Reduced Cellular Model for Cardiac Electromechanical Simulations

Helena C L C Salles[1], João G R Silva[2], Carolina Ribeiro Xavier[3], Bernardo M Rocha[1], Joventino O Campos[1], Rodrigo W dos Santos[1]

[1] Federal University of Juiz de Fora, Juiz de Fora, Brazil
[2] Federal Institute of Brasília, Brasília, Brazil
[3] Federal University of São João del Rei, São João del-Rei, Brazil

Abstract

This work presents a reduced model with only six ordinary differential equations (ODEs) that reproduces cardiac electromechanical activity at the cellular level. Developed from the Bueno-Orovio Minimal Model with simplified calcium and mechanics equations, the proposed model was fitted via genetic algorithms in order to reproduce the biophysically detailed model ToR-ORd-Land behavior. Comparisons with the ToR-ORd-Land showed that the developed model maintains accuracy in reproducing action potential, calcium dynamics, and active tension, with significant computational cost reduction. Tests on electromechanical simulations using a 3D slab mesh proved its efficiency in tissue simulations. This approach offers a unique balance between mathematical simplicity and physiological fidelity, enabling electromechanical simulations at organ scale.

1. Introduction

Cardiac electromechanical modeling is a powerful tool for studying physiological and pathological heart behavior, but its computational complexity remains a major challenge [1]. Simulating the interplay between electrical activation, calcium dynamics, and mechanical contraction requires solving coupled nonlinear systems across multiple spatial and temporal scales.

Traditional biophysically detailed models [2, 3] incorporate intricate cellular mechanisms, such as ion channel kinetics, cross-bridge cycling, and calcium-induced calcium release, but they demand high computational resources in tissue simulations due to their large ODEs systems. While these models achieve high physiological fidelity, their computational cost limits applications in large-scale simulations, such as patient-specific studies or drug screening.

In contrast, simplified models prioritize computational efficiency by reducing the number of variables and equations while preserving qualitative behavior. The proposed model, named MinimalModel_Silva (MMS), bridges this gap: a reduced-order electromechanical model with only six ODEs, derived from the Bueno-Orovio minimal electrical model [4] and coupled to phenomenological equations for calcium and active tension.

By leveraging genetic algorithms for parameter fitting, the model maintains accuracy in reproducing action potentials, calcium transients, and active tension while enabling faster simulations. In order to show the good performance of MMS in 3D simulations, we used a 3D slab mesh to perform electromechanical simulations, comparing the execution time using MMS and ToR-ORd-Land models.

2. Methods

This section outlines the reduced-order model, its calibration through data fitting, and the formulation of tissue electromechanics. We also describe the computational experiments conducted to assess model performance.

2.1. Reduced Model

Action Potential and Coupling: The reduced electromechanical model was developed to capture cardiac electromechanics using a minimal number of differential equations. For this purpose, the model proposed by [4] was adopted for the action potential due to its simplicity and its structure based on three ionic current densities: J_{si} (slow inward), J_{so} (slow outward), and J_{fi} (fast inward). The coupling with the calcium and active tension systems followed a scheme inspired by cardiac physiology, in which the sequence of events occurs in an orderly and interdependent manner. Initially, the electrical activation of cardiac tissue triggers changes in the membrane potential, which in turn regulate the influx and efflux of ions, including calcium. This ionic flow leads to an increase in intracellular calcium concentration, which is essential for the excitation–contraction coupling process. The transient increase in calcium activates the cell's contractile machin-

ery, promoting the interaction between actin and myosin and, consequently, generating mechanical force. Thus, the developed model incorporates this sequence of events, ensuring that electrical activation drives calcium dynamics, which in turn control the generation of active tension and the mechanical response of cardiac tissue.

Reduced Model for Calcium: Calcium dynamics (Equation 1) were modeled using one differential and two algebraic equations, coupled to the electrical system via J_{fi} and J_{si}. Activation (Equation 2) depends on J_{fi} and is regulated by γ_1 (speed) and γ_2 (amplitude). Inactivation (Equation 3) is influenced by J_{si} and controlled by p_1 and p_2 (maximum and minimum values), γ_3 (transition smoothing), and a (transition midpoint).

$$\frac{\mathrm{dCa}}{\mathrm{dt}} = f_{at_{ca}}(J_{fi}) - f_{ina_{ca}}(J_{si})(Ca - Ca_{Diastolic}) \quad (1)$$

$$f_{at_{ca}}(J_{fi}) = \frac{(-J_{fi})^{\gamma_1}}{\gamma_2} \quad (2)$$

$$f_{ina_{ca}}(J_{si}) = \frac{p_1 + p_2}{2} - \frac{p_1 - p_2}{2}\tanh(-\gamma_3(J_{si} - a)) \quad (3)$$

Reduced Model for Active Tension: The modeling of active tension (Equation 4) followed a similar principle, using one differential and three algebraic equations. The term $c_1(J_{fi})$, described by Equation 5, represents the delay in mechanical activation and depends on γ_5. Its activation (Equation 6) is regulated by γ_4 (activation exponent) and γ_7 (amplitude). Inactivation (Equation 7) is controlled by p_3 and p_4 (maximum and minimum values), γ_6 (transition smoothing), and b (transition midpoint).

$$\frac{\mathrm{dTa}}{\mathrm{dt}} = c_1(J_{fi}) f_{at_{ta}}(Ca) - f_{ina_{ta}}(Ca)Ta \quad (4)$$

$$c_1(J_{fi}) = \begin{cases} 0, & \text{if } (-J_{fi})^{\gamma_5} > 0.001 \\ 1, & \text{otherwise} \end{cases} \quad (5)$$

$$f_{at_{ta}}(Ca) = \gamma_7 Ca^{\gamma_4} \quad (6)$$

$$f_{ina_{ta}}(Ca) = \frac{p_3 + p_4}{2} + \frac{p_3 - p_4}{2}\tanh(-\gamma_6(Ca - b)) \quad (7)$$

In this way, an electromechanical model named MinimalModel_Silva (MMS) was developed, structured into three coupled systems: electrical, calcium, and mechanical. The model is composed of 6 differential equations, 15 algebraic equations, and 42 parameters, ensuring an efficient representation of cardiac electromechanical activity.

2.2. Fitting the Model to ToR-ORd-Land Behavior

To achieve the desired simulations and validations, the 42 parameters of the coupled model were optimized using a custom genetic algorithm designed to minimize the discrepancy between MMS and ToR-ORd-Land models for the action potential shape, action potential duration restitution curve, and the maximum derivative restitution curve. Each parameter was encoded as a 10-bit string, using Gray Code to convert it into real values within its respective domain. The algorithm employed genetic operators such as two-point crossover, bit inversion mutation, and elitism to improve convergence. For evaluation, the objective function was defined as a sum of the distances between the simulations and each of the three targets.

2.3. Tissue Electromechanical Model

Tissue electromechanics is modeled by coupling the monodomain model [5], which describes electrical excitation and action potential dynamics, with a cardiac mechanics model [3], which characterizes tissue contraction and deformation under active tension, based on the theory of finite deformations.

The mechanical problem is governed by the following quasi-static equation:

$$\nabla \cdot \mathbf{FS} = 0, \quad \text{in } \Omega_0 \quad (8)$$

where $\mathbf{F}$ is the deformation gradient tensor, S is the second Piola-Kirchhoff stress tensor, and Ω_0 represents the undeformed configuration. We consider the active stress approach, where tissue deformation is triggered by active tension $\mathbf{S}_a$, that represents active force generation at the cellular level. The active stress component is given by $\mathbf{S}_a = T_{ref} T_a \mathbf{f_0} \otimes \mathbf{f_0}$, where $\mathbf{f_0}$ is the fiber direction in the undeformed configuration. The passive response of the tissue is modeled by the Holzapfel-Ogden model [6].

The electrical propagation is governed by the monodomain model, given by:

$$\chi \left(C_m \frac{\partial V}{\partial t} + I_{ion} - I_s \right) = \nabla \cdot (\boldsymbol{\sigma} \nabla V), \quad (9)$$

where $\boldsymbol{\sigma}$ is the conductivity tensor, χ is the surface-to-volume ratio of cells, C_m is the specific membrane capacitance per unit area, V is the transmembrane potential, I_{ion} is the ionic current, and I_s is an externally applied current.

The models are coupled in a one-way approach, such that the monodomain equation is integrated with the cellular model, which generates active tension. This active tension is then transferred to the mechanical problem at each time step to drive tissue deformation. Once the mechanical problem is solved, the resulting displacement field is used to update the deformed configuration and fiber diretion used in electrophysiological computations. Although the electrical and mechanical processes operate on different spatial and temporal scales, a single computational mesh is employed for both problems for the sake of simplicity.

The numerical solutions is carried out using the in-house code known as `cardiax` [7].

2.4. Computational Experiment

In order to assess the performance of MMS in the context of 3D eletromechanical simulations we performed a test using a 3D slab mesh of hexaedral finite elements, with 6859 nodes and 5832 elements with 500 μm of edge length. The x-displacements were fixed on the left face and the y-displacements were fixed on the bottom face.

A stimulus was applied in a region of the mesh, as shown in Figure 1(a), then the electrical wave propagated and the tissue contracted, as presented in Figure 1(b), which represents the deformed configuration at 50 ms and the wireframe represents the undeformed configuration. The active tension was normalized for both models before to use in the tissue simulation. The coupled eletromechanical model was solved using the finite element method, with Crank-Nicolson method to solve monodomain model and forward Euler for the ODE system. For the mechanical model, the resulting nonlinear systems were solved using the Newton method. All the linear systems were solved using the AMGx library with GMRES preconditioned with an algebraic multigrid solver, which runs in graphics processing unit (GPU).

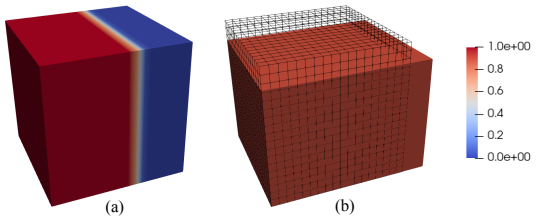


Figure 1. 3D slab electromechanical experiment using MMS model, where colors present the transmembrane voltage. (a) Stimulus applicaton at $[0, 1]$ ms. (b) Deformed tissue at 50 ms.

In order to obtain convergence, we used a time step of 0.05 ms to solve MMS with a $\Delta t = 0.1$ ms for the mechanical solver. While in the ToR-ORd-Land simulation it was necessary to use a time step of 0.001 ms for the celular model and a $\Delta t = 0.01$ ms for the mechanical solver.

The experiments were carried out in a machine with a CPU Intel(R) Core(TM) i5-13400F and a GPU NVIDIA GeForce RTX 4070 TI Super.

3. Results

3.1. Fitting Results

In order to evaluate the capacity of the MMS model to reproduce the cardiac electromechanical activity for the endocardial cell, Figure 2 shows the behavior of the action potential, calcium, and active tension of the ToR-ORd-Land model for endocardial cells and the same curves obtained with the proposed model.

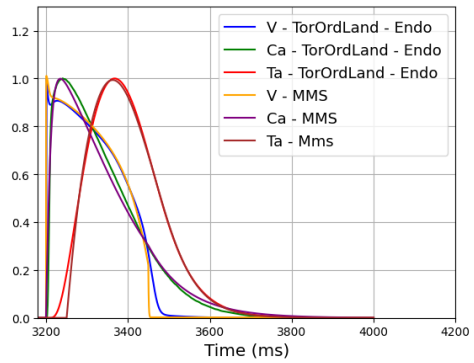


Figure 2. Action potential, calcium and active tension curves for ToR-ORd-Land and MMS after fitting.

The developed model proved to be capable of phenomenologically reproducing the behavior of the systems that are part of the electromechanics for the endocardium. In this scenario, the percentage differences between curves were 3.93% for transmembrane potential, 4.27% for calcium, and 8.98% for active tension. Figure 3 compares the restitution curve for MMS and ToR-ORd-Land, presenting the behavior of MMS model varying the pacing. Besides the significant difference for long APD, the MMS restitution curve captures the behavior of ToR-ORd-Land, and the difference between the curves for short APDs is small.

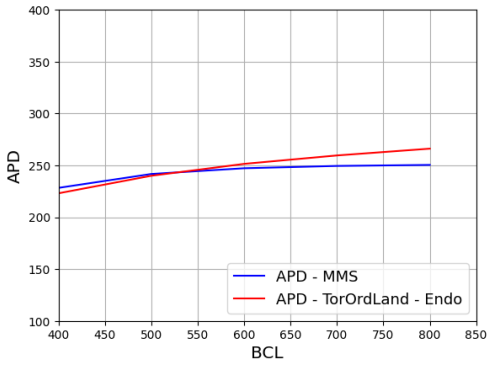


Figure 3. APD vs BCL restitution curve for ToR-ORd-Land and MMS after fitting.

3.2. Performance in 3D Simulation

To evaluate the performance of a 3D electromechanical simulation using MMS, we conducted the computational experiment previously described for the proposed model and compared it with the same simulation using the ToR-ORd-Land model.

The execution time results for both experiments are presented in Table 1. In terms of total execution time, MMS was shown to be $6.5\times$ faster than the ToR-ORd-Land simulation.

The most significant performance gain occurred in the electrical module, where MMS achieved a $33\times$ speedup compared to ToR-ORd-Land. In this context, the main advantage of MMS was observed in the ODE solver, which was $290\times$ faster, while the time required to solve the parabolic component of the monodomain equation was 30× shorter with MMS.

The choice of model also influenced the mechanical solution, which is the computational bottleneck. Specifically, the ToR-ORd-Land simulation required a time step (Δt) that was $10\times$ smaller, resulting in a $5.5\times$ speedup in favor of MMS.

Table 1. Execution time (seconds) spent by different parts of the simulator when using MMS and ToR-ORd-Land models.

Solver module	MMS	ToR-ORd-Land	Speedup
ODEs	0.8	232	$290\times$
Parabolic	70.3	2127	$30\times$
Electrical	71.1	2359	$33\times$
Mechanical	1850	10190	$5.5\times$
Total	1921.1	12549	$6.5\times$

4. Conclusions

This work presented the performance of a reduced cellular model when used in 3D electromechanical simulation with respect to a biophysically detailed ToR-ORd-Land model. The parameter fitting enabled the MMS model to reproduce the behavior of the reference model, in terms of action potential, calcium transients, and active tension.

When both models were used in 3D simulations, the MMS model allowed electromechanical simulations $6.5\times$ faster than ToR-ORd-Land model. This low computational cost was achieved because the proposed model has only 6 ODEs and greater time steps could be used for the electrical and mechanical solvers.

As future works, we intend to use parallel programming for the ODE solver and perform simulations in biventricular meshes, considering the whole cardiac cycle. Furthermore, the model does not consider dependence on sarcomere length or shortening velocity, which are points to be improved in the model.

Acknowledgments

The authors would like to express their thanks to Minas Gerais State Research Support Foundation (FAPEMIG) - PCE-00048-25; APQ-02752-24, APQ-02445-24, APQ-02513-22, FINEP (SOS Equipamentos 2021 AV02 0062/22), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq); Coordenação de Aperfeiçoamento de Pessoal de Ensino Superior (CAPES), SINAPAD Santos-Dumont, and Federal University of Juiz de Fora (UFJF) for funding this work.

References

[1] Rodero C, Baptiste TM, Barrows RK, Lewalle A, Niederer SA, Strocchi M. Advancing clinical translation of cardiac biomechanics models: a comprehensive review, applications and future pathways. Frontiers in Physics 2023;11:1306210.

[2] Margara F, Wang ZJ, Levrero-Florencio F, Santiago A, Vázquez M, Bueno-Orovio A, Rodriguez B. In-silico human electro-mechanical ventricular modelling and simulation for drug-induced pro-arrhythmia and inotropic risk assessment. Progress in Biophysics and Molecular Biology 2021;159:58–74.

[3] de Oliveira BL, Sundnes J, Dos Santos RW. The development of a new computational model for the electromechanics of the human ventricular myocyte. In 2010 Annual International Conference of the IEEE Engineering in Medicine and Biology. IEEE, 2010; 3820–3823.

[4] Bueno-Orovio A, Cherry EM, Fenton FH. Minimal model for human ventricular action potentials in tissue. Journal of Theoretical Biology 2008;253(3):544–560.

[5] Sundnes J, Nielsen BF, Mardal KA, Cai X, Lines GT, Tveito A. On the computational complexity of the bidomain and the monodomain models of electrophysiology. Annals of Biomedical Engineering 2006;34:1088–1097.

[6] Holzapfel GA, Ogden RW. Constitutive modelling of passive myocardium: a structurally based framework for material characterization. Philosophical Transactions of the Royal Society A Mathematical Physical and Engineering Sciences 2009;367(1902):3445–3475.

[7] Campos JO, Dos Santos RW, Sundnes J, Rocha BM. Preconditioned augmented lagrangian formulation for nearly incompressible cardiac mechanics. International Journal for Numerical Methods in Biomedical Engineering 2018; 34(4):e2948.

Address for correspondence:

Joventino de Oliveira Campos
Departamento de Ciência da Computação da UFJF, Juiz de Fora
joventino.campos@ufjf.br