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HOMOGENIZATION APPLIED IN MODELLING SMOOTH MUSCLE TISSUE

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Abstract: *The paper deals with the homogenization method in the context of modelling biological tissues which undergo large deformation. The updated Lagrangian scheme is applied to obtain linear subproblems which can be homogenized using the two scale convergence, cf. [6, 7]. It is suggested how an incremental "macroscopic" constitutive law can be obtained in terms of the homogenized coefficients for contracting smooth muscle cells. A simple (hyperelastic) model of the microstructure with contractile filaments is presented.*

Keywords: smooth muscle, homogenization, large deformation, contractile filaments

1. Introduction

In biological tissues the material is characterized very often as a mixture of solid and fluid (liquid) objects, which form the microstructure. If we look at the smooth muscle tissue at the microscopic scale, we recognize individual muscle cells embedded in the tissue matrix. This is a substance constituted by collagen fibrous components, very viscous fluid (amorphous substance) and some other components. The matrix itself presents a very complicated system with inter-penetration, swelling and electrochemical interactions at the sub-microscopic scale; the models which describe its behaviour are based on the mixture theory and theory of porous materials.

When the muscle cells are activated, they change the shape due to the forces produced by the actin–myosin couples in the cytoskeleton, cf. [3]. This change induces stresses in the surrounding matrix and results also in the mass redistribution in the vicinity of each cell. Besides the complexity of the constitutive laws of all members involved in the force–generating chain, we should notice also the geometrical non-linearity which is caused by large deformations of the microstructure.

The up-to-date constitutive models in biomechanics of soft tissues are based in general upon phenomenological relations between the "macroscopic" deformations and the "macroscopic stress", cf. [8, 4]. Using the theory of mixtures the microstructure of the tissue can be considered in terms of the "pseudo–microscopic components";

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for each one we have to define the constitutive law which is based on the macroscopic deformation. The macroscopic stress is the superposition of the stresses which are induced in the pseudo–microscopic components. The drawback of this approach is evident: we can hardly regard the interactions in the microstructure.

Motivation for the research reported in this paper is to describe and understand the geometrical effects which characterize contraction of the smooth muscle tissue. In this study we shall consider a very simple model of the deforming smooth muscle; its microstructure have the following features.

- The microstructure of the unstressed (unloaded) material is periodic.
- The muscle cells are modelled as incompressible inclusions embedded in the isotropic (compressible) hyperelastic matrix.
- Viscosity of both the matrix and the fluid in the inclusions is neglected.
- The cytoskeleton is modelled using bars which are fitted on the boundary of the muscle cells. The activated contraction is introduced through pre-straining the bars.

The periodicity (at least the local periodicity) of the microstructure is critical for applicability of the homogenization method. Although, in real tissue this assumption is not satisfied accurately, it is possible to find an artificial microstructure which is "statistically equivalent" with the real one and which is periodic. Such a step is used often also when modelling engineering composite materials, for which the strict periodicity cannot be guaranteed in the technological process.

2. Periodicity of the microstructure

We consider a composite material which is constituted by the hyperelastic matrix and periodically spaced microscopic incompressible inclusions. The problem is defined at the macroscale and at the microscale, cf. [1], which are associated with two coordinate systems $\mathcal{X}$ and $\mathcal{Y}$, respectively. The two scales are related each other by the scaling parameter ε, so that

$$y = \frac{x}{\varepsilon}, \;\; x \in \mathcal{X}, \; y \in \mathcal{Y}. \tag{1}$$

As usually we assume the size of the micro-heterogenities is very small and, therefore, we consider $\varepsilon \to +0$. In contrast with the small deformation case when treating large deformation the periodicity assumption is valid only locally in a vicinity of x.

Let $\Omega \subset \mathcal{X}$ be the domain (of dimension 2, or 3) occupied by the composite material and consider the decomposition (see [2] for reticulated structures):

$$\Omega = \Omega_m^\varepsilon \cup T^\varepsilon \cup \partial T^\varepsilon, \tag{2}$$

where Ω_m^ε (the matrix) is a connected domain occupied by the neo-Hookean material, T^ε consists of all disconnected incompressible inclusions. At the microscale equipped with the coordinate system $\mathcal{Y}$ we consider (locally in $\mathcal{X}$) periodic system of cells. The reference cell $Y \in \mathcal{Y}$ is decomposed according to (2), i.e. $Y = Y_m \cup T \cup \partial T$.

The Kirchhoff stress τ_{ij} in the two compartments is defined as follows

$$\begin{aligned} \text{matrix:} \quad & \ldots \quad \tau_{ij} = -J\delta_{ij}\, p + \mu J^{-2/3} \mathrm{dev}\, b_{ij}\ , \\ \text{inclusions (fluid):} \quad & \ldots \quad \tau_{ij} = -J\delta_{ij}\, p\ , \end{aligned}$$

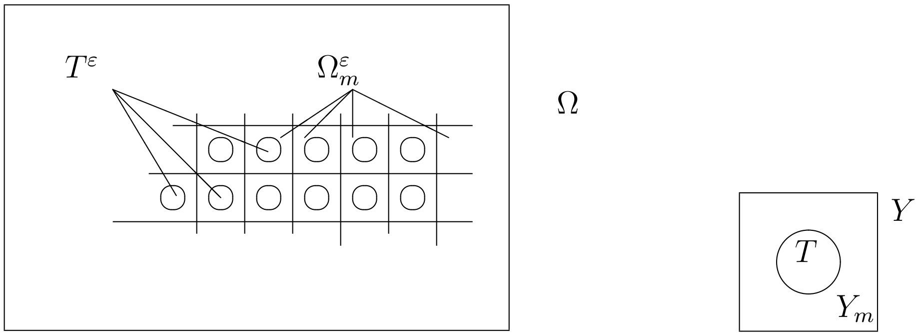

Figure 1: Decomposition of the macroscopic domain Ω (left) and the corresponding decomposition of the reference cell Y (right).

where p is the pressure, b_{ij} is the left Cauchy–Green deformation tensor, $J = \det(b_{ij})^{1/2}$ is the relative volume change and μ is the shear modulus. The stress in whole the domain Ω can be described uniformly as

$$\tau_{ij}^\varepsilon = -J^\varepsilon \delta_{ij} p^\varepsilon + \mu^\varepsilon (J^\varepsilon)^{-2/3} \text{dev } b_{ij}^\varepsilon \ , \tag{3}$$
$$p^\varepsilon = -\gamma^\varepsilon (J^\varepsilon - 1) \ , \tag{4}$$

using oscillating material coefficients $\mu^\varepsilon(x)$ and $\gamma^\varepsilon(x)$

$$\mu^\varepsilon(x) = \begin{cases} \mu, & x \in \Omega_m^\varepsilon \\ 0, & x \in T^\varepsilon, \end{cases} \quad , \quad \gamma^\varepsilon(x) = \begin{cases} \gamma, & x \in \Omega_m^\varepsilon \\ \gamma_\infty, & x \in T^\varepsilon, \end{cases} \quad , \tag{5}$$

where μ, γ and γ_∞ are constants. If $\gamma_\infty \to +\infty$, the inclusions become incompressible.

3. Modelling the contractile filaments

The smooth muscle cell, see Fig. 2, can be modelled as an ellipsoidal balloon filled with the incompressible fluid. It is assumed, that the mechanical properties of the cell depend predominantly on the network of filaments which stiffen the structure. These also involve the contractile filaments which, in response to their activation, develop forces acting on the surface of the cell, being fixed in the dense bodies.

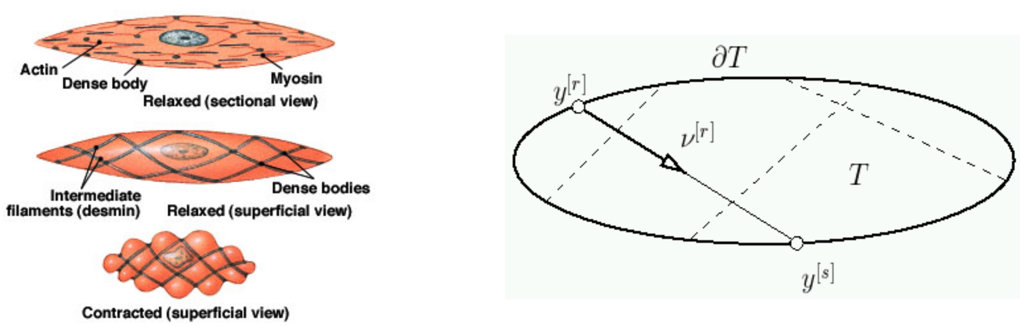

Figure 2: Arrangement of filaments in smooth muscle cell (left); model of contractile fibres (right).

In order to treat action of the contractile filaments at the microscopic reference domain Y, we consider boundary tractions $f_i(y)$, $y \in \partial T$. The virtual work of the filament fixed at $y^{[r]} \in \partial T$ for $r \in \mathcal{I} \equiv \{1,2,3,\dots\}$ is defined in terms of the Dirac distribution function $\delta_D(y^{[r]},y)$ as follows:

$$\int_{\partial T} f_i^{[r]}(y)\, v_i(y)\, dS_y = \int_{\partial T} \bar{f}_i^{[r]}\, \delta_D(y^{[r]},y)\, v_i(y)\, dS_y = \bar{f}_i^{[r]}\, v_i(y^{[r]}) \;, \tag{6}$$

where the $\bar{f}_i^{[r]}$ is the contractile force acting at $y^{[r]}$ and v_i is the virtual displacement. We recall that Y is only the "local" reference domain, which is valid in a neighbourhood of some $x \in \Omega$; for brevity we do not indicate it explicitly in (6).

In fact $\bar{f}_i^{[r]}$ are internal forces of the microstructure; for each index $[r]$ there is $[s]$ such that the points $y^{[r]}$ and $y^{[s]}$ define the bar (the filament) connecting two points on ∂T. Further, it holds that $\bar{f}_i^{[r]} = -\bar{f}_i^{[s]}$. Therefore, the virtual work involving actions of all bars of the cytoskeleton can be written as

$$\int_{\partial T} \sum_{r\in\mathcal{I}} f_i^{[r]}(y)\, v_i(y)\, dS_y = \sum_{r\in\mathcal{I}} \bar{f}_i^{[r]}\, v_i(y^{[r]}) = \sum_{r\in\mathcal{R},s=s(r)} \bar{f}_i^{[r]}\left(v_i(y^{[r]}) - v_i(y^{[s]})\right) \;, \tag{7}$$

where $s = s(r)$ is the corresponding index.

In this paper we consider the following definition of $\bar{f}_i^{[r]}$. Let $\psi(\theta) \geq 0$ be the strain energy function and denote by α the activation parameter; we define

$$\bar{f}_i^{[r]} = \alpha\, \nu_i^{[r]}\, \frac{\partial}{\partial\theta}\psi(\theta^{[r]} - \theta_0) \;,\; i = 1,2,(3) \;, \tag{8}$$

where θ_0 is the *active pre-straining* and $\nu_i^{[r]}$ is directional unit vector of the bar which is associated with the point $y^{[r]}$. We assume that the filaments have no resistance in compression, so that ψ may have the following form:

$$\psi(\theta) = \begin{cases} \frac{1}{6}E\theta^3 \;, & \text{for } \theta \geq 0 \;, \\ 0 \;, & \text{for } \theta < 0 \;, \end{cases} \tag{9}$$

where E is the elasticity constant and θ can be defined as the engineering strain (i.e. the bar elongation related to its initial length). It should be emphasized, that this simple model of active filaments does not allow for capturing dynamical features of muscle contraction. For simplicity we take $\alpha \in \{0;1\}$, so that the intensity of contraction is given purely by the *pre-straining* parameter θ_0; Sthe lesser $\theta_0 < 0$, the higher contraction force can be generated.

From (8),(9) we see that (7) is a nonlinear function of displacements. The first order approximation in displacements yields

$$\left(\bar{f}_i^{[r]}\right)^{\text{new}} \approx \left(\bar{f}_i^{[r]}\right)^{\text{old}} - B_{ik}^{[r]}\Delta u_k^{[r]} \;, \tag{10}$$

where, denoting by $l^{[r]}$ and $l_0^{[r]}$ the actual and the undeformed lengths of the bar, respectively, $B_{ik}^{[r]}$ is given as

$$\begin{aligned} B_{ik}^{[r]} \equiv & \left(\nu_i^{[r]}\nu_k^{[r]} + \delta_{ik}\right)\, \alpha\, \frac{1}{l_0^{[r]}}\frac{\partial}{\partial\theta}\psi(\theta^{[r]} - \theta_0) + \\ & + \nu_i^{[r]}\nu_k^{[r]}\, \alpha\, \frac{1}{l^{[r]}}\frac{\partial^2}{\partial\theta^2}\psi(\theta^{[r]} - \theta_0) \;. \end{aligned} \tag{11}$$

In the following section we formulate the equilibrium equation for $\varepsilon > 0$, i.e. we consider finite scale heterogenities in the macroscopic domain Ω. For this case we also need the corresponding terms which describe action of the filaments.

Let $\Omega_S^{\rho,\varepsilon} \subset \Omega$ such that $\Omega_S^{\rho,\varepsilon} \to \partial T^\varepsilon$ for $\rho \to 0$. The virtual work of the contraction forces is given by

$$\int_{\Omega_S^{\rho,\varepsilon}} \frac{1}{\varepsilon} f_i^\varepsilon(x)\, v_i(x)\, dx \;, \quad \text{where } f_i^\varepsilon(x) = \alpha\, \nu_i^\varepsilon(x) \frac{\partial}{\partial \theta} \psi(\theta^\varepsilon(x) - \theta_0) \;. \tag{12}$$

Above $\theta^\varepsilon(x)$ is the strain in the fibre which is fixed at the point $x \in \Omega_S^{\rho,\varepsilon}$. Introducing the one-to-one mapping $\mathcal{T} : x \to \bar{x}$, $x, \bar{x} \in \Omega_S^{\rho,\varepsilon}$, we define $\theta^\varepsilon(x) = \nu_i^\varepsilon(x)(u_i^\varepsilon(\bar{x}) - u_i^\varepsilon(x))/l_0^\varepsilon(x)$ where u^ε are displacements and $l_0^\varepsilon(x)$ is the undeformed length. To summarize, we treat a system of "continuously" distributed forces in $\Omega_S^{\rho,\varepsilon}$. Using the two-scale convergence for $\varepsilon \longrightarrow 0$ we have that

$$f_i^\varepsilon(x) \rightharpoonup f_i^0(x) \quad \text{weakly in } L_2(\Omega) \;,$$

where $f_i^0(x) = |Y|^{-1} \int_{Y_S^\rho} f_i(x,y)\, dy$, $y = x/\varepsilon$, the microscopic domain Y_S^ρ is associated with $\Omega_S^{\rho,\varepsilon}$. If $\nu_i^\varepsilon(x) = -\nu_i^\varepsilon(\bar{x})$ we have the system of couple-wise applied forces, so that we obtain $f_i^0(x) \equiv 0$. This is the necessary condition, because otherwise the virtual work is unbounded due to presence of $1/\varepsilon$ in (12).

4. Updated Lagrangean formulation

We shall introduce the linearized equilibrium equation (15), where $D_{ijkl}^{TK\,\varepsilon}$ is the Truesdell rate of the Kirchhoff stress, e_{ij} and η_{ij} are the linear and nonlinear parts of the Green strain related to the updated reference configuration

Let $\partial\Omega_D \subset \partial\Omega$ be the part of the boundary where the increments of displacements $\overline{\Delta u}$ are prescribed. We need to define spaces of admissible displacement increments

$$V(\Omega) = \{v \in [W^{1,2}(\Omega)]^n \mid v_i = \overline{\Delta u}_i \text{ on } \partial\Omega_D, i = 1,\dots,n\} \;, \tag{13}$$
$$V_0(\Omega) = \{v \in [W^{1,2}(\Omega)]^n \mid v_i = 0 \text{ on } \partial\Omega_D, i = 1,\dots,n\} \;, \tag{14}$$

where $n = 2,3$ is the dimension of Ω and $W^{1,2}(\Omega)$ is the Sobolev space.

It is now possible to define the deformation (linear) sub-problem for computing the displacement and pressure increments in our heterogeneous material with prestrained fibres: Find $\Delta u^\varepsilon \in V(\Omega)$ and $\Delta p^\varepsilon \in L^2(\Omega)$, so that

$$\begin{aligned}
&\int_{\Omega_m^\varepsilon} D_{ijkl}^{TK\,\varepsilon} e_{kl}(\Delta u^\varepsilon) e_{ij}(v^\varepsilon) \frac{1}{J^\varepsilon}\, dx - \left[\int_{\Omega_m^\varepsilon} \cup \int_{T^\varepsilon} \right] \Delta p^\varepsilon \,\mathrm{div} v^\varepsilon\, dx + \\
&+ \int_{\Omega_m^\varepsilon} \tau_{ij}^\varepsilon\, \delta\eta_{ij}(\Delta u^\varepsilon; v^\varepsilon) \frac{1}{J^\varepsilon}\, dx + \int_{T^\varepsilon} p^\varepsilon \frac{\partial \Delta u_i^\varepsilon}{\partial x_j} \frac{\partial v_j^\varepsilon}{\partial x_i} = \\
&\int_{\Omega_S^{\rho,\varepsilon}} \frac{1}{\varepsilon} f_i^\varepsilon\, v_i^\varepsilon\, dx + L^{\mathrm{new}}(v^\varepsilon) - \int_{\Omega_m^\varepsilon} \tau_{ij}^\varepsilon e_{ij}(v^\varepsilon) \frac{1}{J^\varepsilon}\, dx + \int_{T^\varepsilon} p^\varepsilon \,\mathrm{div} v^\varepsilon\, dx
\end{aligned} \tag{15}$$

for all $v^\varepsilon \in V_0(\Omega)$ and

$$\int_\Omega \frac{1}{\gamma^\varepsilon J^\varepsilon} \Delta p^\varepsilon\, q^\varepsilon\, dx = -\int_\Omega q^\varepsilon \,\mathrm{div}\Delta u^\varepsilon\, dx, \quad \text{for all } q^\varepsilon \in L^2(\Omega) \;. \tag{16}$$

We remark that the above integrals are evaluated over the current reference configuration $\Omega = \Omega(t)$ and $L^{\rm new}(v)$ is the linear functional involving all boundary tractions and volume forces imposed at time $(t+1)$. The new configuration at $(t+1)$ is obtained using the displacement and pressure increments: $u^{\varepsilon\,(t+1)} := u^{(t)} + \Delta u^\varepsilon$, $p^{\varepsilon\,(t+1)} := p^{\varepsilon\,(t)} + \Delta p^\varepsilon$.

5. Microscopic and macroscopic problems

We employ the standard technique to derive equations of the microscopic problem, cf. [1]. For Δu^ε and Δp^ε we use the following asymptotic expansion (The analogous expansion is taken for the test functions v^ε and q^ε.)

$$\Delta u^\varepsilon(x) = \Delta u^0(x) + \varepsilon \Delta u^1(x,y) + \dots\,, \tag{17}$$
$$\Delta p^\varepsilon(x) = \Delta p^0(x,y) + \varepsilon \cdot \dots\,, \tag{18}$$

where $x \in \Omega$, $y \in Y$ and ε is the scaling parameter, i.e. $x = \varepsilon y$. The functions $\Delta u^k(x,y)$ and $\Delta p^k(x,y)$, $k = 0,1,\dots$ are assumed to be Y-periodic. Here we omit the details concerning derivation of the microscopic problem, see [7]. The pressure field in domain T is constant as a function of y (incompressible fluid in a closed volume T), so that we have $p^0(x,y) = \bar{p}^0(x)$ for $y \in T$.

We remark also that due to the term $1/\varepsilon$ involved in the first right hand side in(15), where we substitute $v_i^\varepsilon(x) := 0 + \varepsilon w_i(x/\varepsilon)\vartheta(x)$ with periodic function $w_i(x/\varepsilon)$, we have the following weak convergence in $L_2(\Omega)$ for $\varepsilon \to 0$:

$$\frac{1}{\varepsilon} f_i^\varepsilon(x)\; \varepsilon w_i(x/\varepsilon) \rightharpoonup \frac{1}{|Y|}\int_{Y_S^\rho} f_i(x,y) w_i(y)\, dy\,.$$

Above we use the extension of $f_i^\varepsilon(x)$ by zeros from $\Omega_S^{\rho,\varepsilon}$ to whole Ω. For $\rho \to 0$ the domain integral over Y_S^ρ transforms to the boundary integral over ∂T. So that using results of Section 3 we have for $\rho \to 0$ that

$$\int_{Y_S^\rho} f_i(x,y) w_i(y)\, dy \to \sum_{r \in \mathcal{R}, s = s(r)} \bar{f}_i^{[r]} \left(w_i(y^{[r]}) - w_i(y^{[s]})\right)\,. \tag{19}$$

We shall now introduce the characteristic response functions, which couple the micro- and the macro-responses (we use the abbreviation $\partial_l^x v_k(x) = \partial v_k(x)/\partial x_l$):

$$\Delta u_i^1(x,y) = -\chi_i^{kl}(x,y)\, \partial_l^x \Delta u_k^0(x),\ i = 1,\dots,n \tag{20}$$
$$\Delta p^0(x,y) = -\pi^{kl}(x,y)\, \partial_l^x \Delta u_k^0(x), \tag{21}$$
$$\Delta \bar{p}^0(x) = -\bar{\pi}^{kl}(x)\, \partial_l^x \Delta u_k^0(x). \tag{22}$$

We shall need the space of (locally) admissible displacements [1]:

$$H_\#(Y) \equiv \{v \in [W^{1,2}(Y)]^n \mid v \text{ is Y-periodic, } \int_Y v(y) dy = 0\}. \tag{23}$$

The microscopic problem is defined as follows, cf. [6, 7]. Let the deformed microscopic configuration be in the equilibrium. For a fixed $x \in \Omega$ and $k,l = 1,\dots,n$ find

$\chi^{kl} \in H_{\#}(Y_m)$, $\pi^{kl} \in L^2(Y_m)$ and $\bar{\pi}^{kl} \in \mathbb{R}$, so that

$$\begin{aligned}
& a_{Y_m}(\chi^{kl} - \Pi^{kl},\, w) + b_{Y_m}(\chi^{kl} - \Pi^{kl},\, w) \\
& -(\pi^{kl},\, \mathrm{div}_y w)_{Y_m} + \bar{\pi}^{kl}(1,\, \mathrm{div}_y w)_{Y_m} \\
+ \sum_{\substack{r\in\mathcal{R}\\ s=s(r)}} & B^{[r]}_{ij} \left(\left(\chi^{kl}_j\right)^{[r]} - \left(\chi^{kl}_j\right)^{[s]} - \left(y^{[r]}_l - y^{[s]}_l\right)\delta_{kj}\right)\left(w^{[r]}_i - w^{[s]}_i\right) = 0, \qquad (24)
\end{aligned}$$

$$\forall w \in H_{\#}(Y_m),$$

$$\frac{1}{\gamma}\left(\frac{1}{J}\pi^{kl},\, q\right)_{Y_m} + (q,\, \mathrm{div}_y \chi^{kl})_{Y_m} - (q,\, \mathrm{div}_y \Pi^{kl})_{Y_m} = 0, \qquad (25)$$

$$\forall q \in L^2(Y_m),$$

$$(1, \mathrm{div}_y \chi^{kl})_{Y_m} = -|T|\delta_{kl}\;, \qquad (26)$$

where $\Pi^{kl}_i \equiv y_l\,\delta_{ki}$ and

$$\begin{aligned}
a_{Y_m}(u,v) &= \int_{Y_m} \left(D^{tTK}_{ijkl} + J\bar{p}^0 \delta_{ij}\delta_{kl}\right)\, e^y_{kl}(u)\, e^y_{ij}(v) \frac{1}{J}\, dy\;, \\
b_{Y_m}(u,v) &= \int_{Y_m} \left(\tau_{ij}\delta_{kl} - J\bar{p}^0 \delta_{kj}\delta_{li}\right)\, \partial^y_i u_k\, \partial^y_j v_l\, \frac{1}{J}\, dy\;.
\end{aligned}$$

Eq. (25) results from the constitutive equation for the pressure increment in Y_m, whereas (25) expresses the incompressibility in T. Note that due to the non-symmetry of $\tau_{ij}\delta_{kl}$ in $b_{Y_m}(\cdot,\cdot)$ the characteristic functions are not symmetric in k, l, i.e. $\chi^{kl}_i \neq \chi^{lk}_i$, $\pi^{kl}_i \neq \pi^{lk}_i$, $\bar{\pi}^{kl}_i \neq \bar{\pi}^{lk}_i$.

Using the characteristic response functions we compute the homogenized stiffness coefficients $\hat{\mathcal{Q}}_{ijkl}$; employing the abbreviation $\Xi^{kl} = \chi^{kl} - \Pi^{kl}$ it holds that

$$\begin{aligned}
\hat{\mathcal{Q}}_{ijkl} \equiv & \frac{1}{|Y|}\left[c_{Y_m}(\Xi^{kl}, \Xi^{ij}) + \frac{1}{\gamma}\left(\frac{1}{J}\pi^{ij},\, \pi^{kl}\right)_{Y_m}\right] + \\
& + \frac{1}{|Y|} \sum_{\substack{r\in\mathcal{R}\\ s=s(r)}} B^{[r]}_{mh}\left(\left(\Xi^{kl}_m\right)^{[r]} - \left(\Xi^{kl}_m\right)^{[s]}\right)\left(\left(\Xi^{kl}_h\right)^{[r]} - \left(\Xi^{kl}_h\right)^{[s]}\right)\;,
\end{aligned} \qquad (27)$$

where for simplicity of notation we used $c_{Y_m}(u,v) \equiv a_{Y_m}(u,v) + b_{Y_m}(u,v)$. The stiffness tensor $\hat{\mathcal{Q}}_{ijkl}$ is symmetric only in "$ij\ kl = kl\ ij$".

The macroscopic problem reads as follows: Given distribution of $\hat{\mathcal{Q}}_{ijkl}$, the averaged Cauchy stress $\langle J^{-1}\tau_{ij}\rangle_Y = \int_Y \tau_{ij} J^{-1}\, dy$,

$$\langle J^{-1}\tau_{ij}\rangle_Y = \frac{1}{|Y|}\left[\int_{Y_m} \frac{1}{J}\tau_{ij}\, dy - \bar{p}\,|T| + \sum_{r\in\mathcal{R}} \alpha\, \nu^{[r]}_i\, \nu^{[r]}_j \frac{\partial}{\partial\theta}\psi(\theta^{[r]} - \theta_0)\right]\;, \qquad (28)$$

and the external load functional $L^{\mathrm{new}}(\cdot)$, compute $\Delta u^0 \in V(\Omega)$ such that

$$\int_\Omega \hat{\mathcal{Q}}_{ijkl}\, \partial^x_l \Delta u^0_k\, \partial^x_j v_i\, dx = L^{\mathrm{new}}(v) - \int_\Omega \langle J^{-1}\tau_{ij}\rangle_Y\, e^x_{ij}(v)\, dx, \;\; \forall v \in V(\Omega)\;. \qquad (29)$$

The homogenized coefficients depend on the local deformed microstructures, so that to recover their distribution in Ω large number of microscopic problems should be solved. In [7] an approximation scheme is suggested which makes the problem tractable even for usual computing tools.

6. Computing cell contraction in homogeneous stress field

In this section we illustrate how the topology of the contractile filaments and the mutual position of muscle cells influence deformation and stress in contracting tissue. We may focus on uniform stress fields only, so that for computing the macroscopic deformation we need only one reference microstructure for which we solve the microscopic problems.

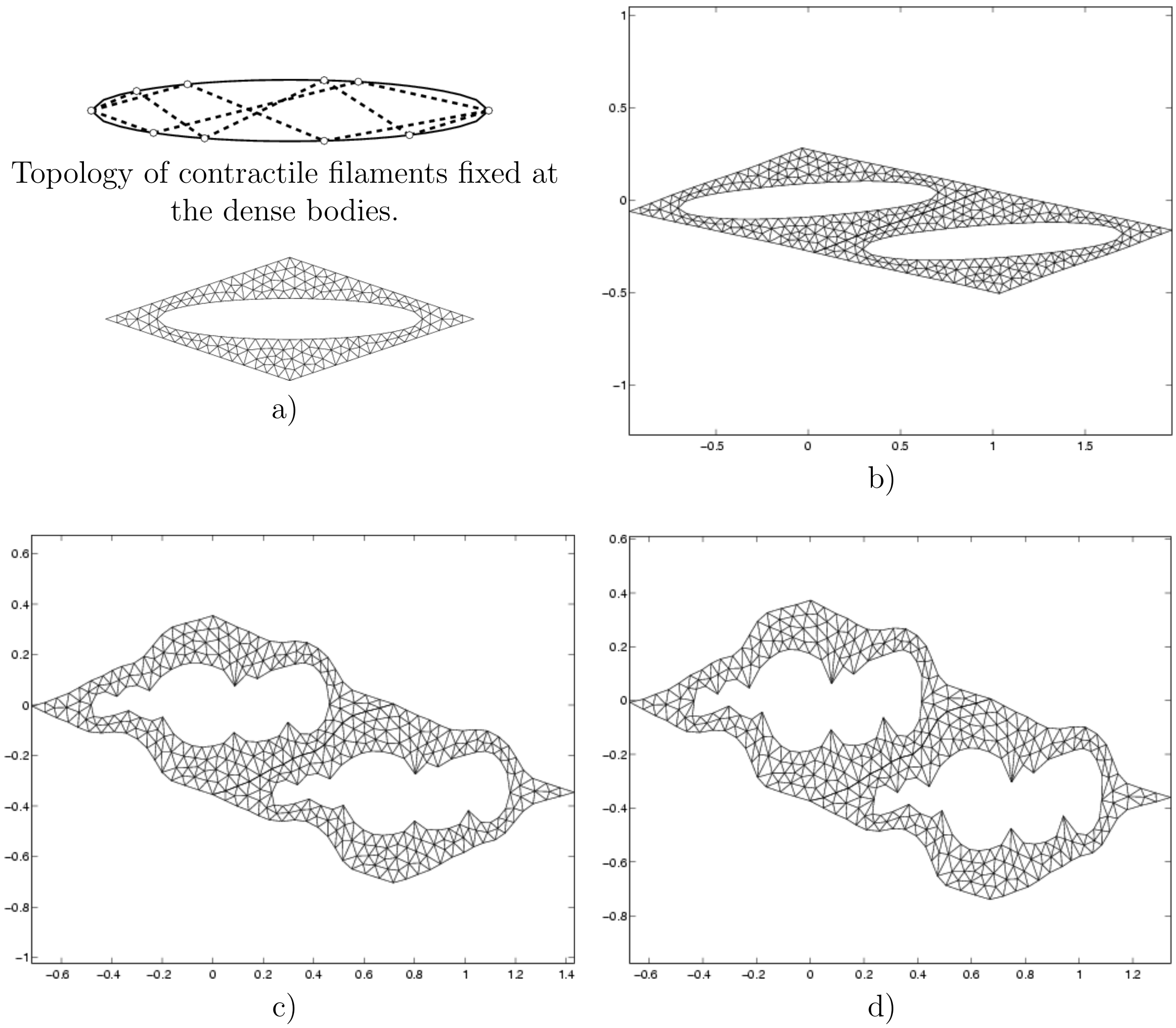

Figure 3: Example 1. Isotonic contraction for the rhombic microstructure: a) smooth muscle cell (top) and the reference cell Y (bottom), b) non-active state, c) active pre-straining $\theta_0 = -0.09$, d) active pre-straining $\theta_0 = -0.30$.

Let $\hat{\boldsymbol{F}}$ be the reference macroscopic deformation gradient. We want to compute the components f_{ij} of $\boldsymbol{f}$, so that we can update: $\boldsymbol{F} = \boldsymbol{f}\hat{\boldsymbol{F}}$. Obviously $f_{ij} - \delta_{ij} = \partial_j^x \Delta u_i^0 \equiv g_{ij}$, which is obtained by solving (29). If the material is subjected to uniform stress field $\bar{\sigma}_{ij}$, then, due to the macroscopic homogeneity, the displacement field Δu_i^0 is also uniform. Consequently, (29) reduces to (for 2D problems(!))

$$\begin{bmatrix} \hat{Q}_{1111}, & \hat{Q}_{1122}, & \hat{Q}_{1112}, & \hat{Q}_{1121} \\ \hat{Q}_{2211}, & \hat{Q}_{2222}, & \hat{Q}_{2212}, & \hat{Q}_{2221} \\ \hat{Q}_{1211}, & \hat{Q}_{1222}, & \hat{Q}_{1212}, & \hat{Q}_{1221} \\ \hat{Q}_{2111}, & \hat{Q}_{2122}, & \hat{Q}_{2112}, & \hat{Q}_{2121} \end{bmatrix} \cdot \begin{bmatrix} g_{11} \\ g_{22} \\ g_{12} \\ g_{21} \end{bmatrix} = \begin{bmatrix} \bar{\sigma}_{11} \\ \bar{\sigma}_{22} \\ \bar{\sigma}_{12} \\ \bar{\sigma}_{21} \end{bmatrix} - \begin{bmatrix} \langle \sigma_{11} \rangle \\ \langle \sigma_{22} \rangle \\ \langle \sigma_{12} \rangle \\ \langle \sigma_{21} \rangle \end{bmatrix}, \qquad (30)$$

where $\langle \sigma_{ij} \rangle$ is the abbreviation for the averaged Cauchy stress employed in (29). It should be remarked that the coefficients $\hat{Q}_{ijkl}$ as well as $\langle \sigma_{ij} \rangle$ in (30) are computed for the reference microstructure Y, which is in equilibrium state; to achieve this state microscopic equilibrium problems must be solved iteratively, cf. [7].

In our numerical simulations we considered two periodic microstructures, the rhombic one, *Example 1*, Fig. 3, and the rectangular one, *Example 2*, Fig. 4. For both the microstructures we choose the same material parameters and the same shape of the cells, however, the topology of the contractile filaments differs. We study the isotonic contraction with the loading stress applied in the "x" axis, i.e. $\langle \sigma_{ij} \rangle = 0$ for $i, j \neq 1$.

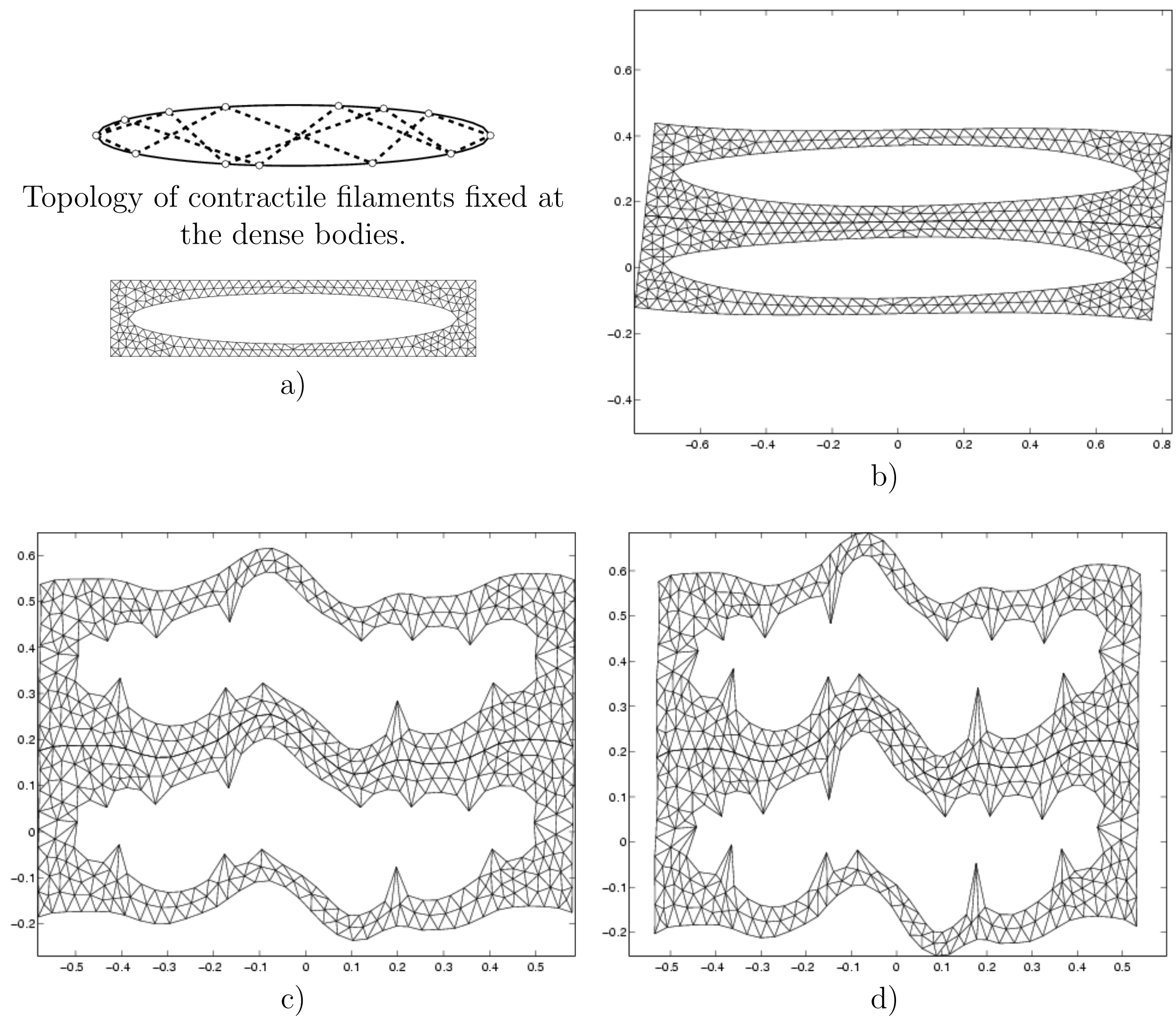

Figure 4: Example 2. Isotonic contraction for the rectangular microstructure: a) smooth muscle cell (top) and the reference cell Y (bottom), b) non-active state, c) active pre-straining $\theta_0 = -0.05$, d) active pre-straining $\theta_0 = -0.30$.

7. Conclusion

In Figs. 3 and 4 we display deformed microstructures, which were computed in a sequence of linear subproblems (30). It is evident that the deformation strongly depends on relative position of the cells, as well as on the topology of the contractile filaments inside the cell. The differences between the macroscopic stretches are introduced in Tab. 1.

	Example 1:		*Example 2:*	
θ_0	-0.05	-0.3	-0.05	-0.3
λ_1	0.82	0.76	0.81	0.74
λ_2	1.17	1.34	1.20	1.30

Tab. 1.

In this paper we presented the simplified model of contracting muscle cells. Advantage of the approach reported here is that it regards very precisely the geometrical features of the microstructure and, thereby, interactions between microscopic constituents (cells and the matrix in this case). One of the crucial difficulties emerges when nonuniform macroscopic deformation develops, as discussed in [6, 7, 9]. The further work will be focussed on modelling the mechanical connections between adjacent cells. Also more complex constitutive laws for the matrix, intracellular substance and the cytoskeleton should be considered; this, however, will be conditional on availability of specific physiological and histological results.

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