hybrid mesh of the papillary muscle was generated at a mean resolution of $75\mu\text{m}$ (PM75), and secondly, a tetrahedral mesh was derived from the hybrid mesh. Tetrahedrization led to the insertion of vertices which increased the number of nodes in the mesh ($\approx 3\%$) and some vertices of the grid were shifted during a volume smoothing step which preserved mesh quality metrics.

Due to the size of the problem, no reference mesh could be generated at a finer resolution with reasonable effort. Hence, only a relative comparisons between the solutions of three different FE formulations were performed, that is, a HM using MFE weighting functions (HM+M), the HM using Lagrange weighting functions (HM+I), and the pure tetrahedral mesh (TM) using linear weighting functions. The main goal here was to demonstrate equivalence of the FE formulations on anatomically realistic high-resolution grids. The solution obtained with the TM was considered as a reference solution since the method is well established and accepted in the field.

Wavefront propagation was simulated in the PM75 model for 40ms and activation times (ATs) were computed at each node of the mesh. ATs were defined as the instant when the upstroke crossed a -40mV threshold. Relative differences in AT between both HM+M and HM+I and TM were computed, as well as between HM+M and HM+I. Since HM and TM meshes were different, it is important to note that the relative deviations $\varepsilon_{\text{HM+M}}$ and $\varepsilon_{\text{HM+I}}$ were computed at the nodes which were shared by both the HM and the TM mesh.

E. Memory usage comparisons

Memory usage is an important factor in large scale bidomain simulations, even when using parallel supercomputers. The two major determinants of memory usage pertinent to the FE part of a bidomain solver are memory requirements for storing stiffness and mass matrices, and for storing the finite element lists. Memory consumption of the MFE formulation was compared to the standard linear FE formulations for 2D and 3D meshes. Two scenarios were considered:

1. A sequence of unit square and unit cube meshes with fixed dimensions of 1cm along each direction were generated. Meshes were successively refined, starting from $100\mu\text{m}$ down to $3.25\mu\text{m}$ resolution in 2D, and from $250\mu\text{m}$ down to $50\mu\text{m}$ in 3D. All meshes of the same resolution used the exact same regular lattice of nodes, independently of the type of elements used. Memory requirements for storing element lists as well as stiffness matrices were measured. Since mass lumping was used, memory requirements for storing mass matrices were identical for all element types and not included in the comparisons.
2. Memory requirements for HM+M and TM meshes were measured for the anatomically realistic PM75 model.

F. Impact upon solver performance

Since the sparsity patterns of the matrices arising from HM (either HM+M or HM+I) and TM discretizations are different, benchmarks were performed to quantify the impact upon

solver performance using the PM75 test case described in Section II-D2 as a benchmark. As a measure for the extra arithmetic work required, for both HM and TM discretizations the maximum, $\widehat{N}_z$, and average, $\bar{N}_z$, number of non-zero entries per row was determined for the FE stiffness matrices $\mathbf{K}_p$ and $\mathbf{K}_{p+e}$ of parabolic and elliptic PDE, respectively.

Furthermore, simulation runs were repeated with HM and TM to compare the performance of sparse matrix-vector multiplication (SpMV) and the number of iterations required for iteratively solving the linear systems. For the HM case only results on HM+M discretizations are reported, since the sparsity pattern is identical to the HM+I case and the minor differences in matrix entry values did not lead to any significant changes in iteration counts. The arithmetic penalty of HM over TM was quantified by measuring the total CPU time spent on SpMV operations and the impact upon iterations statistics, i.e. the average number of iterations per time step was computed by dividing the total number of iterations for the whole simulation runs by the number of timesteps computed.

III. RESULTS

A. Numerical accuracy with analytical testcase

In order to quantitatively assess the numerical accuracy of the MFE approach, solutions of the Poisson problem in 2D and 3D, given by Eq. (1), were computed and the discretization error in the L^2 norm was determined. In 2D, observed convergence rates showed that the macro-quadrangle converges at the same rate as the linear triangle, i.e., the L^2 error is of order h^2 . Similar behavior was observed in the 3D simulations where linear tetrahedral, macro-hexahedral and macro-prismatic elements were employed (Fig. 2).

B. Conduction velocity based analysis of numerical accuracy

Conduction velocity $\bar{g}(H)$ of depolarization wavefronts was measured in strands of tissue for longitudinal, transverse and sheet normal conductivity settings with both the MSH and the TNNP kinetic models for varying discretizations H using various finite element formulations.

A subset of graphs, measured with the MSH kinetic model, is presented in Fig. 3 for the case with longitudinal conductivity settings. We refrained from showing all results since most curves virtually overlapped and, thus, did not provide any additional insight. As shown in Fig. 3, $\bar{g}$ decreased quickly with increasing H . The 5 and 10% errors arose at $H \approx 0.18$ and 0.25, respectively. In terms of h , 10% errors corresponded to a h of $198\mu\text{m}$, $75\mu\text{m}$ and $15\mu\text{m}$ resolution for longitudinal, sheet-transverse and sheet normal conduction velocities. Further, in all cases under study, the approximation error with the MFE formulations was smaller than with the standard linear formulations, although the differences were quite small over the range of H suitable for electrophysiological studies, that is for $H < 0.3$. Finally, the MFE approaches resulted in almost identical $\bar{g}$ curves as the isoparametric elements.

C. Numerical accuracy with anatomically realistic testcase

Relative deviations between $\epsilon_{\text{HM+M}}$ and $\epsilon_{\text{HM+I}}$ were computed for an activation sequence initiated via a point stimulation in a micro-anatomically detailed model of the papillary muscle. Comparing results from the meshes, ATs at 99.70% and 99.87% of the nodes for HM+M and HM+I, respectively, differed by less than 2% from those computed on the TM. The distribution of the deviations is shown in Fig. 4. Comparing HM+M and HM+I revealed that relative deviations in ATs due to the use of different weighting functions were even smaller, with 99.91% of the nodes being within 2%. Overall, differences in AT between

different formulations were very minor and could not be discerned by visual inspection of the activation sequences.

D. Comparing RAM memory usage

RAM memory requirements to store stiffness matrix and element lists are summarized in Tab. II for all meshes using standard continuous piecewise linear FEs and MFEs. In terms of memory usage, the isoparametric hybrid elements and the MFEs are equivalent since they result in the same stencils and thus lead to identical sparsity patterns. Owing to the, on average, denser stencils of hybrid meshes, the MFE approach led to higher memory demands for storing the stiffness matrices, but required less memory to store the finite element lists. These two trends were competing, but overall the use of hybrid meshes led to significant memory savings. The percentage in terms of saved memory increased when going from 2D to 3D: in 2D, savings were in the range between 22% to 26%, whereas in 3D they were between 45% to 51%.

For the PM75 simulation, a total of 358 MBytes were used to store the element list for the TM, but only 117 MB for the hybrid mesh. In this case, the memory demands for storing the TM element list are five times bigger than the FEM stiffness matrix for the same mesh. Using a HM saved 45% of memory which would allow for executing substantially larger setups for a given memory configuration.

E. Solver performance

For the matrices $\mathbf{K}_h$, $\bar{N}_z$ was 13.7 and 22.5 with maxima $\hat{N}_z$ of 31 and 37 for TM and HM discretizations, respectively. Similarly, for $\mathbf{K}_{i+e}$ matrices $\bar{N}_z$ was 14.6 and 23.7 with $\hat{N}_z$ being 39 and 57. This reduced sparsity of HM matrices increased the total time spent on SpMV relative to TM matrices. Benchmarks showed that in the HM case 3433s and 701s were spent on SpMV operations to solve elliptic and parabolic PDE, respectively, whereas only 2678s and 547s were spent in the TM case.

The number of iterations turned out to be slightly smaller for HM matrices. To solve the elliptic PDE, an average of 3.1 and 4.1 iterations were required for HM and TM, respectively, while for the parabolic PDE the numbers were 7.3 and 8.0, suggesting that HM matrices led to quicker convergence.

IV. DISCUSSION

In this study a novel macro element approach for computing finite element shape functions was proposed with the objective to enable the use of hybrid FE meshes for discretization of the cardiac bidomain equations. The numerical accuracy of the macro-elements was studied and compared with standard FE types which were used in numerous previous studies. Both standard FE analysis and comparisons of physiological metrics such as conduction velocity and activation times were performed to demonstrate that the MFEs are of the same numerical accuracy as the accepted standard elements. Using the MFE approach, or other isoparametric FEs which were also investigated in here, allows to discretize the bidomain equations using HM which consist of tetrahedra, hexahedra, prisms and pyramids. Although the use of HM does not provide significant accuracy benefits, it allows to discretize a domain using a much smaller number of elements which leads to substantial RAM memory savings. Further, the MFE approach is very general and can be implemented with ease for any convex polygon in 2D or any convex polyhedra in 3D.

A. Numerical accuracy

The convergence rate of the error of the 2D and 3D Poisson problems using MFEs was shown to be equal to standard finite elements, where the L_2 -error is proportional to h^2 . Therefore, MFEs can be considered to be numerically as accurate as the standard finite elements, used previously [8], [9], [10]. Physiologically driven accuracy metrics based on the dependency of conduction velocities on grid resolution suggested that MFE meshes provide noticeably better accuracy when coarser grids are used. Although this observation supports the notion that MFEs or isoparametric FEs on HMs are at least as accurate as purely TMs, their accuracy advantage is not really compelling. The differences between the methods at small relative discretization factors $H = h/\lambda$ were fairly small and for larger H the overall accuracy was unacceptably low, too low for any practical purposes. Ideally, the solution of the bidomain equations should depend only on the conductivity and ionic model parameters, and not on a particular H . However, this is not always achieved with discretization methods that rely on fixed spatial grids since fairly small H is required to faithfully resolve the steep wavefront of a propagating action potential. For instance, to keep the error in σ smaller than 5% when a wavefront moves in the sheet-normal normal, h has to be smaller than $50\mu\text{m}$. Under conditions of slow decremental conduction with velocities as small as 0.05m/s , even finer resolutions of around $15\mu\text{m}$ are required. Such fine resolutions can be prohibitive with whole organ studies, even when cutting edge high performance computing facilities are used. In this context spatio-temporally adaptive methods may have a distinct advantage [22], [23] by allowing the use of fine spatial resolutions only around the wavefront.

Spatial undersampling phenomena in the context of bidomain simulations lead to an artificial decrease in conduction velocity, effectively reducing the wavelength, which may lead to discrepancies between computer simulations and experiments when the ratio between organ size and wavelength becomes skewed. In pioneering studies, e.g.[24], convergence testing was often conducted to constrain discretization artifacts. For contemporary organ-level studies, however, this is not necessarily feasible since due to the work of generating finer meshes of complex anatomical geometries and/or the computational costs.

Alternatively, inaccuracies secondary to spatial undersampling can be compensated by ad hoc adjustments of conductivity tensors to arrive at a good match with experimentally observed activation patterns. With organ level studies that employ biophysically detailed models of cellular dynamics, ad hoc adjustments are always required, otherwise, the artificial reduction in conduction velocity in the sheet-transverse or sheet-normal direction would be unacceptably large. Typical choices for spatial resolutions range between $\approx 100\mu\text{m}$ [1] and $\approx 250\mu\text{m}$ [25], [26], [27], but coarser meshes have also used [28]. Considering the large number and the high uncertainty in parameters which describe passive and active properties of the myocardium, ad hoc adjustments to match simulations with experiments seem to be well justified and pragmatic. However, further research involving detailed numerical analysis is warranted to better understand the limitations of this approach. Further, there is no unique or universally accepted way to adjust conductivities. Different adjustments may lead to the same conduction velocity, but other relevant properties such as the anisotropy ratio between intracellular and extracellular domain can be altered. Careful analysis of spatial discretization effects is of particular importance when studying pathologies since cases of extremely slow decremental conduction velocity may occur. Under these scenarios it is difficult to decide whether conduction block occurred as a consequence of the pathology or whether it is a numerical artifact.

B. RAM memory requirements

Memory storage requirements are determined by the list of finite elements and by stiffness and mass matrices. The storage required for a single FE may vary depending on a particular

implementation. In the case of this study, memory requirements per element amounted to 60 bytes. HMs fill the volume with a substantially smaller number of elements and, thus, result in shorter FE lists. On the other hand, a single node in a HM, on average, is connected to a larger number of neighboring nodes which leads to a denser stencil and, thus, to higher memory requirements to store the matrices. In general, the memory requirements of storing the FE lists exceed the requirements of storing the matrices, leading to quite substantial memory savings with HMs.

Although the use of HM provides substantial memory savings, the exact percentage depends on numerous factors. Of importance is the chosen temporal discretization technique which determines the number of stiffness and mass matrices, and implementation details such as matrix and FE list storage formats. The savings listed in Tab. II are for one stiffness matrix and one FE list which reflects the case of a monodomain simulation with explicit time stepping. These data can be used to estimate memory savings for a particular numerical scheme, since the decisive factors are the required number of matrices and the FE lists. For instance, with implicit methods, memory savings may be less since an additional matrix is required for assembling the right hand side, but no additional list of elements. With bidomain simulations, memory savings may be less significant. In the absence of a bath, intracellular grid and extracellular grids are identical. Hence, no extra list of elements is required, but an additional stiffness matrix has to be stored, effectively reducing the memory gain. In the more general case of a bidomain with bath, memory savings can be expected to be in the same range as with the explicit monodomain case, since memory is gained with the list of FEs required to discretize the bath volume. Further, numerical schemes which do not implement mass lumping benefit less due to memory requirements for storing the mass matrices which are higher with HMs.

C. Solver performance

The reduced sparsity of HM matrices increased the amount of arithmetic work in SpMV computations which in turn tended to increase execution times. With the PM75 testcase, $\bar{N}_z$ was 62% larger for the HM $\mathbf{K}_i$ matrix compared to the TM variant. Similarly, the increase in $\bar{N}_z$ for $\mathbf{K}_{i+e}$ was 64%.

For this particular testcase, the increased matrix density translated into an increase of 28% in terms of execution time spent on SpMV operations when using a HM discretization. The increase in execution time was noticeably smaller as one would predict from the increase in $\bar{N}_z$. This can be attributed to the slightly quicker convergence of the HM system, but also to the fact that the overall system size of HM systems was slightly smaller, by about ~3%.

D. Implementation aspects

The MFEs proposed in here can be employed to construct basis functions for any convex polygon (2D) or any convex polyhedra (3D). For instance, weighting functions for an octahedron could be constructed using the exact same approach as used in here to construct quadrilaterals, prisms, pyramids and hexahedra elements. Apart from its generality, the MFEs are relatively easier to implement than isoparametric elements such as prisms and pyramids. Firstly, finding the appropriate shape functions [29], [30], [15] for the reference element might not be straightforward (for instance, pyramid elements involve rational shape functions). Secondly, the correct numerical integration rules for the rational functions on pyramids must be derived, and finally, these element types are usually not covered in the FE literature [15].

E. Conclusion

A novel MFE formulation is proposed which is suited for discretizing the bidomain equations on HMs. The method is as accurate as standard FEs used in the field or other isoparametric FEs which were shown to be suited for the bidomain as well. HMs may provide substantial memory savings. The MFE technique may be more general and easier to implement than standard FE techniques since the same construction loop can be used for any convex polygon in 2D or any convex polyhedron in 3D.

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APPENDIX

A. Formal definition of macro finite elements

The definition of the continuous piece-wise linear shape functions on each macro-element can be done systematically in terms of the piecewise linear Lagrangian basis on a virtual simplicial sub-triangulation:

The quadrilateral macro-element

Let M be a quadrilateral with vertices $p_1, \dots, p_4$. Introducing the virtual mid-point is

$p_5 = \frac{1}{4}(p_1 + p_2 + p_3 + p_4)$ yields a virtual sub-triangulation M_h by 4 triangles with piecewise linear Lagrangian hat functions $\{\phi_i\}_{i=1}^5$ with $\phi_i(p_j) = \delta_{i,j}$ for $j = 1, \dots, 5$. The MFE shape functions are defined as

$$\psi_i = \phi_i + \frac{1}{4}\phi_5, \quad i=1, \dots, 4$$

See Fig. 1 for sub-triangulation M_h and shape function ψ_1 .

Remark

The macro-element approach is based on the linear Lagrangian basis functions but fixes the degree of freedom corresponding to the virtual node.

The pyramidal macro-element

Let M be a pyramid with bottom-vertices $p_1, \dots, p_4$ and top-vertex p_5 . Introducing the

virtual mid-point on the bottom face $p_6 = \frac{1}{4}(p_1 + p_2 + p_3 + p_4)$ yields a virtual sub-triangulation M_h by 4 tetrahedra. Let $\{\phi_i\}_{i=1}^6$ denote the (virtual) standard piecewise linear Lagrangian functions on M_h . The MFE shape functions are defined as

$$\psi_i := \phi_i + \frac{1}{4}\phi_6(x), \quad i=1, \dots, 4, \quad \psi_5 := \phi_5$$

The prismatic macro-element

Let M be a prism with bottom-face $p_1, \dots, p_3$ and top-face p_4, p_5, p_6 . Introducing the virtual mid-points p_7, p_8, p_9 on the three quadrilateral faces and interior mid-point $p_{10} = \frac{1}{6} \sum_{i=1}^6 p_i$ yields sub-triangulation M_h by 14 tetrahedra. Let $\{\phi_i\}_{i=1}^9$ Lagrangian denote piece-wise linear functions on M_h . The MFE shape functions are defined as

$$\begin{aligned}\psi_i &:= \phi_i + \frac{1}{4}\phi_9 + \frac{1}{4}\phi_7 + \frac{1}{6}\phi_{10}, & i=1, 4, \\ \psi_i &:= \phi_i + \frac{1}{4}\phi_7 + \frac{1}{4}\phi_8 + \frac{1}{6}\phi_{10}, & i=2, 5, \\ \psi_i &:= \phi_i + \frac{1}{4}\phi_8 + \frac{1}{4}\phi_9 + \frac{1}{6}\phi_{10}, & i=3, 6.\end{aligned}$$

The hexahedral macro-element

Let M be a hexahedron with vertices $p_1, \dots, p_8$. Virtual face-mid-points $p_9, \dots, p_{14}$, on quadrilateral faces and interior mid-point $p_{15} = \frac{1}{8} \sum_{i=1}^8 p_i$ yields sub-triangulation M_h by 24 tetrahedra. Let $\{\phi_i\}_{i=1}^{15}$ denote piecewise linear Lagrangian functions on M_h . The MFE shape functions are defined as

$$\begin{aligned}\psi_1 &:= \phi_1 + \frac{1}{4}\phi_9 + \frac{1}{4}\phi_{14} + \frac{1}{4}\phi_{11} + \frac{1}{8}\phi_{15}, \\ \psi_2 &:= \phi_1 + \frac{1}{4}\phi_9 + \frac{1}{4}\phi_{11} + \frac{1}{4}\phi_{12} + \frac{1}{8}\phi_{15}, \\ \psi_3 &:= \phi_1 + \frac{1}{4}\phi_9 + \frac{1}{4}\phi_{12} + \frac{1}{4}\phi_{13} + \frac{1}{8}\phi_{15}, \\ \psi_4 &:= \phi_1 + \frac{1}{4}\phi_9 + \frac{1}{4}\phi_{13} + \frac{1}{4}\phi_{14} + \frac{1}{8}\phi_{15}, \\ \psi_5 &:= \phi_1 + \frac{1}{4}\phi_{10} + \frac{1}{4}\phi_{14} + \frac{1}{4}\phi_{11} + \frac{1}{8}\phi_{15}, \\ \psi_6 &:= \phi_1 + \frac{1}{4}\phi_{10} + \frac{1}{4}\phi_{11} + \frac{1}{4}\phi_{12} + \frac{1}{8}\phi_{15}, \\ \psi_7 &:= \phi_1 + \frac{1}{4}\phi_{10} + \frac{1}{4}\phi_{12} + \frac{1}{4}\phi_{13} + \frac{1}{8}\phi_{15}, \\ \psi_8 &:= \phi_1 + \frac{1}{4}\phi_{10} + \frac{1}{4}\phi_{13} + \frac{1}{4}\phi_{14} + \frac{1}{8}\phi_{15}.\end{aligned}$$

Obviously, the definition of the shape function is local on each macro-element. Hence, there is no need for additional storage of virtual points or of the virtual sub-triangulation in practical implementation. We summarize the main properties of the suggested macro finite elements:

- the local FE-space macro-element M is continuous and piecewise linear
- the span of the shape functions on the macro-element M includes the complete set of linear polynomials $P^1(M)$ (assuming all quadrilateral faces to be rectangular)
- shape functions are continuous over element interfaces
- by construction, the global basis functions add up to one, i.e. the suggested FE-basis is a partition of unity.

The construction of general polygonal and polyhedral-shaped macro-elements is obvious, as far as the simplicial sub-triangulation does not degenerate.

B. Formal definition of standard Lagrangian finite elements

First-order Lagrangian shape functions on prism M =

$$\{(x_1, x_2, x_3) \in \mathbb{R}_+^3 : x_1 + x_2 \leq 1, 0 \leq x_3 \leq 1\};$$

$$\begin{aligned}
\varphi_1(x) &:= (1 - x_1 - x_2)(1 - x_3), & \varphi_2(x) &:= x_1(1 - x_3), \\
\varphi_3(x) &:= x_2(1 - x_3), & \varphi_4(x) &:= (1 - x_1 - x_2)x_3, \\
\varphi_5(x) &:= x_1x_3, & \varphi_6(x) &:= x_2x_3.
\end{aligned}$$

First-order Lagrangian shape functions on pyramid $M = \{(x_1, x_2, x_3) : -(1 - x_3) \leq x_1, x_2 \leq 1 - x_3, 0 \leq x_3 \leq 1\}$:

$$\begin{aligned}
\varphi_1(x) &:= \frac{1}{4} \left(1 - \frac{x_1}{1-x_3}\right) \left(1 - \frac{x_2}{1-x_3}\right) (1 - x_3), \\
\varphi_2(x) &:= \frac{1}{4} \left(1 + \frac{x_1}{1-x_3}\right) \left(1 - \frac{x_2}{1-x_3}\right) (1 - x_3), \\
\varphi_3(x) &:= \frac{1}{4} \left(1 + \frac{x_1}{1-x_3}\right) \left(1 + \frac{x_2}{1-x_3}\right) (1 - x_3), \\
\varphi_4(x) &:= \frac{1}{4} \left(1 - \frac{x_1}{1-x_3}\right) \left(1 + \frac{x_2}{1-x_3}\right) (1 - x_3), \\
\varphi_5(x) &:= x_3.
\end{aligned}$$

for appropriate quadrature rules see [15]. The non-polynomial nature of pyramidal weighting functions is necessary in order to guarantee C^0 -conformity over element interfaces.

C. Temporal Discretization

An implicit-explicit (IMEX) discretization technique with operator splitting was applied [31], [32] which leads to a three-step scheme, involving the solution of a parabolic PDE, an elliptic PDE and a non-linear system of ODEs:

$$\left[I + \frac{1}{2} \Delta t A_i \right] V^{k*} = \left[I - \frac{1}{2} \Delta t A_i \right] V^k - \Delta t A_i \phi_e^k \quad (8)$$

$$V^{k+1} = V^{k*} - \frac{\Delta t}{C_m} \left(I_{ion}(V^{k*}, \eta^k) - I_{tr} \right) \quad (9)$$

$$\eta_f^{k+1} = \eta_f^k e^{A_f \Delta t} + \frac{A_f}{B_f} (e^{A_f \Delta t} - 1) \quad (10)$$

$$\eta_s^{k+1} = \eta_s^k + \Delta t g(V^{k*}, \eta^k) \quad (11)$$

$$(A_i + A_e) \phi_e^{k+1} = -A_i V^{k+1} + I_e \quad (12)$$

where I is the identity matrix and A_ξ is the discretized $-\nabla \cdot (\bar{\sigma}_\xi \nabla) / (\beta C_m)$ operator with ξ being either i or e ; Δt is time step; V^k , ϕ_e^k and η^k are the temporal discretizations of V_m , ϕ_e and η , respectively, at time $k\Delta t$. State variables are updated using the Rush-Larsen technique where one subvector, η_f , is updated using an analytical solution and the other one, η_s , by applying a forward Euler step. Parameter choices were $C_m = 1 \mu F/cm^2$, $\beta = 1400 cm^{-1}$ and $I_{tr} = 50 e4 \mu A/cm^3$.

Both monodomain and bidomain simulations were conducted. The numerical scheme in the monodomain case is essentially the same, with the minor difference that the step to solve the

elliptic PDE and the term including φ_e in Eq. (5) are omitted, and the conductivity tensor σ_i in Eq. (5) is replaced by σ_m , where the scalar conductivities along each orthotropic axis of the tissue ξ are $\sigma_{m\xi} = \sigma_{i\xi}(\sigma_{i\xi} + \sigma_{e\xi})^{-1} \sigma_{e\xi}$ as in [18].

D. Factors influencing the relative discretization factor H

The relative discretization factor H depends on the chosen spatial discretization, h , relative to the width of the propagating wavefront, ΔX_{up} , that is, $H = h/\Delta X_{up}$. ΔX_{up} can be conveniently approximated by the space constant λ which is a widely used metric to quantify the spatial decay of stimulation-induced changes in V_m with distance from the stimulus site under subthreshold conditions. Along a given direction ξ , since $\Delta X_{up,\xi} \propto \vartheta_\xi$ and $\vartheta_\xi \propto \lambda_\xi$ holds, where ϑ_ξ and λ_ξ are given by

$$\lambda_\xi = \sqrt{\frac{\sigma_{m\xi}}{\beta G_m}}, \quad \vartheta_\xi \sim K \sqrt{\frac{\sigma_{m\xi}}{\beta}} \propto \lambda_\xi, \quad (13)$$

λ_ξ can be used as a surrogate for $\Delta X_{up,\xi}$ if we neglect the temporal variation of the membrane conductance per unit area, G_m , during the upstroke phase. That is, measuring approximation errors as a function $H = h/\lambda_\xi$ provides a direction and velocity independent metric for assessing numerical accuracy.

E. Numerical Solution

The solution of the linear systems associated with the FE discretization were performed using the preconditioned conjugate gradient method (PCG). For the solution of the parabolic system within the Crank-Nicholson scheme a block Jacobi preconditioner together with an incomplete Cholesky ICC(0) sub-block preconditioner were used, where the latter has a zero fill-in level that preserves the sparsity pattern of the matrices [33]. An algebraic multigrid preconditioner was employed to solve the elliptic PDE [34]. The set of ODEs were solved in a decoupled form. A non-standard finite difference solver based on the Rush-Larsen approach [35] was employed to resolve fast transients and a simple forward Euler step was used for slower transients. Details of the ODE solver strategy are described in great detail elsewhere [36].

A time step of $10\mu s$ was used for all simulations involving the calculation of the conduction velocity. Different time steps were used for the PM75 simulations which are described together with the simulation results. The stopping criteria for the iterative solution process was that the unpreconditioned L_2 residual norm was less than 10^{-5} for the elliptic PDE, and less than 10^{-6} for the parabolic PDE. The linear Poisson problem used to investigate the numerical accuracy of the different finite element formulations was solved with the same solver technique as applied to the elliptic PDE of the bidomain equations with the only difference that a smaller tolerance of 10^{-9} was used.

Simulations were carried out with CARP (Cardiac Arrhythmia Research Package) simulator [37], [38], linked against the MPI based PETSc C library version 3.0.0-p7 [39], running on the high performance computing facility CINECA.

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Fig. 1. MFE decomposition using the example of a quadrilateral: four virtual triangles are created sharing center node p_5 . In this case, the weighting function $f(x, y) = \psi_1(x, y)$ corresponding to vertex p_1 is shown. Center node p_5 is weighted with $1/4$.

Fig. 2.

Log-log plots of the L^2 norm of the error $\|u - u_h\|_0$ are shown as a function of h for 2D and 3D testcases on the left and right panel, respectively.

Fig. 3.

Longitudinal conduction velocities $\bar{\vartheta}_l$ measured at different resolutions H for the MSH ionic model in 2D and 3D discretizations of a thin strand. Graphs for conduction velocities $\bar{\vartheta}_s(H)$ and $\bar{\vartheta}_n(H)$ overlapped with $\bar{\vartheta}_l(H)$ and, thus, are not shown.

Fig. 4. Propagating wave in a papillary muscle simulation discretized at $75\mu m$ of mean resolution at several time steps. The lower right panel shows the histogram of relative errors ϵ_{HM+M} in the PM75 simulations.

TABLE I

Harmonic Mean Conductivity Settings (S/m)

Ionic model	Longitudinal	Transverse	Sheet normal
MSH	0.17805	0.07921	0.01992
TNNP	0.12309	0.05463	0.01367

TABLE II

Benchmarking memory usage of stiffness matrices (K) and element lists (Elist) in 2D and 3D

Dimension	Resolution	μm	2D					3D					3D PM	
			100	50	25	12.5	6.25	3.125	200	150	100	50	75	75
K (TM)	MB		0.39	1.54	6.12	24.45	97.73	507.57	12.80	29.22	100.79	799.88	70.17	
			0.69	2.76	11.0	43.98	175.85	703.27	26.27	60.12	208.06	1656.20	112.17	
Elist (TM)	MB		1.83	7.32	29.30	117.19	468.75	1893.17	104.77	218.23	675.59	4760.37	358.13	
			1.03	4.12	16.48	65.92	263.67	1059.63	30.36	63.17	195.36	1375.59	117.98	
Total (TM)	MB		2.22	8.86	35.42	141.64	566.48	2400.74	117.57	247.45	776.38	5560.25	433.42	
Total (HM+M)	MB		1.72	6.88	27.48	109.9	439.53	1762.90	56.63	123.29	403.42	3031.79	235.15	