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SIMPLE MODEL OF THE SMOOTH MUSCLE ISOTONIC CONTRACTION AS A DYNAMICAL SYSTEM

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Summary: *The paper discusses a mathematical model of the isotonic smooth muscle contraction considering the influence of the excitation processes on the sarcolemma and inside the muscle cell.*
The discussed model is based on the approach published in Rosenberg and Svobodová (2010) where the muscle fibre model containing the term corresponding to the state of ATP hydrolysis was proposed. ATP hydrolysis is the main source of muscle energy. This term is considered in the study to be proportional to the intracellular Ca^{2+} concentration, its sigmoidal function respectively. A lot of models of the intracellular Ca^{2+} concentration time evolution have been published. The model introduced in Keener and Sneyd (1998) was chosen.
The model has the form of the dynamical system with 6 DOFs. Its basic dynamical analysis was done. The results from the numerical simulation are consistant with the published experimental results. The periodic solution of the model corresponds in some specific cases to the myogenic vascular response known in medicin.
The advantage of the discussed approach is the natural integration of the active and passive components of the muscle tissue into the model. The model facilitates also the integration of the other sophicticated muscle cell models.

1. Introduction

Many tissues of human and animal organs contain smooth muscles (SMs). Important differences exist between the basic types of muscles and smooth muscles in different organs. Nevertheless, the own biological motor - the actin-myosin sliding mechanism actuated by ATP hydrolysis - is same for all muscle types (smooth, straited and cardiac).

- The regulation of the SM contraction occurs due to the calcium-regulated phosphorylation of myosin rather than the calcium-activated troponin system by the cardiac and straited muscle. The main control parameter is the concentration of the intracellular Ca^{2+}.

- Calcium ionts bind calmodulin. This complex binds myosin light chain kinase (MLCK) and forms an enzyme *Ca-calmodulin-MLCK-complex*. The active enzyme phosphorylates myosin light chain of each myosin head requiring one molecule of ATP.

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- Myosin light chain phosphatase (phosphatase C) is an enzyme that removes a phosphate group from the myosin light chain by active MLCK.
- This phosphate group activates myosin to create the cross-bridges.
- The fast cross-bridges cycling requires further ATP. ATP hydrolysis causes the stractural changes of myosin part and leads to the cross-bridge detachment. The ATPase activity depends on the MLCK-Phosphatase C ratio.
- ATP activity decreases with the MLCK decrease - myosin dephosphorylation - and the cross-bridge release is more difficult. The attached dephosphorylayted cross-bridges lead to the development of the latch state.

Remark: ATP is needed twice during the SM contraction - for myosin phosphorylation and croos-bridge cycling.

The main control parameter of the relative actin-myosin movement is the Ca^{2+} concentration in cytoplasm. The process of the Ca^{2+} influx and outflux in and out of the muscle cell is in generall following (see e.g. Keener and Sneyd (1998)).

- Ca^{2+} inflow from the extracellular medium through
  - voltage-controlled L-type channels - depolarization of the membrane,
  - receptor-operated channels - binding of the external ligand,
  - second-messenger-operated channels - binding of the cellular second messenger,
  - mechanically operated channels - mechanical stimulation.

It should be mentioned that other membrane channels not described here exist.

- Ca^{2+} release from the internal stores (endoplasmic reticulum (ER) or sarcoplasmic reticulum (SR)) regulated by two channels (receptors)
  - ryanodine receptor - calcium-induced calcium release from SR,
  - inositol/triphosphate (IP_3) receptor "*Binding of an extracellular agonist to the receptor in the surface membrane causes the diffusion of* IP_3 *through the membrane.* IP_3 *binds to and activates the* IP_3 *receptors on the ER. The calcium channel opens.*",
  - Ca^{2+} outflow driven by Ca^{2+} pumping out of a cell "*The energy stored in ATP or also the energy of* Na^+ *electromechanical gradient is used. The* Ca^{2+} *concentration in the cytoplasm is lower than the extracellular concentration.*",
  - Ca^{2+} outflow driven by pumping into the internal membrane-bound compartments (e.g. ER or SR) "*The energy stored in ATP or also the energy of* Na^+ *electromechanical gradient is used. The* Ca^{2+} *concentration in the cytoplasm is lower than the concentration inside the internal compartments.*".

Remark: All these ways of Ca^{2+} influx and outflux on the outer cell and internal membranes can create the oscillators - the membrane and intracellular oscillators - which can interface (see Parthimos et al. (1999)). Depending on the type of SM cell the key element for its activation is either the membrane depolarization or the periodic release of Ca^{2+} from the internal stores. The mathematical model of the mentioned processes is shown later.

2. Mechanochemical coupling

Till now the electro-chemical processes only leading to the own SM cell contraction process have been discussed. The own contraction of SM cell is connected also with the mechanical response of other passive tissue components. A lot of diverse models describing the pathway from the processes on the cell level into the macro-effects - like total force in the isometric case or the muscle contraction in the isotonic case - were published.

The growth and remodelling theory of DiCarlo and Quiligotti (2002) together with the laws of irreversible thermodynamics with internal variables (IVT) were used in Rosenberg and Svobodová (2010) to suggest a model of mechanochemical coupling during the SM fibre contraction. Short overview only and the results of the approach are mentioned as follows.

The starting point is an initial configuration $\mathcal{B}_0$ that *growths* and *remodels*, i.e. changes its volume (*growth*), form and anisotropy (*geometrical remodelling*) or material parameters (*material remodelling*). This process is expressed in DiCarlo and Quiligotti (2002) by the tensor $\mathbf{P}$ (further *growth tensor*) that relates the initial configuration to the relaxed one $\mathcal{B}_r$ with zero inner stress. To the real configuration $\mathcal{B}_t$, where the inner stress invoked by growth, geometrical remodelling and external loading can exist, it is related by the deformation tensor $\mathbf{F}$.

The small deformations only are taken into account, the Lagrangian and Eulerian approach is not distinguished. The deformation gradient between configurations $\mathcal{B}_0$ and $\mathcal{B}_t$ can be written as

$$\nabla \boldsymbol{p} = \mathbf{F}\mathbf{P}. \tag{1}$$

Let the velocity of continuum $\boldsymbol{v} = \nabla \dot{\boldsymbol{p}}$ ($\boldsymbol{p}$ is the placement - the mapping between initial and current configurations) and the velocity of growth $\boldsymbol{V} = \dot{\mathbf{P}}\mathbf{P}^{-1}$ be considered.

Further the isothermic case, the existence of chemical reactions and the mass flux are assumed. Taking into account the IVT approach, see Lebon et al. (2008), comparing it with the approach of DiCarlo and Quiligotti (2002), renaming the state and internal variables $\boldsymbol{a} = [\mathbf{F}, \mathbf{P}]$, $\boldsymbol{\xi} \approx \mathbf{K}$, the first law of thermodynamics has the form

$$\dot{f} = \boldsymbol{\tau}_e \cdot \nabla \boldsymbol{v} + \mathbf{C}_e \cdot \mathbf{V} - \mathbf{A} \cdot \dot{\mathbf{K}} - \boldsymbol{\mathcal{A}}_{chem} \cdot \dot{\boldsymbol{Y}}, \tag{2}$$

where $\boldsymbol{\tau}_e$ is the Cauchy stress tensor, $\mathbf{C}_e$ is the generalised external remodelling force. $\mathbf{A}$ is the affinity (or configurational or Eshelby force) conjugate to $\mathbf{K}$ and $\boldsymbol{\mathcal{A}}_{chem} \cdot \dot{\boldsymbol{Y}}$ is the product of the chemical reaction affinity with its rate.

It is supposed that the free energy related to the relaxed configuration f_r depends on $\mathbf{F}, \mathbf{K}, \boldsymbol{Y}$ only. In the initial configuration is then

$$f(\mathbf{F}, \mathbf{P}, \mathbf{K}, \boldsymbol{Y}) = J f_r(\mathbf{F}, \mathbf{K}, \boldsymbol{Y}), \tag{3}$$

where $J = \det\mathbf{P}$. After certain steps described in Rosenberg and Svobodová (2010) is obtained *the first set of constitutive equations*

$$\boldsymbol{\sigma}_e = J\frac{\partial f_r}{\partial \mathbf{F}};\ \mathbf{A} = -J\frac{\partial f_r}{\partial \mathbf{K}};\ \boldsymbol{\mathcal{A}}_{chem} = -J\frac{\partial f_r}{\partial \boldsymbol{Y}};\ Jf_r\mathbf{I} = \boldsymbol{\sigma}_e\mathbf{F} + \mathbf{C}_e, \tag{4}$$

where $\boldsymbol{\sigma}_e = \boldsymbol{\tau}_e\mathbf{P}^{\mathrm{T}}$ is the first Piola-Kirchhoff stress tensor (elastic).

The second law of thermodynamics has the form

$$\dot{f} \leq \boldsymbol{\tau}\cdot\nabla\boldsymbol{v} + \mathbf{C}\cdot\mathbf{V} - \boldsymbol{J}\cdot\nabla(\Delta\bar{\mu}), \tag{5}$$

where $\boldsymbol{J}$ represents the mass flux and $\Delta\bar{\mu}$ is the difference of the chemical potentials. Inserting the first set of constitutive equations (4), considering $\dot{f} = J(\frac{\partial f_r}{\partial \mathbf{F}}\cdot\dot{\mathbf{F}} + \frac{\partial f_r}{\partial \mathbf{K}}\cdot\dot{\mathbf{K}} + \frac{\partial f_r}{\partial \boldsymbol{Y}}\cdot\dot{\boldsymbol{Y}} + f_r\mathbf{I}\cdot\mathbf{V})$, *the second law of thermodynamics* is obtained after certain steps as follows

$$(\boldsymbol{\sigma} - \boldsymbol{\sigma}_e)\cdot\dot{\mathbf{F}} + (\mathbf{C} - Jf_r\mathbf{I} + \boldsymbol{\sigma}\mathbf{F})\cdot\mathbf{V} + \boldsymbol{\mathcal{A}}_{chem}\cdot\dot{\boldsymbol{Y}} + \mathbf{A}\cdot\dot{\mathbf{K}} - \boldsymbol{J}\cdot\nabla(\Delta\bar{\mu}) \geq 0. \tag{6}$$

The term in brackets can be written in the form

$$(\mathbf{C} - Jf_r\mathbf{I} + \boldsymbol{\sigma}\mathbf{F}) = \mathbf{C} - \mathbf{E} \quad \text{where} \quad \mathbf{E} = Jf_r\mathbf{I} - \boldsymbol{\sigma}\mathbf{F} \tag{7}$$

and $(\boldsymbol{\sigma} - \boldsymbol{\sigma}_e) = \boldsymbol{\sigma}_{dis}$ represents the dissipation part of the stress tensor.

The second set of constitutive equations - the evolution equations - can be obtained from (6) according to the linear phenomenological relations using the Onsager's coefficients $L_{\alpha\beta}$ which should satisfy the corresponding inequalities,

$$\begin{aligned}
\boldsymbol{\sigma}_{dis} &= L_{\sigma F}\dot{\mathbf{F}} + L_{\sigma E}(\mathbf{C}-\mathbf{E}) + L_{\sigma\mathcal{A}}\boldsymbol{\mathcal{A}}_{chem} + L_{\sigma A}\mathbf{A} - L_{\sigma\mu}\nabla(\Delta\bar{\mu}),\\
\mathbf{V} &= L_{VF}\dot{\mathbf{F}} + L_{VE}(\mathbf{C}-\mathbf{E}) + L_{V\mathcal{A}}\boldsymbol{\mathcal{A}}_{chem} + L_{VA}\mathbf{A} - L_{V\mu}\nabla(\Delta\bar{\mu}),\\
\dot{\boldsymbol{Y}} &= L_{YF}\dot{\mathbf{F}} + L_{YE}(\mathbf{C}-\mathbf{E}) + L_{Y\mathcal{A}}\boldsymbol{\mathcal{A}}_{chem} + L_{YA}\mathbf{A} - L_{Y\mu}\nabla(\Delta\bar{\mu}),\\
\dot{\mathbf{K}} &= L_{KF}\dot{\mathbf{F}} + L_{KE}(\mathbf{C}-\mathbf{E}) + L_{K\mathcal{A}}\boldsymbol{\mathcal{A}}_{chem} + L_{KA}\mathbf{A} - L_{K\mu}\nabla(\Delta\bar{\mu}),\\
\boldsymbol{J} &= L_{JF}\dot{\mathbf{F}} + L_{JE}(\mathbf{C}-\mathbf{E}) + L_{J\mathcal{A}}\boldsymbol{\mathcal{A}}_{chem} + L_{JA}\mathbf{A} - L_{J\mu}\nabla(\Delta\bar{\mu}).
\end{aligned} \tag{8}$$

These linear dependencies are only one simple possibility, nevertheless it offers a lot of diverse applications. Except the discussed possibility the others exist.

3. One dimensional model of a smooth muscle fibre - isotonic contraction

The structure of a smooth muscle fibre is very complicated comparing with a straited muscle fibre. Consequently one dimensional (1D) model only of the smooth muscle fibre is studied based on the previous equations. The model allows to test basic properties of the smooth muscle. The first validation of the model can be done according to the experimental results.

A lot of different mathematical models of the Ca^{2+} in/ and outflow exist. The precise models are described e.g. in Yang et al. (2003a), Yang et al. (2003b), Parthimos et al. (1999) and Parthimos et al. (2007). The relatively simple ryanodine receptor based model published in Keener and Sneyd (1998) is used at first as follows

$$
\begin{aligned}
\frac{dc}{dt} &= v_c[(k_f x_2 + g_1)(c_s - c) - \frac{p_1 c^2}{p_2^2 + c^2}] + g_2(c_e - c) - \frac{g_1 c^2}{g_2^2 + c^2} + J(t), \\
\frac{dc_s}{dt} &= -(k_f x_2 + g_1)(c_s - c) + \frac{p_1 c^2}{p_2^2 + c^2}, \\
\frac{dy}{dt} &= k_2(\frac{k_1 c}{k_{-1} + k_1 c})(1 - y) - k_{-2} y, \qquad (9) \\
\text{where} & \\
x_2 &= (\frac{k_1 c}{k_{-1} + k_1 c})(1 - y).
\end{aligned}
$$

Following conditions are assumed

- Ca^{2+} leaks into the cell from the cell outside at the rate $g_2(c_e - c)$, where c_e is the external Ca^{2+} concentration, c is the cytoplasmic Ca^{2+} concentration and g_2 is a constant.
- Ca^{2+} leaks into the cell from the SR at the rate $g_1(c_s - c)$, where c_s is the Ca^{2+} concentration in the SR.
- Ca^{2+} is pumped out of the cell at the rate $g_1 c^2/(c^2 + g_2^2)$.
- Ca^{2+} is pumped from the cytoplasm into the SR at the rate $p_1 c^2/(c^2 + p_2^2)$.
- The rate of Ca^{2+} release from the SR through ryanodine receptors is $k_f x_2(c_s - c)$.

The parameter dimensiones are as follows

$$
\begin{aligned}
[k_1] &= \mu\ M^{-1} s^{-1}, [k_{-1}] = [k_2] = [k_{-2}] = [k_f] = [g_1] = [g_2] = s^{-1}, \\
[p_1] &= [q_1] = \mu\ M\ s^{-1}, [c_e] = [q_2] = \mu\ M, [v_c] = 1.
\end{aligned}
$$

$J(t)$ is a flux that expresses the Ca^{2+} influx resulting from the opening of the voltage-gated channels in the sarcolemma. It is a square pulse lasting in the cardiac cell for the period $240ms$ and the amplitude determined the size of the initial $Ca2+$ stimulus.

Let the following dimensionless variables be introduced into (9)

$$
\tau = t\ k_{-1}, u = c/c_e, v = c_s/c_e, \qquad (10)
$$

the equation (9) has the form

$$
\begin{aligned}
\frac{du}{d\tau} &= [\alpha\frac{u}{\beta + u}(1 - y) + 1]\gamma(v - u) - \frac{v_c u^2}{\delta + \eta u^2} + \vartheta(1 - u) - \frac{u^2}{\kappa + \lambda u^2} + \mu(t), \\
\frac{dv}{d\tau} &= -\frac{1}{v_c}[\alpha\frac{u}{\beta + u}(1 - y) + 1]\gamma(v - u) + \frac{u^2}{\delta + \eta u^2}, \qquad (11) \\
\frac{dy}{d\tau} &= \nu\frac{u}{\beta + u}(1 - y) - \psi y,
\end{aligned}
$$

where

$$\begin{aligned}\alpha &= \frac{k_f}{g_1},\ \beta=\frac{k_{-1}}{k_1 c_e},\ \gamma=\frac{v_c g_1}{k_{-1}},\ \delta=\frac{{p_2}^2 k_{-1}}{p_1 c_e},\ \eta=\frac{c_e k_{-1}}{p_1},\\ \vartheta &= \frac{g_2}{k_{-1}},\ \kappa=\frac{{q_2}^2 k_{-1}}{q_1 c_e},\ \lambda=\frac{c_e k_{-1}}{q_1},\ \mu=\frac{J(t)}{c_e k_{-1}},\ \nu=\frac{k_2}{k_{-1}},\ \psi=\frac{k_{-2}}{k_{-1}}.\end{aligned} \tag{12}$$

Let now the muscle fibre be modelled as a 1D continuum of the initial length l_0. Its actual length after growth, remodelling and loading let be l. The relaxed length - after growth and remodelling - is then l_r. For the corresponding deformation gradients $\mathbf{P}=\gamma\mathbf{e}\otimes\mathbf{e}, \mathbf{F}=\varphi\mathbf{e}\otimes\mathbf{e}, \nabla p=\varepsilon\mathbf{e}\otimes\mathbf{e}$, where $\mathbf{e}$ is the unit vector in the muscle fibre direction, the following relations can be written

$$\gamma=\frac{l_r}{l_0},\quad \varphi=\frac{l}{l_r},\quad \varepsilon=\frac{l}{l_0}. \tag{13}$$

For small deformations ($J=1$), free energy has the simple form. It contains the term $\mathcal{A}_{chem}Y$ according to the relation (4)

$$f=f_r=\frac{1}{2}k(\varphi-1)^2+\mathcal{A}_{chem}Y. \tag{14}$$

Fung suggested another form of free energy for the living tissues

$$f=\frac{k}{\lambda}(e^{\frac{\lambda}{2}(\varphi-1)^2}-1)+\mathcal{A}_{chem}Y, \tag{15}$$

where for $\lambda\rightarrow 0$ the same result as in (14) is obtained. The equations (4), (8) have then the following form using the diagonal terms only for the uncoupled case

$$\sigma_e=\frac{\partial f}{\partial\varphi}, \tag{16}$$

$$\sigma_{dis}=h\dot{\varphi}, \tag{17}$$

$$C-E=g\dot{\gamma}\gamma^{-1}, E=f-\varphi\sigma, \tag{18}$$

$$\dot{Y}=L\mathcal{A}_{chem}, \tag{19}$$

$$\dot{k}=-m\frac{\partial f}{\partial k}. \tag{20}$$

Further in this study the new simpler notation of the Onsager's coefficients is introduced as follows $h\equiv L_{\sigma F}, g\equiv L_{VE}, L\equiv L_{Y\mathcal{A}}, m\equiv L_{KA}$ and $k\sim\mathbf{K}$ represents the stiffness as an internal variable. The equations (16)-(20) can be expressed after certain steps in the form

$$
\begin{aligned}
\dot{k} &= m[r - \frac{1}{2}(\frac{l}{l_r} - 1)^2], \\
\dot{l_r} &= \frac{l_r}{g}[\frac{l}{l_r}\tau - \frac{1}{2}k(\frac{l}{l_r} - 1)^2 - C], \\
\dot{l} &= \frac{l_r}{h}\{\tau - k(\frac{l}{l_r} - 1) + h\frac{l}{gl_r}[\frac{l}{l_r}\tau - \frac{1}{2}k(\frac{l}{l_r} - 1)^2 - C]\}.
\end{aligned} \tag{21}
$$

The equations (21) define the dynamical system expressed on the state space $\{l_r, l, k\}$. The parameter r in the first equation of (21) expresses the influence of the diffusion processes on the change of k ($-L_{K\mu}\nabla(\Delta\mu) = r$). Its importance for the whole system stability can be shown, see Rosenberg and Hynčík (2008).

If the dimensionless variables are introduced

$$
\begin{aligned}
k' &= k\sqrt{\frac{|m|}{g}},\ l'_r = \frac{l_r}{l_0},\ t' = \frac{t}{\sqrt{g|m|}}, \\
x &= \frac{l'}{l'_r},\ y = l'_r,\ z = k',\ \frac{l}{l_0} = x \cdot y,
\end{aligned} \tag{22}
$$

the following system of equations is obtained

$$
\begin{aligned}
\dot{x} &= \frac{g}{h}[\tau' - z(x - 1)], \\
\dot{y} &= y[x\tau' - \frac{1}{2}z(x - 1)^2 + C'], \\
\dot{z} &= \mathrm{sgn}m[r - \frac{1}{2}z(x - 1)^2],
\end{aligned} \tag{23}
$$

where

$$
C' = (C - \mathcal{A}_{chem}Y)\sqrt{(|m|/g)}, \tag{24}
$$

$$
\mathcal{A}_{chem}Y\sqrt{(|m|/g)} = p\frac{c^2}{c^2 + {x_0}^2}, \tag{25}
$$

$$
p = p_0 e^{s(\frac{l}{l_0} - \frac{l}{l_0}|_{opt})^2}, \tag{26}
$$

$$
C\sqrt{(|m|/g)} = C_t e^{q(\frac{l}{l_0} - \frac{l}{l_0}|_{opt})^2}. \tag{27}
$$

The notation $\frac{l}{l_0}|_{opt}$ is the optimal sarcomere prolongation with the maximal number of the attached cross-bridges. p_0, x_0, s, q, C_t are the control parameters.

The whole dynamical system representing the isotonic contraction of the smooth muscle fibre consists from the equations (9) and (21) or in the dimensionless form (11) and (23). The equations express the dynamical system with 6 DOFs. The stretch dependent channels can be taken into account and expressed by the parameter g_2 dependent on the stretch of the SM cell as follows

$$g_2 \rightarrow \frac{2g_2}{1+e^{-coup\ y\ (x-x_b)}}, \tag{28}$$

where $coup$ is the parameter describing the influence of the stretch on the flux of Ca^{2+}. If $coup = 0$ the uncoupled case occurs, as was shown previously. x_b is the value for which the influence of the stretch on the flux of Ca^{2+} is zero.

4. Dynamical analysis

The dynamical properties of the system (23) were studied in Rosenberg and Hynčík (2008). In this paper there is paid the attention to the evolution of the Ca^{2+} concentration. The equations (11) define the nonlinear dynamical system. The matrix $[a_{ij}]$ of the range 3×3 is constracted as the partial derivative of the equations (11) right sides according to the variables $\{u, v, y\}$ to analyse the dynamical system properties.

$$\begin{aligned}
a_{11} &= \frac{\alpha\gamma}{\beta+u}(1-y)[\frac{\beta(v-u)}{\beta+u} - u] - \gamma - \frac{2\delta v_c u}{(\delta+\gamma u^2)^2} - \vartheta - \frac{2\kappa u}{(\kappa+\lambda u^2)^2}, \\
a_{12} &= [\alpha\frac{u}{\beta+u}(1-y)+1]\gamma, \\
a_{13} &= -\alpha\gamma(v-u)\frac{u}{\beta+u}, \\
a_{21} &= -\frac{1}{v_c}\{\frac{\alpha\gamma}{\beta+u}(1-y)[\frac{\beta(v-u)}{\beta+u} - u] - \gamma - \frac{2\delta v_c u}{(\delta+\gamma u^2)^2}\}, \\
a_{22} &= -\frac{\gamma}{v_c}[\alpha\frac{u}{\beta+u}(1-y)+1], \\
a_{23} &= \frac{\alpha\gamma}{v_c}(v-u)\frac{u}{\beta+u}, \quad a_{31} = \nu\frac{\beta}{(\beta+u)^2}(1-y), \\
a_{32} &= 0, \quad a_{33} = -\nu\frac{u}{\beta+u} - \psi.
\end{aligned} \tag{29}$$

The results from the numerical simulation are shown as follows.

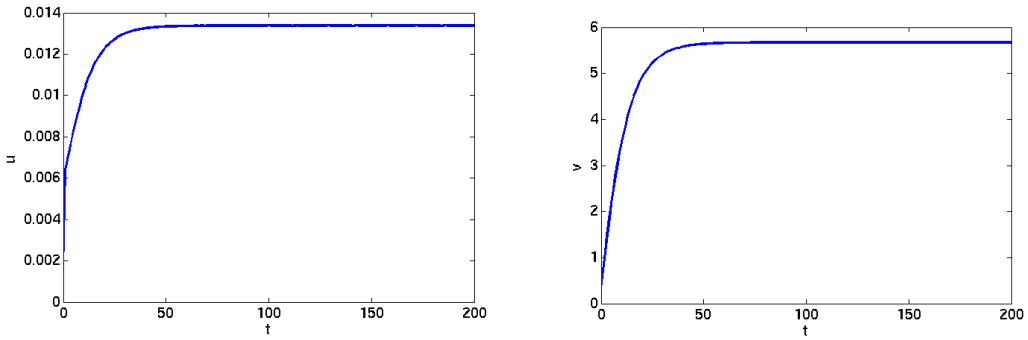

Figure 1: The dimensionless parameters $\{u, v\}$ representing the Ca^{2+} concentration for $\vartheta = 0.1$, where $\alpha = 200, \beta = 0.338, \gamma = 0.01, \delta = 0.00007, \eta = 0.01, \vartheta = 0.1, \kappa = 0.0017, \lambda = 0.6, \mu = 0, \nu = 0.105, v_c = 0.185, \psi = 0.11$.

The parameter ϑ represents the flux of Ca^{2+} through the sarcolemma. If the parameter ϑ changes the eigenvalues $\{d_1, d_2, d_3\}$ of the dynamical system change too. The situation is shown on fig. 2-4. The eigenvalue bifurcation dependence on the parameter ϑ can be observed.

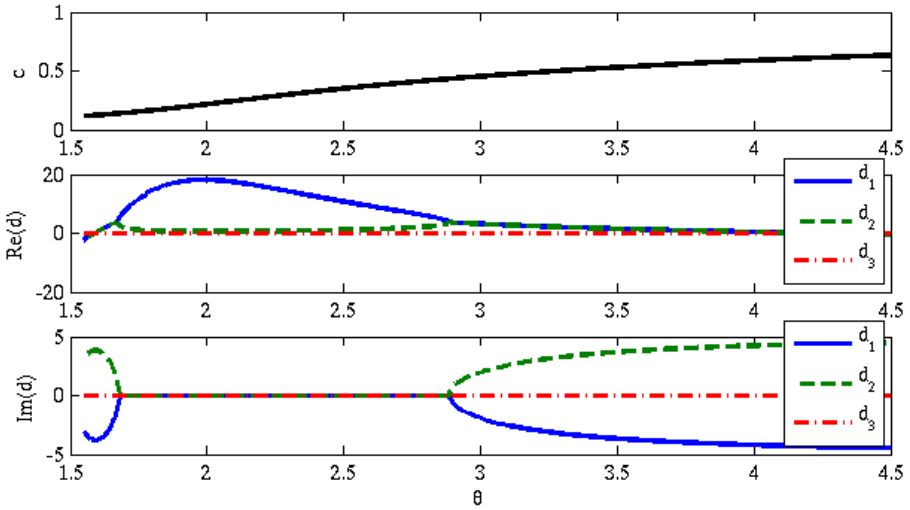

Figure 2: The dependence of the eigenvalues $\{d_1, d_2, d_3\}$ - their real and imaginary parts - on the parameter ϑ. The eigenvalue d_3 is small and negative, e.g. for $\vartheta = 1$ $d_1 = -57.82, d_2 = -0.095, d_3 = -0.127$, for $\vartheta = 2$ $d_1 = 11.205, d_2 = 0.905, d_3 = -0.128$.

The interesting regions are shown on fig. 3 and 4 as follows

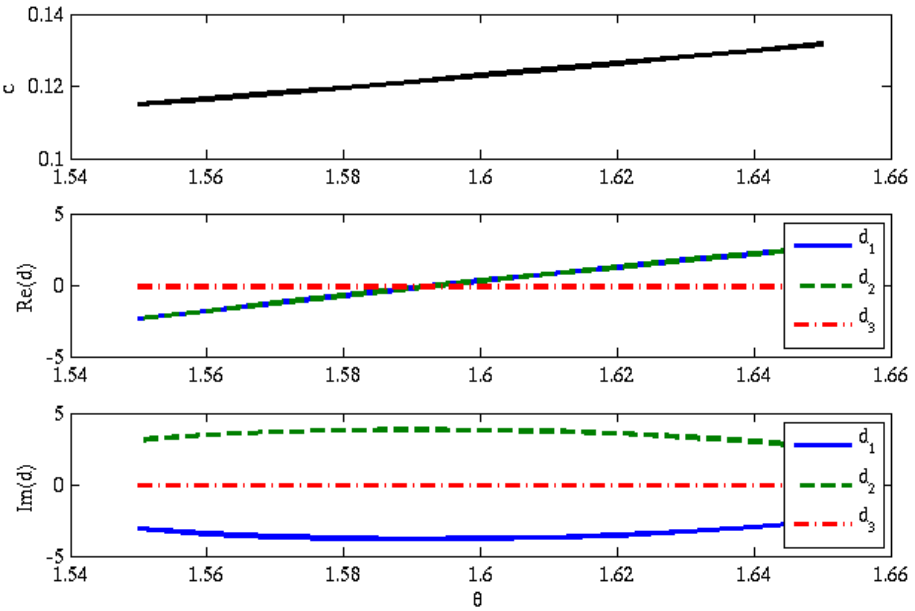

Figure 3: The dependence of the eigenvalues $\{d_1, d_2, d_3\}$ on the parameter ϑ.

The bifurcation for $\theta = 1.595$ is the Hopf's one (see fig. 3). The fix point is non-stable for $\vartheta > 1.595$, the periodical attractor apears.

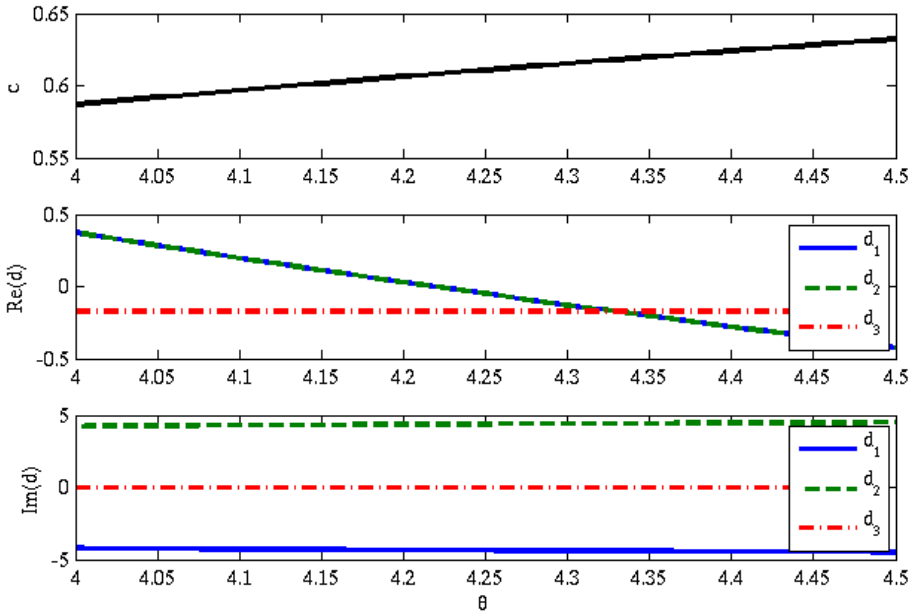

Figure 4: The dependence of the eigenvalues $\{d_1, d_2, d_3\}$ on the parameter ϑ.

The periodical change of the Ca^{2+} concentration can appear for the large value of ϑ see fig. 5 where the response of the muscle fibre is shown. The input data for the following figures are: $k_f = 80, v_c = 0.185, k_1 = 15, k_{-1} = 7.6, g_1 = 0.4, p_1 = 1038, p_2 = 0.12, c_e = 1.5, q_1 = 19, q_2 = 0.08, J = 0.0, k_2 = 0.8, k_{-2} = 0.84, x_0 = 1, p_0 = 0.1859, s = 0, q = 0, \tau = 0.2, opt = 1, C_t = 0.12, m = 1, r = 0.02, coup = 0, x_b = 1, t_{final} = 100, c_0 = 0.00292, c_{s0} = 0.00685, y_0 = 0.00542875$.

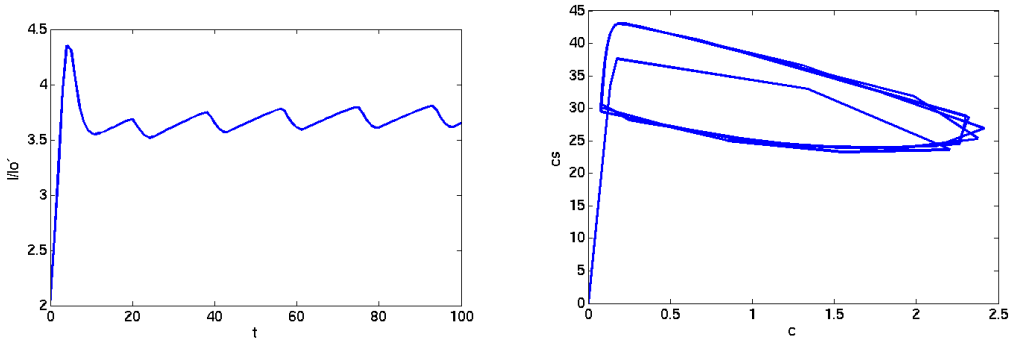

Figure 5: Left - the time evolution of the muscle fibre deformation l/l_0. Right - the relation between c the cytoplasmic Ca^{2+} concentration and c_s the Ca^{2+} concentration in SR. The results were obtained for $g_2 = 15, \vartheta = 1.97$.

The chaotical behaviour (see fig. 6) can be observed in between the stationary state (see fig.1) and the periodical oscillation in the neibourghood of the bifurcation point (see fig. 5).

The behavior of the muscle fibre discussed in the paper was experimentally proved in Parthimos et al. (1999) on the isolated rabbit ear resistance arteries.

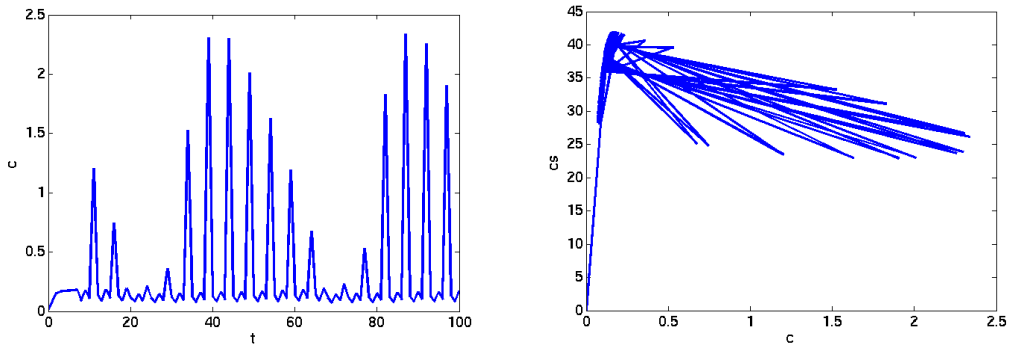

Figure 6: Left - the time evolution of the cytoplasmic Ca^{2+} concentration. Right - the relation between c the cytoplasmic Ca^{2+} concentration and c_s the Ca^{2+} concentration in SR. The results were obtained for $g_2 = 12, \vartheta = 1.578$.

5. Conclusion

The one possible way how to introduce more sophisticated models describing the phosphorylation of the myosin into the basic mathematical model of the isotonic smooth muscle contraction, see e.g. Hai and Murphy (1998), was shown in the paper. The approach increases both the number of DOFs and allows to introduce other known models describing the stimulation of muscle cells influenced by the intracellular calcium concentration. Another possibility is to change the free energy form e.g. taking into account diverse constitutive relations for the passive components of the muscle. The great advantage of the discussed approach seems to be its flexibility allowing to tailor the model to the concrete type of the smooth muscle.

The crucial problem is to identify the large number of the parameters from the experimental data.

The challenging problem is the analysis of the dynamical system properties like the equilibrium points corresponding to the steady state or the bifurcations which can lead to the either periodic or chaotic contractions. Both types of the behavior were experimentally approved on the living tissues.

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