Numerical Simulation of Mechanoelectric Feedback in a Deformed Myocardium

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Abstract—Mechanoelectric feedback manifests itself as a change in myocardial conductivity and the appearance of additional transmembrane currents associated with stretch-activated ion channels. The deformation-conductivity relations were derived by analyzing the microstructural model using the homogenization method. The cardiac tissue was considered as a periodic lattice, where the cells are rectangular prisms filled with an isotropic electrolyte. The conductivity of the gap junctions was taken into account through the boundary conditions on the sides of these prisms and was deemed constant. It is shown that the tensor that is the inverse of the myocardial conductivity tensor can be represented as a sum of the inverse reduced conductivity tensors of the myoplasm and gap junctions. The chosen model is compared with the model from the book by F.B. Sachse, Computational Cardiology, Springer (2004). For the longitudinal conductivity both models agree well for relative extensions in the range from 0.8 to 1.2. When studying the propagation of an excitation wave, the effect of deformation is “diluted” by the extracellular conductivity. In the processes where the extracellular and intracellular media act individually, the effect of deformation on the myocardium is more significant. A model for the activation of channels under complex deformation based on the assumptions that these channels are uniformly distributed over the lateral surface of the cell and respond to a local increase in membrane patch area has been constructed. This model allows the activation of channels to be considered not only when stretched along the fiber, but also when deformed in an arbitrary direction.

Keywords: electromechanical coupling, mechanoelectric feedback, stretch-activated channels, numerical simulation

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1. INTRODUCTION

A cardiac arrhythmia is one of the most common cardiovascular diseases. Studying the causes of this dangerous state can contribute to its timely prevention and treatment.

Macroscopically, the cardiac muscle may be considered as a two conducting media filling the extracellular and intracellular spaces and interacting through a membrane. The cardiac tissue has a significant anisotropy owing to its fibrous-layered organization. The conductivities in different directions can differ by an order of magnitude [1]. The integrity of the intracellular space as a conducting medium is provided by the gap junctions.

Electrical stimulation triggers an increase in the concentration of calcium ions in a cardiac cell, which, in turn, leads to cardiac muscle contraction (electromechanical coupling). Large deformations accompanying the work of the heart exert a strong effect on the electric excitation process (mechanoelectric feedback arises). The following types of mechanoelectric feedback can be identified: a change in myocardial conductivity and the appearance of additional transmembrane currents (stretch-activated ion channels).

The effect of deformation on the contractile apparatus of the muscle cell is close to the mechanoelectric feedback. This type of mechanosensitivity is provided by the following cell processes: a change in the overlap between the thin and thick filaments in the sarcomere; a change in the sensitivity of the contractile apparatus to calcium ions; and a transition related to the release and capture of calcium ions in the sarcomere. The first two processes are fast and affect the myocardium contraction during the cardiac cycle. The third process is slow and is reflected in the regime of contractions in succeeding cycles [2]. The first two processes are presented in most electromechanical coupling models [3–6]. The effect of calcium ion kinetics can be found in [7, 8]. Since the mechanosensitivity is closely related to the electromechanical...
Two approaches are possible when investigating the conductivity of a deformable cardiac tissue [9]: in one (most popular) approach the myocardium is assumed to be an anisotropic fluid in which the conductivity along any of the material axes does not depend on deformation; only the rotation of the conductivity tensor together with the material axes occurs. In the second approach the myocardium is represented as a spatial grid of resistors for which the resistance between any two points does not change under deformation. Each of these approaches has its own carrier: the cytoplasm for the first one and the gap junctions for the second one. An approach that includes both types of carrier is proposed in the book by F.B. Sachse [9], where some parameter varying within the range from zero to one is introduced and its extreme values correspond to these cases.

In this paper we use a model for the change in the intracellular conductivity of the myocardium under its deformation based on the microstructural model from [10]. In the mentioned model the cardiac tissue is in the form of a periodic lattice, where the cells are rectangular prisms filled with an isotropic conducting fluid and the conductivity of the gap junctions is taken into account through the boundary conditions on the prism sides. Then, the intracellular conductivities along and across the fiber are expressed via the cell sizes, lattice periodicity parameters, and electric properties of the myoplasm and gap junctions by the homogenization method and by calculating the total current through the periodic structure. In addition, it was shown in [10] that the extracellular conductivity depends weakly on the linear cell sizes themselves and is determined mainly by the ratio of the cell sizes to the corresponding structure periodicity parameters (the fraction of the extracellular space). Therefore, the extracellular conductivity is expected to be almost unrelated to the deformations.

If the myocardium deformation in the material axes is extension–contraction, then the dependence of the macroscopic conductivities on deformation can be derived using simple generalizations of the model from [10] that take into account the layered structure of the myocardium when substituting the changed sizes into the expressions for the intracellular conductivity. For the more general case where the principal deformation axes are not aligned with the material axes associated with the fibrous-layered structure of the myocardium, shears are present in the myocardium when it is considered in these material axes. An analytical solution based on the model [10] can also be obtained, but only when using the homogenization method in the form presented in [11].

When deriving the dependences of the conductivities on deformation, we made the following assumptions: the cytoplasm is an isotropic electrolyte with a deformation-independent conductivity; the conductivities of the gap junctions are constant; and the cell deformation is identical to the deformation of the medium. This model can be generalized to include the myoplasm anisotropy related to its microstructure. The derivation of the dependence of the conductivity on deformation is described in detail in [12, 13].

In a deformable myocardium transmembrane channels can be activated and, as a consequence, additional sources of electric excitation can arise, which can entail a cardiac arrhythmia. There are a large number of channels that vary in mechanisms of load transfer to one another and response to the load [2, 14–16]. The currently developed models take into account the spatial pattern of deformation insufficiently well. As a rule, the activation of channels depends on their extension along the fiber, which is not obvious for the stretch-activated channels located on the muscle cell membrane.

In this paper we construct a channel activation model in the case of complex deformation under the following assumptions: the channels are uniformly distributed over the lateral cell surface; the channels respond to a local increase in membrane patch area [17, 18]; and the formula in which the extension along the fiber is used is valid for one-dimensional stretch in this direction.

2. THE MYOCARDIUM AS A CONDUCTING MEDIUM

Macroscopically, the cardiac muscle may be considered as two inhomogeneous anisotropic conducting media, extracellular and intracellular, that fill the spaces interacting through a membrane. Each of these two media is characterized by its own conductivity tensor. The model constructed under these assumptions is called the bidomain one and has the form [1]

\[
\nabla \cdot (D_I \nabla V_m) + \nabla \cdot (D_e \nabla V_e) = \chi I_m + \chi I_{is} + I_{is},
\]

\[
\nabla \cdot \left((D_I + D_e) \nabla V_e\right) + \nabla \cdot (D_I \nabla V_m) = I_{es} + I_{es}
\]
under the boundary conditions
\[ n \cdot (D_i \nabla V_i) = -n \cdot (D_e \nabla V_e), \quad (3) \]
\[ n \cdot (D_e \nabla V_e) = 0. \quad (4) \]

Here, \( V_i \) and \( V_e \) are the intracellular and extracellular potentials; \( V_m = V_i - V_e \) is the transmembrane potential; \( D_i \) and \( D_e \) are the intracellular and extracellular conductivity tensors; \( I_m \) is the transmembrane current; \( \chi \) is the cell membrane area per unit volume; \( I_{ts} \) is the transmembrane current source associated, for example, with the action of stretch-activated channels; \( I_{is} \) and \( I_{es} \) are the external sources of the current fed to the intracellular and extracellular media, respectively; \( n \) is a normal vector the cell membrane.

The transmembrane current can be represented as a sum of the capacitive current proportional to the rate of change of the transmembrane potential and the current \( I_{ion} \) due to the motion of ions through the membrane:
\[ I_m = C_m \frac{dV_m}{dt} + I_{ion}(V_m, r). \quad (5) \]

Here, \( C_m \) is the capacitance of the cell membrane; \( r \) is the vector of internal variables whose change with time \( t \) is described by a system of differential equations in the form
\[ \frac{\partial r}{\partial t} - R(V_m, r) = 0. \quad (6) \]

If the conductivity tensors of the intracellular and extracellular spaces are assumed to be similar,
\[ D_e = \Lambda D_i, \quad (7) \]
then the cardiac muscle model is simplified considerably and transforms to
\[ \nabla \cdot (D_m \nabla V_m) = \chi I_m + \chi I_{ts} + I_{is} \quad (8) \]
under the boundary conditions
\[ n \cdot (D_m \nabla V_m) = 0. \quad (9) \]

This model is called the monodomain one; here, \( D_m = (\Lambda/(1 + \Lambda)) D_i \) is its reduced conductivity tensor.

In the case of an isotropic medium, for which the similarity condition for the extra- and intracellular spaces is fulfilled automatically, the results obtained with the bidomain and monodomain models coincide exactly. As regards the anisotropic cardiac tissue models, for them, with the proper choice of parameters, the results describing the propagation of an excitation wave differ insignificantly [18]. In this paper the conductivities of the monodomain model in the material axes will be calculated, according to [18], as a harmonic mean of the corresponding intracellular and extracellular conductivities:
\[ \sigma_m = \sigma_i \sigma_e / (\sigma_i + \sigma_e). \quad (10) \]

However, the bidomain model becomes necessary in those cases when the process of excitation from external factors itself is taken into account and/or when a comparison with the actually measured extracellular potential is required [19]. An overview of such problems can be found in [20, 21]. One of the striking examples in which the bidomain model manifests itself is the formation of virtual electrodes [22]. It turns out that when an electric current is fed to the myocardium, depolarization and hyperpolarization regions can be formed in a small region around the electrode. Their appearance, on the one hand, can lead to the excitation of scroll waves [23] and, on the other hand, can be used in defibrillation [24, 25].

Characteristically, virtual electrodes appear only in the case when the similarity condition (7) is not fulfilled. In this case, it is necessary to solve the complete system (1)–(6) to investigate the excitation development process. However, at a low exciting current strength, to determine the original configuration of virtual electrodes, it will suffice to solve a linearized static bidomain problem:
\[ \nabla \cdot (D_i \nabla V^m) + \nabla \cdot (D_e \nabla V_e) = \chi G_0 \nabla V^m + \chi I_{ts} + I_{is}, \quad (11) \]
\[ \nabla \cdot ((D_i + D_e) \nabla V_e) + \nabla \cdot (D_e \nabla V^m) = I_{is} + I_{es}. \quad (12) \]

Here, \( V^m = V_m - V_{rest} \) is the deviation of the transmembrane potential from the rest potential; \( G_0 = (\partial I_{ion}/\partial V_m)|_{V=V_{rest}} \) is the membrane conductivity linearized in the vicinity of the rest potential.
If relation (7) holds, then the problem (11), (12) becomes degenerate:

$$\nabla \cdot \left( D_m \nabla V_m \right) = \chi G_0 V_m + \chi I_{ns} + \left( \frac{\Lambda}{1 + \Lambda} \right) I_{ns} - \left( \frac{1}{1 + \Lambda} \right) I_{ex}.$$  \hspace{1cm} (13)

Equation (13) does not show the appearance of virtual electrodes, but it has an analytical solution [26] and can be used to check the adequacy of finite-element codes.

3. THE CONDUCTIVITY OF A DEFORMED MYOCARDIUM

The derivation of macroscopic conductivities was based on the microstructural model [10]. In this paper the cardiac tissue was considered as a periodic lattice, where the cells were rectangular prisms filled with an isotropic conducting medium and the conductivity of the gap junctions was taken into account through the boundary conditions on the sides of these prisms (Fig. 1). It was assumed that the cells were adjacent to one another along the fiber and there were gaps between them in the transverse directions. The intracellular conductivities along and across the fiber were expressed via the cell sizes, lattice periodicity parameters, and electric properties of the myoplasm and gap junctions by the homogenization method and by calculating the total current through the periodic structure.

In [10] it was also shown that the extracellular conductivity depends weakly on the linear cell sizes themselves and is determined mainly by the ratio of the cell sizes to the corresponding structure periodicity parameters (i.e., the fraction of the extracellular space). Therefore, the extracellular conductivity is expected to be weakly determined by the deformation.

If the deformation in the material axes is extension–contraction, then the dependence of the macroscopic conductivities on deformation can be derived using simple generalizations of the model, in which the layered structure is taken into account: different conductivities of the gap junctions, cell sizes, and periodicity parameters in two transverse directions. The following assumptions are made when deriving the dependence of the conductivities on deformation in this case:

— the cytoplasm is an isotropic electrolyte with a deformation-independent conductivity \( \sigma_c \);
— the conductivities of the gap junctions are constant;
— the deformations of the cell, the extracellular space, and the medium are identical.

Applying the homogenization method to these equations (by analogy with [10]) and calculating the total electric current through the periodic structure along the material axes \( x_1 \), \( x_2 \), and \( x_3 \) lead to the following relations for the macroscopic conductivities in the corresponding directions:

$$\sigma_1 = \sigma_c \frac{w_{c2} w_{c3}}{w_{p2} w_{p3}} \left( 1 - \frac{1}{1 + \kappa_1} \right), \quad \sigma_2 = \sigma_c \frac{w_{c3}}{w_{p3}} \left( 1 - \frac{1}{1 + h_{c2} \kappa_2} \right), \quad \sigma_3 = \sigma_c \frac{w_{c2}}{w_{p2}} \left( 1 - \frac{1}{1 + h_{c3} \kappa_3} \right).$$  \hspace{1cm} (14)

Here, \( h_{c2} = w_{c2}/l \); \( h_{c3} = w_{c3}/l \); \( \kappa_1 = (g_1)/(\sigma_c w_{c2} w_{c3}) \); \( \kappa_2 = g_2/(\sigma_c w_{c3}) \); \( \kappa_3 = g_3/(\sigma_c w_{c2}) \); \( l \) is the cell length; \( w_{c2}, w_{c3} \) are the transverse cell sizes; \( w_{p2}, w_{p3} \) are the lattice periodicity parameters; \( g_1, g_2, g_3 \) are the total conductivities of the gap junctions on the corresponding sides of the cell-simulating prisms.

Having substituted the cell sizes that changed in the deformation process into relations (14):

$$l = L \lambda_1, \quad w_{c2} = W_{c2} \lambda_2, \quad w_{c3} = W_{c3} \lambda_3,$$  \hspace{1cm} (15)
where \( L, W, W \) are the original sizes, \( \lambda_1, \lambda_2, \lambda_3 \) are the tissue extensions in the material axes, we obtain the sought-for dependences of the macroscopic conductivities:

\[
\frac{1}{\sigma_1} = \left( \frac{1}{\sigma_{c1}} + \frac{\lambda_1\lambda_3}{\sigma_{g1}\lambda_1} \right), \quad \frac{1}{\sigma_2} = \left( \frac{1}{\sigma_{c2}} + \frac{\lambda_1\lambda_2}{\sigma_{g2}\lambda_2} \right), \quad \frac{1}{\sigma_3} = \left( \frac{1}{\sigma_{c3}} + \frac{\lambda_1\lambda_2}{\sigma_{g3}\lambda_3} \right) .
\]

(16)

Here, \( \sigma_{gj} \) are the conductivities of the gap junctions and \( \sigma_{gj}^0 \) are their values in the undeformed state.

In the more general case when the principal deformation axes are not aligned with the material axes associated with the fibrous-layered structure of the myocardium, there are shears relative to the material axes in the myocardium. As a result, the periodic structure that was rectangular in the undeformed state becomes skew-angular under deformation (Fig. 2). The normals in the reference \((N)\) and current \((n)\) configurations are related as \( N = T \cdot n \) (Nanson’s formula); the corresponding conductivities of the gap junctions reduced to the surface are related as \( \sigma = \sigma^\ast \). Here, \( \mathbf{J} \) is the deformation gradient tensor.

Hence, the conductivity equations for the periodic structure will be written as [12]

\[
-\sigma_1 \nabla \varphi^{i,j,k} (l, x_1, x_2, x_3) \cdot n_1 = \gamma_1 (\varphi^{i,j,k} (l, x_1, x_2, x_3) - \varphi^{i+1,j,k} (0, x_1, x_2, x_3)),
\]

(17)

\[
-\sigma_2 \nabla \varphi^{i,j,k} (x_1, w_2, x_3) \cdot n_2 = \gamma_2 (\varphi^{i,j,k} (x_1, w_2, x_3) - \varphi^{i,j+1,k} (x_1, 0, x_3)),
\]

(18)

\[
-\sigma_3 \nabla \varphi^{i,j,k} (x_1, x_2, w_3) \cdot n_3 = \gamma_3 (\varphi^{i,j,k} (x_1, x_2, w_3) - \varphi^{i,j,k+1} (x_1, x_2, 0)),
\]

(19)

\[
(\nabla \varphi^{i,j,k} (l, x_1, x_2, x_3) - \nabla \varphi^{i+1,j,k} (0, x_1, x_2, x_3)) \cdot n_1 = 0,
\]

(20)

\[
(\nabla \varphi^{i,j,k} (x_1, w_2, x_3) - \nabla \varphi^{i,j+1,k} (x_1, 0, x_3)) \cdot n_2 = 0,
\]

(21)

\[
(\nabla \varphi^{i,j,k} (x_1, x_2, w_3) - \nabla \varphi^{i,j,k+1} (x_1, x_2, 0)) \cdot n_3 = 0,
\]

(22)

where \( \varphi^{i,j,k} \) is the intracellular potential of a \((i, j)\) cell on layer \( k \).

Substituting Nanson’s formula and the relations for the conductivities of the gap junctions in the undeformed and deformed states into (17)–(22) and applying the homogenization method in the form proposed in [11], we can derive a formula to calculate the macroscopic conductivity tensor [12]:

\[
d_{jk} = \frac{\sigma V_c}{V_p} \left( \delta_{jk} + F_{jk}^{-1} M^{-1} F_{jk}^{-1} \right),
\]

(23)

where \( V_c \) is the cell volume, \( V_p \) is the periodicity cell volume, \( \delta_{jk} \) is the Kronecker delta,

\[
M = \begin{pmatrix}
-C_{11}^{-1} - \tilde{k}_1 & -C_{12}^{-1} - C_{13}^{-1} \\
-C_{21}^{-1} - C_{22}^{-1} - \tilde{k}_2 & -C_{23}^{-1} \\
-C_{31}^{-1} & -C_{32}^{-1} - C_{33}^{-1} - \tilde{k}_3
\end{pmatrix}.
\]

(24)
Here, \( \kappa_i = (\Gamma_i I)/(\sigma_i J) \); \( \kappa_i = \kappa_i \), \( \kappa_2 = h_2 \kappa_2 \), \( \kappa_3 = h_3 \kappa_3 \); \( C \) is the Cauchy–Green deformation tensor. In Eq. (24) \( C^{-1}_{ij} \) denotes the \( ij \)-the component of the tensor \( C^{-1} \) rather than the reciprocal of \( C_{ij} \).

The macroscopic conductivity tensor can be represented in matrix form as the inverse of the sum of the inverse conductivity tensors for the cytoplasm and gap junctions:

\[
d^{-1} = \beta (d^{-1}_c + d^{-1}_g),
\]

(25)

where

\[
d_c = \sigma_c I,
\]

(26)

\[
d_g = \sigma_g F d_g F^T
\]

(27)

are the reduced conductivity tensors of the cytoplasm and gap junctions, \( d_g \) is the conductivity tensor of the gap junctions in the undeformed state.

Relations (23)–(27) were derived under the assumption of myoplasm conductivity isotropy. The myocardium conductivity anisotropy in this case is a result of only the resistance of the gap junctions. However, owing to the internal structure of the cell containing parallel filamentary structures, myofibrils, the effective conductivity of the myoplasm itself can be anisotropic. The model under consideration can be generalized to include the myoplasm anisotropy if (23) is replaced by the expression

\[
d_c = \overline{R} d^0 \overline{R}^T.
\]

Here, \( d^0 \) is the cytoplasm conductivity tensor in the initial axes and \( \overline{R} \) is the rotation matrix of the anisotropy axes.

The derivation of the dependence of the conductivity on deformation is described in detail in [12, 13].

\section*{4. STRETCH-ACTIVATED CHANNELS}

When the myocardium is deformed, transmembrane channels can be activated in it and, as a consequence, additional sources of electric excitation can appear, which can induce a cardiac arrhythmia. There are a large number of channels that vary in mechanisms of load transfer to them from the tissue and response to the load. The currently developed models take into account the spatial pattern of deformation insufficiently well. In them, as a rule, the activation of channels depends on the extension along the fiber, which is not obvious for the stretch-activated channels located on the muscle cell membrane.

The stretch-activated current \( I_{SAC} \) is calculated as a product of the stretch-dependent activation function \( \lambda (\lambda) \), the conductivity of stretch-activated channels \( G_{SAC} \), and the difference between the transmembrane potential \( V \) and the reversal potential \( V_r \) [16]:

\[
I_{SAC} = \lambda (\lambda) G_{SAC} (V - V_r).
\]

(28)

The values of \( G_{SAC} \) and \( V_r \) are individual for each type of channel. The activation function has a range of values from zero to one and, in the case of contraction, is equal to zero. The general form of this function is shown in Fig. 3 and below we give an example of its writing:

\[
\lambda (\lambda) = \frac{1}{1 + \exp\left(-\alpha (\lambda - \lambda_m)\right)},
\]

where \( \alpha \) and \( \lambda_m \) are empirical parameters.

When the cell is deformed along the fibers, all of the channels located on its lateral surface are in equal conditions; under an arbitrary deformation this is not the case. In this paper we investigate the possibility of generalizing the potential (28) for a complex deformation under the following assumptions:

— the channels are uniformly distributed over the lateral cell surface;
— the channels respond to a local increase in membrane patch area [17, 18];
— the formula in which the extension along the fiber is used is valid for one-dimensional stretch along the fiber.

Consider a fragment of the muscle cell in the material axes represented as a cylinder oriented along the fiber (Fig. 4). Here, the \( a \) axis is directed along the fiber, the \( b \) axis is in a plane tangential to the muscle
layer perpendicular to the fiber, and the $c$ axis is perpendicular to the layer. The normal $\mathbf{N}$ at an arbitrary point of the lateral cylindrical surface of the muscle fiber is then expressed as

$$\mathbf{N} = \mathbf{e}_b \cos \theta + \mathbf{e}_c \sin \theta.$$  \hfill (29)

Here, $\mathbf{e}_b, \mathbf{e}_c$ are the unit vectors of the $b$ and $c$ axes; $\theta$ is the angle between the normal and $\mathbf{e}_b$.

The local change in membrane area can be determined using Nanson’s formula:

$$J_A = \frac{da}{dA} = \left\|F^{-T} \cdot \mathbf{N}\right\|_2 = J\sqrt{\mathbf{N} \cdot F^{-T} \cdot F^{-T} \cdot \mathbf{N}} = J\sqrt{\mathbf{N} \cdot \mathbf{C}^{-1} \cdot \mathbf{N}}.$$  \hfill (30)

Substituting (29) into (30), we obtain the dependence of the local change in membrane area on the components of the Cauchy–Green deformation tensor in the $a$, $b$, and $c$ axes:

$$J_A = \frac{da}{dA} = J\sqrt{C_{bb}^{-1} \cos^2 \theta + C_{cc}^{-1} \sin^2 \theta + 2C_{bc}^{-1} \cos \theta \sin \theta} = \sqrt{\left|C_{bb}\right| \cos^2 \theta + \left|C_{cc}\right| \sin^2 \theta + 2\left|C_{bc}\right| \cos \theta \sin \theta}$$  \hfill (31)

$$= \sqrt{(C_{aa}C_{cc} - C_{ac}^2) \cos^2 \theta + (C_{aa}C_{bb} - C_{ab}^2) \sin^2 \theta + 2(C_{ab}C_{ac} - C_{aa}C_{bc}) \cos \theta \sin \theta}.$$

Here, $x = a, b, c; y = a, b, c; C_{xy}$ and $C_{xy}^{-1}$ are the components of the tensors $\mathbf{C}$ and $\mathbf{C}^{-1}$ in the material axes; $|C|_{xy}$ are the corresponding algebraic complements of the tensor matrix $\mathbf{C}$.

Consider a uniaxial extension $\lambda$ along the fiber: $\lambda_a = \lambda$, $\lambda_b = \lambda_c = \lambda^{-0.5}$. In this case, the Cauchy–Green deformation tensor is

$$\mathbf{C} = \begin{pmatrix} \lambda_a^2 & 0 & 0 \\ 0 & \lambda_b^2 & 0 \\ 0 & 0 & \lambda_c^2 \end{pmatrix} = \begin{pmatrix} \lambda^2 & 0 & 0 \\ 0 & \lambda^{-1} & 0 \\ 0 & 0 & \lambda^{-1} \end{pmatrix}.$$
while the local change in membrane area is constant and equal to

$$J_\lambda = \frac{da}{dA} = \sqrt{\lambda^2 \lambda^{-1} \cos^2 \theta + \lambda^2 \lambda^{-1} \sin^2 \theta} = \lambda^{0.5}. \quad (32)$$

Thus, in (28) we can replace $L(\lambda)$ by $L(J_\lambda^2)$.

Under an arbitrary deformation the local change in membrane area $J_\lambda$ depends on the coordinate $\theta$. Then, instead of (28) we should use the formula that is the result of averaging $L(J_\lambda^2)$ over the angular coordinate $\theta$:

$$I_{SAC} = \bar{L}(C) G_{SAC}(V - V_r), \quad (33)$$

where

$$\bar{L}(C) = \frac{1}{2\pi} \int_0^{2\pi} L(J_\lambda^2(C, \theta)) d\theta, \quad (34)$$

and $J_\lambda(C, \theta)$ is calculated according to (31). As $L(J_\lambda^2)$ we use the function $L(\lambda)$ from (28).

5. RESULTS

For a uniaxial extension we compared the results obtained with our model and the model proposed in [9]. Figure 5 shows the change in parameter $q$—the ratio of the longitudinal intracellular conductivity when stretched along the fiber to the longitudinal intracellular conductivity of an undeformed myocardium. We see that both models agree well for extensions in the range from 0.8 to 1.2 (in the region highlighted in the figure by the gray color). For the transverse conductivity there is a dominance of gap junctions.

We investigated the propagation of an excitation wave in a rectangular region for an extension $\lambda = 1.4$ along the horizontal axis corresponding to the fiber direction. The source of initial excitation was in the middle of the left boundary of the rectangular region. In the problem we solved the monodomain system (6), (8) under the boundary conditions (9) using a numerical algorithm based on the splitting method [1] and implemented in software based on the finite-element

FEniCS library [27]. The results are shown in Table 1, where the ratios of the conductivities of deformed and undeformed cardiac tissues are given, and in Fig. 6. The effect of deformation turns out to be strongly “diluted” by the extracellular conductivity. For this reason, the simulation results presented in Fig. 6 demonstrate slight differences.

The next example illustrates subtler effects. We considered the emergence of depolarization and hyperpolarization regions (the formation of virtual electrodes) under point cathode excitation of the extracellular medium in a two-dimensional rectangular region. This phenomenon takes place in the case when the similarity condition (7) is not fulfilled, which is typical of the real myocardium. The extracellular conduc-
activity tensor is close to the spherical one, while the components of the intracellular conductivity tensor can differ by an order of magnitude. The parameter from [28], which is equal to zero provided that the intracellular (index $i$) and extracellular (index $e$) conductivity tensors of the two media are similar, can be used as a measure of the deviation of these tensors for two-dimensional problems:

$$
\varepsilon = 1 - \frac{\sigma_{ex}/\sigma_{ey}}{\sigma_{ix}/\sigma_{iy}}.
$$

An exact solution of this problem can be obtained only when the extra- and intracellular conductivity tensors are similar, i.e., in the absence of virtual electrodes [29]. As a consequence, an approximate solution [8] was used to estimate the effect of deformation on the configuration of virtual electrodes. The values of the parameter $\varepsilon$ calculated for various dependences of the conductivity on deformation are given in Table 2. The corresponding configurations of virtual electrodes are shown in Fig. 7. The effect of deformation in the presence of virtual electrodes turns out to be more significant.

We also considered the emergence of stretch-activated currents under uniaxial extension $\lambda$ across the fiber (along the $b$ axis). In this case, the Cauchy–Green deformation tensor is

$$
\mathbf{C} = \begin{pmatrix}
\lambda^{-1} & 0 & 0 \\
0 & \lambda^2 & 0 \\
0 & 0 & \lambda^{-1}
\end{pmatrix},
$$

while the local change in membrane area, according to (48), is

$$
J_{a}^2(\theta) = \lambda^{-1}\lambda^{-1} \cos^2 \theta + \lambda^{-1}\lambda^{-1} \sin^2 \theta = \lambda^{-2} \cos^2 \theta + \lambda \sin^2 \theta.
$$

Figure 8 shows the distributions of the local change in intercellular membrane area and the corresponding activation function of the form presented in Fig. 3 in angular coordinate. Much of the membrane is seen to be in a state of contraction and, therefore, most of the channels are not activated. In this case, the Cauchy–Green deformation tensor is

$$
\mathbf{C} = \begin{pmatrix}
\lambda^{-1} & 0 & 0 \\
0 & \lambda^2 & 0 \\
0 & 0 & \lambda^{-1}
\end{pmatrix},
$$

while the local change in membrane area, according to (48), is

$$
J_{a}^2(\theta) = \lambda^{-1}\lambda^{-1} \cos^2 \theta + \lambda^{-1}\lambda^{-1} \sin^2 \theta = \lambda^{-2} \cos^2 \theta + \lambda \sin^2 \theta.
$$

Table 1. Longitudinal conductivity under deformation

| Model          | Type of conductivity | intracellular | reduced according to monodomain model |
|----------------|----------------------|---------------|--------------------------------------|
| Grid of resistors | 1.96                | 1.24          |                                      |
| Our model      | 1.24                | 1.09          |                                      |

Table 2. Change in the parameter of deviation from similarity under deformation

| Quasi-fluid  | Grid of resistors | Our model   |
|--------------|-------------------|-------------|
| 0.596        | 0.853             | 0.768       |

Fig. 6. Propagation of an excitation wave in a rectangular region filled with an excitable medium as a quasi-fluid (a), a grid of resistors (b), and according to our model (c).
case, the ratio of the stretch-activated currents $I_{\text{SAC},b}$ and $I_{\text{SAC},a}$ when stretched across and along the fiber is

$$r = \frac{I_{\text{SAC},b}}{I_{\text{SAC},a}} = \frac{\tilde{L}_b}{\tilde{L}_a} = 0.3531.$$  

Here, $\tilde{L}_a$ and $\tilde{L}_b$ are the values of $\tilde{L}(\mathbf{C})$ when the myocardium is stretched along and across the fibers, respectively.

6. CONCLUSIONS

The following types of mechanoelectric feedback were identified: a change in myocardial conductivity and the appearance of additional transmembrane currents (stretch-activated ion channels).

The intracellular conductivity tensor can be represented as the inverse of the sum of the inverse conductivity tensors for the cytoplasm and gap junctions. When investigating the propagation of an excitation wave, the effect of deformation turns out to be strongly “diluted” by the extracellular conductivity. When investigating subtler effects, such as, for example, the formation of virtual electrodes (when the extracellular and intracellular media act more individually), the effect of deformation is stronger.

We constructed a channel activation model in conditions of complex deformation under the following assumptions: the channels are uniformly distributed over the cell surface; the channels respond to a local increase in intercellular membrane patch area; the formula in which the extension along the fiber is used is valid for a uniaxial extension along the fiber. This model allows the activation of channels to be considered not only when stretched along the fiber, but also in an arbitrary direction.

A more detailed simulation of the connection between the mechanical and electric processes makes it possible to go more deeply into the causes of cardiac arrhythmias and contributes to the timely prevention and treatment of these dangerous states for the human.
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