Modeling the electromechanics of a single cardiac myocyte*

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Abstract. The synchronous and proper contraction of cardiomyocytes is essential for the correct function of the whole heart. Computational models of a cardiac cell may spam multiple cellular sub-components, scales, and physics. As a result, they are usually computationally expensive. This work proposes a low-cost model to simulate the cardiac myocyte's electromechanics. The modeling of action potential and active force is performed via a system of six ordinary differential equations. Cardiac myocyte's deformation that considers details of its geometry is captured using a mass-spring system. The mathematical model is integrated in time using Verlet's method to obtain the position, velocity, and acceleration of each discretized point of the single cardiac myocyte. Our numerical results show that the obtained action potential, contraction, and deformation reproduces very well physiological data. Therefore, the low-cost mathematical model proposed here can be used as an essential tool for the correct characterization of cardiac electromechanics.

Keywords: Mass-spring Systems · Eletromechanical Coupling · Cardiac Myocyte.

1 Introduction

Cardiac diseases are still the first cause of death in the world, taking an estimated 17.9 million lives per year, according to World Health Organization. Modeling this organ is a complex task that begins with the model of a single cardiac myocyte. Computational models of a cardiac cell may spam multiple cellular sub-components, scales, and physics. In general, robust models with partial differential equations are used for the electrical action potential propagation and

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the coupling to the mechanical deformation, i.e., the myocyte contraction [7]. The finite Element Method is widely used in solving these equations, but with high computational costs [3].

For tackling the computational costs, the work of *Silva et al* [10] proposed simplified models that reproduce the most important cardiac mechanics features. These models capture how action potential influences active force, i.e., the so-called electromechanical coupling. These models are based on few differential equations and have low computational costs without losing quality to reproduce the physiological phenomena.

Besides a simple active force model, it is also necessary to implement the passive mechanical model, responsible for restoring a contracted cell to its initial configuration. In this case, a common choice is a mass-spring system (MSS), which represents elastic materials by a finite set of masses connected by springs. The ability to simulate the elastic behavior of bodies in real-time made MSSs of great interest in computer graphics due to its simple formulation and computational performance [6, 1]. They are used in animations and virtual reality applications, especially in simulations of surgeries and biologic tissues [8].

A related work that simulates the heart mechanic with mass-spring systems is presented by Weise *et al.* [12]. It proposes a discrete reaction-diffusion-mechanics model, where Hooke's law describes the elastic properties of the material. The model was used for studying heart phenomena such as the effect of mechano-electrical feedback.

Another works in this field use simplified methods based on cellular automata for simulating the action potential propagation and the active force application. A example of this kind of method is the *Campos et al.* [4], that proposes a meshless simulator, where the 3D geometries are split in a discrete set of masses, connected by springs. Its simple implementation resulted in very fast execution times. Later, *Campos et al.* [5] proposed a more robust cardiac electromechanic simulator, able to handle more complex geometries, with a discretization based on tetrahedrons. It also contains more realistic features, such as volume preservation and anisotropy controlling in a mass spring system. The model reproduced a cycle of contraction and relaxation of a human left ventricle.

In this sense, this work proposes a new tool for cardiac myocyte electromechanics simulation, aiming for low computational costs and correct physiological results. The action potential and active force are modeled by a system of six ordinary differential equations. The active force is responsible for contracting the cell, and then a passive force acts for bringing the cell to its initial configuration. The passive force is modeled by a mass-spring system. The cardiomyocite shape is obtained via a confocal microscopy, which we discretize by a set of point masses connected by springs, in a irregular mesh fashion. Our equations are integrated in time using Verlet's method to obtain the position, velocity, and acceleration of mass point.

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2 Mass-Spring Systems

Mass-spring models have a simple formulation and fast execution time, making them a suitable altenative for modeling elastic materials without the need of higher computational resources. In such systems, masses are connected to their neighbors by springs. Forces can be applied to the system deforming its spatial distribution.

The cardiac tissue does not have a linear stress-strain relation but considering small scale deformations, its contraction can be aproximated by a linear model, using springs. The springs of the system will try to bring the system back to its initial configuration after contraction. The proposed model is described below.

2.1 Mathematical Model

Considering one mass unity as a rigid body, the following Ordinary Diferential Equations can be deduced to integrate trajectory and velocity, according to classical mechanics.

$$F = ma \tag{1}$$

$$v = \frac{\partial x}{\partial t} \tag{2}$$

$$a = \frac{\partial v}{\partial t} \tag{3}$$

This formulation can be manipulated in order to isolate derivatives and then obtaining a linear system with two ODE's.

$$\frac{\partial x}{\partial t} = v \tag{4}$$

$$\frac{\partial v}{\partial t} = \frac{F}{m} \tag{5}$$

The force can be categorized in two different types: passive and active forces. Passive forces are made from particles to its neighboors through the springs when its position changes. The active force is applied as a load external to the system, in this case, modeling the active tension generated by the action potential in the cell. In order to avoid the rigid-body displacement of translation, the mass center of the cell is fixed. Considering only one mass linked to a wall by a spring, as depicted in Figure 1a, the force can be calculated with Hooke's Law. The force exerted will be f_p and the reaction of the wall will be f_r.

$$f_p = -f_r = k(x_L - x_0) \tag{6}$$

We arranged our spring and masses in a regular grid, where masses are connected in a Moore Neighborhood fashion, as depicted in Figure 1b. In this manner, the

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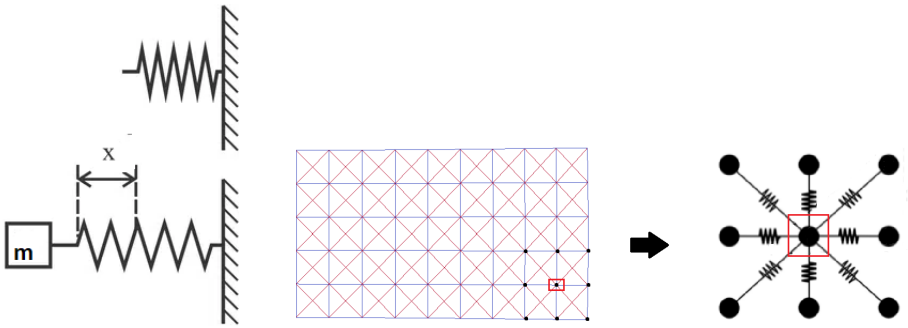

(a) Mass coupled to a spring and its deformation.

(b) Neighborhood of a mass.

Fig. 1. A simple mass-spring system and our mass-spring configuration.

total force exerted in a mass will be the sum of contributions of the neighborhood composed by 8 other masses. Therefore, the total force will be the sum of passive and active forces applied externally to the system. Equation 7 was used to calculate passive forces, that are proportional to the deformation of the spring.

$$f_p = -[k_{elas}(|l| - r)]\frac{l}{|l|} \tag{7}$$

In addition to passive forces and active forces, a viscous damping force is considered. This damping force is calculated as shown in the equation 8.

$$f_p = \left[k_{damping}\frac{(\dot{l} \cdot l)}{|l|}\right]\frac{l}{|l|} \tag{8}$$

After system initialization, a loop starts over a period of time. At each iteration, the sum of passive, active, external and damping forces that a mass receives at a given moment is calculated.

2.2 Critical damping

The spring mass system without the use of damping results in a state in which the energy never dissipates. A factor called Damping Ratio denoted by ξ can be used to calculate damping in a MSSs:

$$\xi = \frac{k_{damping}}{k_{dcritical}}. \tag{9}$$

Considering the equation of motion in the formulation described by equation 10, the critical damping coefficient will be equal to the relation in equation 11. If damping below the critical value is used, the damping ratio will be less than 1,

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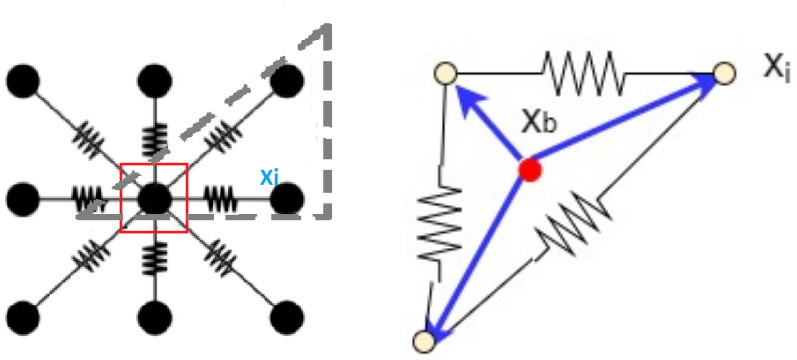
characterizing an under-damped system. If the above value is used, we will have an over-damped system and a damping ratio greater than 1.

$$m\ddot{x} + k_d\dot{x} + k_e x = 0 \tag{10}$$

$$k_{dcritical} = 2\sqrt{km} \tag{11}$$

2.3 Area Preservation

To adjust the cardiac myocyte contraction to obtain a more physiological behavior a force of area preservation is added, i.e., to reproduce the quasi-incompressible feature of the cell.



(a) A mass and one adjacent surface area.

(b) Force applied to preserve the area.

Fig. 2. Surface area preserving.

For each mass, two masses in the neighborhood are visited, forming a triangle, as showed in Figure 2. The baricenter of the formed triangle is calculated using the mean value between the three masses coordinates, displayed in equation 12.

$$x_b = \frac{1}{3}\sum_{j=1}^{3} x_j \tag{12}$$

The direction in wich force is applied is calculated through a vector between the baricenter and the node receiving the preservation force. The force applied will be proportional to a preservation area constant and the area of the triangle formed by the nodes:

$$f_{prev} = -k_{prev} area \frac{(x_i - x_b)}{||x_i - x_b||}. \tag{13}$$

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2.4 Verlet's Numerical Method

Verlet's numerical method was used to solve the mathematical model in order to obtain its position and velocity through time:

Verlet's method can be deduced using Taylor's Series Expansion for progressive and regressive aproximations:

$$X_{t_{n+1}} = X_{t_n} + V_{t_n}\Delta t + \frac{h^2}{2}\frac{F_n}{m} + \frac{h^3}{6}X^{(3)}_{t_n} + O(h^4), \tag{14}$$

$$X_{t_{n-1}} = X_{t_n} - V_{t_n}\Delta t + \frac{h^2}{2}\frac{F_n}{m} - \frac{h^3}{6}X^{(3)}_{t_n} + O(h^4). \tag{15}$$

Adding the two expansions we obtain:

$$X_{t_{n+1}} = 2X_{t_n} + h^2\frac{F_n}{m} - X_{t_{n-1}} + O(h^4). \tag{16}$$

The velocity of the mass can be obtained by Finite Diferences Method in its centered aproximation:

$$V_{t_{n+1}} = \frac{V_{t_{n+1}} - V_{t_{n-1}}}{2h} + O(h^2). \tag{17}$$

Therefore, this method aproximates the position with an error order of h^4 and velocity of h^2.

3 Coupled Eletromechanical Model

For the mass system to model the cardiac myocyte with its contraction characteristics and properties, the applied force must follow a cell active tension that is associated to a cell action potential. To model the cell action potential, the Minimal Model proposed in [2] was used and adjusted to reproduce the model described in [11]:

$$\frac{\mathrm{d}u}{\mathrm{d}t} = -(J_{fi} + J_{so} + J_{si}) \tag{18}$$

$$\frac{\mathrm{d}v}{\mathrm{d}t} = (1 - H(u - \theta_v))(v_\infty - v)/\tau_v^- - H(u - \theta_v)v/\tau_v^+ \tag{19}$$

$$\frac{\mathrm{d}w}{\mathrm{d}t} = (1 - H(u - \theta_w))(w_\infty - w)/\tau_w^- - H(u - \theta_w)w/\tau_w^+ \tag{20}$$

$$\frac{\mathrm{d}s}{\mathrm{d}t} = ((1 + tanh(k_s(u - u_s)))/2 - s)/\tau_s \tag{21}$$

$$J_{fi} = -vH(u - \theta_v)(u - \theta_v)(u_u - u)/\tau_{fi} \tag{22}$$

$$J_{so} = (u - u_o)(1 - H(u - \theta_w))/\tau_o + H(u - \theta_w)/\tau_{so} \tag{23}$$

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$$J_{si} = -H(u - \theta_w)WS/\tau_{si} \tag{24}$$

$$\tau_v^- = (1 - H(u - \theta_v^-))\tau_{v1}^- + H(u - \theta_v^-)\tau_{v2}^- \tag{25}$$

$$\tau_w^- = \tau_{w1}^- + (\tau_{w2}^- - \tau_{w1}^-)(1 + tanh(k_w^-(u - u_w^-)))/2 \tag{26}$$

$$\tau_{so} = \tau_{so1} + (\tau_{so2} - \tau_{so1})(1 + tanh(k_{so}(u - u_{so})))/2 \tag{27}$$

$$\tau_s = (1 - H(u - \theta_w))\tau_{s1} + H(u - \theta_w)\tau_{s2} \tag{28}$$

$$\tau_o = (1 - H(u - \theta_o))\tau_{o1} + H(u - \theta_o)\tau_{o2} \tag{29}$$

$$v_\infty = \begin{cases} 1, & u < \theta_v^- \\ 0, & u \geq \theta_v^- \end{cases} \tag{30}$$

$$w_\infty = (1 - H(u - \theta_o))(1 - u/\tau_{w\infty}) + H(u - \theta_o)w_\infty^*, \tag{31}$$

where $u_o, u_u, \theta_v, \theta_w, \theta_v^-, \theta_o, \tau_{v1}^-, \tau_v^+, \tau_{w1}^-, \tau_{w2}^-, k_w^-, u_w^-, \tau_w^+, \tau_{fi}, \tau_{o1}, \tau_{o2}, \tau_{so1}, \tau_{so2}$, $k_{so}, u_{so}, \tau_{s1}, \tau_{s2}, k_s, u_s, \tau_{si}, \tau_{w\infty}, w_\infty^*$ are 28 adjustable parameters of the model with values reported in [2].

The model presented in [10] proposes two ODE's to capture the cell's active tension triggered by an action potential:

$$\frac{\mathrm{d}Ta_i}{\mathrm{d}t} = c_0(k(V) - Ta_i) \tag{32}$$

$$\frac{\mathrm{d}Ta}{\mathrm{d}t} = \epsilon_1(V, Ta_i)(Ta_i - Ta) \tag{33}$$

$$k(V) = \frac{1}{\sigma\sqrt{2\pi}}\, e^{\frac{-1}{2}(\frac{V-1}{\sigma})^2} \tag{34}$$

$$\epsilon_1(V) = \begin{cases} x_1 \text{ para V} > x_2 \text{ e } Ta_i < x_3 \\ c_0 \qquad\qquad \text{otherwise.} \end{cases} \tag{35}$$

The parameters used were adjusted using a Genetic Algorithm as described before in [10]. The parameters of the coupled electromechanical model are presented in Table 1.

The active tension obtained in equation 33 was multiplied by a factor of 85

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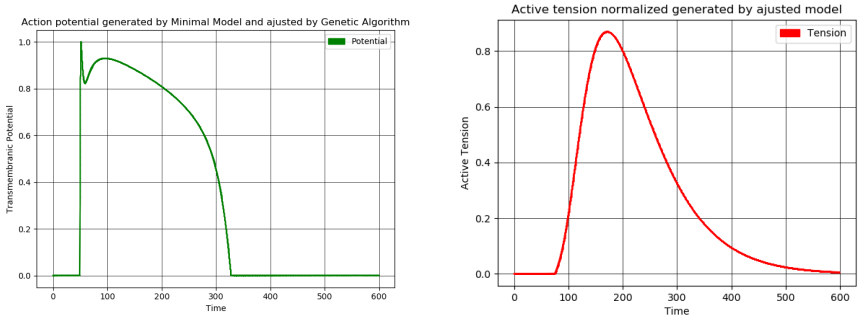
u_o	0.529297	τ_{w2}^-	62.9688	k_{so}	0.253711	c_0	0.0166016
θ_v	0.0673828	u_w^-	58.0469	τ_{s1}	2.36621	x_1	0.0001
θ_w	0.00195313	τ_w^+	0.59668	τ_{s2}	11.4453	x_2	0.78
θ_v^-	0.0976563	τ_{fi}	273.633	k_s	2.25586	x_3	0.2925
θ_o	0.932618	τ_{o1}	0.644532	u_s	0.903321		
τ_{v1}^-	57.7148	τ_{o2}	477.344	τ_{si}	1.76816		
τ_v^+	1101.56	τ_{so1}	14.1992	$\tau_{w\infty}$	0.785157		
τ_{w1}^-	1.96973	τ_{so2}	25.4492	w_∞^*	0.500977		

Table 1. Parameters of the coupled model.



(a) Action potential. (b) Active tension.

Fig. 3. Action potential and active tension.

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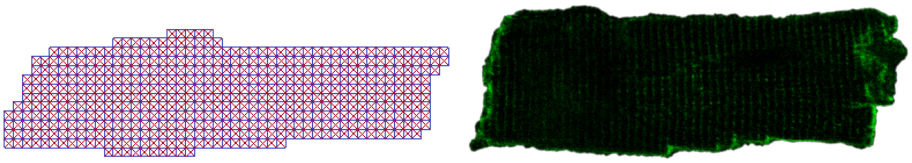
4 Results

4.1 Computational aspects

A C++ code was developed to simulate the coupling of units of masses with springs in horizontal, vertical, and diagonal links, considering the force each mass applies to its neighbors. The tool allows the representation of irregular geometries. This is essential to reproduce the complex geometry of single cardiac myocytes, as presented in Figure 4b, which was obtained in the laboratory. A similar numerical mesh is also presented in Figure 4a.



(a) Generated mesh. (b) Real myocyte image.

Fig. 4. A real myocyte image and its corresponding mesh.

4.2 Numerical results

We tested our model by simulating a cycle of contraction and relaxation. The results for action potential and active tension are presented in Figure 3b. The active force reaches its peak around 170ms, where it applies 100% of stress. After that, it returns to 0% of stress.

The active tension drives the mass-spring system which results in the contraction and relaxation of the single cardiac myocyte, as presented in Figure 5.

Figure 6 shows the shortening of the myocyte in the x-direction. We applied three different values of active stress, $T_a = 30kPa$, $T_a = 40kPa$ and $T_a = 50kPa$ causing a maximum deformation of 12%. The cell responded to active stress as expected, achieving its maximum contraction when stress is maximum.

5 Conclusion

In this work, we present a low-cost model to simulate the electromechanics of a single cardiac myocyte. The modeling of action potential and active force was performed via a system of six ordinary differential equations. Cardiac myocyte's deformation that considers details of its complex geometry was captured using a mass-spring system with an irregular mesh. The mathematical model was integrated in time using Verlet's method to obtain the position, velocity, and

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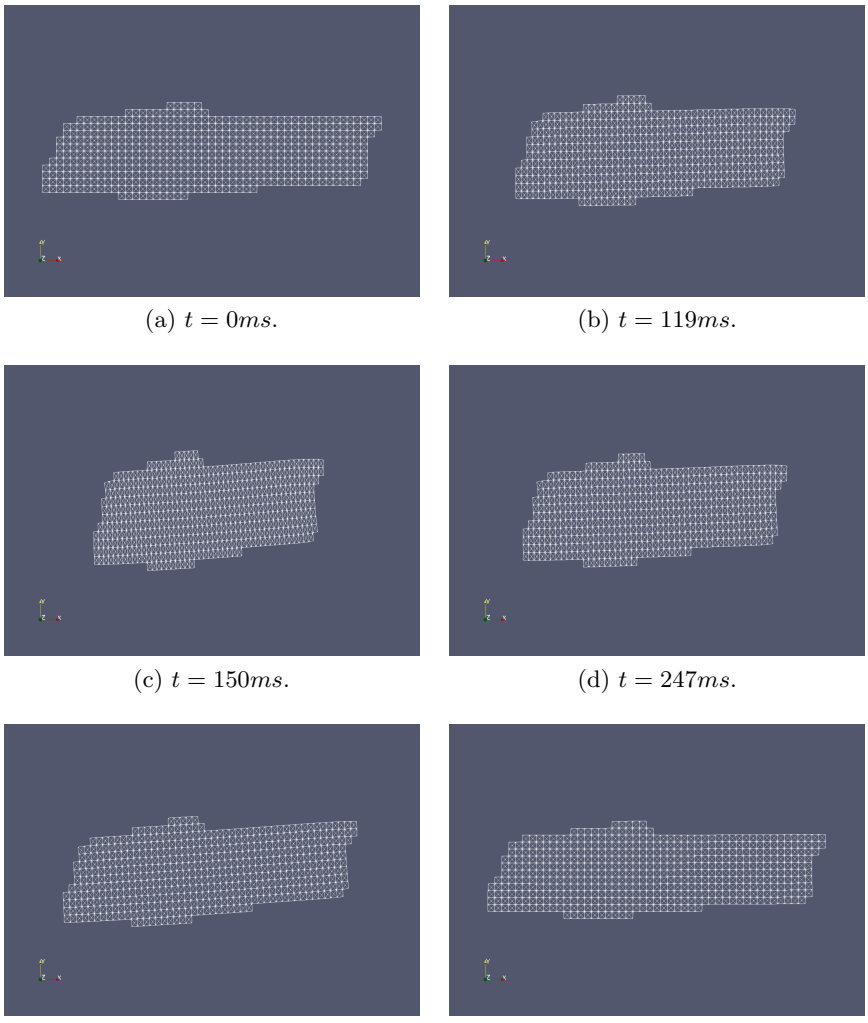

(a) $t = 0ms$. (b) $t = 119ms$.

(c) $t = 150ms$. (d) $t = 247ms$.

(e) $t = 300ms$. (f) $t = 574ms$.

Fig. 5. Simulations results at different time-steps t.

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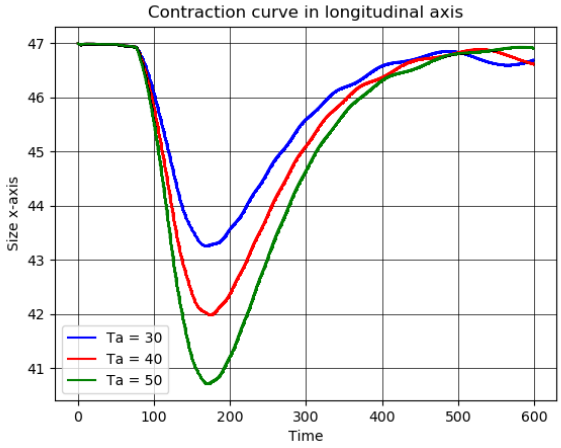

Fig. 6. Contraction curve

acceleration of each discretized point of the single cardiac myocyte. Our numerical results show that the obtained shortening reproduces very well physiological data. The comparison was made considering measures in [9]. In this work, the measured contraction displayed a shortening of 8% to 10% of the cell volum. Therefore, the low-cost mathematical model proposed here can be used as a tool to help the characterization of cardiac electromechanics.

As future work, we intend to perform a sensitivity analysis in order to evaluate the significance of each parameter in the simulations. We also intend to quantitatively compare our simulations to experimental data.

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